UKOSS

UK Obstetric Surveillance System

Seventh Annual Report 2013




We would like to thank all the reporting anaesthetists, midwives, obstetricians, risk managers and other clinicians throughout the UK who have contributed to UKOSS, without whom this work would not have been possible

Royal College of Obstetricians and Gynaecologists

Bringing to life the best in women's health care

npeu National Perinatal Epidemiology Unit

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Knight M, Workman M, Fitzpatrick K, Acosta C, Peirsegaele P, Mistry V, Kurinczuk JJ.
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1. Introduction

The UK Obstetric Surveillance System (UKOSS), a joint initiative between the National Perinatal Epidemiology Unit and the Royal College of Obstetricians and Gynaecologists, was launched in February 2005. The system is designed to be used to survey a range of rare conditions in pregnancy. The system is also supported by the Royal College of Midwives, the Obstetric Anaesthetists Association, the NCT, the Faculty of Public Health, the Department of Health and the Health Protection Agency.

Rare conditions are difficult to study because the identification of even a small number of affected women requires collaboration between large numbers of investigators. Such collaborations are difficult to establish and may be costly, hence uncommon disorders are rarely studied comprehensively on a population basis. The information available about the natural history, prognosis, risk factors and evidence-based practice is therefore very limited. UKOSS draws together clinicians from all hospitals with consultant-led maternity units in the UK in a routine reporting system, thus allowing the straightforward conduct of a changing programme of studies of rare disorders of pregnancy. The information gained from these studies may be used to inform counselling of women, development of guidelines for prevention or treatment, for service planning and for addressing patient safety issues. Completed studies have demonstrated the efficacy of the system for generating this information[1-7].

Studies using UKOSS may be undertaken by any investigator who identifies a suitable topic and secures funding[8]. Suitable disorders to study are those which are uncommon (usually no more than one case per 2000 births annually in the UK); are an important cause of maternal or perinatal morbidity or mortality; and which have research questions that can be addressed using the UKOSS methodology (prospective descriptive, cohort or case-control studies). This report outlines the studies undertaken during the eighth year of surveillance using UKOSS.

2. Methods

Up to four nominated clinicians (anaesthetists, midwives, obstetricians and risk managers) in each hospital with a consultant-led maternity unit in the UK report to UKOSS. Every month, the nominated individuals are sent a report card with a list of conditions currently under surveillance (Figure 1). They are asked to complete a box indicating the number of cases which have occurred in the previous month, or if none, to return the card indicating a nil return. As a guide, only conditions with an estimated incidence of less than one in 2000 births are surveyed, and thus the most common response is a nil return. Nil returns are, however, extremely important as they allow us to confirm the number of women in the denominator birth cohort for each study.

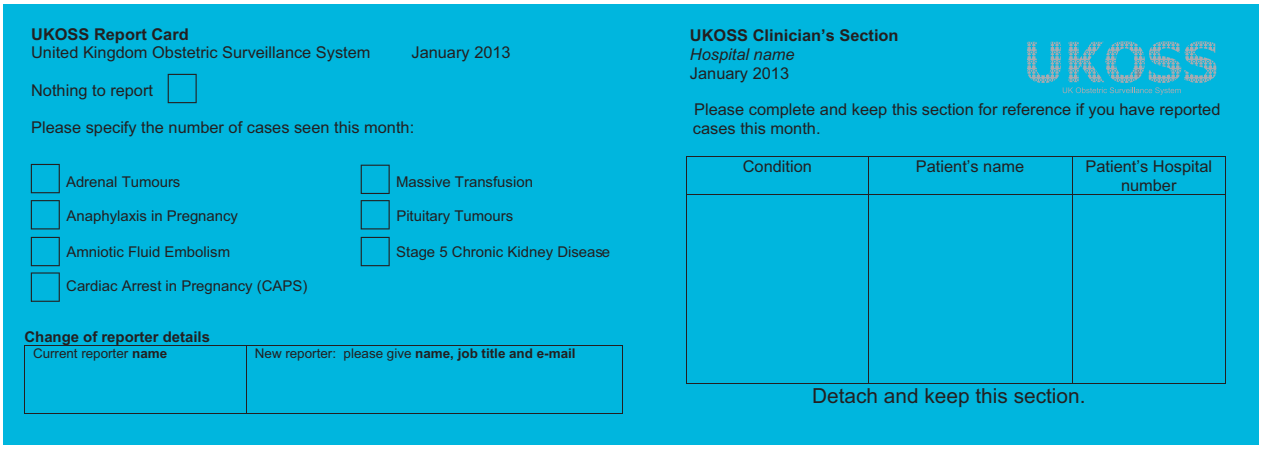
On receiving a case report (return of the monthly card mailing), the UKOSS central team dispatches a data collection form to collect more detailed information about each case. The data collection forms are developed individually for each condition and are designed to be short and easily completed from a woman's case notes without requiring reference to any other sources of information. The data collection forms seek confirmation of the appropriate case definition and additional information on risk factors, management and outcomes according to the protocol relating to each condition. UKOSS does not collect any personally identifiable information, such as women's names, addresses, dates of birth or hospital numbers. Reporting clinicians are asked to keep their own record of the names of women they have reported, in order that they can retrieve the woman's case notes to complete the data collection form. The National Information Governance Board (NIGB) and the Confidentiality and Security Advisory Group for Scotland (CSAGS) have judged that collection of information only, for the purpose of studying incidence and identifying means to improve patient care, which is not individually identifiable and does not lead to any change in management for the individual patient is acceptable without requiring individual patient consent[9,10]. The UKOSS methodology and that of each individual study are approved by Research Ethics Committees.

In order to perform case-control or cohort studies, information is also collected on control or comparison women for some studies. For these studies only, clinicians who report a case are asked to follow specific instructions to identify appropriate comparison women and complete a similar data collection form from their case notes. The process of selecting comparison women is individual to each study.

Examples of questions which can be addressed using UKOSS studies include:

1. Estimating disease incidence; for example UKOSS surveillance of eclampsia demonstrated a 45% reduction in incidence between 1992 and 2005[2].
2. Describing the prevalence of factors associated with near-miss maternal morbidity; for example a UKOSS study estimated that more than 1 in every 1200 women delivering in the UK is extremely obese (BMI 50kg/m^2 or greater)[11].
3. Quantifying risk factors for severe morbidity; for example UKOSS surveillance of uterine rupture showed a significant association with induction or augmentation of labour in women with a previous caesarean delivery[5].
4. Auditing of national guidelines; for example UKOSS surveillance of antenatal pulmonary embolism showed that very few women were not receiving thromboprophylaxis according to Royal College of Obstetricians and Gynaecologists guidelines[3,12].
5. Investigating different management techniques; for example the use of total versus subtotal hysterectomy was examined in the UKOSS study of peripartum hysterectomy for severe haemorrhage but no significant differences in complication rates between the two techniques was found[1].
6. Responding to emerging public health issues; for example in response to the 2009/H1N1 influenza ('swine flu') pandemic, surveillance of women admitted to hospital with confirmed infection was initiated to inform ongoing clinical guidance during the course of the pandemic[13].
7. Describing the outcomes of severe morbidity; for example UKOSS surveillance of 2009/H1N1 influenza showed a significant association with poor pregnancy outcomes[14].
8. Investigating disease progression; for example a comparison of UKOSS data on severe morbidity with information on women who died identified through the UK Confidential Enquiry into Maternal Death showed that women who were older, obese, from routine or manual occupations or unemployed, or of Black African or Caribbean ethnicity were more likely to die[15].
9. Informing public health policy; for example the UKOSS study showing poor perinatal outcomes in pregnant women with 2009/H1N1 influenza[14] was used as evidence to recommend universal immunisation of pregnant women against influenza[16].

Figure 1: UKOSS Report Card



UKOSS Report Card
United Kingdom Obstetric Surveillance System January 2013

Nothing to report ☐

Please specify the number of cases seen this month:

☐ Adrenal Tumours
☐ Anaphylaxis in Pregnancy
☐ Amniotic Fluid Embolism
☐ Cardiac Arrest in Pregnancy (CAPS)
☐ Massive Transfusion
☐ Pituitary Tumours
☐ Stage 5 Chronic Kidney Disease

Change of reporter details

Current reporter **name**	New reporter: please give **name, job title and e-mail**

UKOSS Clinician's Section
Hospital name
January 2013

UKOSS
UK Obstetric Surveillance System

Please complete and keep this section for reference if you have reported cases this month.

Condition	Patient's name	Patient's Hospital number

Detach and keep this section.

3. Participation

All 212 units with consultant-led maternity units in the UK contribute to UKOSS. This represents 100% participation of eligible units and effectively means that the denominator for all UKOSS studies is the entire birth cohort in the UK. The mean monthly card return rate during 2012 was 93% (Figure 2), with regional return rates varying between 88% and 99% (Figure 3). These card return rates continue the high rates obtained during the first seven years of reporting, and are a testament to the dedication of reporting clinicians throughout the UK.

Figure 2: UKOSS national card return rates January-December 2012

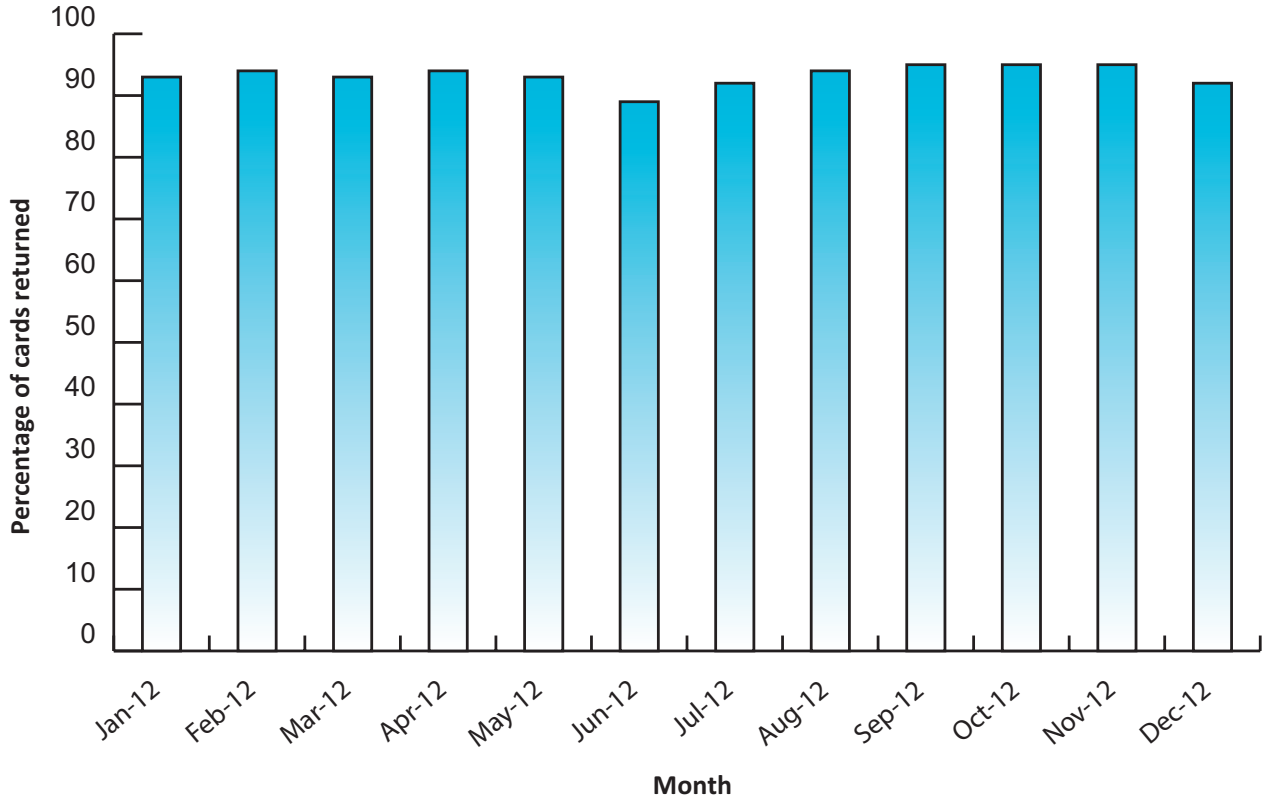
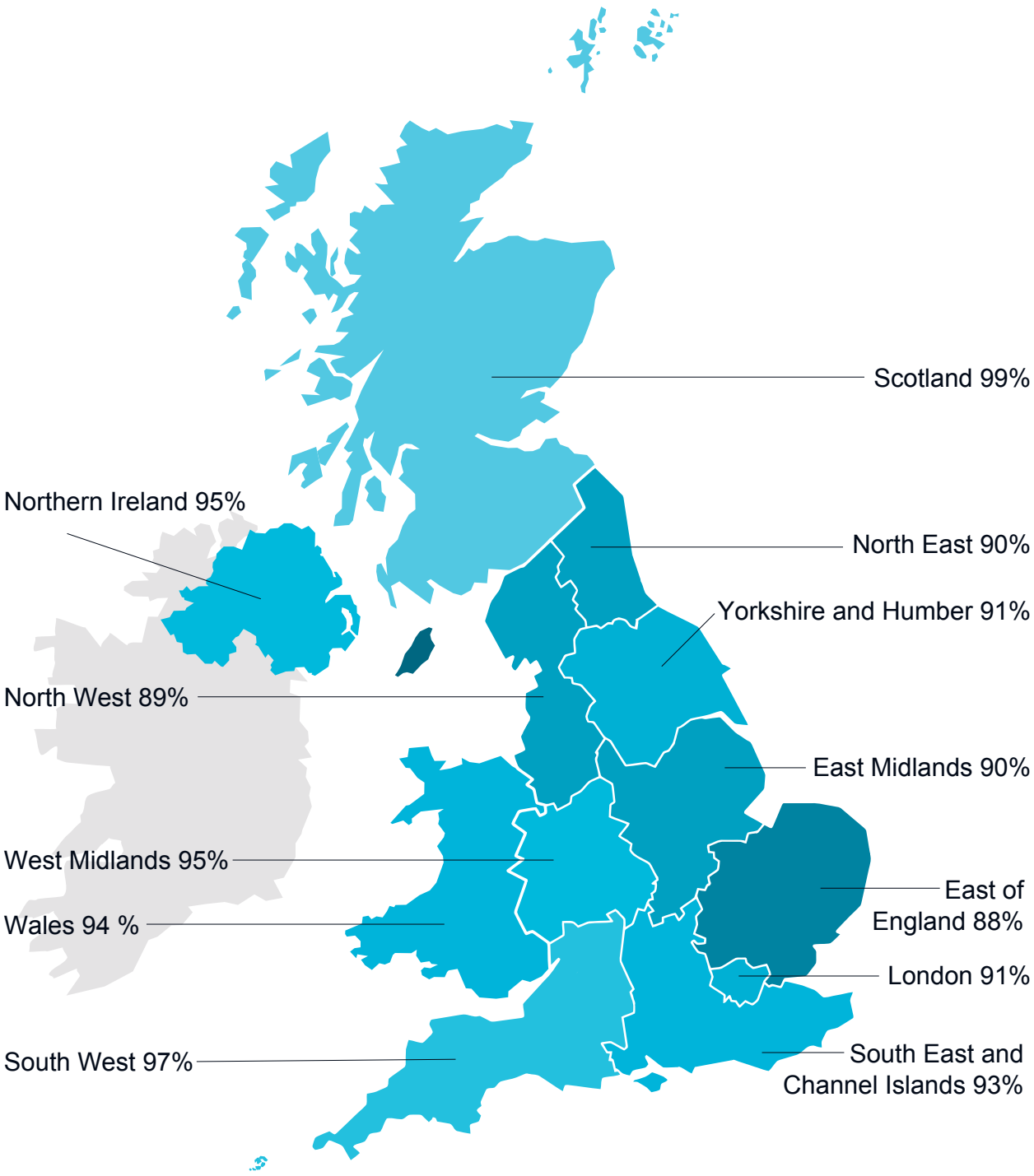


