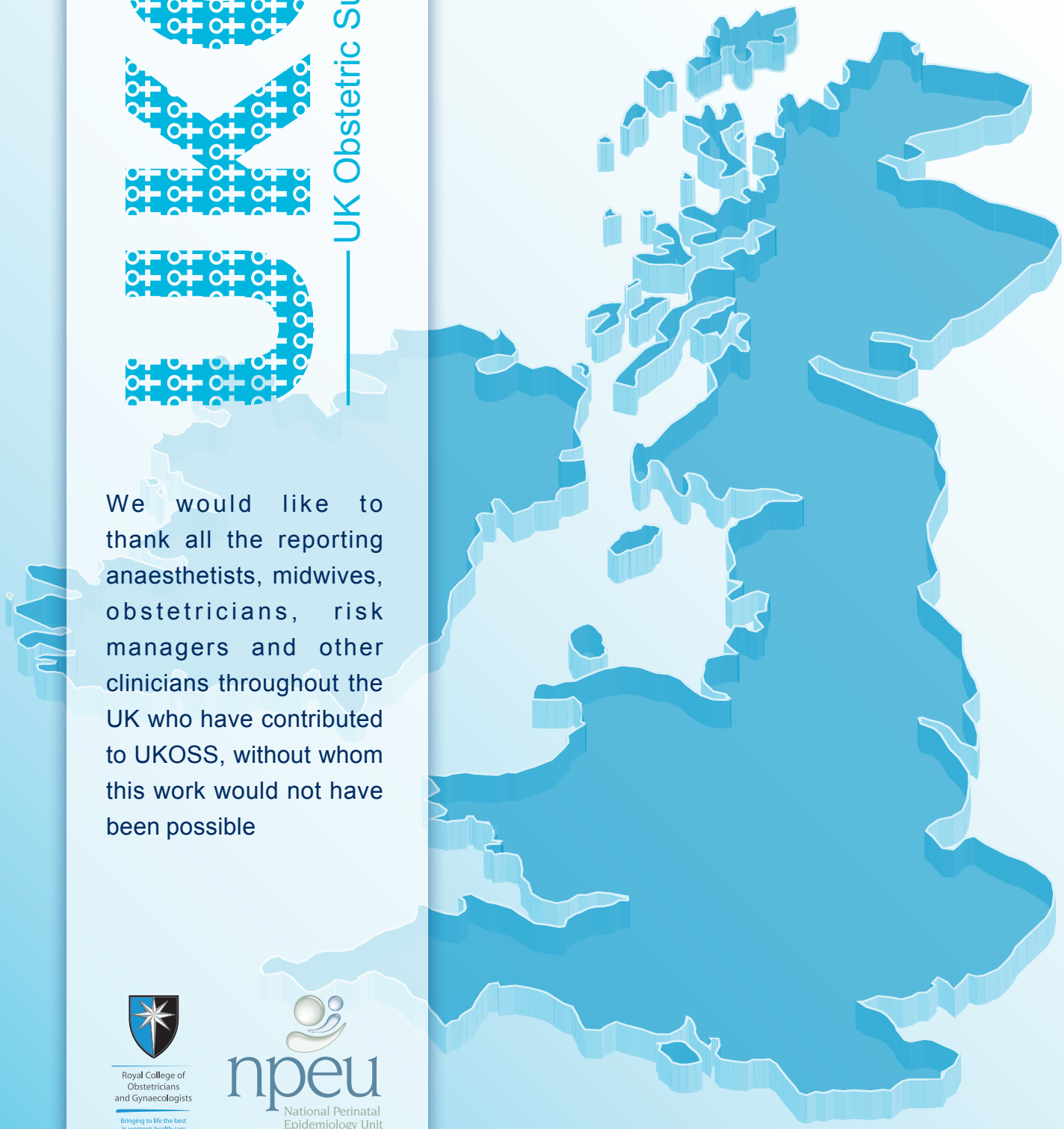
UKOSS

UK Obstetric Surveillance System

Eleventh Annual Report 2017



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
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National Perinatal Epidemiology Unit

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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 UK. UKOSS 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 Public Health England.

In the UK, where maternal death is rare, UKOSS provides a 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 data (1). Since its inception, UKOSS has successfully generated evidence to guide prevention and management of major obstetric complications, inform policy, service planning and address patient safety issues and emerging public health issues (1-7). This has encouraged Australia, New Zealand and several countries in Europe to establish similar systems (8).

Studies using UKOSS may be undertaken by any investigator who identifies a suitable topic and secures funding (9). 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. This report outlines the studies undertaken during the twelfth year of surveillance using UKOSS.

