

UKOSS

UK Obstetric Surveillance System

Eighth Annual Report 2014



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



National Perinatal
Epidemiology Unit

This report should be cited as:

Nair M, Workman M, Fitzpatrick K, Peirsegaele P, Kurinczuk JJ, Knight M. UKOSS Annual Report 2014.
Oxford: National Perinatal Epidemiology Unit (2014)

Table of Contents

1. Introduction	1
2. Methods	1
3. Participation	3
4. Studies	5
4.1. Study Timetable	5
4.2. Studies completed in 2013	6
4.2.1 Massive Transfusion in Major Obstetric Haemorrhage	6
4.2.2 Pituitary Tumours	7
4.3. Studies in progress	8
4.3.1 Adrenal Tumours in Pregnancy	8
4.3.2 Amniotic Fluid Embolism	9
4.3.3 Anaphylaxis in Pregnancy	10
4.3.4 Aspiration in Pregnancy	11
4.3.5 Cardiac Arrest in Pregnancy	12
4.3.6 Chronic Kidney Disease Stage 5	13
4.3.7 Epidural Haematoma or Abscess	14
4.3.8 Gastric Bypass in Pregnancy	15
4.3.9 Pregnancy at Advanced Maternal Age	16
4.3.10 Prosthetic Heart Valves	17
4.3.11 Severe Primary Immune Thrombocytopenia (ITP) in Pregnancy	18
4.4. Future studies	19
4.4.1 Vasa Praevia	19
5. Publications	21
5.1. Association of severe intrahepatic cholestasis of pregnancy with adverse outcomes: a prospective population-based case-control study	21
5.2. Ethnic variations in severe maternal morbidity in the UK – a case-control study	21
5.3. Risk factors, management and outcomes of HELLP and ELLP Syndromes	22
5.4. Pregnancy outcomes in liver and cardiothoracic transplant recipients: a UK National Cohort Study	22
5.5. The management and outcomes of placenta accreta/increta/percreta in the UK: a population-based descriptive study	23
5.6. The UK Obstetric Surveillance System: impact on patient safety	23
5.7. Variation in severe maternal morbidity according to socioeconomic position: a UK national cohort study	24
5.8. Abstracts	24
5.9. UKOSS Publications to date	25
6. Acknowledgements	28
7. References	30

1. Introduction

The UK Obstetric Surveillance System (UKOSS), a joint initiative between the National Perinatal Epidemiology Unit (NPEU) and the Royal College of Obstetricians and Gynaecologists, was launched in February 2005. This national system has been used to study a range of rare disorders of pregnancy through a system of ongoing data collection, made possible through multi-centre collaborations across the UK¹. UKOSS is also supported by the Royal College of Midwives, the Obstetric Anaesthetists Association, the National Childbirth Trust (NCT), the Faculty of Public Health, the Department of Health and the Health Protection Agency.

In the UK, where maternal death is rare, UKOSS provides the platform to generate robust evidence about the risk factors for severe life-threatening complications related to pregnancy and childbirth. Clinicians from all hospitals with consultant-led maternity units in the UK report cases for conditions that are under surveillance, within a designated period, through this routine reporting system. This minimises the possibility of selection bias and inclusion of false positive cases. Furthermore, UKOSS enables collection of detailed information to answer specific clinical questions which cannot be otherwise answered by studies that use routinely collected data¹. Since its inception, UKOSS has successfully generated evidence to guide prevention and management of major obstetric complications, inform policies, service planning and address patient safety issues¹⁻⁷. This has encouraged Australia, New Zealand and several countries in Europe to establish similar systems⁸.

Studies using UKOSS may be undertaken by any investigator who identifies a suitable topic and secures funding⁹. 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). Examples of questions that have been addressed using UKOSS studies are provided in Box 1 overleaf. This report outlines the studies undertaken during the ninth year of surveillance using UKOSS.

2. Methods

This rolling programme is maintained through case notification cards sent to all consultant-led obstetric units in the UK every month with an approach of 'nil-reporting'. We anticipate that all women who experience a condition investigated through UKOSS will be admitted to a consultant-led unit even if their initial care is provided in a different maternity setting. 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 and to ensure that cases are not missed.

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 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^{10, 11}. 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.

Box 1: Examples of questions which can be addressed using UKOSS studies

1. Estimating disease incidence
 - UKOSS surveillance of eclampsia demonstrated a 45% reduction in incidence between 1992 and 2005³.
2. Describing the prevalence of factors associated with near-miss maternal morbidity
 - A UKOSS study estimated that in 2007-8 more than 1 in every 1200 women delivering in the UK was extremely obese (BMI 50kg/m² or greater)¹².
3. Quantifying risk factors for severe morbidity
 - UKOSS surveillance of uterine rupture showed a significant association with induction or augmentation of labour in women with a previous caesarean delivery⁶.
 - UKOSS surveillance also showed that women with prior caesarean delivery and placenta praevia diagnosed antenatally had an increased odds of having placenta accreta/increta/percreta¹³.
 - UKOSS surveillance of 2009/H1N1 influenza showed a significant association with poor pregnancy outcomes¹⁴.
4. Investigating different management techniques
 - Use of total versus subtotal hysterectomy was examined in the UKOSS study of peripartum hysterectomy but no significant differences in complication rates between the two techniques were found^{1, 2}.
5. Investigating disease progression
 - 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 die¹⁵.
6. Auditing of national guidelines
 - 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, 16}.
7. Responding to emerging public health issues
 - In response to the 2009/H1N1 influenza ('swine flu') pandemic, surveillance of women admitted to hospital with confirmed infection was initiated and informed ongoing changes to clinical guidance concerning pregnancy during the course of the pandemic¹⁷.
8. Informing public health policy
 - UKOSS study showing poor perinatal outcomes in pregnant women with 2009/H1N1 influenza¹⁴ was used as evidence to recommend universal immunisation of pregnant women against seasonal influenza¹⁸.