Figure 3: Map showing regional card return rates during 2012

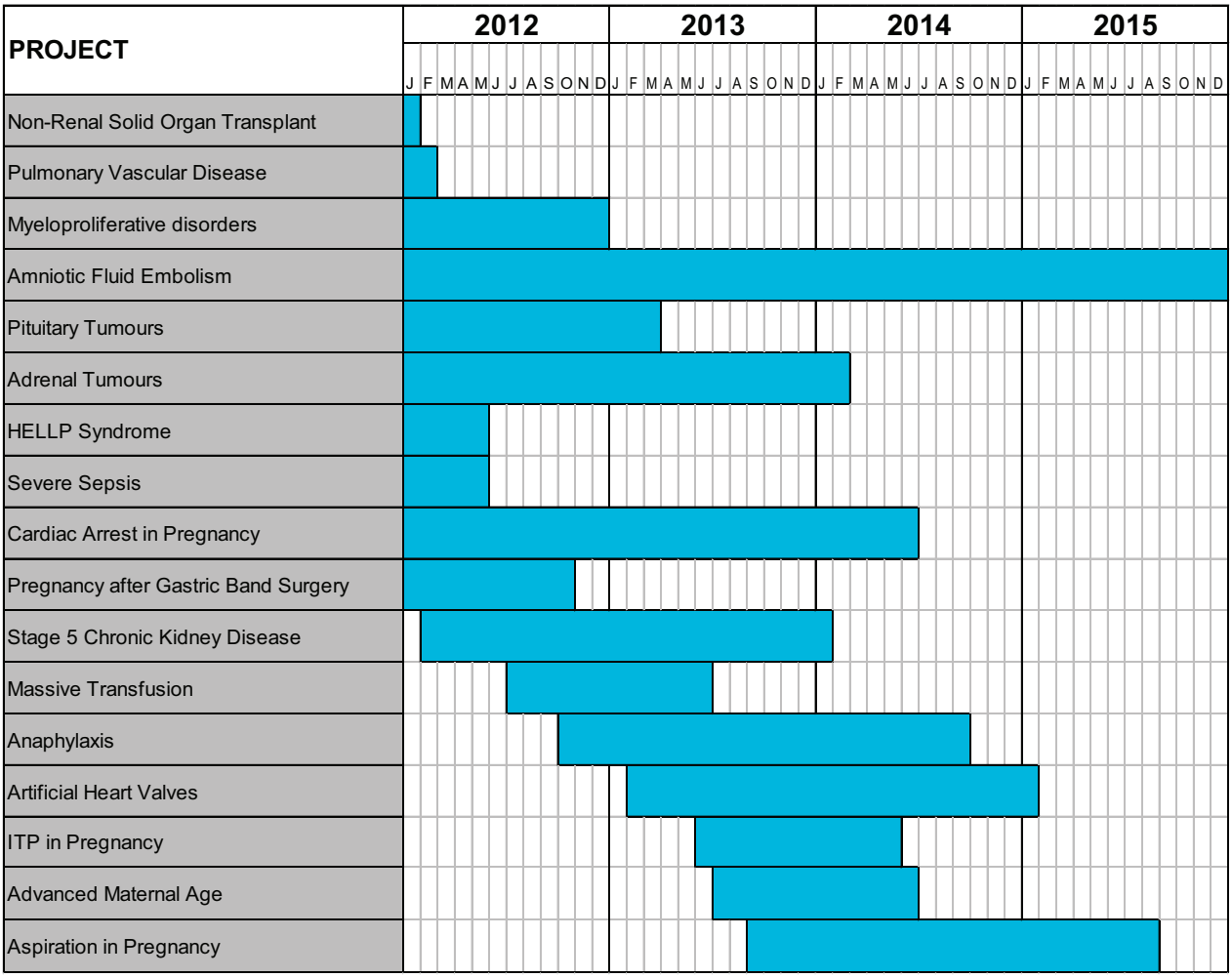


4. Studies

Unless otherwise specified, the results included in this report represent analysis of cases reported and data available up to February 2013. All studies have been funded through a grant to the NPEU from the Department of Health (reference number: 006 0034) except where indicated. Please note the data presented are provisional, not peer reviewed and definitive conclusions should not be drawn from them.

4.1. Study Timetable

Figure 4: Provisional UKOSS Study Data Collection Timetable 2012-2015



4.2. Studies completed in 2012

4.2.1 Gastric Banding in Pregnancy

Key points

- Laparoscopic Adjustable Gastric Band (LAGB) insertion is the primary surgical method of surgical weight reduction in the UK.
- LAGB insertion is increasing rapidly and the increase in gastric banding in women of reproductive age has resulted in increasing numbers of pregnancies following gastric banding.
- Management of pregnancy following gastric band surgery is not well defined.
- This study aimed to describe the epidemiology and management of gastric banding in pregnancy in the UK and suggests that band inflation may be associated with lower weight in pregnancy and lower BMI gain than band deflation.

Background

The impact of obesity on pregnancy is well established; obesity negatively impacts on maternal, fetal and neonatal wellbeing[17]. Laparoscopic Adjustable Gastric Band (LAGB) insertion is the primary surgical method of weight reduction in the UK. LAGB insertion is increasing rapidly both in the private sector and in the NHS, with an estimated 1,700 bands inserted in women under the age of 40 years in 2007. The increase in gastric banding in women of reproductive age has resulted in increasing numbers of pregnancies following gastric banding. Nevertheless, management of pregnancy following gastric band surgery has not been well defined. In most reports, women who conceive following LAGB have the band deflated for the duration of the pregnancy[18] because of concerns regarding hyperemesis and poor nutritional intake. Deflating the gastric band has the adverse effect of excessive weight gain[19] and subsequent pregnancy complications. However, pregnancy following LAGB has been shown to be well tolerated and studies have also demonstrated a reduction in incidence of gestational diabetes[20-22], maternal hypertension[20-23] and caesarean delivery[23] when compared to obese controls.

Case definition

Any woman with a confirmed ongoing pregnancy following laparoscopic adjustable gastric band surgery.

Surveillance Period

November 2011 - October 2012

Interim Results

To date complete, checked and verified data has been received for 67 cases. 32 (48%) women had their band inflated for the duration of pregnancy. 29 (43%) women underwent band deflation pre- or during pregnancy. In the remainder of cases band management was unknown. There were no differences in baseline characteristics between the two groups. No inflation related adverse symptoms were reported. Mean weight gain and increase in pregnancy BMI both appeared lower (BMI change significantly lower $p<0.05$) in the inflation group (weight gain inflation 6.4kg, deflation 11.6kg; BMI change inflation 2.0, deflation 4.2).

There were no statistically significant differences in outcomes of pregnancy between the two groups, however, it is important to note that the small number of cases limit the power of these analyses to identify a difference as statistically significant.

Conclusions

In this preliminary analysis, band inflation in pregnancy was generally well tolerated and potentially associated with reduced pregnancy weight gain. Analysis of complete data is needed to confirm benefit and guide management.

Investigators

Dimitrios Siassakos, Amanda Jefferys, Elinor Medd, Judith Hyde, Mary Lynch, Andrew Johnson, Tim Draycott, Southmead Hospital, Bristol.

Funding

This study is funded by a grant from North Bristol Hospitals NHS Trust.

4.2.2 HELLP syndrome

Key points

- There has been no comprehensive UK study of the risk factors for HELLP syndrome to date.
- There is debate about the optimal management of women who develop the syndrome prior to 34 weeks of gestation when the maternal and fetal status is reassuring and there is uncertainty regarding risk factors for adverse outcomes.
- This study aimed to estimate the incidence of HELLP syndrome in the UK and investigate and quantify the associated risk factors, management and outcomes and also to explore whether any factors are associated with poor outcomes.
- The study showed that expectant/conservative management is rarely used in the UK and therefore this study cannot provide clear evidence about the risks/benefits of this approach.

Background

HELLP syndrome is a serious complication of pregnancy characterised by haemolysis, elevated liver enzymes and a low platelet count[24]. In the absence of haemolysis, the condition has been called ELLP syndrome. Incidence estimates vary from 0.5 to 7.6 per 1000 deliveries[25,26] and between 8% and 24% of cases with severe pre-eclampsia/eclampsia[26,27]. Although there have been reports that women with HELLP syndrome are more likely to be older, of white ethnicity and multiparous[28-30] and the majority, although not all, have signs of pre-eclampsia[31], there has been no comprehensive study of the risk factors for this complication.

There is a consensus that prompt delivery is indicated when HELLP syndrome develops after 34 weeks of gestation or when fetal or maternal conditions deteriorate. However, there is debate about the optimal management of women who develop the syndrome prior to 34 weeks of gestation when the maternal and fetal status is reassuring. There is also uncertainty regarding risk factors for adverse outcomes. This study aimed to estimate the incidence of HELLP and ELLP syndrome in the UK, to investigate and quantify the associated risk factors, management and outcomes and to explore whether any factors are associated with poor outcomes.

Case definition

All pregnant women identified as having **new onset** of the following:

Elevated liver enzymes, defined as:

Serum aspartate aminotransferase (AST) ≥70 U/L
OR
Gamma-glutamyltransferase (γ-GT) ≥70 U/L
OR
Alanine aminotransferase (ALT) ≥70 U/L

AND

Low platelets, defined as platelet count < 100 $x10^9$/l.

AND

EITHER
Haemolysis, defined by abnormal peripheral blood smear or serum lactate dehydrogenase (LDH) levels ≥600 U/L or total bilirubin ≥20.5 µmol/l
OR
Hypertension, defined as a systolic blood pressure ≥ 140 mmHg or a diastolic blood pressure ≥ 90 mmHg
OR
Proteinuria, defined as 1+ (0.3 g/l) or more on dipstick testing, a protein:creatinine ratio of 30 mg/mmol or more on a random sample, or a urine protein excretion of 300 mg or more per 24 hours

Surveillance Period

June 2011 - May 2012

Results

Up to December 2012 there were 257 notified cases. Data were received for 229 of these cases (89%); 14 cases were subsequently reported by clinicians as not cases and data collection forms were received for the remaining 215 notified cases. A total of 180 women met the case definition. 110 of the women had haemolysis and can be considered to have HELLP syndrome, representing an estimated incidence of 1.38

per 10,000 maternities (95% CI 1.13-1.66). A further 70 of the women met the case definition, but did not have haemolysis and can be considered to have ELLP syndrome, representing an estimated incidence of 0.88 per 10,000 maternities (95% CI 0.68-1.11).

Of the women with HELLP syndrome, 64% were diagnosed antenatally at a median gestation of 35 weeks (range 21-41). 54% (37/68) of antenatally diagnosed women had a planned management of immediate delivery and delivered a median of 3 hours 37 minutes after diagnosis (range 53 minutes - 21 hours 26 minutes); 43% (29/68) had a planned management of delivery within 48 hours and delivered a median of 11 hours 40 minutes after diagnosis (range 1 hour 28 minutes - 74 hours 43 minutes); only 2/68 had a planned attempt at expectant/conservative management, with one delivering 3 days and the other 12 days after diagnosis.

Overall, 42% (46/110) of women with HELLP received corticosteroids (only three for maternal indications, two of whom were diagnosed postpartum), 77% (84/109) were given antihypertensive medication and 78% (86/110) were given magnesium sulphate. Severe morbidity was noted in 15% (16/110) of the women with HELLP syndrome and one women died (case fatality rate 1%, 95% CI 0.02-5%). Major complications were reported in 9% (10/111) of infants born to women with HELLP syndrome and there were two perinatal deaths (perinatal mortality rate 18 per 1,000 total births, 95% CI 2-62) and one late neonatal death (late neonatal morality rate 9 per 1,000 live births, 95% CI 0.2-48). All HELLP syndrome cases associated with major maternal or perinatal complications occurred in women delivered within 48 hours of diagnosis or in women diagnosed postpartum.

Interim Conclusions

HELLP syndrome is associated with severe maternal and infant morbidity and mortality. Expectant/conservative management is rarely used in the UK and therefore this study cannot provide clear evidence about the risks/benefits of this approach. Further analysis of these data, including quantification of risk factors for the syndrome, is currently underway.

Investigators

Kate Fitzpatrick, Marian Knight, Jenny Kurinczuk, Maria Quigley, NPEU;

Kim Hinshaw, Sunderland Royal Hospital;

Peter Brocklehurst, Institute for Women's Health UCL;

Sue Sellers, United Bristol Hospitals NHS Trust;

Mervi Jokinen, RCM;

Shona Golightly, CMACE;

Gwyneth Lewis, Department of Health;

James Walker, NPSA;

Jane Bell, Oxfordshire PCT;

Jenny Furniss, Lay representative.