2. Methods

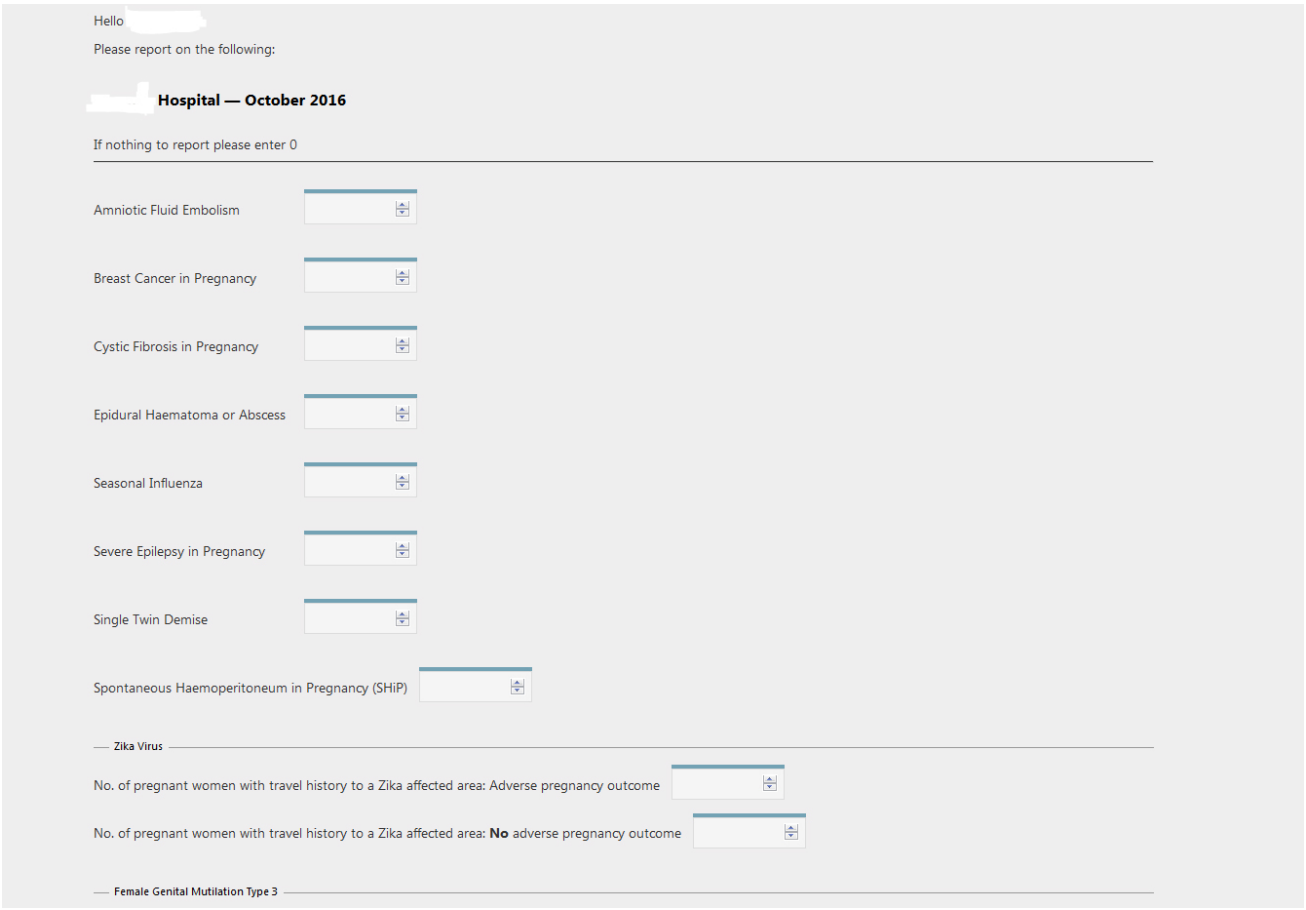
Whereas in the past a card returned by post was used for notification the programme is now maintained through online report submission requested from all consultant-led obstetric units in the UK every month with an approach of 'nil-reporting'. We anticipate that all women who experience a condition investigated through UKOSS will be admitted to a consultant-led unit even if their initial care is provided in a different maternity setting. Nominated clinicians (from anaesthetists, midwives and obstetricians to risk managers and data analysts) in each hospital with a consultant-led maternity unit in the UK report to UKOSS. Every month, the nominated individuals are sent a report request email containing a unique link to an online report submission page 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 complete the box with '0'. 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 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 about 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, hospital or NHS 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 has Research Ethics Committee approval.

In order to perform case-control or cohort studies, information is also collected about 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.

Figure 1: UKOSS Electronic Report Submission Page

This has replaced the original postcard notification system.



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

1. Estimating disease incidence
    - Analysis of the UKOSS severe sepsis study showed that the incidence of confirmed severe maternal Group B streptococcal sepsis was very low(12).
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/m^2 or greater) (13).
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 delivery (6).
    - UKOSS surveillance also showed that women with prior caesarean delivery and placenta praevia diagnosed antenatally had an increased odds of having placenta accreta/increta/percreta (14).
    - UKOSS surveillance of 2009/H1N1 influenza showed a significant association with poor pregnancy outcomes (15).
4. Investigating different management techniques
    - 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 were found (1, 2).
5. Investigating disease progression
    - A comparison of the characteristics of women who died identified through the MBRRACE-UK Confidential Enquiry into Maternal Death with UKOSS data on control women showed that 66% of the increased risk of maternal death from direct and indirect causes at the population level could be attributed to medical comorbidities(16).
6. Auditing of national guidelines
    - UKOSS surveillance of antenatal pulmonary embolism (PE) showed that very few women who had a PE were not receiving thromboprophylaxis according to Royal College of Obstetricians and Gynaecologists guidelines (17, 18).
7. Responding to emerging public health issues
    - Surveillance of ZIKV associated adverse pregnancy outcomes was rapidly instituted in 2016 in response to the WHO declaration of a global public health emergency (19).
8. Informing public health policy
    - UKOSS study showing poor perinatal outcomes in pregnant women with 2009/H1N1 influenza (15) was used as evidence to recommend universal immunisation of pregnant women against seasonal influenza (20).

3. Participation

All 199 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 report rate during 2016 was 88% (Figure 2), with regional return rates varying between 79% and 97% (Figure 3). These report return rates continue the high rates obtained during the first ten 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 2016