Figure 1: UKOSS Report Card

<p>UKOSS Report Card United Kingdom Obstetric Surveillance System January 2014</p> <p>Nothing to report <input type="checkbox"/></p> <p>Please specify the number of cases seen this month:</p> <table style="width: 100%;"> <tr> <td><input type="checkbox"/> Adrenal Tumours</td> <td><input type="checkbox"/> Aspiration in Pregnancy</td> </tr> <tr> <td><input type="checkbox"/> Advanced Maternal Age</td> <td><input type="checkbox"/> Cardiac Arrest in Pregnancy</td> </tr> <tr> <td><input type="checkbox"/> Amniotic Fluid Embolism</td> <td><input type="checkbox"/> Epidural Haematoma</td> </tr> <tr> <td><input type="checkbox"/> Anaphylaxis in Pregnancy</td> <td><input type="checkbox"/> Primary ITP in Pregnancy</td> </tr> <tr> <td><input type="checkbox"/> Artificial Heart Valves</td> <td><input type="checkbox"/> Stage 5 Chronic Kidney Disease</td> </tr> </table> <p>Change of reporter details</p> <table style="width: 100%;"> <tr> <td style="width: 50%;">Current reporter name</td> <td style="width: 50%;">New reporter: please give name, job title and e-mail</td> </tr> </table>	<input type="checkbox"/> Adrenal Tumours	<input type="checkbox"/> Aspiration in Pregnancy	<input type="checkbox"/> Advanced Maternal Age	<input type="checkbox"/> Cardiac Arrest in Pregnancy	<input type="checkbox"/> Amniotic Fluid Embolism	<input type="checkbox"/> Epidural Haematoma	<input type="checkbox"/> Anaphylaxis in Pregnancy	<input type="checkbox"/> Primary ITP in Pregnancy	<input type="checkbox"/> Artificial Heart Valves	<input type="checkbox"/> Stage 5 Chronic Kidney Disease	Current reporter name	New reporter: please give name, job title and e-mail	<p>UKOSS Clinician's Section <i>Hospital name</i> January 2014</p> <p>Please complete and keep this section for reference if you have reported cases this month.</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 33%;">Condition</th> <th style="width: 33%;">Patient's name</th> <th style="width: 33%;">Patient's Hospital number</th> </tr> </thead> <tbody> <tr> <td style="height: 100px;"></td> <td></td> <td></td> </tr> </tbody> </table> <p style="text-align: center;">Detach and keep this section.</p>	Condition	Patient's name	Patient's Hospital number			
<input type="checkbox"/> Adrenal Tumours	<input type="checkbox"/> Aspiration in Pregnancy																		
<input type="checkbox"/> Advanced Maternal Age	<input type="checkbox"/> Cardiac Arrest in Pregnancy																		
<input type="checkbox"/> Amniotic Fluid Embolism	<input type="checkbox"/> Epidural Haematoma																		
<input type="checkbox"/> Anaphylaxis in Pregnancy	<input type="checkbox"/> Primary ITP in Pregnancy																		
<input type="checkbox"/> Artificial Heart Valves	<input type="checkbox"/> Stage 5 Chronic Kidney Disease																		
Current reporter name	New reporter: please give name, job title and e-mail																		
Condition	Patient's name	Patient's Hospital number																	

3. Participation

All 210 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 2013 was 94% (Figure 2), with regional return rates varying between 87% and 99% (Figure 3). These card return rates continue the high rates obtained during the first eight 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 2013

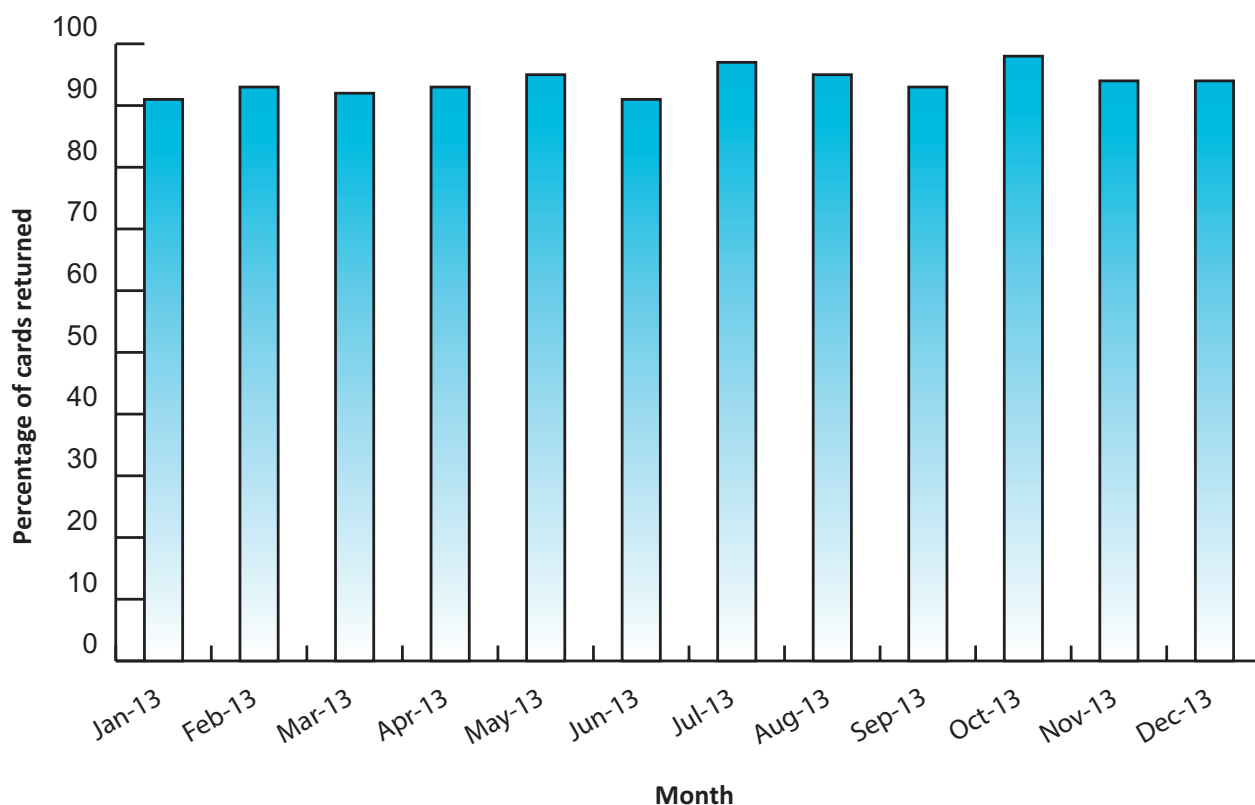
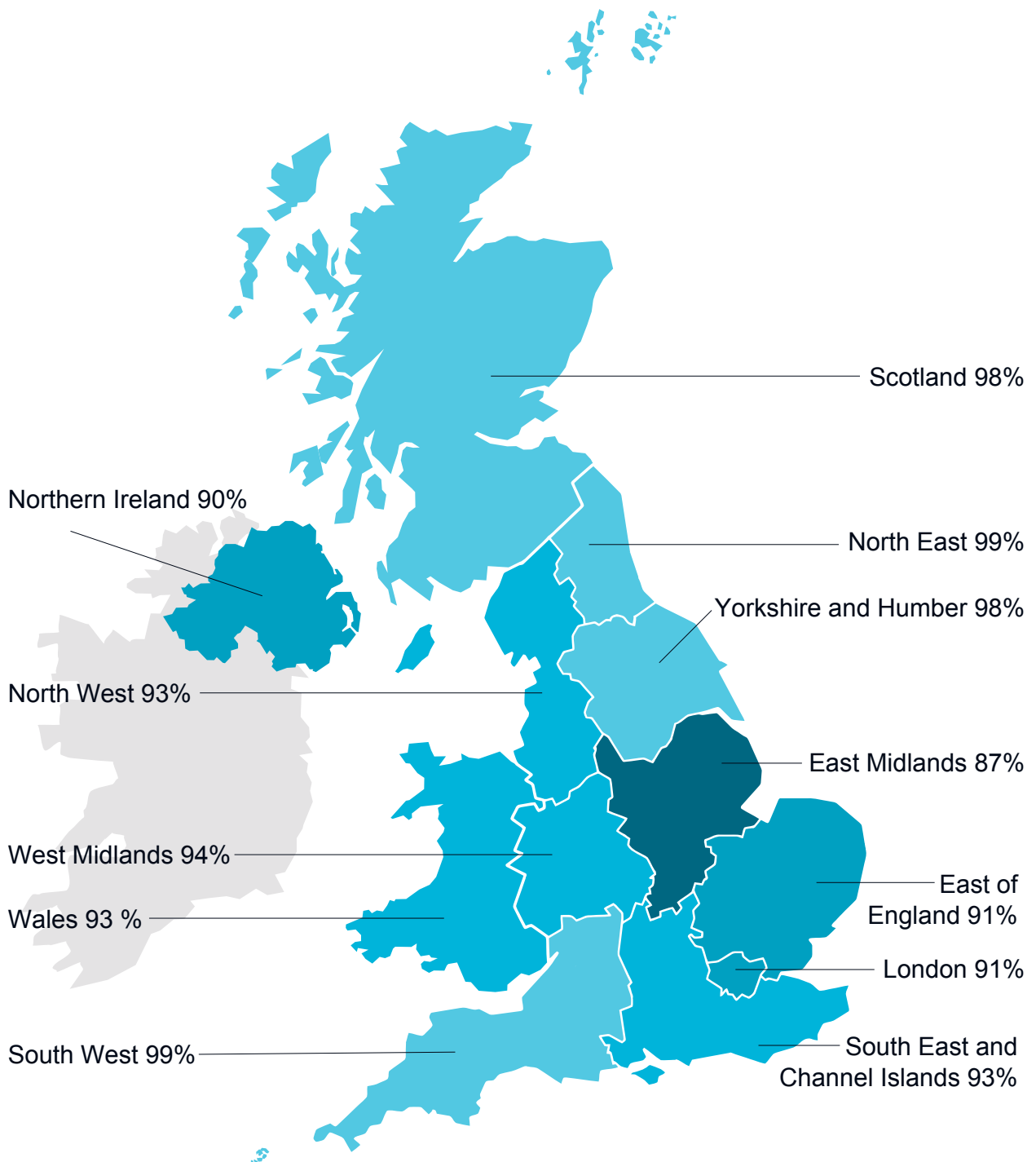