Funding

This study has been funded by the National Institute for Health Research as part of the UK National Maternal Near-miss Surveillance Programme (UKNeS).*

UKNeS
The National Maternal Near-miss Surveillance Programme

4.2.3 Myeloproliferative Disorders

Key points

- Historical literature suggests myeloproliferative disorders are associated with increased maternal and fetal morbidity and mortality.
- There have been no prospective national studies to estimate the incidence or outcomes of myeloproliferative disorders, persistent thrombocytosis or erythrocytosis in pregnancy.
- This study of myeloproliferative disorders, persistent thrombocytosis or erythrocytosis in pregnancy aimed to investigate the incidence, management and outcomes for mother and infant.

Background

The Myeloproliferative disorders (MPDs) are clonal haematological malignancies characterised by over production of mature blood cells and a chronic clinical course. They include polycythaemia vera (PV), primary myelofibrosis (PMF) and essential thrombocythaemia (ET). The most extensive literature of the epidemiology and outcome of pregnancy exists for ET with approximately 461 pregnancies reported[32]; for PV and PMF the literature is more limited, reporting mostly single centre studies. MPD especially PV and PMF in pregnancy are thus under-researched, our understanding of them is poor and any interventions used in current clinical practice are rarely based on robust evidence. Prospective data collection on known and occult MPDs in pregnancy using UKOSS provides valuable information into the epidemiology and complications of MPD in pregnancy.

Case definition

All pregnant women in the UK identified as having:

EITHER	a myeloproliferative disorder (essential thrombocythaemia, polycythaemia vera, myelofibrosis), diagnosed by a consultant haematologist according to WHO guidelines
OR	a thrombocytosis (platelet count persistently greater than 600 $x10^9$/l)
OR	an erythrocytosis (haemoglobin persistently greater than 16.5g/dl) .

Surveillance Period

January 2010 – December 2012

Interim Results

Up to January 2013, 85 cases of myeloproliferative disorders in pregnancy were reported. Information has been received for 69 of these cases (81%). There were 17 cases which were subsequently reported by clinicians as not cases, five duplicate reports and three further cases did not meet the case definition. There were thus 44 confirmed cases in an estimated 2,396,640 maternities. This gives an incidence estimate in the UK of 1.8 cases per 100,000 maternities (95% CI 1.3 to 2.5 per 100,000). The cases diagnosed were predominantly essential thrombocythemia (20 cases - 69%), five women had thrombocytosis (17%), three women had polycythaemia vera (10%) and there was one case of myelofibrosis (3%).

Interim Conclusion

We are in the process of finalising data collection for this study and it is not possible to draw any definitive conclusions at this stage.

Investigators

Sue Robinson, Claire Harrison, Susan Bewley, Gabriella Gray, Guy's and St Thomas' Hospital.

Funding

This study was funded by a grant from the Guy's and St Thomas' Charity

4.2.4 Pregnancy in Non-renal Solid Organ Transplant Recipients

Key points

- There have been over 14,000 reports of pregnancy in transplant recipients worldwide.
- The UK National Transplantation Pregnancy Register no longer collects information.
- Immunosuppressive regimens are continually developing.
- This study aimed to provide a national picture of the incidence of pregnancy in non-renal solid organ transplant recipients and assess the role of immunosuppressive regimens and other factors in the outcomes of women and their infants.

Background

Despite initial concerns about the advisability of pregnancy in solid-organ transplant recipients, there have now been reports of over 14,000 births to women with transplanted organs[33]. Most studies are centre-based and retrospective[34]. Three voluntary registers have collected data at various times: the US National Transplantation Pregnancy Register (1991-present)[35], the UK Transplant Pregnancy Register (1994-2001)[34] and the European Dialysis and Transplant Association Registry (1960-1992)[36]. This UK register, however, no longer collects information. The objective of this project was to collect information about pregnancy outcomes amongst current solid organ transplant recipients in the UK and describe the outcomes for women and their infants. The project was divided into two studies; this reports data from the second part of the study to investigate outcomes in women with non-renal solid organ transplants.

Case definition

All pregnant women with a transplanted solid organ, including heart, lung, liver, pancreas and small bowel. Isolated renal, corneal and bone marrow transplant recipients were excluded.

Surveillance Period

January 2007 – January 2012

Results

110 cases of pregnancy in non-renal solid organ transplant recipients were reported and data collection forms were returned for 98 cases (89%). There were 13 cases which were subsequently reported by clinicians as not cases and there were 13 duplicate reports leaving 72 confirmed cases. We identified 59 pregnancies amongst 52 liver transplant recipients, and 13 pregnancies amongst 13 women with cardiothoracic transplants and compared them with a group of comparison women identified in previous UKOSS studies.

Women with a liver transplant had a median period of 6 years from transplant to conception (range 0-20). They were significantly more likely than comparison women to have pre-eclampsia (14% vs 4%; OR 4.3, 95%CI 1.5-11.2) and to deliver at less than 37 completed weeks (43% vs 8%; OR 8.6, 95% CI 4.8-15.2). There was no difference in the proportion delivering at less than 32 completed weeks. Overall amongst women with liver transplants, four pregnancies were lost or terminated, 54 infants were liveborn and one stillborn. No women with liver transplants died.

Women with cardiothoracic transplants had a median of 9 years from transplant to conception (range 2-16). One pregnancy miscarried; there were two stillbirths amongst 13 births. One woman died.

Conclusions

Women with liver and cardiothoracic transplants can have successful pregnancies, although pregnancy complications and loss are frequent.

Investigators

Marian Knight, Peter Brocklehurst, Jenny Kurinczuk, NPEU;

Catherine Nelson-Piercy, Guy's and St Thomas' Hospital.

4.2.5 Pulmonary Vascular Disease

Key points

- Pulmonary vascular disease in pregnancy is widely considered to pose an extreme risk of maternal death.
- There have been no recent prospective case series to assess this risk.
- This study showed that maternal pulmonary vascular disease in pregnancy is extremely rare in the UK.
- Neither maternal nor infant mortality appears to be as high as previously reported. However, we cannot exclude the possibility that this is because some women, particularly those with more severe disease, choose not to continue with their pregnancies.

Background

Pre-existing or gestational occurrence of pulmonary vascular disease, including Eisenmenger's syndrome, primary and secondary pulmonary hypertension, is one of the rare conditions widely considered to pose an extreme risk of maternal death[37]. In the triennium 2006-2008, two maternal deaths in the UK were attributable to pulmonary vascular disease; and between 1994 and 2008 there were 23 maternal deaths in the UK associated with this rare condition[38]. Eisenmenger's syndrome is estimated to carry a maternal mortality rate of 40% per pregnancy[39], with an infant mortality rate of 10-15%[37]. A systematic review of the literature in 1998 suggested that the maternal mortality rate had remained unchanged over the previous 20 years[37]. However, the authors of this review recognised that there may be inherent biases in published reports of pregnancy in women with pulmonary vascular disease in pregnancy and called for more information from detailed prospective case series in order to differentiate the risks of pregnancy and eventually provide an optimal plan of management. Cases in the UK were collected prospectively on a voluntary basis by the UK Registry of High Risk Obstetric Anaesthesia[40], however, problems with ascertainment caused the register to cease to collect data. The objective of this prospective study through UKOSS was to provide an appropriate national case series with good ascertainment to allow comprehensive study of the epidemiology and current management of Eisenmenger's syndrome and pulmonary hypertension in pregnancy.

Case definition

EITHER Pulmonary hypertension: defined as (1) a mean (not systolic) pulmonary artery pressure equal to or greater than 25mmHg at rest or 30 mmHg on exercise in the absence of a left-to-right shunt or (2) a pulmonary artery systolic pressure greater than 36mmHg[41]. Pulmonary hypertension may be primary (no cause identified) or secondary (known cause identified, for example, vasculitis, connective tissue disease, chronic pulmonary thromboembolism, sickle cell disease, drug use),

OR Eisenmenger's syndrome: defined as pulmonary hypertension secondary to an uncorrected left-to-right shunt from a ventricular septal defect, an atrial septal defect or a patent ductus arteriosus[42].

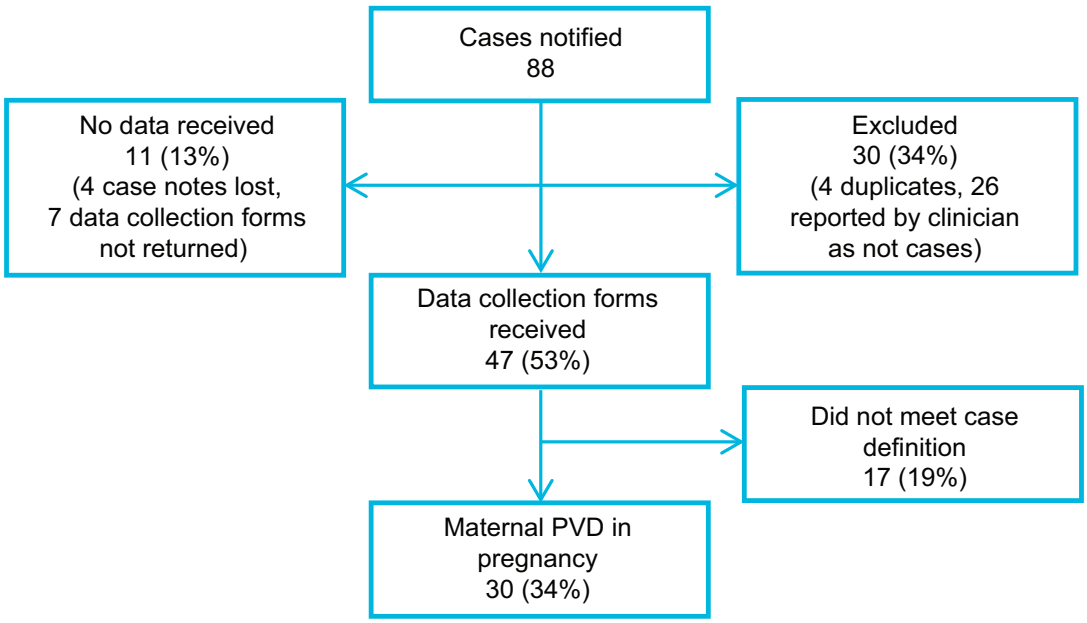
Surveillance Period

March 2006 – February 2012

Results

A total of 88 cases were reported during the study period and data were returned for 81 cases (92%). There were four duplicate cases, four cases whose case notes were lost and 26 cases were subsequently reported not to be cases by the notifying clinician. Of the 26 reported as not cases, 20 did not meet the case criteria, and 6 had a pulmonary embolism with no pulmonary hypertension. Seventeen cases for which we received data collection forms did not meet the case criteria; eleven had no pulmonary artery pressure measurement, four had a thromboembolic event with no pulmonary hypertension, one case had a pulmonary artery pressure below the threshold and one case reported neonatal pulmonary hypertension rather than maternal. There were thus 30 confirmed cases of maternal pulmonary vascular disease in pregnancy; an estimated incidence of 0.6 cases per 100,000 maternities (95% CI 0.4 to 0.9 per 100,000).

Figure 5: Case reporting and completeness of data collection, Pulmonary Vascular Disease.



The aetiologies of the thirty cases were as follows: fifteen cases (50%) of primary pulmonary hypertension; eight cases (26.7%) of secondary pulmonary hypertension; six cases (20%) of Eisenmenger's syndrome; one case (3.3%) of pulmonary hypertension was unspecified. Of the cases with secondary pulmonary hypertension, mitral valve disease accounted for four cases (50%), recurrent thromboembolic events for two cases (25%), and Systemic Lupus Erythematosus (SLE) and obstructive sleep apnoea for one case each (12.5% each).

Twenty-four women (80%) proceeded with their pregnancies and six (20%) underwent terminations. Of the completed pregnancies, there were no fetal losses and all infants survived the immediate neonatal period. Seventeen women were delivered by caesarean section (68%) and two had instrumental deliveries (8%); the remaining six (24%) had spontaneous vaginal deliveries. Two women died, both of whom continued with their pregnancies into the third trimester (overall case fatality 6.7%, 95% CI 0.8 to 22%; case fatality amongst women with continuing pregnancies 8.3%, 95% CI 1.0 to 27%).

Conclusions

Maternal pulmonary vascular disease in pregnancy is extremely rare in the UK. Neither maternal nor infant mortality appears to be as high as previously reported. However, we cannot exclude the possibility that this is because some women, particularly those with more severe disease, choose not to continue with their pregnancies. Further analysis of these data, and checking of case ascertainment with the MBRRACE-UK Confidential Enquiry into Maternal Deaths data is currently underway.

Investigators

Marian Knight, Vikash Mistry, Jenny Kurinczuk, NPEU;

Steve Yentis, Imperial College London;

Catherine Nelson-Piercy, Guys and St Thomas' Hospital.

4.2.6 Severe Maternal Sepsis

Key points

- Mortality due to severe maternal sepsis has increased in the UK and is now the leading cause of direct maternal death in the UK.
- Underlying each maternal death is a much larger number of cases of sepsis-related morbidity; however there has been no national-level study to measure the incidence or risk factors for this condition in the UK.
- This study shows that there is a significant burden of severe maternal sepsis in the UK, with almost one third of cases due to genital tract sepsis.
- Further analysis is underway to fully investigate the associated risk factors.

Background

Maternal sepsis is a severe complication of pregnancy or birth, which if untreated, can rapidly progress along a continuum of severity to septic shock and eventually death. In the UK, the incidence of fatal maternal sepsis has increased over the last two decades. In the late 1980s the maternal mortality rate (MMR) due to sepsis was 0.4/100,000 maternities, while in the period from 2006-2008 the MMR increased to 1.13/100,000[43]. This places sepsis as the leading cause of direct maternal death, surpassing hypertensive disorders[43,44]. Underlying each maternal death is a much larger number of cases of morbidity during pregnancy and the puerperium[45]. Given the recent increase in maternal deaths and incidence of morbidity in the general population due to sepsis[46], an understanding of the risk factors in the UK of obstetric sepsis morbidity before death occurs is needed to better target potential points of clinical intervention and prevent poor outcomes for mothers and their infants.

While there are several well-established risk factors for maternal sepsis including caesarean section[47-49] and anaemia[48,50], there has been no national-level study of the incidence or risk factors for this complication in the UK. The aim of this study, therefore, was to carry out a population-based case-control study using UKOSS to estimate the incidence of severe maternal sepsis in the UK, to investigate and quantify the associated risk factors, causative organisms, management and outcomes and to explore whether any factors are associated with poor outcomes.

