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.
This report should be cited as:

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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 and for service planning. Completed studies have demonstrated the efficacy of the system for generating this information\(^1\)\(^-\)\(^5\).

Studies using UKOSS may be undertaken by any investigator who identifies a suitable topic\(^7\). 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 suitably addressed using the UKOSS methodology (prospective descriptive, cohort or case-control studies). This report outlines the studies undertaken during the seventh 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 tick 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, including 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\(^8\)\(^,\)\(^9\). 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:

Estimating disease incidence; for example UKOSS surveillance of eclampsia demonstrated a 45% reduction in incidence between 1992 and 2005.

1. 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/m² or greater).

2. Quantifying risk factors for severe morbidity; for example UKOSS surveillance of uterine rupture haemorrhage showed a significant association with induction or augmentation of labour in women with a previous caesarean delivery.

3. 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.

4. 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.

5. 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.

6. Describing the outcomes of severe morbidity; for example UKOSS surveillance of 2009/H1N1 influenza showed a significant association with poor pregnancy outcomes.

7. 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 Deaths 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.

Figure 1: UKOSS Report Card

<table>
<thead>
<tr>
<th>Condition</th>
<th>Patient’s name</th>
<th>Patient’s Hospital number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenal Tumours</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic Fluid Embolism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac Arrest in Pregnancy Study (CAPS)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastric Banding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HELLP Syndrome</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Please specify the number of cases seen this month:
3. Participation

All 219 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 2011 was 94% (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 six 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 2011
Figure 3: Map showing regional card return rates during 2011

Scotland 99%
North East 97%
Yorkshire and Humber 94%
East Midlands 93%
East of England 88%
London 94%
South East and Channel Islands 90%
Northern Ireland 94%
North West 88%
West Midlands 96%
Wales 96%
South West 95%
4. Studies

Unless otherwise specified, the results included in this report represent analysis of cases reported and data available up to February 2012. All studies have been funded through a grant to the NPEU from the Department of Health 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 2011-2015
4.2. Studies completed in 2011

4.2.1 Aortic Dissection

**Key points**
- Aortic dissection in pregnancy is a significant cause of maternal morbidity and mortality.
- Changes in birth patterns, with a rise in older mothers and increased prevalence of obesity may contribute to an increased occurrence of aortic dissection in the UK.
- There have been no prospective studies to estimate the incidence of this disease and its investigation and management during pregnancy.
- This study estimates that the national incidence of aortic dissection is 0.8 cases per 100,000 maternities in the UK. This national initiative has helped characterise the management of women with aortic dissection in the UK.

**Background**
Aortic dissection in pregnancy is a life-threatening event to both mother and baby and accounts for 14% of maternal cardiac deaths. Although rare, an association between pregnancy and aortic dissection has been reported and its incidence in pregnancy is thought to be rising. Approximately 50% of cases of aortic dissection in women under the age of 40 occur whilst they are pregnant\(^\text{15}\). Patients presenting with aortic dissection may do so with a wide array of symptoms and the condition may be missed or symptoms mistaken for other diseases in pregnancy\(^\text{16,17}\). There is often an over-cautious approach by clinicians to imaging studies required for the diagnosis of aortic dissection for fear of radiation effects on the baby and this may hinder prompt diagnosis\(^\text{16,17}\). Untimely delays in treatment of this disease can lead to potentially catastrophic consequences, since the mortality rate increases by 1% each hour if left untreated\(^\text{18}\).

This study aimed to estimate the national incidence of aortic dissection in pregnancy and describe the presentation, investigation, management and maternal-fetal outcomes of this disease in the UK.

**Case definition**
Cases are defined as any women in whom the diagnosis of:
1. Aortic dissection (also referred to as dissecting aortic aneurysm) was confirmed using suitable imaging (Echocardiography, Computed tomography, Magnetic Resonance Imaging) or
2. Aortic dissection confirmed at surgery or postmortem.

Cases should be recorded for women with new onset aortic dissection and those with pre-existing aortic dissection or previous aortic repair prior to pregnancy.

**Surveillance Period**
Sept 2009 – Sept 2011

**Results**
By the close of this study, there were 12 confirmed cases of aortic dissection in pregnancy. The estimated national incidence is 0.8 per 100,000 maternities (95% CI: 0.5-1.5 per 100,000). The mean age of women with the disease was 37 years. There were 7 cases of type A aortic dissection and 3 of type B aortic dissection using Stanford criteria. Only one case was reported in association with Marfan’s disease; one woman had preexisting aortic coarctation and a bicuspid aortic valve.

Seventy-five percent of the women presented with anterior chest pain and 58% with back pain. Of the confirmed cases with full data available, 66% received antihypertensives mainly as an intravenous preparation (7/8 cases). Only two women required more than three anti-hypertensives to control blood pressure. Three women were managed conservatively whilst 5 women received an aortic root replacement.

Overall there were 4 deaths and 8 survivors (case fatality 33%, 95% CI 10-65%).

**Interim Conclusions**
This study suggests that there are very few cases of aortic dissection in pregnancy in the UK and in this series two thirds of women survived this potentially devastating disease. The last triennial report of the UK Confidential Enquiry into maternal deaths reported seven deaths attributable to aortic dissection over the three year period. To ensure there has been no under ascertainment of cases in the UK, work is ongoing to check other sources for identification of cases. Extensive work to date, including through various professional societies and the Intensive Care National Audit and Research Centre database does not
indicate significant underascertainment of cases. We however would be grateful if clinicians could check with their colleagues in their department, in radiology and surgical departments to retrospectively report any cases that should previously have been reported to UKOSS since the study began in September 2009.