Figure 3: Map showing regional card return rates during 2013



4. Studies

Unless otherwise specified, the results included in this report represent analysis of cases reported and data available up to January 2014. 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 2012-2016

PROJECT	2013												2014												2015												2016											
	J	F	M	A	M	J	J	A	S	O	N	D	J	F	M	A	M	J	J	A	S	O	N	D	J	F	M	A	M	J	J	A	S	O	N	D	J	F	M	A	M	J	J	A	S	O	N	D
Amniotic Fluid Embolism	[Active]																																															
Pituitary Tumours	[Active]												[Inactive]																																			
Adrenal Tumours	[Active]																																				[Inactive]											
Cardiac Arrest in Pregnancy	[Active]																								[Inactive]																							
Stage 5 Chronic Kidney Disease	[Active]																		[Inactive]																													
Massive Transfusion	[Active]												[Inactive]																																			
Anaphylaxis	[Active]																																										[Inactive]					
Artificial Heart Valves	[Active]																								[Inactive]																							
ITP in Pregnancy	[Inactive]												[Active]																								[Inactive]											
Advanced Maternal Age	[Inactive]												[Active]																								[Inactive]											
Aspiration in Pregnancy	[Inactive]												[Active]																																			
Epidural Haematoma	[Inactive]																								[Active]																							
Gastric Bypass in Pregnancy	[Inactive]																								[Active]												[Inactive]											
Vasa Praevia	[Inactive]																								[Active]												[Inactive]											

4.2. Studies completed in 2013

4.2.1 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 women with massive haemorrhage.
- Current guidance for management of massive haemorrhage in pregnant women is based on the findings of studies carried out on trauma patients although there is no evidence to support this.
- This study described the incidence, management and clinical outcomes of massive transfusion in MOH in the UK and further analysis will investigate the management factors that are associated with improved outcomes.

Background

Major obstetric haemorrhage (MOH) resulting in massive transfusion (MT), is a significant cause of maternal morbidity¹⁹. 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 coagulopathy²⁰.

In recent years, much of the drive for new approaches to the management of bleeding comes from studies of patients with trauma which showed that standard MT protocols are less effective in treating major bleeding²¹. Thus, 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 validity and usefulness of standard coagulation tests (PT, APTT) in the management of MT.

Case definition

All pregnant women of 20 weeks gestation or more identified as having >8 units of red blood cell (RBC) transfusion within a 24 hour period.

Surveillance Period

July 2012 – June 2013

Results

A total of 181 cases of MT due to MOH were identified by the end of the surveillance period. The median estimated blood loss was 6000mL (IQR: 4500–8000). The main causes for MOH were uterine atony (40%) and placenta accreta/increta/percreta (16%). The median worst (IQR) platelet count was $68 \times 10^9/l$ (50-95), APTT-ratio 1.3 (1.0–1.9) and fibrinogen 1.4 (0.8–2.2). In 33% of the women APTT-ratio was >1.5x baseline, 27% had fibrinogen <1.0g/dl and in 25% of cases the platelet count was $<50 \times 10^9/l$. Fresh frozen plasma (FFP), cryoprecipitate and platelets were transfused in 99%, 61% and 77% of women. The median (IQR) RBC, FFP and cryoprecipitate transfused were 10 (8-1), 6 (4–8), and 2 units (2–4), with the first FFP and cryoprecipitate transfused after a median of 4 (3–6) and 7 RBC units (6–9) respectively. 45% of women underwent hysterectomy, 2 died, 82% were admitted to ITU/HDU, and 28% developed additional major morbidity.

Interim Conclusions

Guideline criteria for plasma/platelet transfusion were fulfilled in only 25% of these severe cases, indicating that further research is needed to define transfusion triggers in MOH. Further analysis of these data is currently underway.

Investigators

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Simon Stanworth, John Radcliffe Hospital;

Peter Collins, Rachel Collis, Cardiff University;

Marian Knight, UKOSS.

Funding

NHS Blood and Transplant Trust Fund.



Blood and Transplant

4.2.2 Pituitary Tumours

Key points

- Pituitary tumours produce hormones that can have a detrimental effect on pregnancy. As the pituitary gland enlarges in size during pregnancy, the tumour may also compress surrounding structures.
- This was the first national study to evaluate maternal and fetal mortality and morbidity related to pituitary tumours in pregnancy.
- The evidence 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. 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 radiation²². 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 failure²². Cushing's disease is associated with high fetal morbidity (spontaneous abortion 5%, stillbirth 6% and prematurity 43%)²³. There is very little literature on the use of medication in the management of these conditions in pregnancy.

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

Results

Of 119 cases notified to UKOSS, 71 met the case definitions: 49 macroprolactinoma; 16 non-functioning pituitary tumours; 3 acromegaly and 3 Cushing's disease (thus 6 GH and ACTH-secreting tumours). Hence these tumours are all rare with an incidence of 1.8 macroprolactinomas per 100,000 pregnancies (95% CI 1.3-2.4), 0.6 non-functioning pituitary tumours per 100,000 (95% CI 0.3-1.0), and 0.1 GH and ACTH-secreting tumours per 100,000 (95% CI 0.02-0.3). Five women with macroprolactinoma (10%) and 6 with non-functioning pituitary tumours (38%) had surgery or radiotherapy before pregnancy. Overall there were 9 cases of tumour expansion, (14%). Women with pituitary tumours in pregnancy did not have significantly increased adverse outcome events (miscarriage, termination of pregnancy, pre-eclampsia, congenital abnormalities, prematurity, stillbirth and NICU admission) compared to controls, but note the low power of this analysis to detect a clinically important difference as statistically significant.