Case definition

Any pregnant or recently pregnant woman (up to 6 weeks postpartum) diagnosed with severe sepsis (irrespective of the source of infection).

Only women diagnosed as having severe sepsis by a senior clinician were reported.

A severe sepsis case would be expected to include women in one of the following groups:

1. Death related to infection or suspected infection.
2. Any women requiring level 2 or level 3 critical care (or obstetric HDU type care) due to severe sepsis or suspected severe sepsis.
3. A clinical diagnosis of severe sepsis.

   As a guide, clinical diagnosis of severe sepsis would usually be in association with 2 or more of the following:

   a. Temperature > 38°C or < 36°C on 2 occasions at least 4 hours apart.
   b. Heart rate > 100 beats/ minute on 2 occasions at least 4 hours apart.
   c. Respiratory rate >20/ minute on 2 occasions at least 4 hours apart.
   d. White cell count > $17x10^9$/L or < $4x10^9$/L or with > 10% immature band forms, measured on 2 occasions.

Surveillance Period

June 2011 – May 2012

Interim Results

There have been 487 cases of severe sepsis reported to UKOSS. Information has been received for 440 cases (90%). There were 33 cases that were subsequently reported by clinicians as not cases, eight for which the case notes had been lost and 29 further cases did not meet the case definition criteria. There were five duplicate reports, leaving 365 confirmed cases giving an estimated incidence of 4.6 per 10,000 maternities (95% CI 4.1-5.1). Data were also obtained for 719 controls.

Laboratory confirmed infection (LCI) was reported for 223 (61%) severe sepsis cases and a source of infection was identified for 257 cases (70%). Overall, the largest proportion of cases was due to genital tract infection (31%) and the organism Escherichia coli (E. coli) (20.3%). Infection by Group A

streptococcus was responsible for 11% of severe postpartum sepsis cases. Sociodemographic and medical history characteristics of women with severe sepsis compared to control women are listed in table 1 (350 cases at time of analysis).

Interim Conclusions

At this point in the analysis, there appears to be a significant difference in several demographic, clinical and delivery characteristics between cases and controls. Further analyses will elucidate the burden of severe maternal sepsis on a national level, as well as investigate further the significant risk factors.

Investigators

Colleen Acosta, Marian Knight, Jenny Kurinczuk, Peter Brocklehurst, Maria Quigley, NPEU;

Sue Sellers, United Bristol Hospitals NHS Trust; Nuala Lucas, Northwick Park Hospital;

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Funding

This study has been funded by the National Institute for Health Research as part of the UK National Maternal Near-miss Surveillance Programme (UKNeS).*

Table 1: Characteristics of sepsis cases and controls

	Cases n (%) n=350	Controls n (%) n=719	χ^2 P-value
Risk Factor			
Sociodemographic factors			
Age (years)			<0.0001
<25	115 (32.9)	150 (20.9)	
25-34	176 (50.3)	414 (57.6)	
≥35	59 (16.9)	155 (21.6)	
Ethnic group			0.015
White	218 (63.1)	501 (69.9)	
Black and other minority	131 (36.9)	216 (30.1)	
Socio-economic group			0.001
Managerial and professional occupations	63 (18.9)	177 (25.4)	
Intermediate or manual	152 (45.7)	346 (49.6)	
Student or unemployed	118 (35.4)	174 (25.0)	
Obstetric and medical history			
Late booking			0.149
Yes	82 (23.4)	141 (19.6)	
No	268 (76.6)	578 (80.4)	
Parity			0.001
0	189 (54.0)	312 (43.4)	
≥1	161 (46.0)	407 (56.6)	
Multiple pregnancy			0.043
Yes	9 (2.6)	7 (1.0)	
No	340 (97.4)	710 (99.0)	
Smoked during pregnancy			0.095
Yes	96 (27.8)	165 (23.0)	
No	250 (72.3)	551 (77.0)	
BMI at booking (kg/m^2)			0.988
<18.5	14 (4.0)	26 (3.6)	
18.5<25	154 (44.0)	320 (44.5)	
25<30	89 (25.4)	185 (25.7)	
≥30	93 (26.6)	188 (26.2)	
Diabetes			0.368
Yes	9 (2.6)	26 (3.6)	
No	341 (97.4)	693 (96.4)	
Mode of delivery*			<0.0001
Spontaneous vaginal	55 (21.2)	421 (58.9)	
Operative vaginal	39 (15.1)	96 (13.4)	
Pre-labour caesarean	62 (23.9)	110 (15.4)	
Caesarean after labour onset	103 (39.8)	88 (12.3)	

* Percentage of postpartum cases only (n=289)

4.3. Studies in progress

4.3.1 Adrenal Tumours

Key points

- Adrenal tumours secrete excessive hormones which adversely affect maternal and fetal health.
- Adrenal tumours are managed with specific drugs or surgery, but it is not known how these affect the mother, the fetus or the neonate.
- This study will investigate the current incidence of rare adrenal tumours including phaeochromocytomas, those associated with Conn's Syndrome and Cushing's Syndrome. It will describe their current management and the associated outcomes for women and their infants and help develop guidelines for their optimal management.

Background

Tumours of the adrenal glands are very rare[51] and information in the medical literature on the incidence, their management in pregnancy and maternal, fetal and neonatal outcomes is limited. Phaeochromocytomas, tumours associated with Conn's Syndrome, and adrenal or pituitary tumours linked to Cushing's Syndrome produce excess steroid hormones which are associated with major pregnancy complications[52,53], including major maternal and fetal morbidity[54] and mortality[55,56]. Adrenal tumours are linked to higher rates of hypertension[51], diabetes[54] and pre-eclampsia, as well as fetal death, intrauterine growth restriction, fetal hypoxia[57], fetal distress[51,58], spontaneous abortion, stillbirth and prematurity[54]. Currently, there are no data on the incidence of adrenal tumours in pregnancy in the UK and the associated maternal, fetal and neonatal morbidity and mortality. In addition, there are few guidelines on the appropriate pharmacological or surgical management of these tumours during pregnancy. Therefore, this study will examine the effects of the drugs used to treat these in relation to maternal or fetal and neonatal complications and whether the timing of the surgery to remove the tumours is important. This will help the development of guidelines on the management of adrenal tumours in pregnancy with the ultimate aim of improving maternal and infant outcomes.

Case definition

Any pregnant women in the UK with a functioning adrenal neuroendocrine tumour, including women diagnosed pre-pregnancy who have not undergone surgery to remove the tumour.

INCLUDED:

PHAEOCHROMOCYTOMA	Neuroendocrine adrenal tumour secreting catecholamines (dopamine, nor-adrenaline, adrenaline, metadrenaline and normetadrenaline).
CUSHING'S SYNDROME	Adrenal cortex tumour secreting excessive amounts of cortisol.
CONN'S SYNDROME	Adrenal cortex adenoma secreting excessive amounts of aldosterone.
EXCLUDED:	Women with non-functioning adrenal tumour.

Surveillance Period

March 2011 - February 2014

Interim Results

Up to January 2013, 19 cases of adrenal tumours in pregnancy were reported. Information has been received for 17 of these cases (89%). There were five cases which were subsequently reported by clinicians as not cases and one duplicate report. One case was reported as lost. Four further cases did not meet the case definition. There were thus six confirmed cases in an estimated 1,531,422 maternities. This gives an incidence estimate in the UK of 0.4 cases per 100,000 maternities (95% CI 0.1 to 0.9 per 100,000). The six confirmed cases included four women with Conn's syndrome and two women with phaeochromocytoma.

Interim Conclusions

Data collection for this study is still incomplete and it is not possible to draw any definitive conclusions at this stage. However, these preliminary results suggest that adrenal tumours in pregnancy are extremely rare.

Investigators

Catherine Williamson, Kimberly Lambert, Imperial College London;

David McCance, Royal Victoria Hospital.

Funding

This study is funded by SPARKS

4.3.2 Amniotic Fluid Embolism

Key points

- Amniotic fluid embolism (AFE) is a leading cause of maternal mortality in the UK today but estimates of incidence and mortality vary widely.
- The estimated incidence using active surveillance through UKOSS is more than twice that obtained through passive registration.
- AFE is associated with induction of labour and caesarean delivery in the UK population.
- There is no evidence of an increase in incidence over the eight years of UKOSS surveillance.

Background

Amniotic fluid embolism (AFE) has been consistently identified by the UK Confidential Enquiry into Maternal Deaths as a leading cause of maternal mortality[15,43]. Estimates of incidence vary tenfold between 1.3 and 12.5 per 100,000 pregnancies[59]. Estimates of the case fatality of this condition also vary widely[60], from as much as 86% to more recent estimates of 16-30%. Recent retrospective administrative database analyses suggest possible links with induction of labour and caesarean delivery[61,62], and a wide range of treatments have been described in case reports[60]. A database of voluntary notifications was established in the UK to collect information on epidemiology and management[63]; this register was incorporated into UKOSS to improve ascertainment and allow a comprehensive study of the epidemiology and current management. Analysis of UKOSS data on AFE up to February 2009 showed that AFE occurrence was significantly associated with induction of labour and multiple pregnancy, and that an increased risk was also noted in older ethnic minority women. Caesarean delivery was associated with postnatal amniotic fluid embolism[64].

Case definition

EITHER	A clinical diagnosis of AFE (acute hypotension or cardiac arrest, acute hypoxia or coagulopathy in the absence of any other potential explanation for the symptoms and signs observed)
OR	A pathological diagnosis (presence of fetal squames or hair in the lungs).

Surveillance Period

February 2005 – ongoing

Interim Results

In the eight years of surveillance to date, 169 cases of AFE in pregnancy have been reported. Information has been received for 164 cases (97%). There were 21 cases which were subsequently reported by clinicians as not cases and nine duplicate reports. Fifteen further cases did not meet the case definition criteria. There were thus 119 confirmed cases, in an estimated 6,192,052 maternities. This gives an incidence estimate in the UK of 1.9 cases per 100,000 maternities (95% CI 1.6 to 2.3 per 100,000).

Interim Conclusions

There is no evidence of a significant change in the incidence of AFE over the past eight years. The incidence rate is comparable to that documented in other high resource countries using similar methodology[65]. However, in view of the extreme rarity of this condition and the significant associated mortality, surveillance through UKOSS is ongoing in order to further investigate risk factors and describe outcomes following the use of different management techniques.

Investigators

Marian Knight, NPEU

Funding

This study has been funded by the National Institute for Health Research as part of the UK National Maternal Near-miss Surveillance Programme (UKNeS).*

4.3.3 Anaphylaxis in Pregnancy

Key points

- Although rare, anaphylaxis during pregnancy can be associated with significant adverse outcomes for both mother and infant and can be fatal.
- There are published guidelines for the management of anaphylaxis in adults, however there is little information about how anaphylactic shock in pregnancy should be managed in order to optimise the outcome for both mother and baby.
- This study will collect information about the incidence, management and outcomes of anaphylaxis in pregnancy in the UK.

Background

Anaphylaxis is severe and potentially fatal systemic hypersensitivity reaction. It is characterised by a combination of life-threatening airway, breathing or circulatory problems with skin or mucosal changes[66]. Current estimates of incidence suggest that maternal anaphylaxis occurs in approximately 1 in 30,000 pregnancies, although this is based on limited evidence[67]. There is currently no published information relating to the incidence of anaphylaxis during pregnancy available for the UK and although this condition is rare, the importance of studying it is highlighted by a number of case studies showing that anaphylaxis during pregnancy can be associated with significant adverse outcomes for both mother and infant[68-71].

Anaphylaxis can be caused by a wide variety of agents and it is unclear as to whether the risk factors for anaphylaxis in the general population such as age, concomitant co-morbidities and previously documented hypersensitivity can accurately predict risk of anaphylaxis in pregnancy[72,73]. The recent proposed and actual policy changes with regard to antibiotic administration in pregnancy, including the use of prophylactic antibiotics up to one hour prior to delivery by caesarean section and the use of prophylactic antibiotics for maternal group B streptococcal carriage in labour[71,72], have the potential to impact on the incidence and/or outcomes of anaphylaxis during pregnancy, making this study very timely.

Case definition

All pregnant women in the UK identified as having anaphylaxis according to the following definition[74].

Anaphylaxis is defined as a severe, life-threatening generalised or systemic hypersensitivity reaction. The following three criteria must be met for a diagnosis of anaphylaxis to be made:

1. A life-threatening airway problem and/or breathing problem and/or circulatory problem
2. Sudden onset and rapid progression of symptoms
3. Skin and/or mucosal changes

A life-threatening airway problem is taken to include:

- Laryngeal or pharyngeal oedema
- Hoarse voice
- Stridor

A life-threatening breathing problem is taken to include:

- Shortness of breath and raised respiratory rate
- Wheeze
- Decreased oxygen saturations
- Confusion secondary to hypoxia
- Cyanosis
- Respiratory exhaustion or respiratory arrest

A life-threatening circulatory problem is taken to include:

- Signs of shock such as faintness, pallor or clammy skin
- Tachycardia >100bpm
- Systolic BP <90mmHg
- Decreasing level of consciousness
- Signs of ischaemia on ECG
- Cardiac arrest

Surveillance Period

October 2012 – September 2014

Interim Results

This study is at an early stage. Up to January 2013, 11 cases of Anaphylaxis in Pregnancy had been reported. Information has been received for five of these cases (45%). There was one case which was subsequently reported by clinicians as not a case. There are thus four confirmed cases to date.

Interim Conclusions

Data collection for this study is still incomplete and it is not possible to draw any definitive conclusions at this stage.

Investigators

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Nuala Lucus, Northwick Park Hospital;

Derek Tuffnell, Bradford Teaching Hospitals, NHS foundation Trust;

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Rhiannon D'Arcy, Oxford University Hospitals.

Funding

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PRUMHC
POLICY RESEARCH UNIT - MATERNAL HEALTH & CARE

UKNeS
The National Maternal Near-miss Surveillance Programme

4.3.4 Cardiac Arrest in Pregnancy

Key points

- The risk of death following a cardiac arrest in pregnancy is extremely high for both mother and child, but both can be resuscitated if fast action is taken.
- Cardiac arrest is managed by resuscitation and periarrest/perimortem caesarean section (PMCS).
- There is little information on survivors of cardiac arrest or PMCS.
- This study will investigate the current incidence of cardiac arrest and PMCS in pregnancy. It will describe the current management by resuscitation and PMCS, the associated outcomes for women and their infants and will help to develop guidelines for optimal management.