**Investigators**
Sheba Jarvis, Mandish Dhanjal, Richard Gibbs, Catherine Williamson
Imperial College Healthcare NHS Trust, Queen Charlotte’s and Chelsea Hospital

**Funding**
Heart Research UK.

### 4.2.2 Placenta Accreta

**Key points**
- Placenta accreta 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 section.
- There is a debate about the optimal diagnostic and management techniques.
- This study shows that placenta accreta/increta/percreta is still uncommon in the UK, but is associated with preterm delivery and significant maternal morbidity.
- Further analysis of these data, including quantification of risk factors for placenta accreta/increta/percreta, is currently underway.

**Background**
The presence of placenta accreta/increta/percreta is associated with major pregnancy complications, including life-threatening maternal haemorrhage, uterine rupture, peripartum hysterectomy and maternal death, as well as complications associated with surgical removal including damage to bladder, ureters and other organs. Placenta accreta 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 section. However, the risk associated with these factors has not been quantified on a population basis in the UK.

There is also a debate about the optimal diagnostic and management techniques for placenta accreta. This study aimed to describe the current management of placenta accreta in the UK and associated outcomes for women and their infants. In addition, this study planned to estimate the national incidence of placenta accreta in the UK and identify the extent to which previous caesarean section and older maternal age are risk factors in this population. This information will enable appropriate future service planning, provide accurate information which can be used when counselling women about the risks associated with caesarean section and will be used to develop management guidelines, and provide a baseline incidence against which future trends can be monitored.

**Case definition**
Any pregnant woman in the UK identified as having placenta accreta using the following definition:

- **EITHER** Placenta accreta / increta / percreta diagnosed histologically following hysterectomy or postmortem.
- **OR** An abnormally adherent placenta, requiring active management, including conservative approaches where the placenta is left in situ.
- **EXCLUDED** Women who have had a manual placental removal with minimal or moderate difficulty but required no additional active management.

**Surveillance Period**
May 2010 – April 2011
**Results**

187 cases were reported during the study period. Information was received for 160 of these cases (86%). There were a total of 134 confirmed cases representing an estimated incidence in the UK of 1.7 cases per 10,000 maternities (95% CI 1.4 to 2.0). There were no maternal deaths, but women with placenta accreta/increta/percreta had a median estimated total blood loss of 3050mls (range 200-24,000mls). 79% (104/131) had blood products given, 69% (92/134) were admitted to ITU/HDU and 59% (79/134) had a hysterectomy. Figure 1 shows the variety of other therapies that were used to treat active haemorrhage.

There were no stillbirths and two early neonatal deaths amongst the 134 infants born to mothers with placenta accreta/increta/percreta, equating to a perinatal mortality rate of 14.9 per 1000 (95% CI 1.8-52.8), not significantly different from the national rate of 7.5 per 1000. However, just over half of the women delivered prior to 37 weeks gestation (51%, 55/130).

**Figure 1. Therapies used to treat haemorrhage in women with placenta accreta/increta/percreta**

![Therapies Used to Treat Haemorrhage](image)

**Conclusions**

Overall placenta accreta/increta/percreta is still uncommon in the UK, but is associated with preterm delivery and significant maternal morbidity. Further analysis of these data, including quantification of risk factors for placenta accreta/increta/percreta, is currently underway.

**Investigators**

Marian Knight, Kate Fitzpatrick, Jenny Kurinczuk, Peter Brocklehurst, Maria Quigley, NPEU; Sue Sellers, United Bristol Hospitals NHS Trust; Mervi Jokinnen, RCM; Shona Golightly, Independent; Gwyneth Lewis, University College London; James Walker, RCOG; Alison Burton, 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).**
4.2.3 Severe Obstetric Cholestasis

Key points

- Obstetric cholestasis (OC) is associated with an increased risk of adverse fetal outcomes.
- The risk of adverse fetal outcomes is thought to be increased in women with severe cholestasis.
- There are no prospective national studies to estimate the incidence or outcomes of severe cholestasis in pregnancy.
- This study suggests severe OC is commoner than previously estimated and that there is a relationship between bile acid levels and adverse pregnancy outcomes.

Background

Obstetric cholestasis is a pregnancy specific liver disorder that affects about 1 in 200 women in the UK. It typically presents in the third trimester with maternal pruritus and deranged liver function, including raised serum bile acids. The maternal symptoms and biochemical abnormalities resolve rapidly after delivery and OC is therefore considered to be a cause of transient hepatic impairment for the mother. However, OC is associated with an increased incidence of adverse fetal outcomes, including spontaneous preterm labour, fetal distress and sudden intrauterine death\(^24\).

Several studies have demonstrated a correlation between the maternal serum bile acid level and the risk of adverse fetal events\(^25-28\). The most definitive of these studies investigated the incidence and outcomes of OC in a Swedish population of 45,000 women, including 690 with OC\(^25\). The data from this study demonstrate that the risk of meconium staining of the amniotic fluid, green staining of the placenta and fetal membranes, asphyxial events and preterm delivery is increased by 1-2% for every additional 1 µmol/L of maternal serum bile acids. However, this did not reach statistical significance for women with mild or moderate elevations in maternal fasting serum bile acid levels, but was significant for those with severe cholestasis defined as fasting serum bile acid levels greater than 40 µmol/L. Several small studies have reported the incidences of adverse fetal outcomes in the UK population\(^29,30\), but none have been able to demonstrate a correlation with maternal serum bile acid level.