Interim Conclusions

All pituitary tumours in pregnancy are rare; however, non-functioning pituitary tumours are more common than previously thought. Further analysis of these data will be undertaken to investigate factors associated with tumour expansion.

Investigators

K Lambert, K Rees, C Williamson, M Dhanjal, Imperial College Healthcare NHS Trust;
D McCance, Royal Victoria Hospital, Belfast.

Funding

This study is funded by SPARKS.



4.3. Studies in progress

4.3.1 Adrenal Tumours in Pregnancy

Key points

- Adrenal tumours secrete excessive hormones which adversely affect maternal and fetal health.
- Maternal 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 is investigating the current incidence of rare maternal adrenal tumours including pheochromocytomas, those associated with Conn's Syndrome and Cushing's Syndrome. It will describe their current management and the resultant outcomes for women and their infants, and help develop guidelines for their optimal management.

Background

Tumours of the adrenal glands are very rare²⁴ and information in the medical literature about their incidence and management during pregnancy, and associated maternal, fetal and neonatal outcomes is limited. Pheochromocytomas, 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^{25, 26}, including major maternal and fetal morbidity²³ and mortality^{27, 28}. Adrenal tumours are linked to higher rates of hypertension²⁴, diabetes²³ and pre-eclampsia among pregnant women. These can also lead to intrauterine growth restriction, fetal hypoxia²⁹, fetal distress^{24, 30}, spontaneous abortion, stillbirth, prematurity²³ and fetal death. 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. This study is examining the effects of the drugs used to treat these tumours in relation to maternal, fetal and neonatal complications and timing of the surgery to remove the tumours. 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:

PHAECHROMOCYTOMA 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 2015

Interim Results

Up to January 2014, 27 cases of adrenal tumours in pregnancy were reported. Information has been received for 26 of these cases (96%). Of these, there were five cases which were subsequently reported by clinicians as not cases and two duplicate reports. The notes were reported as lost for one case. Eight further cases did not meet the case definition. There were thus 10 confirmed cases in an estimated 2,272,979 maternities. This gives an incidence estimate in the UK of 0.4 cases per 100,000 maternities (95% CI 0.2 to 0.8 per 100,000). The 10 confirmed cases included 5 women with pheochromocytoma, 4 women with Conn's Syndrome and one with Cushing's Syndrome.

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; however estimates of incidence and mortality vary widely.
- The estimated incidence using active surveillance through UKOSS is more than twice that obtained through previous 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 nine years of UKOSS surveillance.

Background

AFE has been consistently identified by the UK Confidential Enquiry into Maternal Deaths as one among the leading causes of maternal mortality^{15, 31}. Estimates of incidence vary tenfold between 1.3 and 12.5 per 100,000 pregnancies³². Estimates of the case fatality of this condition also vary widely³³, 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^{34, 35} and a wide range of treatments have been described in case reports³³. A database of voluntary notifications³⁶ 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 AFE³⁷.

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 nine years of surveillance until January 2014, 186 cases of AFE in pregnancy have been reported. Information has been received for 179 of these cases (96%). Of these, there were 23 cases which were subsequently reported by clinicians as not cases, one set of case notes was reported as lost, and there were 11 duplicate reports. Twenty-one further cases did not meet the case definition. One additional case was identified through MBRRACE-UK and there were also four cases reported through UKOSS that were classified by MBRRACE-UK as not AFE cases following confidential review. There were thus 120 confirmed cases, in an estimated 7,001,438 maternities. This gives an incidence estimate in the UK of 1.7 cases per 100,000 maternities (95% CI 1.4 to 2.1 per 100,000). A range of management strategies were used; 26% (31/120) of women had a hysterectomy, 22% (26/120) of women were treated with factor VIIa, 3% (3/120) of women had exchange transfusion and 3% (4/120) of women had plasma exchange.

Interim Conclusions

There is no evidence of a significant change in the incidence of AFE over the past nine years. The incidence rate is comparable to that documented in other high resource countries using similar methodology. 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

Derek Tuffnell, Bradford Teaching Hospitals NHS Foundation Trust;
Marian Knight, Kate Fitzpatrick, 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 for both.
- 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 is collecting information about the incidence, management and outcomes of anaphylaxis in pregnancy in the UK.

Background

Anaphylaxis is a severe and potentially fatal systemic hypersensitivity reaction. It is characterised by a combination of life-threatening airway, breathing and/or circulatory problems with skin or mucosal changes³⁸. Current estimates of incidence suggest that maternal anaphylaxis occurs in approximately 1 in 37,000 pregnancies, although this is based on limited evidence³⁹. 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 infant⁴⁰⁻⁴³.

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^{44, 45}. 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 for maternal group B streptococcal carriage in labour^{43, 44} have the potential to impact on the incidence and/or outcomes of anaphylaxis during pregnancy, making this study very timely.

Case 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. Skin and/or mucosal changes
3. Sudden onset and rapid progression of symptoms

However, skin and/or mucosal features in particular may not be evident if treatment is rapidly implemented, so **include all women in whom the final clinical diagnosis is anaphylaxis, irrespective of the presence or absence of skin/mucosal changes.**

Surveillance Period

October 2012 – September 2015

Interim Results

Up to January 2014, 31 cases of anaphylaxis in pregnancy had been reported. Information has been received for 26 of these cases (84%). There were seven cases which were subsequently reported by clinicians as not cases and one set of notes reported as lost. Three further cases did not meet the case definition criteria. Thus, there were 15 confirmed cases until January 2014 in an estimated 1,004,984 maternities, giving an estimated incidence of 1.5 per 100,000 maternities (95% CI 0.8 to 2.5 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. However, the preliminary results suggest that the incidence of maternal anaphylaxis in the UK is about half of that reported in a study from Texas, USA³⁹.

Investigators

Marian Knight, NPEU;
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Kim Hinshaw, Sunderland Royal Hospital;
Nuala Lucas, Northwick Park Hospital;
Derek Tuffnell, Bradford Hospitals;
Benjamin Stenson, Edinburgh Royal Infirmary;
Rhiannon D'Arcy, Oxford University Hospitals.

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)* and as part of the programme of work of the Policy Research Unit in Maternal Health and Care (reference number: 108/0001).



4.3.4 Aspiration in Pregnancy

Key points

- Pulmonary aspiration is the most common cause of death in association with complications of airway management.
- Pregnant women are at increased risk of aspiration due to a number of factors including delayed gastric emptying.
- Current policies recommend a light diet in established labour; however it is not clear whether this change to policy on oral intake will impact on the incidence of maternal aspiration.
- This study is collecting data to estimate the incidence of maternal aspiration in the UK. It will identify other associated factors and investigate the outcomes for mothers and infants in order to further inform current guidance.

Background

Pulmonary aspiration is defined as the inhalation of foreign material below the level of the vocal cords and into the lower respiratory tract^{46, 47}. A recent national audit conducted by the Royal College of Anaesthetists (NAP4) identified aspiration as the most common cause of death in association with complications of airway management⁴⁸. 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 labour⁴⁹. 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^{50, 51}. However, recent National Institute for Health and Care 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'⁵². 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 devices⁴⁸.

Case definition

All women in the UK at 20 weeks gestation or greater with a final diagnosis of pulmonary aspiration during pregnancy or delivery or 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 (eg. 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.

Surveillance Period

September 2013 – August 2016

Interim Results

Up to January 2014, two cases of aspiration in pregnancy were reported. Information has been received for both of these cases (100%). One of these was a confirmed case and the other did not meet the case definition.