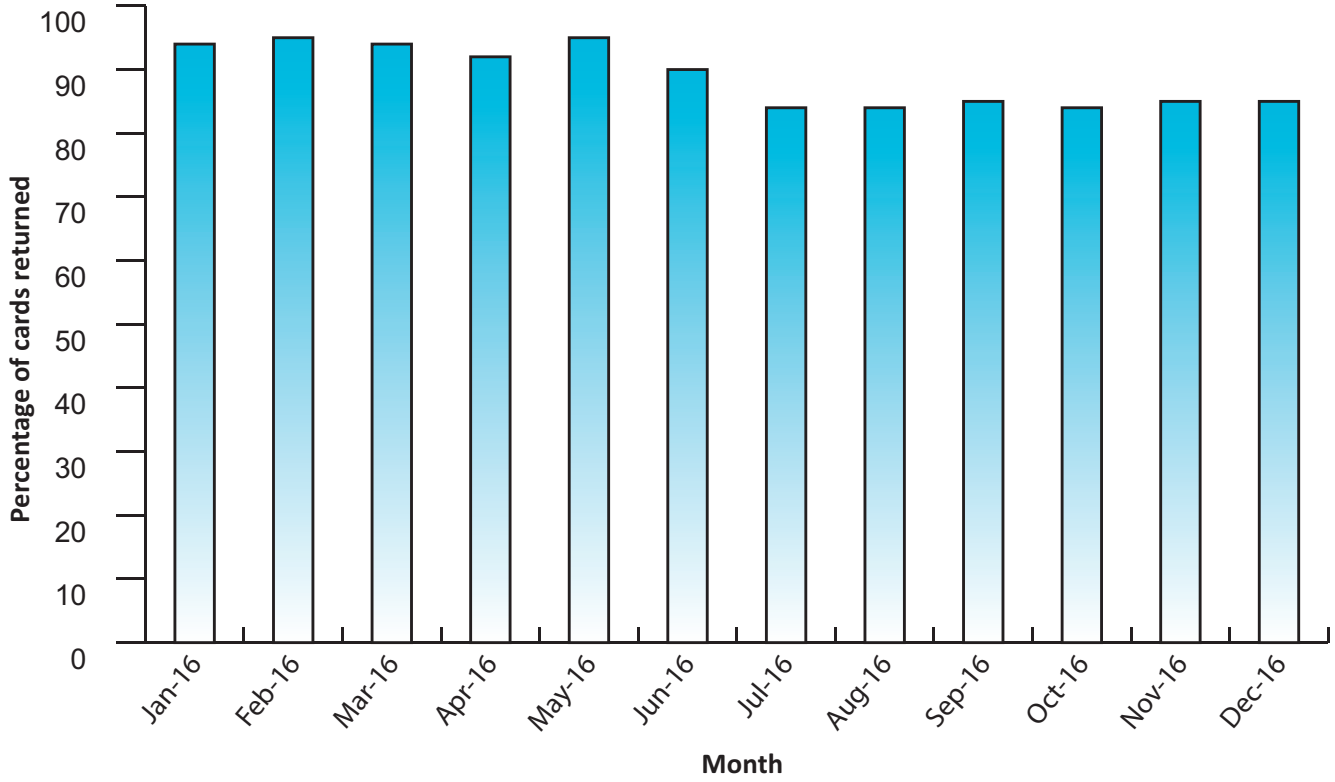
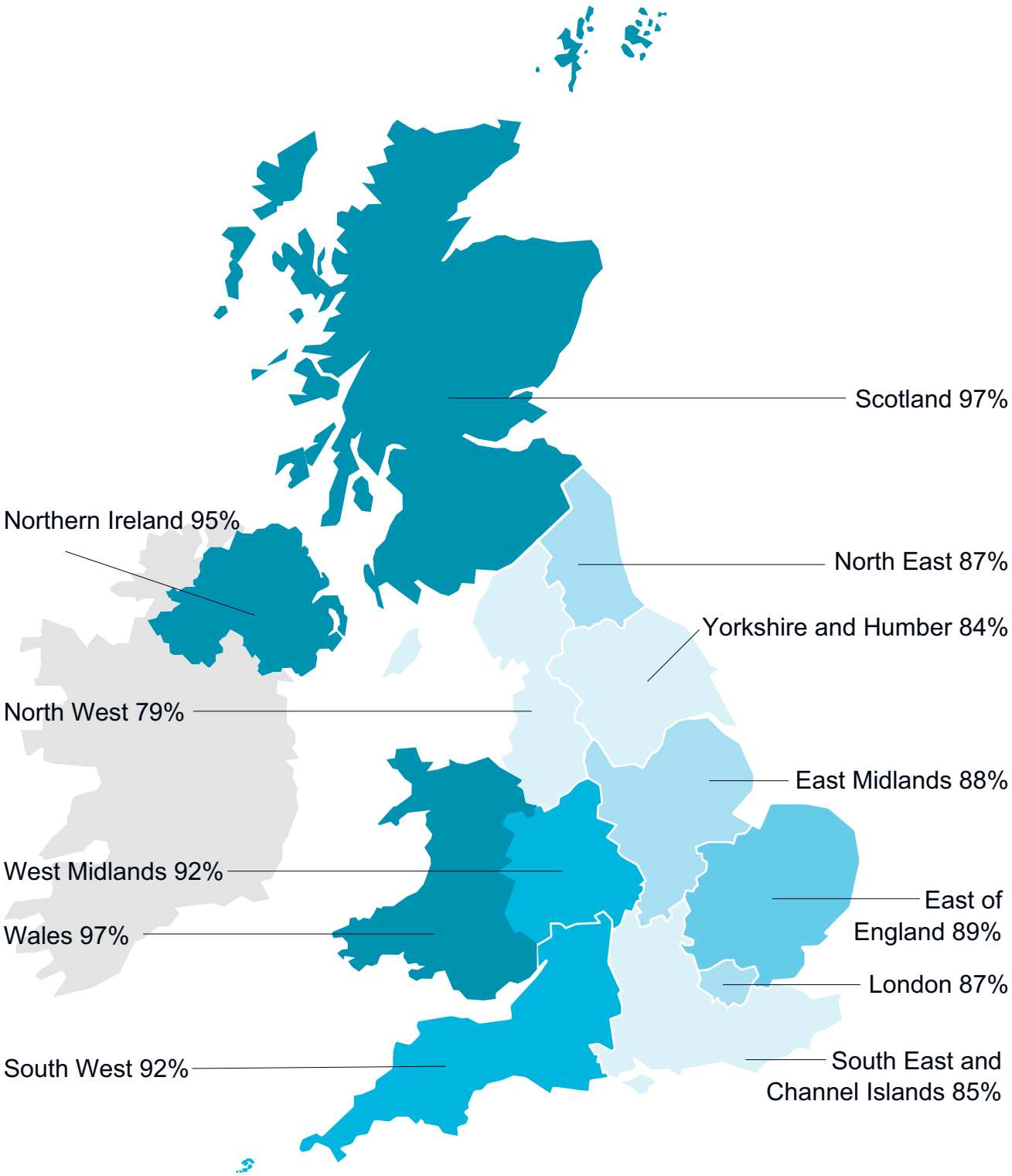