Case definition

Any woman in the UK identified as having severe obstetric cholestasis using the following definition:

Pruritus in the absence of a rash and in association with a single maternal serum bile acid level greater than or equal to 40 µmol/L at any time point in the pregnancy

EXCLUDED: Women with obstetric cholestasis but with bile acid levels less than 40 µmol/L.

Surveillance Period

June 2010 - May 2011

Results

881 cases were reported during the study period and data were returned for 837 cases (95%). There were 16 duplicate cases reported and 143 cases did not meet the case criteria. There were 678 confirmed cases of severe obstetric cholestasis.

The results are currently being analysed. However, preliminary analysis using unadjusted logistic regression and generalised additive models suggests that there are relationships between maternal serum bile acid levels and meconium stained amniotic fluid, spontaneous preterm labour, Apgar score < 7 at five minutes post delivery and stillbirth. We are currently undertaking further analysis to determine the effect of maternal age, ethnicity, body mass index and gestational week at delivery on these outcomes.

Interim Conclusions

Severe OC, defined as affected pregnancies in which the serum bile acid level is >40µmol/L, is commoner than anticipated. There is a relationship between the level of serum bile acids and adverse pregnancy outcome in severe OC when defined in this way.

Investigators

Catherine Williamson, Victoria Geenes, Imperial College London
Marian Knight, NPEU

Funding

This study is funded by Wellbeing of Women.
4.2.4 Sickle Cell Disease in Pregnancy

Key points
• Sickle Cell Disease is the most common genetic disease in the UK and is associated with significant mortality and morbidity during pregnancy.
• There are no prospective national studies to estimate the incidence or outcomes of pregnancy in patients with Sickle Cell Disease.
• This study suggests that pregnancy in women with sickle cell disease is a time of high morbidity with more than half of women reporting painful crises and a quarter admitted to ICU after delivery.

Background
Sickle Cell Disease (SCD) is the most common genetic disorder worldwide and in the UK, with 12-15,000 affected individuals in the UK. SCD is a multi-organ disorder characterised by intermittent episodes of severe pain which may require hospital admission for treatment, and other complications including chest disease, pulmonary hypertension, stroke, retinopathy, renal failure, avascular necrosis and leg ulcers.

There are some historical data, most from outside the UK, showing a high incidence of maternal and fetal complications in SCD, but no contemporary or recent prospective data from the UK. The number of deliveries in women with SCD has increased markedly over recent years, from 25-30 deliveries across the whole UK in the 1970s, to the current situation of approximately 150-250 deliveries per year. There is also a lack of consensus about the best management strategies for optimum care of these women, although it is clear that good committed obstetric care is of vital importance. SCD has great geographical variability across the UK, with the greatest numbers of deliveries occurring in London or other major conurbations such as Manchester and Birmingham, but with small numbers of deliveries distributed across the UK. This lack of knowledge about incidence of pregnancy, makes it difficult to plan services, to plan optimal care, or in the long term to plan further trials into best practice. This study aimed to collect data about incidence across the UK and describe current management practice.

Case definition
Any woman in the UK identified as having sickle cell disease using the following definition:

Sickle cell disease including
    homozygous sickle cell disease
    compound heterozygous conditions of haemoglobin S with haemoglobin C, D, E, O-Arab or Beta thalassaemia.

Pregnancies in women with sickle cell trait are excluded.

Surveillance Period
February 2010 – February 2011

Results
162 cases were reported during the study period and data were returned for 133 cases (82%). There were 12 duplicate cases reported and 13 cases did not meet the case criteria. There were 108 confirmed cases of sickle cell disease. The majority of women were from African (68%) or Caribbean (20%) background. Patients were anaemic at booking with haemoglobin levels of 5.5-12.5g/dl (median 9.3g/dl).

Problems were commonly reported during this pregnancy and 57 women (52%) experienced a painful sickle cell crisis during pregnancy, 14/57 were admitted to hospital with painful crisis, 8 on a single occasion, 5 patients on two occasions and one women on four occasions. Seven women (6%) had acute chest syndrome, a life threatening complication of sickle cell disease characterised by pulmonary signs and symptoms and infiltration on the Chest X-Ray. Twenty-six women (24%) received ante-natal blood transfusion.

Four miscarriages/terminations, 3 stillbirths and 94 live births were reported. Eleven women had not delivered at the time of data completion, so outcome data on this pregnancy is not available. 24% of women were admitted to ITU in the peri-partum period. 15% of women reported a sickle cell crisis in the 6 weeks following delivery.

Interim Conclusions
Further analysis of these results is underway, including comparison with the normal population. The currently available results suggest that pregnancy in women with sickle cell disease is a time of significant morbidity. There were no reports of maternal mortality, but morbidity was high with 52% of women
reporting antenatal painful crises, 6% of women having acute chest syndrome and 24% of women having antenatal blood transfusion. The reasons for and timing of blood transfusion in pregnancy need further investigation. One previous randomised trial showed that prophylactic blood transfusion decreased maternal pain but did not impact on other maternal and fetal outcomes, but the high incidence of complications and high numbers of women receiving blood transfusion in this study suggest that the risks and benefits of prophylactic antenatal transfusion should be further investigated.