Background

Cardiac arrest in pregnancy affects around 1 in 30,000 women[75]; incidence is thought to be rising due to the increasing age and morbidity of the antenatal population in the UK. The risk of death for mother and child is extremely high but some causes of cardiac arrest are reversible. Aggressive resuscitation is required, including caesarean section in most cases over 20 weeks gestation. The importance of rapid delivery after cardiac arrest for maternal benefit is becoming a widely accepted practice and there is evidence to suggest that MOET (Managing Obstetric Emergencies & Trauma) training in obstetric resuscitation is leading to an increase in the use of PMCS in maternal cardiac arrest in the UK[76] and in Europe[77]. In the UK 52 cases of PMCS were recorded between 2003-2005 amongst women who subsequently died[15].

There is, however, minimal information on survivors of cardiac arrest or PMCS. This study will investigate the incidence, management (including PMCS) and outcomes of maternal cardiac arrest including both women who survive and women who die. This information will be used to establish optimal management guidelines to improve survival of mother and infant.

Case definition

Any woman who has received immediate basic life support (BLS) (i.e. chest compressions and, if possible, ventilation breaths) at any point in pregnancy, up to the point of delivery of the baby. **Note** that women requiring ventilatory support only, are **not** included.

Surveillance Period

July 2011 - June 2014

Interim Results

Up to March 2013, 91 cases of cardiac arrest in pregnancy were reported. Information has been received for 72 of these cases (79%). There were 13 cases which were subsequently reported by clinicians as not cases, two duplicate reports and 23 further cases did not meet the case definition. There were thus 34 confirmed cases in an estimated 1,398,255 maternities. This gives an incidence estimate in the UK of 2.4 cases per 100,000 maternities (95% CI 1.7 to 3.4 per 100,000). In 25 women (74%) perimortem caesarean section was carried out. 11 women (32%) died.

Interim Conclusions

Data collection for this study is still incomplete and it is not possible to draw any definitive conclusions at this stage.

Investigators

Virginia A. Beckett, Laura McCarthy, Bradford Teaching Hospitals NHS Trust;

Paul Sharpe, University Hospitals of Leicester NHS Trust;

Marian Knight, NPEU.

Funding

This study is funded by Wellbeing of Women.

WELLBEING OF WOMEN

4.3.5 Massive Transfusion in Major Obstetric Haemorrhage

Key points

- Major obstetric haemorrhage (MOH) is a significant cause of maternal morbidity however, there is no consensus on optimal transfusion support for patients with massive haemorrhage.
- Currently there is a drive to adapt the management of massive haemorrhage in pregnant women based on the findings of studies carried out on trauma patients although there is no evidence to support this change.
- This study will describe the incidence, management and clinical outcomes of major obstetric haemorrhage in the UK and investigate whether any management factors are associated with improved outcomes.

Background

Major obstetric haemorrhage (MOH), resulting in massive transfusion (MT), accounts for up to 80% of all maternal morbidity[78]. As there is no universally accepted definition for MOH, incidence estimates vary depending upon how it is defined. The most critical feature of MOH is the development of disseminated intravascular coagulopathy (DIC) which, unlike DIC that follows major haemorrhage in trauma or surgery, occurs quite early in the course of the haemorrhage. The situation is further complicated by the fact that during massive haemorrhage volume resuscitation with fluid and blood can lead to dilutional coagulopathy[79].

In recent years, availability of rapid new diagnostic testing and the introduction of new haemostatic resuscitation strategies have challenged our thinking on optimal transfusion support for patients with massive haemorrhage. Much of the drive for new approaches to the management of bleeding has come from studies of patients with trauma. In trauma-induced haemorrhage it is now believed that standard MT protocols are less effective in treating major bleeding[80]. Although studies from bleeding trauma patients have some limitations, they have raised some important questions about the optimum management of patients with massive bleeding. Increasingly, the 'high-ratio' protocols are being adapted and applied to patients with other major bleeding (including MOH) with no supporting evidence. Further investigation is required to enable the generation of evidence-based clinical guidance, as well as the identification of new avenues for research including, among others, interventional clinical trials.

Case definition

All pregnant women of 20 weeks gestation or more identified as having ≥8 units of RBC transfusion within a 24 hour period.

Surveillance Period

July 2012 – June 2013

Interim Results

Up to January 2013, 149 cases of Massive transfusion due to Major Obstetric Haemorrhage were reported. Information has been received for 93 of these cases (62%). There were 11 cases which were subsequently reported by clinicians as not cases, one duplicate report and 13 further cases did not meet the case definition. There were thus 68 confirmed cases in an estimated 466,085 maternities. This gives a provisional incidence estimate in the UK of 1.4 cases per 10,000 maternities (95% CI 1.1 to 1.8 per 100,000).

Interim Conclusions

Data collection for this study is still incomplete and it is not possible to draw any definitive conclusions at this stage.

Investigators

Laura Green, NHS Blood and Transplant & Barts and the London Hospital;

Simon Stanworth, John Radcliffe Hospital;

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Marian Knight, UKOSS.

Funding

NHS Blood and Transplant Trust Fund.

NHS
Blood and Transplant

4.3.6 Pituitary Tumours

Key points

- Pituitary tumours produce hormones that can have a detrimental effect on pregnancy; as the pituitary enlarges in size during pregnancy, the tumour may also compress surrounding structures.
- This will be the first national study to evaluate maternal and fetal mortality and morbidity of pituitary tumours in pregnancy.
- This information will be used to develop guidelines for the management of women with pituitary tumours in pregnancy.

Background

Pituitary Tumours are rare and complicate approximately 1 in 4500 pregnancies in the UK. These tumours often secrete hormones, which in excess can have devastating effects on the mother and the unborn baby. In addition, many pituitary tumours require treatment with specific drugs or surgery, and this can also result in adverse outcomes for the fetus or neonate.

Macroprolactinoma is a benign tumour of the pituitary that is 1cm or more in diameter. The risk of enlargement of untreated macroprolactinoma in pregnancy is approximately 26%, compared to 3% in women previously treated with surgery and/or radiation[81]. Pituitary tumours that secrete excess hormones are associated with a higher incidence of maternal mortality and morbidity. Cushing's disease and acromegaly are both associated with an increased incidence of hypertension (potentially leading to pre-eclampsia), diabetes and cardiac failure[81]. Cushing's disease is associated with high fetal morbidity (spontaneous abortion 5%, stillbirth 6% and prematurity 43%)[54]. There is very little literature on the use of medication in the management of these conditions in pregnancy.

Following this study we will be able to provide comprehensive information on maternal/fetal outcome related to medications used to treat pituitary tumours and this will be used as the basis for the development of clinical management guidelines.

Case definition

All women in the UK with a pituitary tumour in pregnancy excluding a microprolactinoma (a prolactin-secreting tumour less than 1cm diameter).

This will include women diagnosed in pregnancy and those diagnosed pre pregnancy with a macroprolactinoma, Cushing's disease, acromegaly, thyrotrophinomas or non-functioning pituitary tumours.

Surveillance Period

March 2010 - March 2013

Interim Results

Up to March 2013, 118 cases of pituitary tumours in pregnancy were reported. Information has been received for 102 of these cases (86%). There were 28 cases which were subsequently reported by clinicians as not cases and four duplicate reports. Fifteen further cases did not meet the case definition. There were thus 55 confirmed cases in an estimated 2,463,285 maternities. This gives an incidence estimate in the UK of 2.2 cases per 100,000 maternities (95% CI 1.7 to 2.9 per 100,000). The 55 confirmed cases included 36 women with prolactinomas, 12 women with non-functioning tumours, three women with Cushing's disease, three women with acromegaly and one woman with thyrotrophinoma.

Interim Conclusions

Data collection for this study is still incomplete and it is not possible to draw any definitive conclusions at this stage.

Investigators

K Lambert, C Williamson, M Dhanjal, Imperial College Healthcare NHS Trust;

D McCance, Royal Victoria Hospital, Belfast.

Funding

This study is funded by SPARKS

4.3.7 Prosthetic Heart Valves in Pregnancy

Key points

- Lifelong anticoagulation is required to prevent thrombosis in women with artificial heart valves.
- Warfarin, the usual anticoagulant, can cause fetal abnormalities. Low molecular weight heparin (LMWH) injections can be used instead and these are safe for the baby, but concerns have been expressed about their efficacy in protecting the mother against heart valve thrombosis.
- This study will provide population-based information about the risks associated with an artificial heart valve in pregnancy and the different anticoagulation regimes in order to inform future management guidance.

Background

Women with mechanical prosthetic heart valves require lifelong anticoagulation, usually with warfarin, to prevent valve thrombosis. During pregnancy their thrombotic risk increases (estimated to be as high as 29%[82] with a 2.9% maternal mortality rate[83]). Thus, the need for effective anticoagulation is greater. Warfarin treatment throughout pregnancy appears to have the lowest risk of maternal thrombotic complications[83] but is associated with a higher fetal loss rate (estimates as high as 59%)[82] and can have damaging effects on the fetus[83]. In contrast, unfractionated heparin or low molecular weight heparin are safe for the fetus, but doubts have been expressed about their efficacy in preventing maternal thrombotic complications[84]. Factors, such as the type and position of the mechanical valve, choice of anticoagulant regime and patient compliance may all affect the rate of thrombosis.

Counselling of women with artificial heart valves about the risks during pregnancy is difficult due to the paucity of good data relating to maternal or fetal outcomes. Recommendations from various expert groups have suggested that since there is no ideal anticoagulant regime, women should be given the information and encouraged to choose their therapy[85]. Whilst the concept of 'informed choice' is appealing, there is a need for accurate information on which to base this choice. The aim of this study is to provide population based estimates of the incidence of maternal and fetal complications with the different anticoagulant regimes. This would help optimise the future management of pregnant women with artificial valves, to obtain the best outcomes for mother and baby.

Case definition

All women with artificial mechanical prosthetic heart valves in the UK, who become pregnant during the study period, irrespective of the outcome of the pregnancy.

This includes any woman in whom one or more heart valves have been replaced with an artificial mechanical prosthetic heart valve eg Starr-Edwards ball in cage, Bjork-Shiley tilting disc or St Jude's bi-leaflet valve.

EXCLUDED

Women with a bioprosthetic valve eg Carpentier-Edwards, Medtronic Intact or Hancock, women with a homograft or women who have had a valvotomy or valvoplasty (unless they also have an artificial mechanical prosthetic heart valve).

Surveillance Period

February 2013 – January 2015

Interim Results and Conclusion

Data collection for this study has just commenced and results and conclusions are not yet available.

Investigators

Sarah Vause, Bernard Clarke, Clare Tower, Charles Hay, Central Manchester University Hospitals NHS Trust;

Marian Knight, NPEU.

Funding

This study is funded by Wellbeing of Women.

WELLBEING OF WOMEN

4.3.8 Chronic Kidney Disease Stage 5

Key points

- Pregnancy in women with Chronic Kidney Disease (CKD) Stage 5 is associated with poor fetal outcomes and an increased incidence of maternal complications.
- Dialysis strategies for the management of this group of women are continually developing; however the effects on both mother and fetus of changes in dialysis dose are not well defined.
- This study will collect information about the incidence, management and outcomes of pregnancy in women with CKD Stage 5 in the UK.

Background

Current advice given to women pre-pregnancy with CKD Stage 5 is to delay conception until they receive a renal transplant, which is associated with restored fertility and improved pregnancy outcomes. Women ineligible for prospective transplantation are counselled regarding high rates of fetal loss, severe preterm delivery, fetal growth restriction and small for gestational age infants and maternal complications including pre-eclampsia. Dialysis strategies are continually developing, however more intensive dialysis regimes are likely to be associated with treatment related complications (e.g. infection, fluid volume shifts) which may have consequences for both mother and fetus.

Furthermore, the dialysis dose (urea clearance) has not yet been shown to be predictive of fetal outcome[86,87]. More information is needed about the intrauterine effects and neonatal consequences of changes in dialysis dose. This project will collect information about pregnancy outcomes amongst current women with CKD Stage 5 during pregnancy in the UK and assess the role of dialysis regimens and other factors in the outcomes of women and their infants. Outcomes will be compared with women with renal transplants matched for age, parity and ethnicity. This information is important to inform future management and counselling of these women; in particular to provide a direct comparison of pregnancy outcomes between different forms of renal replacement therapy i.e. dialysis and transplantation.

Case definition

Any pregnant woman identified as having CKD Stage 5 prior to, or during their pregnancy.

This would usually include any pregnant woman in one of the following groups:

- A woman with an estimated glomerular filtration rate (eGFR) <15mls/min/1.73m^2 pre-pregnancy
- A woman receiving peritoneal or haemodialysis at conception
- A woman with a serum creatinine >300umol/l pre-pregnancy
- A woman with a serum creatinine >250umol/l on two or more occasions during pregnancy
- A woman commenced on peritoneal or haemodialysis to treat chronic kidney disease during pregnancy

Surveillance Period

February 2012 – January 2014

Interim Results

Up to January 2013, 21 cases of Chronic Kidney Disease were reported. Information has been received for 14 of these cases (72%). There was one duplicate report and three cases did not meet the case definition. There were thus 10 confirmed cases in an estimated 799,003 maternities. This gives an incidence estimate in the UK of 1.3 cases per 100,000 maternities (95% CI 0.6 to 2.3 per 100,000).

Interim Conclusion

At this stage, it appears that pregnancy amongst with women with CKD stage 5 is very uncommon. However, we will also be seeking additional sources of cases to maximise case ascertainment.

Investigators

Catherine Nelson-Piercy (Principal Investigator), St Thomas' Hospital, London;

Kate Bramham, Maternal and Fetal Research Unit, King's College London.

Funding

The Lauren Page Trust

4.4. Future studies

These studies have been approved by the UKOSS Steering Committee to commence in 2013/14.

4.4.1 Pregnancy at advanced maternal age in the UK

Key points

- Childbearing at advanced maternal age is becoming increasingly common in high income countries. Furthermore, developments in assisted reproductive technologies may contribute to an increasing incidence of pregnancies in women outside of the normal reproductive age.
- Many studies have reported an association between advanced maternal age and adverse maternal and infant outcomes. However, few studies have quantified the risks in women of very advanced maternal age.
- This study will describe the characteristics, management and outcomes of women giving birth at very advanced maternal age in the UK and will estimate the risk of adverse outcomes attributable to advanced maternal age.