Figure 3: Map showing regional card return rates during 2016

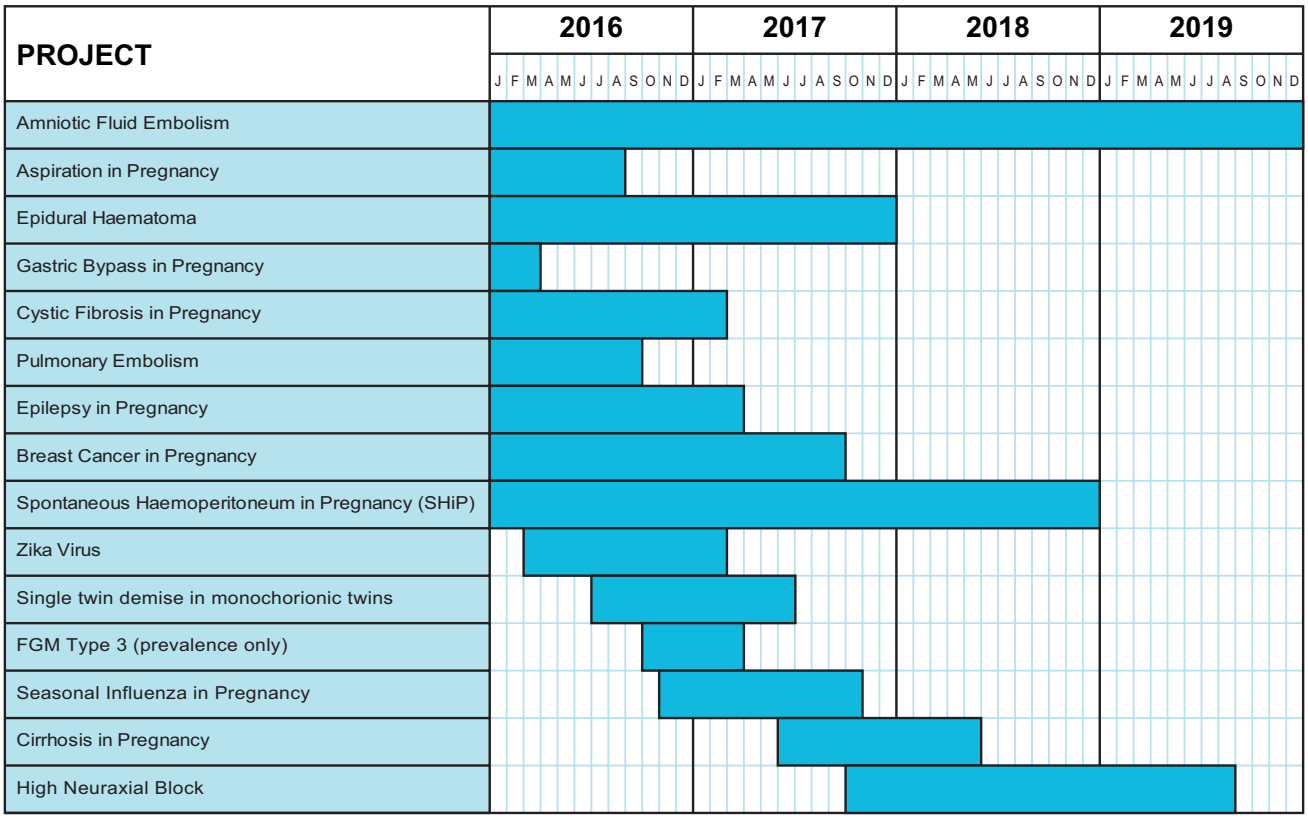


4. Studies

Unless otherwise specified, the results included in this report represent analysis of cases reported and data available up to February 2017. Please note the data presented are provisional (unless specified), not peer reviewed and definitive conclusions should not be drawn from them.

4.1 Study Timetable

Figure 4: Provisional UKOSS Study Data Collection Timetable 2016-2019



4.2 Studies completed in 2016

4.2.1 Pulmorary 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 recent change to policy on oral intake will impact on the incidence of maternal aspiration.
- The aim of this study was to estimate the incidence of maternal aspiration in the UK, 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 (21, 22). 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 management (23). The factors increasing the risk of aspiration associated with pregnancy include the gravid uterus, progesterone-mediated lower oesophageal sphincter relaxation, lower gastric pH and delayed gastric emptying during labour (24). 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 (25, 26). 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" (27). It is not clear whether the change to policy on oral intake has impacted on the frequency of maternal aspiration. In addition to a potential increased risk in association with changes in oral intake policy, other known risk factors for aspiration, for example obesity, are becoming more common in the pregnant population. There are thus concerns that maternal aspiration and the consequent risks of severe maternal morbidity and mortality may become an increasing problem in the UK obstetric population. Balanced against this is the increasing use of airway devices, for example second generation supraglottic airway devices, which may protect more effectively against aspiration in the emergency situation than classic devices (23).

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 (e.g. vomiting after induction of anaesthesia or gastric contents seen in the oropharynx).

AND

- Symptoms/signs of respiratory compromise requiring supplementary oxygen and antibiotics or level 2 or level 3 (HDU or ITU) respiratory support, in the absence of any other clear cause.

Classical radiological findings may or may not be present.

Surveillance Period

September 2013 – August 2016

Interim Results

There were 12 confirmed cases of aspiration in an estimated 2,245,080 maternities, representing an incidence of 5.6 per 1,000,000 maternities (95% CI 2.8-9.3). Nine cases (75%) occurred in association with general anaesthesia (GA); an estimated 1.9 per 10,000 GAs (95% CI 0.9-3.6), based on an estimated 16,000 obstetric GAs in the UK annually (28). Three cases occurred when the woman was semi-conscious for other reasons. Seven of the 9 women who were undergoing general anaesthesia received prior antacid prophylaxis (78%); 7 of 9 (78%) were known to have had fluid intake within the preceding 6 hours. Seven of 11 women who underwent radiological investigation (63%) showed X-ray signs consistent with aspiration. One woman died (case fatality 8%).

Interim Conclusions

- Gastric aspiration in pregnancy or immediately postpartum in the UK is extremely rare. Reassuringly, there does not appear to be a substantial number of cases associated with oral intake in labour following the change in policy.

Investigators

Marian Knight, Manisha Nair, Alice Gooda, Jenny Kurinczuk, NPEU;
David Bogod, Nottingham City Hospital;
Audrey Quinn, Leeds General Infirmary;
D Nuala Lucas, Northwick Park Hospital.

Funding

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

4.2.2 Gastric Bypass in Pregnancy

Key points

- Obesity is associated with significant maternal and fetal complications during pregnancy and birth.
- Gastric bypass surgery is increasingly being 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 rising dramatically 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)(29). The adverse consequences of obesity on maternal and perinatal health are well established (30).

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 carried out as 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 loss (31). 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 reviews (30-32) 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 surgery (31-34). Complications such as intestinal hernias, nutritional deficiencies (32, 33) and birth defects (34) 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 1 year after bypass surgery (30, 35). However, studies have shown similar maternal and neonatal outcomes between patients who conceived during the first post-operative year, and those who conceived later (30, 36).