**Investigators**

Jo Howard, Eugene Oteng-Ntim, Guy’s and St Thomas’ NHS Foundation Trust

**Funding**

Guy’s and St Thomas’ Charity
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 develop guidelines for their optimal management.

Background

Tumours of the adrenal glands are very rare and information in the medical literature on the incidence, their management 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, including major maternal and fetal morbidity and mortality. 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. 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 allow for 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 2013

Interim Results

Up to March 2012 14 cases of adrenal tumours in pregnancy were reported. Information has been received for 10 of these cases (71%). There were three cases which were subsequently reported by clinicians as not cases and one duplicate report. Two further cases did not meet the case definition. There were thus five confirmed cases in an estimated 798,634 maternities. This gives an incidence estimate in the UK of 0.6 cases per 100,000 maternities (95% CI 0.2 to 1.5 per 100,000). The five confirmed cases included four women with Conn’s syndrome and one woman 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. We are currently investigating whether this study can be extended to include Australia and New Zealand, through AMOSS, the Australasian Maternity Outcomes Surveillance System.

Investigators

Catherine Williamson, Kimberly Lambert, Imperial College London
David McCance, Royal Victoria Hospital

Funding

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 seven 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\(^4\). Estimates of incidence vary tenfold between 1.3 and 12.5 per 100,000 pregnancies\(^1\). Estimates of the mortality rate from this condition also vary widely\(^2\), from as much as 86% to more recent estimates of 16-30%. Recent retrospective database analyses suggest possible links with induction of labour and caesarean delivery\(^3,4\), and a wide range of treatments have been described in case reports\(^2\). A database of voluntary notifications was established in the UK to collect information on epidemiology and management\(^5\); 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\(^6\).

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 seven years of surveillance to date 153 cases of AFE in pregnancy have been reported. Information has been received for 143 cases (93%). There were 21 cases which were subsequently reported by clinicians as not cases and seven duplicate reports. Thirteen further cases did not meet the case definition criteria. There were thus 102 confirmed cases, in an estimated 5,385,726 maternities. This gives an incidence estimate in the UK of 1.9 cases per 100,000 maternities (95% CI 1.5 to 2.3 per 100,000).

Interim Conclusions
There is no evidence of a significant change in the incidence of AFE over the past seven years. The incidence rate is comparable to that documented in other high resource countries using similar methodology\(^7\). 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.

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 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 1:30 000 women; 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 and in Europe. In the UK 52 cases of PMCS were recorded between 2003-2005 amongst women who subsequently died.

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

Please report 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 2012 33 cases of cardiac arrest in pregnancy were reported. Information has been received for 18 of these cases (55%). There were six cases which were subsequently reported by clinicians as not cases and six further cases did not meet the case definition. There were thus eight confirmed cases in an estimated 532,423 maternities. This gives an incidence estimate in the UK of 1.5 cases per 100,000 maternities (95% CI 0.6 to 3.0 per 100,000). In 5 women (62.5%) perimortem caesarean section was carried out. 2 women (25%) 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.
4.3.4 Gastric Banding in Pregnancy

Key points
- Laparoscopic Adjustable Gastric Band (LAGB) insertion is the primary surgical method of 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 will use UKOSS to describe the epidemiology and management of gastric banding in pregnancy in the UK and use this information to develop future guidelines for optimal management.

Background
The impact of obesity on pregnancy is well established; obesity negatively impacts on maternal, fetal and neonatal wellbeing. Laparoscopic Adjustable Gastric Band (LAGB) insertion is the primary surgical method of surgical weight reduction in the UK. It involves application of an adjustable silicone balloon around the upper portion of the stomach, resulting in a small upper stomach pouch and a narrowed outlet, which limits the stomach’s capacity to intake food and increases the feeling of fullness. These two effects assist subsequent weight loss. 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 because of concerns regarding hyperemesis and poor nutritional intake. Deflating the gastric band has the adverse effect of excessive weight gain 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, maternal hypertension and caesarean delivery when compared to obese controls.

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

Surveillance Period
September 2011 - August 2012

Interim Results
Up to March 2012 70 cases of gastric banding in pregnancy were reported. Information has been received for 37 of these cases (53%). There were four cases which were subsequently reported by clinicians as not cases. Eleven further cases did not meet the case definition. There were thus 22 confirmed cases in an estimated 332764 maternities. This gives an incidence estimate in the UK of 6.6 cases per 100,000 maternities (95% CI 4.1 to 10.0 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
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.
4.3.5 HELLP Syndrome

Key points

- There has been no comprehensive 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 some controversy regarding risk factors for adverse outcome.
- This study will estimate the incidence of HELLP syndrome in the UK and will investigate and quantify the associated risk factors, management and outcomes and will also explore whether any factors are associated with poor outcomes.

Background

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

Case definition

All pregnant women identified as having HELLP syndrome defined as 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 x109/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

Interim Results

Up to March 2012 161 cases of HELLP were reported. Information has been received for 100 of these cases (62%). There were six cases which were subsequently reported by clinicians as not cases and 10 further cases did not meet the case definition. There were thus 84 confirmed cases in an estimated 598,976 maternities. This gives an incidence estimate in the UK of 14.0 cases per 100,000 maternities (95% CI 11.2 to 17.4 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

Kate Fitzpatrick, Marian Knight, Jenny Kurinczuk, Peter Brocklehurst, Maria Quigley, NPEU;
Sue Sellers, United Bristol Hospitals NHS Trust; Mervi Jokinen, RCM;
Shona Golightly, Independent; Gwyneth Lewis, University College London;
James Walker, RCOG; Alison Burton, Oxfordshire PCT; Jenny Furniss, Lay representative

Funding

This study has been funded by the NIHR as part of the UK National Maternal Near-miss Surveillance Programme (UKNeS).**
4.3.6 Myeloproliferative Disorders in Pregnancy

**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 will investigate the incidence, management and outcomes for mother and infant.