Interim Conclusions

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

Investigators

Marian Knight, Vikash Mistry, Jenny Kurinczuk, NPEU;
David Bogod, Nottingham City Hospital;
Audrey Quinn, Leeds General Infirmary.

Funding

This study has been funded as part of the programme of work of the Policy Research Unit in Maternal Health and Care (reference number:108/0001).



4.3.5 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 about survivors of cardiac arrest or PMCS.
- This study is investigating 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 women⁵³; the 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 UK⁵⁴ and in Europe⁵⁵. In the UK 52 cases of PMCS were recorded between 2003-2005 amongst women who subsequently died¹⁵. There is, however, minimal information on survivors of cardiac arrest or PMCS.

Case definition

Any woman who has received immediate basic life support (BLS) (i.e. chest compressions and usually ventilation breaths) at any time in pregnancy and the immediate postpartum period. Note that women requiring ventilatory support only, are **not** included.

Surveillance Period

July 2011 - June 2014

Interim Results

Up to January 2014, 143 cases of cardiac arrest in pregnancy were reported. Information has been received for 123 of these cases (86%). There were 43 cases which were subsequently reported by clinicians as not cases, five duplicate reports and 17 further cases did not meet the case definition. There were thus 58 confirmed cases in an estimated 2,071,982 maternities. This gives an incidence estimate in the UK of 2.8 cases per 100,000 maternities (95% CI 2.1 to 3.6 per 100,000). In 41 women (71%) perimortem caesarean section was carried out; 23 women (40%) died.

Interim Conclusions

Data collection for this study is still incomplete and it is not possible to draw any definitive conclusions at this stage. However, it appears that cardiac arrest is not uncommon among the UK obstetric population; an estimated 1 in 35,000 women developed cardiac arrest during pregnancy.

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.



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4.3.6 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 of changes in dialysis dose on mother and fetus 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. This information is important to inform future management and counselling of these women.

Background

Current pre-pregnancy advice given to women with CKD Stage 5 is to delay conception until they receive a renal transplant to restore fertility and improve 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 adverse consequences for the mother and fetus. Furthermore, the dialysis dose (urea clearance) has not yet been shown to be predictive of fetal outcome^{56, 57}. More information is needed about the intrauterine effects and neonatal consequences of changes in dialysis dose. This project will collect contemporary information about pregnancy outcomes amongst women who currently have 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 to compare 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 CKD during pregnancy

Surveillance Period

February 2012 – January 2014

Interim Results

There were a total of 19 confirmed CKD stage 5 cases at the end of the surveillance period in an estimated 1,607,974 maternities of in the UK. This gives an incidence of 1.2 cases per 100,000 maternities (95% CI 0.7 to 1.9 per 100,000).

Interim Conclusions

The results show that pregnancy among women with CKD stage 5 is uncommon. Additional sources of data are being investigated to ensure all cases have been fully ascertained prior to further data analysis.

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.

4.3.7 Epidural Haematoma or Abscess

Key points

- Epidural haematoma and epidural abscess are clinically severe and can cause permanent damage unless diagnosed and treated rapidly.
- The current incidence of both conditions is not fully known yet women are counselled regularly.
- In the case of epidural haematoma, the potential for iatrogenic coagulopathy with Low Molecular Weight Heparin (LMWH) is increasing. Without information about when regional analgesia is safe, women might be denied effective pain relief unnecessarily and equally, regional techniques may well be used at an inappropriate time.
- Both conditions can affect any obstetric unit that offers regional analgesia/anaesthesia and is not limited to high-risk tertiary referral centres.

Background

Approximately 140,000 epidurals are placed annually for labour analgesia in the UK. These are two major but rare complications which merit study as they both occur in an occult manner leading to problems with diagnosis and further management⁵⁸. Vertebral canal haematoma is a very rare but potentially devastating complication occurring either during placement or more typically after removal of an epidural catheter. Epidural abscess formation tends to follow a slower course, with symptoms developing over several days. Diagnosis in both cases can be difficult but delay in recognition and treatment leads rapidly to permanent neurological deficit. These complications are commonly mentioned in the pre-procedure counselling given to women.

Existing estimates of the incidence of epidural haematoma are based on retrospective studies or meta-analysis of the same and are obviously subject to ascertainment bias in that it is unlikely that all obstetric cases are reported in the available literature⁵⁹. The data themselves come from studies from up to and over 20 years old and practice has changed, not least in the increasing use of LMWH.

Case definition

All pregnant women identified as having an epidural haematoma or abscess after a regional anaesthetic technique or attempt at technique.

Surveillance Period

January 2014 – December 2017

Interim Results and Conclusion

This study is at a very early stage. Up to March 2014, 2 cases of epidural haematoma or abscess were reported. So far information has been received for one case. It is thus not possible to draw any definitive conclusions at this stage.

Investigators

Felicity Plaat, Imperial College Healthcare.

Funding

This study is funded by the National Institute for Academic Anaesthesia – The Obstetric Anaesthetists Association Grant.



4.3.8 Gastric Bypass in Pregnancy

Key points

- Obesity is associated with significant maternal and fetal complications during pregnancy and birth.
- Gastric bypass surgery is being increasingly used to treat women of reproductive age, resulting in an increased number of pregnancies following gastric bypass surgery.
- Guidelines for optimal management of pregnancy following gastric bypass surgery have not yet been established.

Background

The prevalence of maternal obesity is dramatically rising in the UK, with approximately 5% of women having a BMI of 35 or over at some point in pregnancy. Indeed, 2% of women giving birth are morbidly obese (BMI>40)⁶⁰. The adverse consequences of obesity on maternal and perinatal health are well established⁶¹.

Gastric bypass surgery is an effective procedure used to achieve weight loss in people with morbid obesity. The most commonly performed surgery is a Roux-en-Y gastric bypass, which can be an open or laparoscopic procedure. It involves creating a small pouch from the stomach and reconnecting this to a section of the small intestine, bypassing the larger, remaining stomach. These anatomical changes reduce food intake and absorption, thereby inducing weight loss⁶². The increase in gastric bypass surgery amongst women of reproductive age has resulted in an increasing number of pregnancies following bypass surgery.

Several studies and reviews⁶¹⁻⁶³ have analysed pregnancy outcomes following bariatric surgery. Reports show that pregnancy following gastric bypass surgery is largely safe for both mother and child. Studies demonstrate a reduction in obesity-related gestational complications such as gestational diabetes and maternal hypertension. However, there appears to be conflicting results regarding the incidence of intrauterine growth restriction and mode of delivery following bariatric surgery⁶²⁻⁶⁵. Complications such as intestinal hernias, nutritional deficiencies^{63, 64} and birth defects⁶⁵ in pregnancies following gastric bypass surgery have also been cited. Studies conducted thus far emphasise the importance of appropriate monitoring and effective nutritional control, although this is not currently defined.

There is a need for robust evidence regarding how long to delay pregnancy following bariatric surgery. Due to the potential nutritional deficiencies and concomitant complications associated with rapid weight loss, current advice is to delay pregnancy for one year after bypass surgery^{61, 66}. However, studies have shown similar maternal and neonatal outcomes between patients who conceived during the first post-operative year, and those who conceived after^{61, 67}.

Case definition

Any woman with a confirmed ongoing pregnancy following gastric bypass surgery. Include all types of surgery (Roux-en-Y, duodenal switch, gastric sleeve or other).