Background

Childbearing at advanced maternal age is becoming increasingly common in high income countries. Furthermore, developments in assisted reproductive technologies, including IVF egg donation, may contribute to an increasing incidence of pregnancies in women outside of the normal reproductive age. In England and Wales the average age at childbearing has increased steadily since the mid-1970s from 26.4 in 1975 to 29.5 in 2010, with a corresponding rise in the proportion of women delivering in their 30s and 40s[88].

Many studies have reported an association between advanced maternal age and adverse maternal and infant outcomes[89-91]. However, the majority of studies have reported outcomes in women aged ≥35 years or women aged ≥40 years. These studies therefore include only a small number of the oldest mothers and have not specifically addressed the risks associated with very advanced maternal age. Carolan[92] recently reviewed the literature published between 2001 and 2011 on maternal and perinatal outcomes in high-income countries in relation to very advanced maternal age (≥45 years). Only ten studies were identified: most were conducted over a long time-period; very few made any attempt to control for potential confounding factors; the control groups used for comparison varied widely; and none of the studies were conducted in the UK.

Case definition

All pregnant women in the UK of 20 weeks gestation or more, who are aged 48 years or older at their estimated date of delivery.

Main Research questions

- What are the characteristics of women giving birth at very advanced maternal age in the UK?
- What proportion of pregnancies in these women follow assisted reproductive technologies?
- How are these women managed?
- What are the risks of adverse outcomes for mother and infant associated with very advanced maternal age?

Investigators

Kate Fitzpatrick, Marian Knight, Jenny Kurinczuk, NPEU;

Derek Tuffnell, Bradford Teaching Hospitals NHS Foundation Trust.

Funding

This study has been funded by the National Institute for Health Research as part of the UK National Maternal Near-miss Surveillance Programme (UKNeS).*

4.4.2 Pulmonary Aspiration in Pregnancy

Key points

All women in the UK at 20 weeks gestation or greater identified as having a clinical diagnosis of pulmonary aspiration during their pregnancy.

A clinical diagnosis of pulmonary aspiration would normally be based on one or more of the following:

- Directly witnessed aspiration event.
- The presence of foreign material in the tracheobronchial tree confirmed by direct visualisation (either laryngoscopically or bronchoscopically).
- Chest radiograph showing new changes consistent with aspiration (infiltration, consolidation or radio-opaque foreign body).
- Signs and symptoms consistent with aspiration (dyspnoea, tachypnoea, pleuritic chest pain, hypoxia, crepitations or wheeze) in the absence of any other clear cause.

Background

Pulmonary aspiration is defined as the inhalation of foreign material below the level of the vocal cords and into the lower respiratory tract[93,94]. A recent national audit conducted by the Royal College of Anaesthetists (NAP4) identified aspiration as the commonest cause of death in association with complications of airway management[95]. The factors increasing the risk of aspiration associated with pregnancy include the gravid uterus, progesterone-mediated lower oesophageal sphincter relaxation, lower gastric pH and delayed gastric emptying during labour[96]. It has therefore been common practice for maternity units to restrict fluid and oral intake during active labour to reduce the risk of aspiration should the need for an unplanned general anaesthetic occur[97,98]. However, recent National Institute for Health and Clinical Excellence (NICE) guidelines have changed and now recommend that 'women may eat a light diet in established labour unless they have received opioids or they develop risk factors that make general anaesthetic more likely'[99]. It is not clear whether the change to policy on oral intake will impact on the frequency of maternal aspiration. In addition to a potential increased risk in association with changes in oral intake policy, other known risk factors for aspiration, for example obesity, are becoming more common in the pregnant population. There are thus concerns that maternal aspiration, and the consequent risks of severe maternal morbidity and mortality may become an increasing problem in the UK obstetric population. Balanced against this is the increasing use of airway devices, for example second generation supraglottic airway devices, which may protect more effectively against aspiration in the emergency situation than classic devices[95].

Case definition

Any woman with a final diagnosis of pulmonary aspiration during pregnancy or delivery up to postpartum discharge from hospital.

Maternal pulmonary aspiration includes women with the following features

- Women who have had an unprotected airway while unconscious, semi-conscious or paralysed

AND

- A clinical history consistent with regurgitation of stomach contents and pulmonary aspiration (e.g vomiting after induction of anaesthesia or gastric contents seen in the oropharynx)

AND

- Symptoms / signs of respiratory compromise requiring supplementary oxygen and antibiotics or level 2 or level 3 (HDU or ITU) respiratory support, in the absence of any other clear cause
- Classical radiological findings may or may not be present

Main research questions

- What is the incidence of maternal pulmonary aspiration in pregnancy in the UK?
- What are the characteristics of pregnant women with pulmonary aspiration?
- How is maternal pulmonary aspiration in pregnancy managed in the UK?
- What are the maternal, fetal and neonatal outcomes following maternal pulmonary aspiration in pregnancy?
- What are the prognostic indicators associated with maternal pulmonary aspiration in pregnancy?

Investigators

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4.4.3 Severe Primary Immune Thrombocytopenia (ITP) in Pregnancy

Key points

- Primary Immune Thrombocytopenia (ITP) is an acquired immunological disorder characterised by an isolated low platelet count.
- This condition can be acquired during women's reproductive years and is known to develop in pregnancy, but there are no accurate estimates of UK incidence.
- Additionally, there are no high quality prospective studies or randomised clinical trials to inform management of the mother or the delivery.
- This study seeks to estimate the current incidence and describe management and outcomes of severe ITP in pregnancy in the UK.

Background

Primary Immune Thrombocytopenia (ITP) is an acquired immunological disorder characterized by an isolated low platelet count (thrombocytopenia) necessary for normal clotting function. It is defined as a blood peripheral platelet count of <100 x 10^9/l and the absence of any initiating or underlying cause such as antiphospholipid antibody syndrome, SLE or viral infections[100]. This condition can be acquired during women's reproductive years and is known to develop in pregnancy. The current incidence of ITP in pregnancy is not yet estimated accurately. Discrepancies in definition and clinical criteria have led to a wide range of estimates reported to be between 0.1 and 1 case per 1000 pregnancies[101,102]. ITP accounts for 3% of cases of thrombocytopenia in pregnancy[102].

Current treatment recommendations for ITP in pregnancy are largely based on clinical experience and expert consensus[100]. There are no high quality prospective studies or randomized clinical trials to inform management of the mother or the delivery. First line treatments include corticosteroids and/or immunoglobulin. Second line treatments include combination therapy of high dose methylprednisolone and IVIg, and rarely splenectomy (advised in the second trimester)[100]. Without clear guidance or a strong evidence base for treatment of this rare condition it is unknown how this patient cohort is currently managed in the UK. This study seeks to estimate the current incidence and describe management and outcomes of severe ITP in pregnancy in the UK.

Case definition

Any pregnant woman who has been diagnosed with thrombocytopenia with a platelet count of <50 x 10^9/l at any point in her pregnancy prior to delivery where obstetric and hereditary causes for thrombocytopenia have been excluded (ie. pre-eclampsia, HELLP syndrome, acute fatty liver of pregnancy, known antiphospholipid antibody syndrome or other hereditary thrombocytopenias)

OR

Any pregnant woman diagnosed with an isolated thrombocytopenia where a clinical decision to treat the thrombocytopenia prior to delivery of the infant has been made.

Women with secondary immune thrombocytopenia are **excluded**.

Main Research questions

- What is the current incidence of severe primary ITP in pregnancy in the UK?
- What indications or factors determine a clinician's decision to commence active treatment of severe primary ITP in pregnancy in the UK?
- How is severe primary ITP managed in pregnancy in the UK?
- What is the current incidence of maternal morbidity and mortality in this cohort of patients?
- What is the current incidence of neonatal morbidity and mortality in this cohort of patients?

Investigators

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Funding

The ITP Support Association

itp
Immune
Thrombocytopenic
Purpura

5. Publications

5.1. Antenatal management and outcomes of gastroschisis in the UK

Published Article

Overton TG, Pierce MR, Gao H, Kurinczuk JJ, Spark P, Draper ES, Marven S, Brocklehurst P, Knight M. Antenatal management and outcomes of gastroschisis in the U.K. Prenat Diagn. 2012;32(13):1256-62.

Key points

- The birth prevalence of gastroschisis is increasing worldwide, yet little evidence exists concerning the optimal monitoring strategies after diagnosis.
- The aim of this study was to describe the UK prevalence, antenatal management and outcomes of affected pregnancies.
- The overall estimated birth prevalence of gastroschisis was 4.2 cases per 10,000 total births (95% CI 3.6-4.8).
- Estimates based on these data suggest that four per 100 fetuses surviving to the third trimester are stillborn (95% CI 2–6), four per 100 affected infants born alive die in the neonatal period (95% CI 1–10) and fewer than 1% of surviving infants die in the postnatal period (0.7 per 100 infants, 95% CI 0–2).
- Infants were variably monitored with growth scans (90%), umbilical artery Doppler ultrasound (85%), cardiotocography (65%) and biophysical profile (27%). Bowel measurements were undertaken for only 113 infants (52%).
- Eighty-nine women (43%) were induced and 63 (31%) laboured spontaneously.
- There were no statistically significant differences in growth measurements or gestation at delivery between babies who were stillborn or liveborn or those who died and those who survived, but note that this analysis has limited power to detect any differences as statistically significant due to the low number of deaths.
- The variability in management and paucity of evidence on antenatal monitoring approaches suggests there may be a place for randomised trials of fetal surveillance strategies in order to develop the evidence to improve outcomes for the at-risk fetus with gastroschisis.

5.2. Failed tracheal intubation in obstetric anaesthesia

Published Articles

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

Key points

- The incidence of failed intubation for general anaesthesia among the pregnant population is estimated to be up to eight times that of the non-pregnant population, however, there are no national data in the UK.
- Concerns about the risk of the condition when emergency obstetric anaesthesia is required may be associated with a move to planned elective surgery.
- The aims of this study were to estimate the national incidence of failed intubation in obstetric general anaesthesia, to quantify the associated risk factors, and to describe how failed intubation is currently managed in the UK.
- The overall incidence was one in 224 general anaesthetics (95% confidence interval (CI) 1 in 179 to 1 in 281).
- Failed intubation was associated with obesity, with a 6% increase in the odds of failed intubation with every 1kg/m^2 increase in BMI (adjusted odds ratio (aOR) 1.06, 95% CI 1.00-1.13).

- Maternal age (aOR 1.07, 95% CI 1.01-1.14 for every one year increase) and making an assessment of the airway (aOR 3.06, 95% CI 1.18-7.88 if a Mallampati score was recorded) were also significantly associated.
- Management was very variable; the most common rescue procedure was the use of a classical laryngeal mask airway (68% of cases).
- There were four cases of gastric aspiration amongst the 57 women with failed intubation (8%), but there were no significant differences in rates of either maternal or neonatal intensive care unit admission amongst cases and controls. No women died.
- The study suggests that the risk of failed intubation is low, but continuing monitoring is important in view of the increasing prevalence of obesity and older maternal age amongst the obstetric population.

5.3. Incidence and risk factors for placenta accreta/increta/percreta in the UK

Published Article

Fitzpatrick KE, Sellers S, Spark P, Kurinczuk JJ, Brocklehurst P, Knight M. Incidence and Risk Factors for Placenta Accreta/Increta/Percreta in the UK: A National Case-Control Study. PLoS One. 2012;7(12):e52893.

Key points

- The presence of placenta accreta/increta/percreta is associated with major pregnancy complications, and is thought to be becoming more common, due to a number of factors including rising maternal age at delivery and an increasing proportion of deliveries by caesarean.
- The aims of this study were to estimate the incidence of placenta accreta/increta/percreta in the UK and to investigate and quantify the associated risk factors.
- 134 women were diagnosed with placenta accreta/increta/percreta between May 2010 and April 2011 and 256 control women; an estimated incidence of 1.7 per 10,000 maternities.
- Women who had a previous caesarean delivery (aOR 14.41, 95% CI 5.63–36.85), other previous uterine surgery (aOR 3.40, 95% CI 1.30–8.91), an IVF pregnancy (aOR 32.13, 95% CI 2.03–509.23) and placenta praevia diagnosed antepartum (aOR 65.02, 95% CI 16.58–254.96) had raised odds of having placenta accreta/increta/percreta.
- There were also raised odds of placenta accreta/increta/percreta associated with older maternal age in women without a previous caesarean delivery (aOR 1.30, 95% CI 1.13–1.50 for every one year increase in age).
- The estimated incidence is 577 per 10,000 (1 in 17) in women with both a previous caesarean delivery and placenta praevia; there is a need to maintain a high index of suspicion of abnormal placental invasion in such women and preparations for delivery should be made accordingly.

5.4. Incidence, risk factors, management and outcomes of stroke in pregnancy

Published Article

Scott CA, Bewley S, Rudd A, Spark P, Kurinczuk JJ, Brocklehurst P, Knight M. Incidence, risk factors, management, and outcomes of stroke in pregnancy. Obstet Gynecol. 2012; 120(2 Pt 1):318-24.

Key points

- Stroke is an important cause of morbidity and mortality, the incidence of which is likely to increase due to an ageing population. However, estimates of the incidence of stroke associated with pregnancy vary widely.

- This study was designed to estimate the incidence of antenatal stroke in the UK and to identify risk factors associated with stroke during pregnancy. Information about the clinical features, current management, survival and prognosis of antenatal strokes was also obtained in order to develop guidance and improve the care of women having an antenatal stroke.
- Thirty cases of antenatal stroke were reported giving an estimated incidence of 1.5 cases per 100,000 maternities (95% CI 1.0-2.1). The incidences of non-haemorrhagic and haemorrhagic stroke were 0.9 (95% CI 0.5-1.3) and 0.6 (95% CI 0.3-1.0) per 100,000 maternities respectively.
- Factors associated with increased risk of antenatal stroke were history of migraine (OR 8.5, 95% CI 1.5-62.1), gestational diabetes (OR 26.8, 95% CI 3.2-∞), and pre-eclampsia or eclampsia (OR 7.7, 95% CI 1.3-55.7).
- There was wide variation in the use of pharmacological and surgical management, and organised stroke unit care.
- There were six stroke-related maternal deaths giving a case fatality rate of 20% of all strokes, and 50% of haemorrhagic strokes, and a mortality rate of 0.3 (95% CI 0.1–0.6) per 100,000 maternities.
- This study suggests that the risk of a stroke during pregnancy is low, however the poor outcomes in terms of morbidity and mortality and variations in care highlight the importance of such women receiving specialist stroke care.
- Clinicians should be aware of the increased risk in women with a history of migraine, gestational diabetes and pre-eclampsia or eclampsia.