**Background**

The aim of the proposed study is to use the UK Obstetric Surveillance System to describe the epidemiology of myeloproliferative disorders (MPDs), persistently increased number of platelets or red cells in pregnancy. 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 for epidemiology and outcome of pregnancy exists for ET with approximately 461 pregnancies reported; 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 interventions used in current clinical practice are rarely based on robust evidence. Prospective data collection on known and occult MPDs in pregnancy using UKOSS will provide 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 x10⁹/l)

OR an erythrocytosis (haemoglobin persistently greater than 16.5g/dl).

**Surveillance Period**

January 2010 – December 2012

**Interim Results**

Up to March 2012 50 cases of myeloproliferative disorders in pregnancy were reported. Information has been received for 41 of these cases (82%). There were 10 cases which were subsequently reported by clinicians as not cases and one further case did not meet the case definition. There were thus 30 confirmed cases in an estimated 1,730,374 maternities. This gives an incidence estimate in the UK of 1.7 cases per 100,000 maternities (95% CI 1.2 to 2.5 per 100,000). The cases diagnosed were predominantly essential thrombocythemia (25 cases - 86%), three women had Polycythaemia vera (10%) and there was one case of Myelofibrosis (3%)

**Interim Conclusions**

Data collection for this study is still incomplete 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**

Guy’s and St Thomas' Charity
4.3.7 Pituitary Tumours in Pregnancy

Key points

- Pituitary tumours produce hormones that can have a detrimental effect on pregnancy; as the pituitary enlarges in size during pregnancy, 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. 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. Cushing’s disease is associated with high fetal morbidity (spontaneous abortion 5%, stillbirth 6% and prematurity 43%). 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 1.0cm diameter).

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

Surveillance Period

March 2010 - March 2013

Interim Results

Up to March 2012 78 cases of pituitary tumours in pregnancy were reported. Information has been received for 63 of these cases (81%). There were 14 cases which were subsequently reported by clinicians as not cases and one duplicate report. Twelve further cases did not meet the case definition. There were thus 36 confirmed cases in an estimated 781,376 maternities. This gives an incidence estimate in the UK of 1.2 cases per 100,000 maternities (95% CI 0.5 to 2.2 per 100,000). The 36 confirmed cases included 23 women with prolactinomas, seven women with non-functioning tumours, three women with Cushing disease and three women with Acromegaly.

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

SPARKS
4.3.8 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 will 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. Most studies are centre-based and retrospective. Three voluntary registers have collected data at various times: the US National Transplantation Pregnancy Register (1991-present), the UK Transplant Pregnancy Register (1994-2001) and the European Dialysis and Transplant Association Registry (1960-1992). This UK register, however, no longer collects information. The objective of this project is 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 is divided into two studies: the first to investigate outcomes in women with renal transplants has now stopped collecting data; this second study to investigate outcomes in women with other solid organ transplants is ongoing.

**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 are excluded.

**Surveillance Period**

January 2007 – January 2012

**Interim Results**

110 cases of pregnancy in non-renal solid organ transplant recipients were reported and data collection forms were returned for 96 cases (87%). There were eight cases which were subsequently reported by clinicians as not cases and there were 13 duplicate reports leaving 75 confirmed cases.

Women with a liver transplant had a median 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 infants. One woman died.

**Interim Conclusions**

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

**Investigators**

Marian Knight, Peter Brocklehurst, Jenny Kurinczuk, NPEU
Catherine Nelson-Piercy, Guy’s and St Thomas’ Hospital
4.3.9 Pulmonary Vascular Disease in Pregnancy

**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.
- Novel methods of management may impact on case outcomes.
- This study will provide a national picture of the incidence of the disease, its epidemiology and management.

**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\(^72\); between 1991 and 2005 there were 25 maternal deaths in the UK associated with this condition. Eisenmenger’s syndrome is estimated to carry a maternal mortality rate of 40% per pregnancy\(^73\), with an infant mortality rate of 10-15%\(^72\). A systematic review of the literature in 1998 suggested that the maternal mortality rate had remained unchanged over the previous 20 years\(^72\). However, the authors of this review recognise that there may be inherent biases in published reports of pregnancy in women with pulmonary vascular disease in pregnancy and call 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\(^74\), however, problems with ascertainment caused the register to cease to collect data. The objective of this prospective study through UKOSS is 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.

**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\(^75\). 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, atrial septal defect or patent ductus arteriosus\(^76\)

**Surveillance Period**
March 2006 – February 2012

**Interim Results**
To date, 88 cases of pulmonary vascular disease have been reported, with further information received for 74 cases (84%). There were 26 cases which were subsequently reported by clinicians as not cases, 13 cases which did not meet the case definition criteria and four duplicate reports, leaving 31 confirmed cases, an estimated incidence of 0.7 cases in 100,000 maternities (95% CI 0.5 to 1.0 per 100,000).