Excluded: Any woman who had a gastric band.

Surveillance Period

April 2014 – March 2015

Interim Results and Conclusion

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

Investigators

Katie Cornthwaite, Dimitrios Siassakos, Judith Hyde, Tim Draycott, Andrew Johnson, Southmead Hospital, Bristol.

Funding

This study is funded by North Bristol NHS Trust.

4.3.9 Pregnancy at Advanced Maternal Age

Key points

- Pregnancies at advanced maternal age are becoming increasingly common in high income countries. In addition, 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 is collecting data to 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 40s⁶⁸.

Many studies have reported an association between advanced maternal age and adverse maternal and infant outcomes⁶⁹⁻⁷¹. 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. Carolan⁷² 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.

Surveillance Period

July 2013 – June 2014

Interim Results

Until the end of January 2014, 201 cases of advanced maternal age in pregnancy have been reported. Information has been received for 133 of these cases (66%). There were three duplicate cases reported, 13 did not meet the case definition and 16 were reported in error. Thus a total of 101 pregnancies in women with advanced maternal age were reported at the end of January 2014 in an estimated 468,992 maternities. This gives an estimated incidence in the UK of 21.5 per 100,000 maternities (95% CI 17.5 to 26.2 per 100,000 maternities).

Interim Conclusions

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

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).*



4.3.10 Prosthetic Heart Valves

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 is investigating the risks associated with an artificial heart valve in pregnancy and the effects of 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%⁷³) with a 2.9% case fatality rate⁷⁴. Thus, the need for effective anticoagulation is greater. Warfarin treatment throughout pregnancy appears to be associated with lowest risk of maternal thrombotic complications⁷⁴ but is associated with a higher fetal loss (estimates as high as 59%)⁷³, and can have damaging effects on the fetus⁷⁴. In contrast, unfractionated heparin or LMWH are safe for the fetus, but doubts have been expressed about their efficacy in preventing maternal thrombotic complications⁷⁵. 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 therapy⁷⁶. 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 e.g Starr-Edwards ball in cage, Bjork-Shiley tilting disc or St Jude's bi-leaflet valve.

Excluded: Women with a bioprosthetic valve e.g 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

Up to January 2014, 38 cases of pregnancy in women with mechanical prosthetic heart valves have been reported. Information has been received for 32 cases (84%) in an estimated 803,987 maternities. Of these, 21 are confirmed cases, one did not meet the case definition, seven were reported in error and there were three duplicate cases. The incidence of pregnancy in women with artificial mechanical prosthetic heart valves is estimated to be 2.6 per 100,000 maternities in the UK (95% CI 1.6 to 4.0 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

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.

4.3.11 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 is investigating the current incidence rate and aims to describe the management and outcomes of severe ITP in pregnancy in the UK.

Background

Primary Immune Thrombocytopenia (ITP) is an acquired immunological disorder characterised by an isolated low platelet count (thrombocytopenia) necessary for normal clotting function. It is defined as a blood peripheral platelet count of $<100 \times 10^9/l$ and the absence of any initiating or underlying cause such as antiphospholipid antibody syndrome, SLE or viral infections⁷⁷. 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^{78, 79}. ITP accounts for 3% of cases of thrombocytopenia in pregnancy⁷⁹.

Current treatment recommendations for ITP in pregnancy are largely based on clinical experience and expert consensus⁷⁷. There are no high quality prospective studies or randomised 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)⁷⁷. Without clear guidance or 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 $<50 \times 10^9/l$ 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.

Excluded: Women with secondary immune thrombocytopenia.

Surveillance Period

June 2013 – January 2015

Interim Results

Up to January 2014, 78 cases of ITP in pregnancy have been reported. Information has been received for 61 cases (78%). Of these, eight cases were reported in error, one set of case notes was reported lost and 12 did not meet the case definition. Thus, there are currently 40 known confirmed cases in an estimated 535,991 maternities. This gives an estimated incidence in the UK of 7.5 per 100,000 maternities (95% CI 5.3 to 10.2 per 100,000); however, this may be a significant underestimate as data collection is still incomplete.

Interim Conclusions

This study is not yet complete and it is not possible to draw any definitive conclusions at this stage.

Investigators

Angharad Care, Liverpool Women's Hospital;

Zarko Alfirevic, University of Liverpool/Liverpool Women's Hospital;

Marian Knight, NPEU.

Funding

The ITP Support Association.



4.4. Future studies

This study has been approved by the UKOSS Steering Committee to commence in 2014/15.

4.4.1 Vasa Praevia

Key points

- Vasa praevia carries no major risk to the mother but is associated with significant risk to the fetus.
- Currently routine screening for vasa praevia is not advised by the RCOG and is not supported by the National Screening Committee, on the basis of insufficient information on the case definition, natural history and epidemiology of the condition.
- There is also uncertainty on the accuracy and practical application of the best test to diagnose vasa praevia, and there is no agreed management pathway from women with confirmed vasa praevia and for women with some risk factors in the absence of vasa praevia.
- This study will estimate the incidence of vasa praevia in the UK over one year and examine the clinical management of the condition as well as maternal and neonatal outcomes.

Background

Vasa praevia (VP) describes fetal vessels coursing through the fetal membranes (amnion and chorion) over the internal cervical os and below the fetal presenting part, unprotected by placental tissue or the umbilical cord. Risk factors include bilobed placenta, accessory placental lobes, velamentous cord insertion, multiple pregnancy and in vitro fertilisation (IVF). Data are limited but the reported incidence varies between one in 2000 and one in 6000 pregnancies.

Vasa praevia carries no major risk to the mother but is associated with significant risk to the fetus. When the fetal membranes rupture, the unprotected fetal vessels are at risk of disruption with consequent fetal haemorrhage. Loss of relatively small amounts of blood can have major fetal implications because the fetus has a relatively small blood volume. Planned caesarean section before labour onset and before rupture of the fetal membranes has occurred is believed to prevent damage to the fragile fetal vessels, and antenatal diagnosis of vasa praevia with planned caesarean section near to term is reported to lead to survival rates of up to 97%⁸⁰. The incidence of undiagnosed and asymptomatic vasa praevia is unknown and has not been previously investigated in the UK.

Currently routine screening for vasa praevia is not advised by the RCOG guideline on management of placenta praevia, and is not supported by the National Screening Committee⁸¹. This is because “there is insufficient information on the case definition, natural history and epidemiology of the condition”. There is also uncertainty on the accuracy and practical application of the best test to diagnose vasa praevia, and there is no agreed management pathway from women with confirmed vasa praevia and for women with some risk factors in the absence of vasa praevia. This study will estimate the incidence of vasa praevia in the UK over one year and examine the clinical management of the condition as well as maternal and neonatal outcomes.

Case definition

Any woman in the UK with at least one of the following:

1. Suspected VP on antenatal U/S >18 weeks gestation, and confirmed VP on antenatal U/S >31 weeks gestation (if not delivered prior to 31 weeks).
2. Palpation or visualisation of the fetal vessels during labour.
3. Rupture of membranes with bleeding associated with fetal death/exsanguination or severe neonatal anaemia.
4. Antenatal or intrapartum bleeding of fetal origin with pathologic CTG and/or positive Apt test.
5. VP documented in medical records as reason for admission and caesarean section.