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 2016

Results

After exclusion of duplicate cases, 211 pregnant women met the inclusion criteria. This suggests a UK prevalence rate for women pregnant following gastric bypass surgery of approximately 13.7 per 100,000 maternities based on 768,162 UK maternities in 2015. This compares with a UK prevalence rate of 18.0 per 100,000 maternities for women pregnant with a gastric band in 2012.

In this cohort, 63% of women were classified as obese at booking, with 13% classified as extremely obese. The majority of women had Roux-en-Y bypass surgery (n=69, 32.7%), although type of bypass surgery was unknown in 97 women (46%). 30 women (14.2%) conceived within 1 year of surgery (surgery to conception interval unknown in 14 cases).

60% (n=127) of women received dietary advice during pregnancy and 88% (n=185) were given dietary supplements. However, only 39.8% (n=84) of women had a dietician involved in their care and 33% (n=70), an endocrinologist. 89% (n=187) of women had a third trimester ultrasound and 62% (n=131) were screened for gestational diabetes.

Twenty women (9%) experienced surgical complications during pregnancy. One woman died and one baby was stillborn.

Preliminary Conclusions

This preliminary analysis shows that pregnancies following gastric bypass surgery are uncommon but high risk. Despite bypass surgery, rates of obesity in pregnancy remain high. Moreover, there is an appreciable risk of surgical complications during pregnancy, with one woman dying as a result in this cohort. Management appears to vary and involvement of multi-professional specialists is inconsistent. Although current advice is to delay pregnancy for at least 1 year after surgery, a number of women conceived within a year of surgery.

It is not possible to draw any more definitive conclusions at this stage. Further analysis is needed to assess if there are any differences in outcomes with time-period between surgery and conception. Comparisons will also be made with pregnancies following gastric banding.

Investigators

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

Funding

This study is funded by North Bristol NHS Trust.

North Bristol NHS Trust

4.2.3 Pulmonary Embolism (DiPEP)

Key points

- Thromboembolic disease, including pulmonary embolism (PE) is the current leading cause of direct maternal mortality in the UK.
- The investigations used to diagnose PE carry risks of radiation exposure, reaction to contrast media and false positive diagnosis, are inconvenient for patients and incur costs for the health services.
- This study forms a part of a larger study (DiPEP) aiming to estimate the diagnostic accuracy, effectiveness and cost-effectiveness of strategies for selecting pregnant or postpartum women with suspected PE for imaging.

Background

Thromboembolic disease, including pulmonary embolism (PE) has been identified as the leading cause of direct maternal mortality in the UK (37), but can be difficult to diagnose. Pregnant and postpartum women with appropriately diagnosed and treated PE have a low risk of adverse outcomes, so accurate diagnosis can result in substantial benefits. However, the investigations used to diagnose PE (diagnostic imaging with VQ scanning or CT pulmonary angiography) carry risks of radiation exposure, reaction to contrast media and false positive diagnosis, are inconvenient for patients and incur costs for the health services. Clinicians therefore face a difficult choice when deciding how to investigate suspected PE in pregnant and postpartum women, between risking the potentially catastrophic consequences of missed diagnosis if imaging is withheld and risking iatrogenic harm to women without PE if imaging is over-used.

Current practice

Guidelines from the RCOG (38) recommend that pregnant or postpartum women with suspected PE should all receive diagnostic imaging. Current data suggest that use of this unselective approach is resulting in a low prevalence of PE among those investigated. The most recent studies of suspected PE in pregnancy report prevalence of between 1.4 and 4.2%, while audit data from Sheffield Teaching Hospitals NHS Foundation Trust show a prevalence of 2% among those undergoing imaging. We therefore appear to be exposing 50 women (and fetuses in pregnant women) to the risks of diagnostic imaging for every one woman who actually has PE.

These recommendations for pregnant and postpartum women contrast with National Institute for Health and Care Excellence (NICE) guidelines for the general (non-pregnant) population with suspected PE, for whom diagnostic imaging is selectively used based upon structured clinical assessment and D-dimer measurement (39).

Case definition

EITHER	PE is confirmed using suitable imaging (angiography, computed tomography, echocardiography, magnetic resonance imaging or ventilation-perfusion scan)
OR	PE is confirmed at surgery or post-mortem
OR	a clinician has made a diagnosis of PE with signs and symptoms consistent with PE present, and the patient has received a course of anticoagulation therapy (>1 week)

Surveillance period

March 2015 – September 2016

Interim Results

165 women with confirmed PE were identified over a 19-month period through UKOSS, an estimated incidence of 1.4 per 10,000 maternities (95% CI 1.2-1.6). The incidence of PE did not differ significantly from the incidence in 2005-6 (p=0.531). 9 of the women with confirmed PE died, a case fatality of 5.5% (95% CI 2.5-10.1). D-dimers were measured in 49 women with confirmed PE (30%), with a median level of 1437ng/mL, range 200-20000. A clinical decision rule has been developed assessing the following elements for inclusion: age, BMI, past medical and family history, current symptoms, signs, ECG and chest x-ray abnormalities and D-dimer levels.

Conclusions

This is the largest and most comprehensive study to date of diagnostic methods to select pregnant or post-partum women with suspected PE for imaging. Further work is underway to investigate the new and existing clinical decision rules.

Investigators

Steve Goodacre, Matt Stevenson, Michael Campbell, Judith Cohen, Fiona Elizabeth Lecky, University of Sheffield; Beverley J Hunt, Catherin Nelson-Piercy, Guy's and St. Thomas' NHS Foundation Trust; Wee-Shian Chan, BC Women's Hospital and Health Care, Canada; Steven Thomas, Sheffield Teaching Hospitals NHS Foundation Trust; Marian Knight, NPEU.

Funding

This study has been funded by NIHR HTA.

4.3 Studies in progress

4.3.1 Amniotic Fluid Embolism

Key points

- Amniotic fluid embolism (AFE) is a leading cause of direct maternal mortality in the UK; however estimates of incidence and mortality vary widely.
- AFE is associated with older maternal age, multiple pregnancy, placenta praevia, induction of labour, instrumental vaginal and caesarean delivery in the UK population.
- There is no evidence of an increase in incidence over the nine years of UKOSS surveillance.
- Further investigation is needed to establish whether earlier treatments can reverse the cascade of deterioration leading to severe outcomes.
- This study forms part of a wider multi-country study using the International Network of Obstetric Surveillance Systems (INOSS).