Thirteen of the cases were attributed to congenital heart disease, two to chronic thromboembolism, one to sleep apnoea, seven to idiopathic pulmonary arterial hypertension, one to connective tissue disease and a further seven had no cause for pulmonary hypertension identified. Sixteen of these cases were known prior to pregnancy and fifteen were diagnosed during pregnancy or immediately postnatally. Two women died (case fatality 6%, 95% CI 1-24%).

**Interim Conclusions**
Pulmonary vascular disease in pregnancy is extremely rare in the UK. However, the preliminary results from this study suggest that mortality may not be as high as previously reported.
4.3.10 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 will describe, on a population level, the incidence of severe maternal sepsis in the UK, associated risk factors, causative organisms, management and outcomes and investigate whether any factors are associated with poor outcomes.

Background

Maternal sepsis can be a severe complication of pregnancy or birth, which if untreated, can rapidly progress along a continuum of severity to septicaemic shock and eventually death. In the UK, the incidence of fatal maternal sepsis has increased over the last two decades. In the late 1980’s 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. This places sepsis as the leading cause of direct maternal death, surpassing hypertensive disorders. Underlying each maternal death is a much larger number of cases of morbidity during pregnancy and puerperium. Given the recent increase in maternal deaths and morbidity incidence in the general population due to sepsis, 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 and anaemia, 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, is 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).

Report only cases diagnosed as having severe sepsis by a senior clinician.

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 > 17x10⁹/L or < 4x10⁹/L or with > 10% immature band forms, measured on 2 occasions.

Surveillance Period

June 2011 – May 2012

Interim Results

To date there have been 388 cases of severe sepsis reported to UKOSS. Information has been received for 244 cases (63%) There were 21 cases which were subsequently reported by clinicians as not cases and 21 further cases did not meet the case definition criteria. There were four duplicate reports, leaving 198 confirmed cases.

Nine cases (4.1%) were undelivered at the time of diagnosis, and 41 (18.9%) cases were diagnosed with septic shock. The most common causative organisms among pathologically confirmed cases were: E. Coli (32.8%), Group A streptococcus (14.9%) and Group B streptococcus (11.9%).
**Interim Conclusions**

At this point in the study, there appears to be a significant difference in several demographic, clinical and delivery characteristics between cases and controls. Further analyses at the end of data collection will elucidate the burden of severe maternal sepsis on a national level, as well as reveal if the differences in characteristics seen currently are indeed significant risk factors for severe sepsis.

**Investigators**

Colleen Acosta, Marian Knight, Jenny Kurinczuk, Peter Brocklehurst, Maria Quigley, NPEU;
Sue Sellers, United Bristol Hospitals NHS Trust; Nuala Lucas, Northwick Park Hospital;
Mervi Jokinen, RCM; Shona Golightly, Independent; Gwyneth Lewis, University College London;
James Walker, RCOG; Alison Burton, Oxfordshire PCT; Jenny Furniss, Lay representative

**Funding**

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

![UKNeS Logo](image-url)
4.3.11 Stage 5 Chronic Kidney Disease in Pregnancy

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. 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/1.73m² 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 and Conclusion

This study is at a very early stage and data collection has only just commenced. No conclusions can be drawn at this stage.

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 2012 / 2013.

4.4.1 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. There is always rapid onset and progression of symptoms. Current estimates of incidence suggest that maternal anaphylaxis occurs in approximately 1 in 30,000 pregnancies, although this is based on limited evidence. 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.

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. 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 have the potential to impact on the incidence and/or outcomes of anaphylaxis during pregnancy, making this study very timely.

Beyond adhering to the best practice algorithm for management of anaphylaxis in an adult, there is little known about how anaphylactic shock in pregnancy should be managed in order to optimise the outcome for both mother and baby.

Case definition
The cases will be all pregnant women in the UK identified as having anaphylaxis as identified by the following definition:

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
Main research questions

- What is the current incidence of anaphylaxis during pregnancy in the UK?
- What are the causative agents implicated in anaphylactic reaction during pregnancy?
- How is anaphylaxis during pregnancy managed in the UK?
- What are the maternal, fetal and immediate neonatal outcomes following anaphylactic reaction during pregnancy?
- What are the factors associated with poor outcomes for mother or infant?

Investigators

Marian Knight, NPEU; Peter Brocklehurst, Institute for Women’s Health UCL; Kim Hinshaw, Sunderland Royal Hospital; Nuala Lucus, Northwick Park Hospital; Derek Tuffnell, Bradford Hospitals; Benjamin Stenson, Edinburgh Royal Infirmary; Rhiannon D’Arcy, Oxford University Hospitals
4.4.2 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 patients 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 80% of all maternal morbidity\(^4\). As there is no universally accepted definition for MOH, its incidence varies depending on 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 on 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\(^5\).

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 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\(^6\). Although studies from bleeding trauma patients have some limitations, they have raised some important questions on 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.

Clinical studies of massive bleeding in trauma have also raised concerns about the role and value of standard coagulation tests (PT, APTT). These are in vitro tests, largely developed and validated for patients with inherited bleeding disorders. Moreover, the time required to obtain their results limits their usefulness in the management of MT and increases its complexity resulting in suboptimal transfusion therapy and maybe contributing to poor outcome. 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 (excluding cell salvage) within a 24hr period.

Surveillance Period

01st September 2012 - 31st August 2013

Main Research questions

- What proportion of women with MOH receive plasma transfusions?
- Is there any correlation between the use of additional blood components and clinical outcomes?
- What are the coagulation abnormalities at the time of MOH?
- Is there any correlation between clinical outcomes and (a) coagulation abnormalities and (b) other products administered?