AND at least one of:

6. Clinical examination of the placenta confirming intact or ruptured velamentous vessels. These may be a velamentous insertion of the umbilical cord or exposed fetal vessels between placental lobes.
7. Pathological confirmation of vasa praevia.
8. Torn umbilical cord or placenta (hence unable to provide placental examination).

Main Research questions

- What is the incidence of diagnosed/symptomatic vasa praevia in the UK over one year?
- What are the risk factors for vasa praevia comparing prospectively collected cases with UKOSS historical controls?
- How is the pregnancy managed following the diagnosis of vasa praevia (diagnosed (i) antenatally and (ii) intrapartum)?
- What are the maternal and neonatal outcomes of pregnancies complicated by vasa praevia (diagnosed (i) antenatally and (ii) intrapartum)?

Investigators

George Attilakos, UCLH;

Anna David, Institute for Women's Health UCL;

Peter Brocklehurst, Institute for Women's Health UCL.

Funding

This study has been funded by the UCLH NIHR Research Capability Fund.

5. Publications

5.1. Association of severe intrahepatic cholestasis of pregnancy with adverse outcomes: a prospective population-based case-control study

Published Article

Geenes V, Chappell LC, Seed PT, Steer PJ, Knight M, Williamson C. (2014). Association of severe Intrahepatic cholestasis of pregnancy with adverse pregnancy outcomes: A prospective population-based case-control study. *Hepatology*. 2014 Apr;59(4):1482-91.⁸²

Key points

- Previous retrospective case series have suggested that intrahepatic cholestasis of pregnancy (ICP) is associated with adverse fetal outcomes, but there have been concerns over possible biases in these studies.
- The aim of this study was to describe the pregnancy complications in a national cohort of women with severe ICP and to compare these with pregnancy complications in a cohort of unaffected women and with national rates where available.
- 713 confirmed cases of severe ICP were identified, giving an estimated incidence of 9.2 cases per 10,000 maternities.
- Women with a singleton pregnancy affected by severe ICP (n=669) had increased odds of preterm delivery (adjusted odds ratio (aOR) 5.39, 95% CI 4.17 to 6.98), neonatal unit admission (aOR 2.68, 95% CI 1.97 to 3.65) and stillbirth (aOR 2.58, 95% CI 1.03 to 6.49) compared to control women, and these risks rose with increasing maternal serum bile acid concentrations.
- Seven of the ten stillbirths in ICP cases were associated with co-existing pregnancy complications.
- The risks of preterm delivery (both spontaneous and iatrogenic) and stillbirth were also raised when compared with national data.
- These findings support the case for close antenatal monitoring of pregnancies affected by severe ICP.

5.2. Ethnic variations in severe maternal morbidity in the UK – a case-control study

Published Article

Nair M, Kurinczuk JJ, Knight M. (2014) Ethnic variations in severe maternal morbidity in the UK – a case-control study. *PLoS One*. 2014 Apr; 9(4): p. e95086.⁸³

Key points

- Previous studies showed a higher risk of maternal morbidity amongst black and other minority ethnic (BME) groups, but were unable to investigate whether this excess risk was concentrated within specific BME groups in the UK. This study analysed the specific risks and investigated reasons for any disparity.
- Cases included in this analysis were women who were reported from previous UKOSS studies to have one of the following ten conditions of severe maternal morbidity: antenatal pulmonary embolism, eclampsia, acute fatty liver of pregnancy (AFLP), amniotic fluid embolism (AFE), peripartum hysterectomy, stroke in pregnancy, uterine rupture, placenta accreta, HELLP syndrome and severe sepsis.
- The study demonstrated a significantly higher risk of severe morbidity among women belonging to the Pakistani (adjusted odds ratio (aOR)=1.43; 95% CI=1.07 to 1.92), Bangladeshi (aOR=1.74; 95% CI=1.05 to 2.88), black Caribbean (aOR=1.80; 95% CI=1.14 to 2.82), black African (aOR=1.83; 95% CI=1.39 to 2.40) and other non-white (non-Asian) ethnic minority groups (aOR=1.56; 95% CI=1.05 to 2.33) compared with white European women.

- Factors including inadequate utilisation of ANC, parity, smoking, pre-existing medical problems and age explained only a small part of this increased risk.
- Compared with white European women, the odds of inadequate utilisation of ANC services were higher among black African (OR=4.46; 95% CI=1.47 to 11.48) and Caribbean (OR=4.35; 95% CI=0.49 to 18.19) women.
- As the population of ethnic minority groups in the UK continue to increase, it is important to focus on these ethnic disparities and investigate the possible pathways for prevention of severe maternal morbidity among BME groups.

5.3. Risk factors, management and outcomes of HELLP and ELLP Syndromes

Published Article

Fitzpatrick KE, Hinshaw K, Kurinczuk JJ, Knight M. (2014) Risk factors, management, and outcomes of hemolysis, elevated liver enzymes, and low platelets syndrome and elevated liver enzymes, low platelets syndrome. *Obstet. Gynecol.* 2014 Mar;123(3):618-27.⁸⁴

Key points

- HELLP and ELLP syndromes are serious but uncommon pregnancy complications. Several management questions remain to be addressed, including the timing of delivery in women developing HELLP/ELLP preterm.
- The aim of this study was to use UKOSS to conduct a national, case-control study of HELLP/ELLP to investigate risk factors, management and outcomes.
- 129 women with HELLP and 81 women with ELLP were identified between June 2011 and May 2012.
- Women with HELLP were more likely to be older, (aOR 1.9, 95%CI 1.1 to 3.1), nulliparous (aOR=4.2, 95%CI 2.5 to 7.0), have had a previous gestational hypertensive disorder (aOR=3.5, 95%CI 1.5 to 8.1), and have a multiple pregnancy (aOR=4.5, 95%CI 1.5 to 14.1) than control women.
- 138 women (66%) were diagnosed antenatally with HELLP/ELLP; 51% had planned management of immediate delivery and 43% had delivery planned within 48 hours. Only seven women (5%) had planned expectant (conservative) management.
- Women with HELLP syndrome were more likely than women with ELLP syndrome to have a blood transfusion (46% vs 21%, p<0.001) and to have additional severe morbidity (13% vs 1%, p=0.003).
- There were no significant differences in outcomes (blood transfusion, intensive care unit admission, additional severe maternal morbidity or major infant complications) between women with planned immediate delivery and those with planned delivery within 48 hours.
- This suggests that a short delay in delivery, of up to 48 hours, may be considered when monitoring is reassuring and there are good clinical reasons for a delay, such as to allow administration of corticosteroids for fetal lung maturation.

5.4. Pregnancy outcomes in liver and cardiothoracic transplant recipients: a UK National Cohort Study

Published Article

Mohamed-Ahmed O, Nelson-Piercy C, Bramham K, Gao H, Kurinczuk JJ, Brocklehurst P, Knight M. (2014) Pregnancy Outcomes in Liver and Cardiothoracic Transplant Recipients: A UK National Cohort Study. *PLoS One.* 2014 Feb 19;9(2):e89151.⁸⁵

Key points

- The majority of studies reporting outcomes in transplant recipients have focused on women with kidney transplants, and have included retrospective, voluntary registries or single centre studies.
- The aim of this study was to use UKOSS to conduct a national, prospective cohort study of pregnancy outcomes in liver and cardiothoracic transplant recipients.