Background

AFE remains one of the leading causes of direct maternal mortality in high-income countries. Estimates of incidence vary from 1.9 to 7.7 per 100,000 maternities. Estimates of the case fatality of this condition also vary widely from 11% to 43%. There is also little consistency in the factors reported to be associated with the occurrence of AFE and very limited data regarding factors associated with severe outcomes.

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

Up to April 2017, 246 cases were reported. Information has been received for 235 of these (96%). Of these, 22 do not meet the case definition, 36 were subsequently reported by clinicians as not cases, 14 were found to be duplicates and the hospital notes for one were reported as lost.

Interim Conclusions

Following analysis of cases reported up to January 2014, the results of which were published in 2015, further investigation is needed to establish whether earlier treatments can reverse the cascade of deterioration leading to severe outcomes. A multi-country analysis will be conducted during 2018.

Investigators

Kate Fitzpatrick, Marian Knight, NPEU;

Derek Tuffnell, Bradford Teaching Hospitals NHS Foundation Trust.

Funding

Wellbeing of Women have funded this multi-country study.

4.3.2 Breast Cancer in Pregnancy

Key Points

- The diagnosis of breast cancer in pregnancy can have devastating consequences for women and their families.
- Treatment regimens vary and we do not know either the incidence of newly diagnosed breast cancer in pregnancy or the short-term outcomes for women and their babies.
- Little is known about what choices women make when continuing with pregnancy.
- The knowledge gained from this study will enable further study of all breast cancer in pregnancy and longer term outcomes in the UK.

Background

The actual incidence of breast cancer in pregnancy in the UK is not known. Estimates from other countries range from 2.4 to 7.8 cases per 100,000 births. This gives an estimated 18 to 61 cases per year in the UK. We are seeing women with a history of breast cancer now becoming pregnant as survival rates increase, but surveillance of this would form a further study in the future.

Although the incidence of breast cancer rises with age, the observation that many women are delaying their families until later in life means that the incidence of breast cancer arising for the first time in pregnancy may be rising. At the other end of the scale, for women under 30, a significant proportion (more than 10%) of breast cancers may be associated with pregnancy, or within a year afterwards.

The diagnosis of breast cancer in pregnant women may be difficult (40) and there is a potential for under-treatment of the mother and iatrogenic prematurity for the fetus. Due to its relative rarity, we lack a standardised approach to managing these women. There is also an apparent contradiction between advice in Europe in general (41) and UK specific advice from the RCOG about the timing of interventions and delivery (42). A group in Australia and New Zealand are conducting a similar study, which will make comparisons hugely informative (43).

It is clear that such cases should be managed within a multidisciplinary team within established cancer networks, in close liaison with obstetric and paediatric teams. Treatment is influenced by a number of factors, including histological grade, receptor and HER 2* status and suspicion of metastases. There is variation in approach to surgery and chemotherapy regimens that have yet to be described. A 2 – 3 week gap is recommended after last chemotherapy prior to delivery in order to reduce the problems of neonatal neutropenia, for example, but this may not always be possible or planned.

Case Definition

Any women meeting one of the following criteria:

- Newly diagnosed cases of breast cancer during pregnancy
- Pathological diagnosis of breast cancer during pregnancy
- Confirmed diagnosis of breast cancer during pregnancy determined from the medical record

Excluded:

- Breast cancer diagnosed before pregnancy
- Recurrence of breast cancer in current pregnancy

Surveillance Period

October 2015 – September 2017

Interim Results and Conclusions

Up to April 2017, 92 cases of newly diagnosed breast cancer in pregnancy were reported. To date information has been received for 69 (75%) cases. Of these 14 were reported in error/did not meet the case criteria and 3 were found to be duplicates. It is not possible to draw any definitive conclusions at this stage.

Investigators

Philip Banfield, Claudia Hardy, BCUHB North Wales;
Julie Jones, North Wales Cancer Centre;
Sarah Davies, Lynda Sackett, BCU Health Board North Wales;
Marian Knight, NPEU.

Funding

This study is being funded by the Betsi Cadwaladr University Health Board (BCUHB)

4.3.3 Cystic Fibrosis in Pregnancy

Key points

- The number of recorded pregnancies in the UK of women with cystic fibrosis (CF) has increased over the past 5 years.
- Pre-pregnancy lung function is often cited as the most important factor in predicting the outcomes of pregnancy for both mother and baby; however it is necessary to clarify the current outcomes in women with CF across the spectrum of lung function.
- This study aims to provide reliable incidence and risk estimates and describe different management strategies across the UK, giving an accurate representation of current practice and outcomes.

Background

Advances in the care of people with CF have led to increasing survival, such that the median predicted survival age of patients in the UK with CF is now 41.4 years, and 53% of all females with the disease are over the age of sixteen. Fertility in menstruating females with CF is near normal (44) , and increasingly medical professionals are confronted with issues regarding fertility, family planning and pregnancy in this patient group.

Pre-pregnancy lung function is often cited as the most important factor in predicting the outcome of pregnancy for both mother and baby. Maternal forced expiratory volume in one minute (FEV_1) of less than 60% correlates with increased risk of premature delivery, delivery by caesarean section and adverse fetal outcomes such as low birth weight and perinatal death (45, 46). Based on the limited published evidence, a guideline was published in 2008 for the management of pregnant women with CF (47) which states that along with pre-existing pulmonary hypertension and cor pulmonale, an FEV_1 of less than 50% predicted should be suggested as an absolute contraindication to pregnancy. However, successful pregnancies have been documented in women with much greater impairment in lung function and pre-pregnancy FEV_1 between 20% and 30% predicted are reported (45), leading to the suggestion that advising such women to avoid pregnancy may be unwarranted. Further study is clearly necessary to clarify the current outcomes for pregnancy in women with CF across the spectrum of lung function.

It is anticipated that the results obtained from this study will guide medical professionals in supporting the care of women both planning and during pregnancy and ultimately enabling them to make informed choices regarding pregnancy and planning a family.

Case Definition

All pregnant women with a diagnosis of CF confirmed by CF mutation genotyping either prior to or during the current pregnancy who are booked for antenatal care in a UK obstetric unit.

Surveillance Period

March 2015 – February 2017

Interim Results

Up to April 2017, 99 cases of cystic fibrosis in pregnancy were reported. Information has been received for 84 cases (85%). Of these, 14 were reported in error, three cases were duplicates and one case could not be completed due to lost hospital notes.