Investigators

Laura Green NHS Blood and Transplant & Barts and the London Hospital
Simon Stanworth, NHS Blood and Transplant Oxford
Peter Collins, Cardiff University
Marian Knight, NPEU
5. Publications

5.1. Amniotic fluid embolism incidence, risk factors and outcomes: a review and recommendations

Published Article

Key points
- The aim of this study was to examine population-based regional or national data from five high-resource countries in order to investigate incidence, risk factors and outcomes of AFE and to investigate whether any variation identified could be ascribed to methodological differences between the studies.
- We reviewed available data sources on the incidence of AFE in Australia, Canada, the Netherlands, the United Kingdom (UKOSS data) and the USA.
- The reported incidence of AFE ranged from 1.9 cases per 100 000 maternities (UK) to 6.1 per 100 000 maternities (Australia).
- There was a clear distinction between rates estimated using different methodologies.
- Older maternal age and induction of labour were consistently associated with AFE.
- Recommendation 1: Comparisons of AFE incidence estimates should be restricted to studies using similar methodology. The recommended approaches would be either population-based database studies using additional criteria to exclude false positive cases, or tailored data collection using existing specific population-based systems.
- Recommendation 2: Comparisons of AFE incidence between and within countries would be facilitated by development of an agreed case definition and an agreed set of criteria to minimise inclusion of false positive cases for database studies.
- Recommendation 3: Groups conducting detailed population-based studies on AFE should develop an agreed strategy to allow combined analysis of data obtained using consistent methodologies in order to identify potentially modifiable risk factors.
- Recommendation 4: Future specific studies on AFE should aim to collect information on management and longer-term outcomes for both mothers and infants in order to guide best practice, counselling and service planning.

5.2. Delayed postpartum eclampsia

Published Articles

Key points
- The overall rate of eclampsia in developed countries has declined; however, the proportion of cases of eclampsia occurring postpartum is thought to have increased. Trends towards decreasing lengths of postnatal hospital stay have led to concerns about possible adverse effects of such early discharge, including risks of morbidity from hypertensive disorders.
- The aim of this study was to use the data from the 2005-6 UKOSS eclampsia study to estimate the incidence of delayed postpartum eclampsia and to investigate whether maternal characteristics and outcomes were different between women with delayed (12 hours or longer after delivery) or early postpartum eclampsia.
- Seventy-six women had postpartum eclampsia, representing an incidence of 1.0/10 000 (95% CI 0.7–1.2/10 000) maternities.
• Among the women having postpartum eclampsia, 70% (n=53) of women had their first fit in the 12 hours immediately following delivery, 11% (n=8) during hours 12–24, 5% (n=4) during the 24–48 hours after delivery and 14% (n=11) more than 48 hours after delivery.

• Maternal characteristics, biological and clinical symptoms in the week preceding eclampsia, maternal and neonatal outcomes were not significantly different in the delayed eclampsia group in comparison with the early postpartum eclampsia group, with the exception of a higher caesarean delivery rate in women with delayed eclampsia [13 (57%) vs. 6 (11%); odds ratio 10.1, 95% CI 3.12–33.3].

• This study suggests that the majority of cases of postpartum eclampsia in the UK occur in the first 12 hours following delivery. Beyond this, the risk of eclampsia is very low.

5.3. Myocardial infarction in pregnancy

Published Article

Key points
• Cardiac disease is a leading cause of maternal deaths in the developed world, responsible for one fifth of all maternal deaths in the UK.
• The aim of this study was to estimate the incidence of myocardial infarction (MI) in pregnancy and up to one week postpartum in the UK and describe risk factors, management and outcomes.
• Twenty-five cases of MI in pregnancy were reported, giving an estimated incidence of 0.7 per 100,000 maternities (95%CI 0.5-1.1), which may represent an underestimate of the true incidence.
• Many risk factors identified were both recognisable and modifiable: maternal age (aOR 1.3 for every one year increase, 95%CI 1.2-1.4), smoking (aOR 3.1, 95%CI 1.3-7.5), hypertension (aOR 8.1, 95%CI 1.5-42.3, p=0.018), twin pregnancy (aOR 11.3, 95%CI 2.9-44.6) and pre-eclampsia (aOR 4.5, 95%CI 1.2-17.2) were all independently associated with MI in pregnancy.
• Fifteen women (60%) underwent coronary angiography; nine (60%) had coronary atherosclerosis, three (21%) had coronary artery dissection, one (7%) had a coronary thrombus, and two (13%) had normal coronary arteries. No women died.
• Management of MI in pregnancy was highly variable, indicating a clear need for further information regarding the safety and outcomes of different interventions.
• The addition of pregnancy status as a compulsory field in cardiac audit databases would enable routine collection of this information.