- There were 62 pregnancies in 56 liver transplant recipients and 14 pregnancies in 14 cardiothoracic transplant recipients (including 10 heart, three lung and one heart-lung recipient) between January 2007 and January 2012.
- Liver transplant recipients, in comparison to cardiothoracic, had similar livebirth rates (92% vs. 87%) but better fetal outcomes (median gestational age 38 weeks vs. 35 weeks; median birthweight 2698g vs. 2365g), fewer caesarean deliveries (47% vs. 62%), fewer maternal intensive care (ICU) admissions (19% vs. 29%) and fewer neonatal ICU admissions (25% vs. 54%).
- Nine women (12%) were taking mycophenolate mofetil at conception, which was associated with adverse fetal outcomes.
- This study shows that pregnancy in transplant recipients may have successful outcomes, but complication rates are high, emphasising the role of pre-conception counselling and further research into the long-term effects on maternal and graft survival rates.

5.5. The management and outcomes of placenta accreta/increta/percreta in the UK: a population-based descriptive study

Published Article

Fitzpatrick KE, Sellers S, Spark P, Kurinczuk JJ, Brocklehurst P, Knight M. (2014) The management and outcomes of placenta accreta, increta, and percreta in the UK: a population-based descriptive study. *BJOG*. 2014 Jan; 121(1):62-70.⁸⁶

Key points

- Placenta accreta/increta/percreta is thought to be becoming more common, however, there are limited data to guide evidence-based management.
- The aim of this study was to describe the management and outcomes of the condition in a national cohort.
- 134 women with placenta accreta/increta/percreta were identified, in 50% of whom (66/133) the condition was suspected antenatally.
- In women with a final diagnosis of placenta increta or percreta, antenatal diagnosis is associated with reduced levels of haemorrhage (median blood loss 2750ml versus 6100ml, $p=0.008$) and a reduced need for blood transfusion (59% versus 94%, $p=0.014$).
- Women diagnosed antenatally were more likely to receive preventive therapies for haemorrhage.
- Women in whom no attempt was made to remove the placenta, either prior to hysterectomy or prior to conservative management, had lower estimated blood loss (median 1750ml versus 3700ml, $p=0.001$) and fewer received a blood transfusion (57% versus 86%, $p < 0.001$) than women in whom an attempt was made to remove the placenta.
- These findings support current RCOG and other guidelines which recommend that, in the presence of accreta/increta/percreta, if the placenta fails to separate, no attempt is made to remove it prior to a planned attempt at uterine conservation or hysterectomy.

5.6. The UK Obstetric Surveillance System: impact on patient safety

Published Article

Knight M, Lindquist A. (2013) The UK Obstetric Surveillance System: Impact on Patient Safety. *Best Practice & Research Clinical Obstetrics & Gynaecology*. 27(4): 621-630.¹

Key points

- This study summarises the contributions made by UKOSS in generating high-quality evidence on risk factors and clinical management of rare complications of pregnancy and childbirth since its inception in 2005.
- Data collected using UKOSS have been used to address a range of patient safety issues both at local and national levels including safety of different treatment options and have been found to provide the next best level of evidence in situations where randomised-controlled trials are challenging.

- Information collected through UKOSS and other such routine surveillance systems can be used as an aid for service planning, to track quality improvement initiatives, as a benchmark against which hospital level disease incidence and outcomes can be compared, to inform and audit national guidelines, and to monitor the effect of changes in practice or policy.
- Studies can be introduced rapidly in response to newly arising safety concerns.
- Ongoing surveillance is needed to establish whether recommendations from UKOSS studies continue to result in improved outcomes and patient safety.

5.7. Variation in severe maternal morbidity according to socioeconomic position: a UK national cohort study

Published Article

Lindquist A, Knight M, Kurinczuk JJ. (2013) Variation in severe maternal morbidity according to socioeconomic position: a UK national case-control study. *BMJ Open*. 2013 Jun 20;3(6). pii: e002742.⁸⁷

Key points

- The aim of this study was to investigate the independent risk of severe maternal morbidity associated with socioeconomic position (defined by occupation) in the UK.
- The study used data from six UKOSS studies in a secondary analysis of AFE, AFLP, eclampsia, peripartum hysterectomy, therapies for peripartum haemorrhage and uterine rupture.
- The findings show that women from the lowest socioeconomic group were 1.22 times (95% CI 0.92 to 1.61) more likely to experience severe maternal morbidity compared with women from the highest group after accounting for other known risk factors.
- The findings suggest that there might be an independent association between socioeconomic position and severe maternal morbidity in the UK, but further studies are required to confirm and investigate the reasons for this association in a country where healthcare is universal and free at the point of access.

5.8. Abstracts

The following abstracts were submitted/ presented at meetings in 2013:

- Management and Outcomes of HELLP Syndrome in the UK. British Maternal and Fetal Medicine 16th Annual Conference, April 2013.
- Conditions triggering local incidence reviews in UK hospital maternity units. British Maternal and Fetal Medicine 16th Annual Conference, April 2013.
- Incidence, causes and outcomes of severe maternal sepsis morbidity in the UK. British Maternal and Fetal Medicine 16th Annual Conference, April 2013.
- Ethnic variations in severe maternal morbidity in the UK – a national study. Global Women's Research Conference 2013.

5.9. UKOSS Publications to date

2005

Knight M, Kurinczuk JJ, Tuffnell D, Brocklehurst P. (2005). "The UK Obstetric Surveillance System for rare disorders of pregnancy." *BJOG* 112(3): 263-265.

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2008

Knight M, Kurinczuk JJ, Spark P, Brocklehurst P. (2008). "Caesarean delivery and peripartum hysterectomy." *Obstet Gynecol* 111(1): 97-105.

Knight M, Nelson-Piercy C, Kurinczuk JJ, Spark P, Brocklehurst P. (2008). "A prospective national study of acute fatty liver of pregnancy in the UK." *Gut* 57(7): 951-956.

Knight M on behalf of UKOSS (2008). "Antenatal pulmonary embolism: risk factors, management and outcomes." *BJOG* 115(4): 453-461.

2009

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Kayem G, Kurinczuk JJ, Alfirevic Z, Spark P, Brocklehurst P, Knight M. (2011). "Uterine compression sutures for the management of severe postpartum hemorrhage." *Obstet Gynecol* 117(1): 14-20.

Knight M, Pierce M, Seppelt I, Kurinczuk JJ, Spark P, Brocklehurst P, McLintock C, Sullivan E. (2011). "Critical illness with AH1N1v influenza in pregnancy: a comparison of two population-based cohorts." *BJOG* 118(2): 232-239.

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6. Acknowledgements

These studies would not have been possible without the contribution and enthusiasm of the UKOSS reporting clinicians who notified cases and completed the data collection forms; we are very grateful for their contribution.

Funding

This is an independent report from studies which are part-funded by the Policy Research Programme in the Department of Health. The views expressed are not necessarily those of the Department. Studies are additionally funded by Wellbeing of Women, the Obstetric Anaesthetists Association (OAA), North Bristol NHS Trust, ITP Support, UCLH Research Capability Fund, The Lauren Page Trust and SPARKS.

*These sections of the report present independent research funded by the National Institute for Health Research (NIHR) under its Programme Grants for Applied Research Programme (Programme Grant RP-PG-0608-10038). The views expressed are those of the author(s) and not necessarily those of the NHS, NIHR or the Department of Health.

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