Interim Conclusions

Final data collection and analysis is currently ongoing and will be reported in 2018.

Investigators

Lucy Mackillop, Anna Ashcroft, Stephen Chapman, Oxford University Hospitals NHS Trust.

Funding

This study has been funded by Wellbeing of Women.

4.3.4 Epidural Haematoma or Abscess

Key points

- Epidural haematoma and epidural abscess are clinically severe and can cause permanent neurological 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 are not limited to high-risk tertiary referral centres.

Background

Approximately 140,000 epidurals are placed annually for labour analgesia in the UK. There are two major but rare complications which merit study as they both occur in an occult manner leading to problems with diagnosis and further management (48). 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 literature (49). 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

Up to April 2017, 19 cases of epidural haematoma or abscess have been reported. Information has been received for 17 cases (89%) of which 4 were reported in error and one was a duplicate.

Interim Conclusions

Data collection for this study is still incomplete although current data suggest the condition is slightly more common than previously estimated.

Investigators

Felicity Plaat, Imperial College Healthcare;
Marian Knight, NPEU.

Funding

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

4.3.5 Epilepsy in Pregnancy

Key points

- Epilepsy is the most common neurological disorder encountered in pregnancy and affects one percent of the UK population (50, 51).
- The majority of women with epilepsy can expect a normal pregnancy, however epilepsy continues to be an important indirect cause of death for a small minority of women.
- It is clear from successive confidential enquiries the management of women with epilepsy who die can be improved(37).
- There have been repeated calls amongst the research community for high-quality, prospective data enabling the value of current policy recommendations to be assessed (52-54).

Background

Amongst women presenting for maternity care, approximately 1 in 200 are receiving treatment for epilepsy, with a mortality risk that is amongst 10 times greater than that of the general maternity population (100 versus 11 per 100,000 maternities respectively) (55, 56).

Between 2010 and 2012, 14 maternal deaths were attributed to epilepsy (maternal mortality risk =0.04/100,000), more than any direct cause of death with the exception of thrombosis, and unchanged from 2006-2008(37). Of these 14 deaths, 12 were classified as cases of 'Sudden Unexplained Death in Epilepsy' (SUDEP)(37). Whilst the definition of SUDEP implies a diagnosis of exclusion, expert-consensus maintains that generalised tonic-clonic seizure activity is likely to be a significant component of the phenomenon and should be considered as a sentinel event leading up to death (52, 57). As such, it follows logically that women in whom generalised tonic-clonic seizure activity persists during pregnancy represent a severe disease phenotype amongst women with epilepsy, with an increased risk of mortality.

Treatment goals for women with epilepsy in pregnancy target a seizure free 'steady-state' before conception on the basis that 1) the risk of seizures during pregnancy reduces as a function of the length of the seizure-free period before conception, and 2) those women who are able to remain seizure free for >12 months prior to conceiving are highly unlikely to have a recurrence of seizure activity when pregnant (53, 56, 58). Whilst this is certainly feasible for the majority of women, it is clear that seizures persists for a minority of women in whom it is considered that treatment plans are adequate (59). What is unclear amongst this group of women with poorly controlled epilepsy, is the relative contribution of women with severe, drug-resistant epilepsy versus the proportion of women whose disease management is suboptimal, or in whom fears about the potential for teratogenic side effects when using anti-epileptic drugs compromises their treatment adherence.

To date, the majority of published data describing maternal outcomes are derived from secondary analyses of studies assessing the safety and efficacy of anti-epileptic drug use in terms of fetal outcomes and are thus subject to a range of biases; primarily as the consequence of selecting only those women requiring anti-epileptic drugs for management of epilepsy but also by excluding cases that result in maternal death through restricting follow-up to include only live newborns (60). As a consequence, the extent to which findings can be generalised to the wider pregnant population as the basis for policy and guideline development must be questioned.

Case Definition

Any pregnant women in the UK who fulfil at least one of the following criteria:

1. A woman with epilepsy who dies during pregnancy or up to day 42 postpartum, where the cause of death is directly attributed to the consequences of epilepsy, including SUDEP
2. A woman with epilepsy who is admitted to hospital for management of generalised tonic-clonic seizures during pregnancy or postpartum period
3. All women being treated with >3 anti-epileptic drugs at any point during their pregnancy

Surveillance Period

October 2015 – March 2017

Interim Results

Up to April 2017, 268 cases of epilepsy in pregnancy were reported with information received for 233 cases (87%). Of these 233, 97 were reported in error/did not meet the case criteria, 9 were duplicates and 4 cannot be completed due to lost hospital notes. Data have also been collected for 205 control women.

Interim Conclusions

Analysis will be undertaken in the autumn of 2017. It is not possible to draw any definitive conclusions at this stage.

Investigators

Bryn Kemp and Marian Knight, NPEU;
Andrew Kelso, Barts Hospitals
David Williams, University College London Hospitals.

Funding

This study is part-funded by the National Institute for Health Research (NIHR) as part of a Professorship award to Professor Marian Knight.

NHS
National Institute for Health Research

4.3.6 Female Genital Mutilation Type 3

Key points

- Female Genital Mutilation (FGM) is commonly performed in parts of Africa, Asia and the Middle East; there are no identifiable health benefits associated with FGM.
- Good quality research evidence about the complications associated with FGM is sparse and there is none from the UK.
- The available evidence, largely from Africa, suggests that FGM is associated with substantial antenatal and delivery complications and poor fetal outcomes.
- The prevalence of FGM in pregnancy in the UK is currently based on unreliable estimates.

Background

Female Genital Mutilation/Cutting is defined by the WHO as “all procedures involving partial or total removal of the external female genitalia or other injury to the female genital organs for non-medical reasons (61). There are four types of FGM of which type 3 (Infibulation) is the most extreme. Long term gynaecological complications include scarring, infections, menstrual complications and sexual dysfunction (62). Psychological harm and post-traumatic stress disorder have also been described (63). Despite widespread practice and misconceptions about FGM there are no identified health benefits associated with FGM (61, 62).

Evidence about pregnancy related impacts is relatively sparse as illustrated by a recent systematic review and meta-analysis; none of the studies included were from the UK and were generally poor quality (64). However, the findings indicate an increased risk of prolonged labour, lacerations, instrumental delivery, dystocia, and obstetric haemorrhage; whereas there was no significant association with caesarean section and episiotomy. Of note fetal outcomes were not assessed and it is not possible to directly relate the findings to the contemporary management of pregnancy and delivery in the UK.