5.5. Multiple repeat caesarean section

Published Article

Cook J, Jarvis S, Knight M, Dhanjal M. Multiple repeat caesarean section in the UK: incidence and consequences to mother and child. A national, prospective, cohort study. BJOG. 2013; 120(1):85-91.

Key points

- The incidence of caesarean delivery is increasing, but it is not known to what extent this results in multiple repeat caesarean procedures in the UK, nor the outcomes of pregnancy in this group.
- The aim of this study was to estimate the incidence of multiple repeat caesarean section (MRCS) (five or more) in the UK, and to describe the outcomes for women and their babies relative to women having fewer repeat caesarean sections.
- Ninety-four women undergoing MRCS were identified over one year, giving an estimated UK incidence of 1.2 per 10,000 maternities (95% CI, 0.97-1.47).
- Women with MRCS had significantly more major obstetric haemorrhages (>1500 ml) (aOR, 18.6; 95% CI 3.89-88.8), visceral damage (aOR, 17.6; 95% CI 1.85-167.1) and critical care admissions (aOR, 15.5; 95% CI 3.16-76.0), than women with lower order repeat caesarean sections.
- Women with MRCS who also had placenta praevia or accreta were at highest risk of complications.
- Neonates of mothers having MRCS were significantly more likely to be born prior to 37 weeks of gestation (OR, 6.15; 95% CI 2.56-15.78) and therefore had higher rates of complications and admissions.
- This study shows that MRCS is associated with greater maternal and neonatal morbidity than fewer caesarean sections. Importantly, the associated maternal morbidity is largely secondary to placenta praevia and accreta; in women undergoing MRCS who do not have these conditions, risks are lower.

5.6. Pregnancy in renal transplant recipients

Published Article

Bramham K, Nelson-Piercy C, Gao H, Pierce M, Bush N, Spark P, Brocklehurst P, Kurinczuk JJ, Knight M. Pregnancy in Renal Transplant Recipients: A UK National Cohort Study. Clin J Am Soc Nephrol. 2013 Feb;8(2):290-8.

Key points

- Most studies reporting pregnancy outcomes in women with kidney transplants are either single-centre studies, small, or report historical cohorts identified over long periods.
- The aim of this study was to collect information about pregnancy outcomes among a current cohort of all kidney transplant recipients in the UK.
- There were 105 pregnancies identified in 101 recipients between January 1, 2007 and December 31, 2009.
- Pre-eclampsia developed in 24% compared with 4% of a comparison cohort.
- 52% of women with kidney transplants delivered preterm, significantly higher than the national rate of 8%.
- Twenty-four infants (24%) were small for gestational age (<10th centile).
- Potential predictive factors for poor pregnancy outcome included >1 previous kidney transplant (P=0.03), first trimester serum creatinine >125 mmol/L (P=0.001), and diastolic BP >90 mmHg in the second (P=0.002) and third trimesters (P=0.05).
- This study shows that most pregnancies in the UK in women with kidney transplants are successful but rates of maternal and neonatal complications remain high.

5.7. Abstracts

The following abstract was presented at meetings in 2012 and are available on our website www.npeu.ox.ac.uk/ukoss:

Placenta accreta/increta/percreta: Incidence, risk factors, management and outcomes. Presented at British Maternal and Fetal Medicine 2012 conference, April 2012.

5.8. UKOSS Publications to date

Knight, M., J. J. Kurinczuk, et al. (2005). “The UK Obstetric Surveillance System for rare disorders of pregnancy.” BJOG 112(3): 263-265.

Knight, M., J. Kurinczuk, et al. (2005). “UK Obstetric Surveillance System uncovered.” RCM Midwives 8(1): 38-39.

Knight, M. on behalf of UKOSS (2007). “Eclampsia in the United Kingdom 2005.” BJOG 114(9): 1072-1078.

Knight, M. on behalf of UKOSS (2007). “Peripartum hysterectomy in the UK: management and outcomes of the associated haemorrhage.” BJOG 114(11): 1380-1387.

Knight, M., J. J. Kurinczuk, et al. (2008). “Cesarean delivery and peripartum hysterectomy.” Obstet Gynecol 111(1): 97-105.

Knight, M., C. Nelson-Piercy, et al. (2008). “A prospective national study of acute fatty liver of pregnancy in the UK.” Gut 57(7): 951-956.

Knight, M. (2008). “Antenatal pulmonary embolism: risk factors, management and outcomes.” BJOG 115(4): 453-461.

Knight, M., J. J. Kurinczuk, et al. (2009). “Tuberculosis in pregnancy in the UK.” BJOG 116(4): 584-588.

Knight, M., J. J. Kurinczuk, et al. (2009). “Inequalities in maternal health: national cohort study of ethnic variation in severe maternal morbidities.” BMJ 338: b542.

Knight, M., W. Callaghan, et al. (2009). “Trends in post-partum haemorrhage in high resource countries.” BMC Pregnancy and Childbirth 9: 55.

Knight, M., D. Tuffnell, et al. (2010). “Incidence and risk factors for amniotic-fluid embolism.” Obstet Gynecol 115(5): 910-917.

Knight, M., J. J. Kurinczuk, et al. (2010). “Extreme obesity in pregnancy in the United Kingdom.” Obstet Gynecol 115(5): 989-997.

Homer, C. S., J. J. Kurinczuk, et al. (2010). “A novel use of a classification system to audit severe maternal morbidity.” Midwifery 26(5): 532-536.

Yates, L. M., M. Pierce, et al. (2010). “Influenza A/H1N1v in pregnancy: An investigation of the characteristics of affected women and the relationship to pregnancy outcomes for mother and infant.” Health Technol Assess 14(34): 109-182.

Kayem, G., J. J. Kurinczuk, et al. (2011). “Uterine compression sutures for the management of severe postpartum hemorrhage.” Obstet Gynecol 117(1): 14-20.

Knight, M., M. Pierce, et al. (2011). “Critical illness with AH1N1v influenza in pregnancy: a comparison of two population-based cohorts.” BJOG 118(2): 232-239.

Homer, C. S., J. J. Kurinczuk, et al. (2011). “Planned vaginal delivery or planned caesarean delivery in women with extreme obesity.” BJOG 118(4): 480-487.

Knight, M., M. Pierce, et al. (2011). “The incidence and outcomes of fetomaternal alloimmune thrombocytopenia: a UK national study using three data sources.” Brit J Haematol 152(4): 460-468.

Lewis, G. E., R. Cantwell, et al. (2011). “Saving Mothers’ Lives: Reviewing maternal deaths to make motherhood safer: 2006-2008. The Eighth Report of the Confidential Enquiries into Maternal Deaths in the United Kingdom.” BJOG 118 Suppl 1: 1-203.

Kayem G, Kurinczuk JJ, et al. (2011) “Specific second-line therapies for postpartum haemorrhage: a national cohort study.” BJOG.118 (7):856-64.

Kayem G, Kurinczuk JJ, et al. (2011), “Maternal and obstetric factors associated with delayed postpartum eclampsia: a national study population.” Acta Obstet Gynecol Scand. 2011 Sep;90(9):1017-23.

M Pierce, JJ Kurinczuk, et al. (2011) “Perinatal outcomes after maternal 2009/H1N1 infection: national cohort study.” BMJ 2011;342:d3214

Kayem G, Kurinczuk J, et al. (2011) “Risk factors for progression from severe maternal morbidity to death: a national cohort study.” PLoS One. 2011;6(12):e29077.

Fitzpatrick KE, Kurinczuk JJ, et al. (2012) “Uterine Rupture by Intended Mode of Delivery in the UK: A National Case-Control Study.” PLoS Med 9(3): e1001184.

Knight, M, et al, (2012) “Amniotic fluid embolism incidence, risk factors and outcomes: a review and recommendations.” BMC Pregnancy and Childbirth, 2012. 12(1): 7.

Scott CA, Bewley S, et al. (2012) “Incidence, risk factors, management, and outcomes of stroke in pregnancy.” Obstet Gynecol. 2012; 120(2 Pt 1):318-24.

Fitzpatrick KE, Sellers S, et al. (2012) “Incidence and risk factors for placenta accreta/increta/percreta in the UK: a national case-control study.” PLoS One. 2012;7(12):e52893.

Overton TG, Pierce MR, et al. (2012) “Antenatal management and outcomes of gastroschisis in the U.K.” Prenat Diagn. 2012;32(13):1256-62.

Cook J, Jarvis S, Knight M, Dhanjal M. (2013) “Multiple repeat caesarean section in the UK: incidence and consequences to mother and child. A national, prospective, cohort study.” BJOG. 2013; 120(1):85-91.

Quinn AC, Milne D, et al. (2013) “Failed tracheal intubation in obstetric anaesthesia: 2 yr national case–control study in the UK.” Br J Anaesth. 2013;110(1):74-80.

Bush N, Nelson-Piercy C, et al. (2013) “Myocardial infarction in pregnancy and postpartum in the UK.” Eur J Prev Cardiol. 2013 Feb; 20(1):12-20.

Bramham K, Nelson-Piercy C, et al. (2013) “Pregnancy in Renal Transplant Recipients: A UK National Cohort Study.” Clin J Am Soc Nephrol. 2013 Feb;8(2):290-8.

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References

1. Knight, M., Peripartum hysterectomy in the UK: management and outcomes of the associated haemorrhage. BJOG, 2007. 114(11): p. 1380-7.
2. Knight, M., Eclampsia in the United Kingdom 2005. BJOG, 2007. 114(9): p. 1072-8.
3. Knight, M., Antenatal pulmonary embolism: risk factors, management and outcomes. BJOG, 2008. 115(4): p. 453-61.
4. Knight, M., et al., Tuberculosis in pregnancy in the UK. BJOG, 2009. 116(4): p. 584-8.
5. Eds. Knight, M., et al., Cesarean delivery and peripartum hysterectomy. Obstet Gynecol, 2008. 111(1): p. 97-105.
6. Knight, M., et al., A prospective national study of acute fatty liver of pregnancy in the UK. Gut, 2008. 57(7): p. 951-6.
7. Knight M. and A. Lindquist, The UK Obstetric Surveillance System: Impact on patient safety. Best Practice and Research Clinical Obstetrics & Gynaecology, 2013 Mar 30. pii: S1521-6934(13)00033-3. doi: 10.1016/j.bpobgyn.2013.03.002. [Epub ahead of print]
8. UKOSS. [Accessed April 2013]; Available from: *http://www.npeu.ox.ac.uk/ukoss/survey-applications*.
9. Confidentiality and Security Advisory Group for Scotland, 2001, The Scottish Executive: Edinburgh.
10. Department of Health. Guidance Notes: Section 60 of the Health and Social Care Act 2001. [Accessed April 2013]; Available from: *http://webarchive.nationalarchives.gov.uk/+/www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4108953*.
11. Knight, M., et al., Extreme obesity in pregnancy in the United Kingdon. Obstet Gynecol, 2010. 115(5) p. 989-97.
12. Nelson-Piercy, C., Thrombosis and Embolism during Pregnancy and the Puerperium, Reducing the Risk (RCOG Green-top guideline no. 37a). [Accessed June 2013]; Available from: *http://www.rcog.org.uk/womens-health/clinical-guidance/reducing-risk-of-thrombosis-greentop37a*.
13. Yates, L.M., et al., Influenza A/H1N1v in pregnancy: An investigation of the characteristics of affected women and the relationship to pregnancy outcomes for mother and infant. Health Technol Assess, 2010. 14(34): p. 109-82.
14. Pierce, M., et al., Perinatal outcomes after maternal 2009/H1N1 infection: national cohort study. BMJ, 2011. 342: p. d3214.
15. Lewis, G.E., ed. The Confidential Enquiry into Maternal and Child Health (CEMACH). Saving Mothers Lives: reviewing maternal deaths to make childhood safer - 2003-2005. ed. L.G. (Ed)2007, CEMACH: London.
16. Nicoll, A., Poor pregnancy outcomes associated with maternal infection with the A(H1N1) 2009 virus during the pandemic - findings from a European cohort study. European Center for Disease Prevention and Control (ECDC) [Review] 18 Jul 2011; Available from: *http://www.ecdc.europa.eu/en/activities/sciadvice/Lists/ECDC%20Reviews/ECDC_DispForm.aspx?List=512ff74f-77d4-4ad8-b6d6-bf0f23083f30&ID=1157&MasterPage=1*.
17. Usha Kiran, T.S., et al., Outcome of pregnancy in a woman with an increased body mass index. BJOG, 2005. 112(6): p. 768-72.
18. Weiss, H.G., et al., Pregnancies after adjustable gastric banding. Obesity Surgery, 2001. 11(3): p. 303-306.
19. Sheiner, E., et al., Pregnancy outcome in patients following different types of bariatric surgeries. Obesity Surgery, 2009. 19(9): p. 1286-1292.
20. Dixon, J.B., M.E. Dixon, and P.E. O'Brien, Birth outcomes in obese women after laparoscopic adjustable gastric banding. Obstetrics & Gynecology, 2005. 106(5 Pt 1): p. 965-972.
21. Ducarme, G., et al., Obstetric outcome following laparoscopic adjustable gastric banding. International Journal of Gynaecology and Obstetrics, 2007. 98(3): p. 244-247.
22. Skull, A.J., et al., Laparoscopic adjustable banding in pregnancy: safety, patient tolerance and effect on obesity-related pregnancy outcomes. Obesity Surgery, 2004. 14(2): p. 230-235.
23. Dixon, J.B., M.E. Dixon, and P.E. O'Brien, Pregnancy after Lap-Band surgery: management of the band to acheive healthy weight outcomes. Obesity Surgery, 2001. 11(1): p. 59-65.
24. Weinstein, L., Syndrome of hemolysis, elevated liver enzymes, and low platelet count: a severe consequence of hypertension in pregnancy. American Journal of Obstetrics & Gynecology, 1982. 142(2): p. 159-67.