5.4. Perinatal outcomes of 2009/H1N1 influenza

Published Article
Perinatal outcomes after maternal 2009/H1N1 infection: national cohort study
M Pierce, JJ Kurinczuk, P Spark, P Brocklehurst, M Knight on behalf of UKOSS. BMJ 2011;342:d3214

Key points
• The first analyses into the effects of 2009/H1N1 influenza “swine flu” in pregnancy focused primarily on maternal morbidity and mortality.
• Few studies followed-up women after their original hospital admission, thus the effect of infection on pregnancy outcome was not fully investigated.
• The aim of this study was to follow-up women admitted to hospital with confirmed 2009/H1N1 identified through UKOSS during the second wave of pandemic infection in September 2009 to January 2010 to assess the risk of adverse fetal and infant outcomes.
• Pregnancy outcome data were obtained for 94% of women (n=256).
• The perinatal mortality was higher amongst infants born to infected women (39 per 1,000 total births, 95%CI 19 to 71) compared to infants of uninfected women (7 per 1,000 total births, 95%CI 3 to 13) (p<0.001).
• This was principally explained by an increase in the stillbirth rate (27 per 1,000 total births vs 6 per 1,000 total births; p=0.001).
• Infants of infected women were also more likely to be born prematurely (aOR 4.0, 95%CI 2.7 to 5.9).
• This study emphasises the importance of immunisation against influenza for all pregnant women to prevent both poor maternal and perinatal outcomes.

5.5. Risk factors for progression from severe maternal morbidity to death

Published Article

Key points
• Women continue to die unnecessarily during or after pregnancy in the developed world.
• The aim of this analysis was to compare women with severe maternal morbidity, identified through UKOSS, with women who died from the same conditions, identified from the UK Confidential Enquiries into Maternal Deaths between 2003 and 2008.
• Women were included if they had eclampsia, antenatal pulmonary embolism, amniotic fluid embolism, acute fatty liver of pregnancy or antenatal stroke.
• The women who died were older (age 35+ years aOR 2.36, 95%CI 1.22-4.56), more likely to be of black ethnicity (aOR 2.38, 95%CI1.15-4.92), and unemployed, routine or manual occupation (aOR 2.19, 95%CI1.03-4.68). We also observed an association with obesity (BMI ≥ 30kg/m2aOR 2.73, 95%CI 1.15-6.46).
• Women from vulnerable populations in the UK thus remain at increased risk of maternal death in the presence of severe maternal morbidities.
• It is not clear whether the increased risk of death was related to difficulties in access to maternal care through physical (location) or cultural factors.
• There is a place for more in depth studies to determine exactly why the presence of these factors makes women more likely to die, but it is evident that there is a place for public health action to reverse the rising trends in maternal age at childbirth and clinical action to mitigate its effects, and to reduce the burden of obesity in pregnancy.
• In addition, development and evaluation of services to mitigate the risk of dying associated with being of black Caribbean or African ethnicity and being unemployed or from routine or manual socioeconomic groups is essential.

5.6. Specific second-line therapies for postpartum haemorrhage

Published Article

Key points
• Several specific second-line therapies for postpartum haemorrhage have been introduced into obstetric practice recently and are used widely, although little is known about their effectiveness on a population basis.
The aim of this study was to describe the characteristics of women managed with rFVIIa, uterine compression sutures, interventional radiology including intra-arterial balloon or embolisation, and pelvic vessel ligation, and to estimate the success rate for each therapy, defined as control of PPH without the need for additional management strategies or hysterectomy.

As the first of these specific therapies used, uterine compression sutures were successful in 75% of women (95%CI 67-81%), pelvic vessel ligation in 36% (95%CI 13-65%) interventional radiology in 86% (95%CI 57-98%) and factor VII in 31% (95%CI 11-59%). Rates of success were not significantly different in women managed first with intrauterine (balloon) tamponade.

Cases managed with factor VII and ligation tended to be more clinically complex.

Overall, 71 (26%) women had a hysterectomy for ultimate control of their haemorrhage.

This study gives an overview of the efficacy of these specific second-line therapies in a population setting. However, further investigation, including particularly assessment of cost-effectiveness, is needed to inform guidelines on the use of these therapies and provision of interventional radiology services.

5.7. Uterine rupture

Published Article

Key points
- Recent reports of the risk of morbidity due to uterine rupture are thought to have contributed to a decrease in the number of women attempting a vaginal birth after caesarean section.
- The aims of this study were to estimate the incidence of true uterine rupture in the UK and to investigate and quantify the associated risk factors and outcomes, based on intended mode of delivery.
- The estimated incidence of uterine rupture was 2 per 10,000 maternities overall; 21 and 3 per 10,000 maternities in women with a previous caesarean delivery planning vaginal or elective caesarean delivery respectively.
- Amongst women with a previous caesarean delivery, odds of rupture were also increased in women who had two or more previous caesarean deliveries (aOR 3.02, 95%CI 1.16-7.85) and less than 12 months since their last caesarean delivery (aOR 3.12, 95%CI 1.62-6.02).
- A higher risk of rupture with labour induction and oxytocin use was apparent (aOR 3.92, 95%CI 1.00-15.33).
- Two women with uterine rupture died (case fatality 1.3%, 95%CI 0.2-4.5%). There were 18 perinatal deaths associated with uterine rupture among 145 infants (perinatal mortality 124 per 1000 total births, 95%CI 75-189).
- This study shows that although uterine rupture is associated with significant mortality and morbidity, even amongst women with a previous caesarean section planning a vaginal delivery, it is a rare occurrence.
- For women with a previous caesarean section, risk of uterine rupture increases with number of previous caesarean deliveries, a short interval since the last caesarean section and labour induction and/or augmentation, and these factors should be considered when counselling and managing the labour of women with a previous caesarean section.

5.8. Abstracts

The following abstracts were presented at meetings in 2011 and are available on our website www.npeu.ox.ac.uk/ukoss:

Multiple repeated caesarean section in the UK: What is the incidence and what are the consequences to mother and child? Presented at the Perinatal Medicine 2011 conference, June 2011

5.9. UKOSS Publications to date


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