25. Waterstone, M., S. Bewley, and C. Wolfe, Incidence and predictors of severe obstetric morbidity: case-control study. BMJ, 2001. 322(7294): p. 1089-93; discussion 1093-4.
26. Martin, J.N.Jr., et al., The spectrum of severe preeclampsia: comparative analysis by HELLP (hemolysis, elevated liver enzyme levels, and low platelet count) syndrome classification. American Journal of Obstetrics & Gynecology, 1999. 180(6 Pt 1): p. 1373-84.
27. Gasem, T., et al., Maternal and fetal outcome of pregnancy complicated by HELLP syndrome. Journal of Maternal-Fetal & Neonatal Medicine, 2009. 22(12): p. 1140-3.
28. Sibai, B.M., et al., Maternal-perinatal outcome associated with the syndrome of hemolysis, elevated liver enzymes, and low platelets in severe preeclampsia-eclampsia. American Journal of Obstetrics & Gynecology, 1986. 155(3): p. 501-9.
29. Sibai, B.M., The HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets): much ado about nothing? American Journal of Obstetrics & Gynecology, 1990. 162(2): p. 311-6.
30. Audibert, F., et al., Clinical utility of strict diagnostic criteria for the HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome. American Journal of Obstetrics & Gynecology, 1996. 175(2): p. 460-4.
31. Sibai, B.M., Diagnosis, controversies, and management of the syndrome of hemolysis, elevated liver enzymes, and low platelet count. Obstetrics & Gynecology, 2004. 103(5 Pt 1): p. 981-91.
32. Barbui, T. and G. Finazzi, Myeloproliferative disease in pregnancy and other management issues. Hematology Am Soc Hematol Educ Program, 2006: p. 246-52.
33. McKay, D.B. and M.A. Josephson, Pregnancy in recipients of solid organs--effects on mother and child. N Engl J Med, 2006. 354(12): p. 1281-93.
34. Sibanda, N., et al., Pregnancy after organ transplantation: a report from the UK Transplant pregnancy registry. Transplantation, 2007. 83(10): p. 1301-7.
35. Armenti, V.T., et al., Report from the national transplantation pregnancy registry (NTPR): outcomes of pregnancy after transplantation. Clin Transpl, 2004: p. 103-14.
36. Rizzoni, G., et al., Successful pregnancies in women on renal replacement therapy: report from the EDTA Registry. Nephrol Dial Transplant, 1992. 7(4): p. 279-87.
37. Weiss, B.M., et al., Outcome of pulmonary vascular disease in pregnancy: a systematic overview from 1978 through 1996. J Am Coll Cardiol, 1998. 31(7): p. 1650-7.
38. Nelson-Piercy, C., Cardiac Disease: in Saving Mothers' Lives: Reviewing maternal deaths to make motherhood safer: 2006-2008. The Eighth Report of the Confidential Enquiries into Maternal Deaths in the United Kingdom, R. Cantwell, et al., Editors. 2011, BJOG. p. 109-15.
39. Lewis, G., ed. Why mothers die 2000-2002, Confidential Enquiry into Maternal and Child Health 2004, Royal College of Obstetricians and Gynaecologists: London.
40. Dob, D.P. and S.M. Yentis, UK registry of high-risk obstetric anaesthesia: report on cardiorespiratory disease. Int J Obstet Anesth, 2001. 10(4): p. 267-72.
41. Thorne, S., et al., Pregnancy and contraception in heart disease and pulmonary arterial hypertension. J Fam Plann Reprod Health Care, 2006. 32(2): p. 75-81.
42. Yentis, S.M., P.J. Steer, and F. Plaat, Eisenmenger's syndrome in pregnancy: maternal and fetal mortality in the 1990s. Br J Obstet Gynaecol, 1998. 105(8): p. 921-2.
43. Lewis, G.E., et al., Saving Mothers' Lives: Reviewing maternal deaths to make motherhood safer: 2006-2008. The Eighth Report of the Confidential Enquiries into Maternal Deaths in the United Kingdom. BJOG : an international journal of obstetrics and gynaecology, 2011. 118 Suppl 1: p. 1-203.
44. Benhamou, D., et al., [The seventh report of the confidential enquiries into maternal deaths in the United Kingdom: comparison with French data]. Ann Fr Anesth Reanim, 2009. 28(1): p. 38-43.
45. Zwart, J.J., et al., Obstetric intensive care unit admission: a 2-year nationwide population-based cohort study. Intensive Care Med, 2010. 36(2): p. 256-63.
46. Padkin, A., et al., Epidemiology of severe sepsis occurring in the first 24 hrs in intensive care units in England, Wales, and Northern Ireland. Crit Care Med, 2003. 31(9): p. 2332-8.
47. Kramer, H.M., et al., Maternal mortality and severe morbidity from sepsis in the Netherlands. Acta Obstet Gynecol Scand, 2009. 88(6): p. 647-53.
48. Maharaj, D., Puerperal pyrexia: a review. Part I. Obstet Gynecol Surv, 2007. 62(6): p. 393-9.
49. Yokoe, D.S., et al., Epidemiology of and surveillance for postpartum infections. Emerg Infect Dis, 2001. 7(5): p. 837-41.

50. van Dillen, J., et al., Maternal sepsis: epidemiology, etiology and outcome. Curr Opin Infect Dis, 2010. 23(3): p. 249-54.
51. Robar, C., et al., Current diagnosis and management of aldosterone-producing adenomas during pregnancy. The Endocrinologist, 1998. 8: p. 403-408.
52. Grodski, S., et al., Phaeochromocytoma in pregnancy. Intern Med J, 2006. 36(9): p. 604-6.
53. Lindsay, J.R. and L.K. Nieman, Adrenal disorders in pregnancy. Endocrinol Metab Clin North Am, 2006. 35(1): p. 1-20, v.
54. Lindsay, J.R., et al., Cushing's syndrome during pregnancy: personal experience and review of the literature. J Clin Endocrinol Metab, 2005. 90(5): p. 3077-83.
55. Ahlawat, S.K., et al., Pheochromocytoma associated with pregnancy: case report and review of the literature. Obstet Gynecol Surv, 1999. 54(11): p. 728-37.
56. Schenker, J.G. and I. Chowers, Pheochromocytoma and pregnancy. Review of 89 cases. Obstet Gynecol Surv, 1971. 26(11): p. 739-47.
57. Bakri, Y.N., et al., Pheochromocytoma and pregnancy: report of three cases. Acta Obstet Gynecol Scand, 1992. 71(4): p. 301-4.
58. Matsumoto, J., et al., Primary aldosteronism in pregnancy. J Nippon Med Sch, 2000. 67(4): p. 275-9.
59. Gilbert, W.M. and B. Danielsen, Amniotic fluid embolism: decreased mortality in a population-based study. Obstet Gynecol, 1999. 93(6): p. 973-7.
60. Tuffnell, D.J., Amniotic Fluid Embolism. Current Opinion in Obstetrics and Gynaecology, 2003. 15: p. 119-122.
61. Abenhaim, H.A., et al., Incidence and risk factors of amniotic fluid embolisms: a population-based study on 3 million births in the United States. Am J Obstet Gynecol, 2008. 199(49): p. e1-e8.
62. Kramer, M.S., et al., Amniotic-fluid embolism and medical induction of labour: a retrospective, population-based cohort study. Lancet, 2006. 368: p. 1444-1448.
63. Tuffnell, D.J., United kingdom amniotic fluid embolism register. BJOG, 2005. 112(12): p. 1625-9.
64. Knight, M., et al., Incidence and risk factors for amniotic-fluid embolism. Obstet Gynecol, 2010. 115(5): p. 910-7.
65. Knight, M., et al., Amniotic fluid embolism incidence, risk factors and outcomes: a review and recommendations. BMC Pregnancy Childbirth, 2012. 12(1): p. 7.
66. Soar, J., et al., Emergency treatment of anaphylactic reactions--guidelines for healthcare providers. Resuscitation, 2008. 77(2): p. 157-169.
67. Mulla, Z.D., M.S. Ebrahim, and J.L. Gonzalez, Anaphylaxis in the obstetric patient: analysis of a statewide hospital discharge database. Annals of Allergy, Asthma & Immunology, 2010. 104(1): p. 55-59.
68. Stannard, L. and A. Bellis, Maternal anaphylactic reaction to a general anaesthetic at emergency caesarean section for fetal bradycardia. BJOG: An International Journal of Obstetrics & Gynaecology, 2001. 108(5): p. 539-540.
69. Gallagher, J.S., Anaphylaxis in pregnancy. Obstetrics & Gynecology, 1988. 71(3, Part 2): p. 491.
70. Entman, S.S., and K.J. Moise, Anaphylaxis in pregnancy. Southern Medical Journal, 1984. 77(3): p. 402.
71. Sengupta, A. and J.K. Kohli, Antibiotic prophylaxis in cesarean section causing anaphylaxis and intrauterine fetal death. Journal of Obstetrics and Gynaecology Research, 2008. 34(2): p. 252-254.
72. Khan, R., E. Anastasakis, and R. Kadir, Anaphylactic reaction to ceftriaxone in labour. An emerging complication. Journal of obstetrics and gynaecology, 2008. 28(7): p. 751-753.
73. Harboe, T., et al., Cardiopulmonary distress during obstetrical anaesthesia: attempts to diagnose amniotic fluid embolism in a case series of suspected allergic anaphylaxis. Acta anaesthesiologica scandinavica, 2006. 50(3): p. 324-330.
74. Resuscitation Council (UK), Emergency treatment of anaphylactic reactions; guidelines for healthcare professionals, 2008.
75. Morris, S. and M. Stacey, Resuscitation in pregnancy. BMJ, 2003. 327(7426): p. 1277-9.
76. RCOG, Managing obstetric emergencies and trauma: MOET course manual. 2nd ed2007, London: RCOG.
77. Dijkman, A., et al., Cardiac arrest in pregnancy: increasing use of perimortem caesarean section due to emergency skills training? BJOG, 2010. 117(3): p. 282-7.

78. Lennox, C. Scottish Confidential Audit of Severe Maternal Morbidity (SCASMM) 7th Annual Report. 2011; Available from: *http://www.healthcareimprovementscotland.org/programmes/reproductive,_maternal__child/programme_resources/scasmm.aspx*.
79. Leslie, S.D. and P.T. Toy, Laboratory hemostatic abnormalities in massively transfused patients given red blood cells and crystalloid. American Journal of Clinical Pathology, 1991. 96(6): p. 770-773.
80. Hess, J.R., J.B. Holcomb, and D.B. Hoyt, Damage control resuscitation: the need for specific blood products to treat the coagulopathy of trauma. Transfusion, 2006. 46(5): p. 685-686.
81. Molitch, M.E., Pituitary tumors and pregnancy. Growth Horm IGF Res, 2003. 13 Suppl A: p. S38-44.
82. Sadler L., L. McCowan, H. White, A. Stewart, M. Bracken, R. North, Pregnancy outcomes and cardiac complications in women with mechanical, bioprosthetic and homograft valves. BJOG, 200. 107: p. 245-253.
83. Chan W.S., S Anand, J.S. Ginsberg, Anticoagulation of pregnant women with mechanical heart valves: A systematic review of the literature. Arch Intern Med, 2000. 160: p. 191.
84. Roberts N, D. Ross, S.K. Flint, R. Arya, M. Blott, Thromboembolism in pregnant women with mechanical prosthetic heart valves anticoagulated with low molecular weight heparin. BJOG, 2001. 108: p. 327-329.
85. Eds. Steer, P.J., M.A Gatzoulis and P. Baker, Consensus views arising from the 51st Study Group: Heart Disease and Pregnancy. RCOG Press, 2006.
86. Luders, C., et al., Obstetric outcome in pregnant women on long-term dialysis: a case series. Am J Kidney Dis, 2010. 56(1): p. 77-85.
87. Asamiya, Y., et al., The importance of low blood urea nitrogen levels in pregnant patients undergoing hemodialysis to optimize birth weight and gestational age. Kidney Int, 2009. 75(11): p. 1217-22.
88. Office for National Statistics, Live Births In England and Wales by Characteristics of Mother 1, 2010, 2011.
89. Balasch, J. and E. Gratacos, Delayed childbearing: effects on fertility and the outcome of pregnancy. Current Opinion in Obstetrics & Gynecology, 2012. 24(3): p. 187-93.
90. Montan, S., Increased risk in the elderly parturient. Current Opinion in Obstetrics & Gynecology, 2007. 19(2): p. 110-2.
91. Hansen, J.P., Older maternal age and pregnancy outcome: a review of the literature. Obstetrical & gynecological survey, 1986. 41(11): p. 726-42.
92. Carolan, M., Maternal age >/=45 years and maternal and perinatal outcomes: A review of the evidence. Midwifery, 2013. 29(5): 479-89.
93. Clayton, T. and R. Prout, Critical incidents: pulmonary aspiration. Anaesthesia and Intensive Care Medicine, 2004. 5(9): p. 297-298.
94. Lykens, M.G. and D.L. Bowton, Aspiration and acute lung injury. International Journal of Obstetric Anesthesia, 1993. 2: p. 236-240.
95. Cook, T., et al., 4th National Audit Project of the Royal College of Anaesthetists and the Difficult Airway Society: Major complications of airway management in the United Kingdom. The Royal College of Anaesthetists and The Difficult Airway Society, 2011.
96. Pinder, A., Complications of obstetric anaesthesia. Current Anaesthesia and Critical Care, 2006. 17: p. 151-162.
97. National Collaborating Centre for Women's and Children's Health: Caesarean section. NICE Clinical Guideline. London: RCOG Press, 2011. 2nd edition: p. 116.
98. Singata, M., J. Tranmer, and G.M.L. Gyte, Restricting oral fluid and food intake during labour. Cochrane Database of Systematic Reviews, 2010(1).
99. National Collaborating Centre for Women's and Children's Health: Intrapartum care: care of healthy women and their babies during childbirth. NICE Clinical Guideline. London: RCOG Press, 2007: p. 83-36.
100. Provan, D., et al., International consensus report on the investigation and management of primary immune thrombocytopaenia. Blood, 2010. 115(2): p. 168-186.
101. Segal, J.B. and N.R. Powe, Prevalence of immune thrombocytopenia: analyses of administrative data. J Thromb Haemost, 2006. 4: p. 2377-2383.
102. Sainio S, K.R., S. Riikonen, K. Teramo, Maternal thrombocytopenia at term: a population based study. Acta Obstet Gynecol Scand, 2000. 79: p. 744-749.

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