Available data about FGM in the UK are sparse, as a consequence prevalence estimates are based on the analysis of maternal place of birth data derived from birth registrations and the application of estimates of FGM practices in different countries (65). From this it is estimated that 1.2% of women giving birth in the UK have undergone FGM, of these it is estimated that 0.9% (9 in 1,000) have FGM type 3, but there is considerable uncertainty about the true prevalence. However, if this is an accurate estimate this would make the condition too frequent for a UKOSS study (frequency limit 1 in 2,000) and cases may be clustered in a small number of centres resulting in too great a data collection burden. For this reason **an initial study to solely estimate the prevalence was carried out** to assess whether it would be possible to conduct a full UKOSS study of FGM.

Mandatory data collection of FGM is underway in England. However, this data collection requires submission of patient-identifiable data, a cause of concern for some clinicians (66). With only 50% of eligible acute Trusts currently returning data centrally, under-ascertainment remains problematic.

Case definition

Any pregnant woman in the UK who fulfils the following criteria:

- A woman identified on examination during pregnancy or at delivery who has been subject to infibulation: narrowing of the vaginal opening through the creation of a covering seal. The seal is formed by cutting and repositioning the labia minora or majora with or without removal of the clitoris.
- Include also women whose infibulation has been reversed by de-infibulation prior to this pregnancy.

Surveillance Period

1st October 2016 – 31st March 2017

Interim results and conclusions

Over a six month period 195 cases of FGM were reported and case reports continue to be submitted. Using the data we will estimate completed the prevalence and consult the UKOSS steering committee regarding the conduct of a full UKOSS study.

Investigators

Jenny Kurinczuk and Marian Knight, NPEU;
Brenda Kelly, John Radcliffe Hospital, Oxford;
Sarah Creighton, University College London Hospitals.

Funding

This study is funded by the Department of Health as part of the programme of work of the Policy Research Unit in Maternal Health and Care.

PRUMHC
POLICY RESEARCH UNIT - MATERNAL HEALTH & CARE

4.3.7 Seasonal Influenza in Pregnancy

Key points

- Women continue to die in the UK from influenza in pregnancy from subtypes of influenza other than A/H1N1.
- It is unclear whether there is also an ongoing burden of severe morbidity from seasonal influenza.
- The aim of this study is to identify women hospitalised with seasonal influenza in pregnancy, in order to investigate associated factors, management and outcomes.

Background

Pregnancy is known to be a risk factor for severe influenza, as evidenced by the influenza A/H1N1 pandemic in 2009-10. However, women continue to die in the UK from influenza in pregnancy from subtypes of influenza other than A/H1N1, and while it is clear that these deaths are usually in unvaccinated women, it is unclear whether there is also an ongoing burden of severe morbidity from seasonal influenza. This project, therefore, aims to collect data nationally using the UK Obstetric Surveillance System, on all women hospitalised with seasonal influenza in pregnancy, in order to investigate associated factors, management and outcomes.

Case Definition

Any pregnant women hospitalised with confirmed or suspected influenza in pregnancy. Include women admitted with secondary pneumonia in whom preceding influenza infection is confirmed on testing.

Surveillance Period

November 2016 – October 2017

Interim Results

Up to April 2017 86 cases of seasonal influenza have been reported. Data have been received for 46 (53%) cases. Of these 3 were reported in error/did not meet the case criteria.

Interim Conclusions

There was a clear peak in cases over the winter period, but data collection will continue for a full calendar year.

Investigators

Marian Knight, NPEU
Jenny Kurinczuk, NPEU
Maria Quigley, NPEU
Peter Brocklehurst, University of Birmingham
Patrick O'Brien, University College London

Funding

This study is part funded by the Department of Health as part of the programme of work of the Policy Research Unit in Maternal Health and Care and part funded by the National Institute for Health Research Health Technology Assessment Programme.

4.3.8 Single Intrauterine Fetal Demise (sIUD) in Mononchorionic Twins

Key points

- Monochorionic (MC) twins constitute 20-30% of all twin pregnancies and 2.6-6.2% will have a single intrauterine fetal death.
- This event is associated with increased risk of premature delivery and perinatal mortality and morbidity for the other twin.
- There is a lack of robust data regarding the incidence of single twin demise; interventions offered; maternal, fetal and neonatal outcomes and any prognostic indicators.
- The knowledge gained from this study will enable recommendations for the management of monochorionic twin pregnancies following single twin demise and improve the counselling and management.

Background

Perinatal mortality is increased in multiple compared to singleton pregnancies, with single twin demise presenting a rare but unique perinatal problem with reported incidence of single twin demise after 14 weeks between 2.6 to 6.2 percent of all twin pregnancies (67). Fetal morbid sequelae may include prematurity, death of the surviving

fetus or survival with perinatal morbidity (68). In addition, maternal morbidity has been reported as increased with higher (than background) rates of pre-eclampsia, coagulopathy and sepsis (69, 70). Management of pregnancies complicated by intrauterine death in a twin may be challenging as controversy exists regarding the optimal time of delivery, the frequency of antenatal surveillance, the appropriate investigations to determine cerebral impairment and the effects on maternal wellbeing (both physical and psychological) of retaining one dead fetus. Current evidence is limited by small numbers and significant heterogeneity in terms of diagnosis, investigation, management and postnatal follow-up.

Case Definition

Any women in the UK with a monochorionic twin pregnancy with single twin demise after 14 weeks gestation, defined as:

a) Monochorionic twin pregnancy – chorionicity confirmed at first trimester scan (<14 weeks) due to ultrasonic absence of the lambda sign (an echogenic V-shaped chorionic projection of tissue in dichorionic placentation).

b) Single intrauterine fetal death – intrauterine death of one twin (including spontaneous single twin demise or selective feticide).

EXLUDE: Multiple pregnancies where multifetal pregnancy reduction has taken place.

Surveillance Period

July 2016 – June 2017

Interim Results

Up to April 2017 99 cases have been reported. Data have been received for 71 (72%) cases. Of these 24 (34%) were reported in error/did not meet the case criteria and 5 were duplicate reports.

Interim Conclusions

Fewer cases than anticipated have been reported, and additional checks of case ascertainment are underway.

Investigators

Mark Kilby, Katie Morris, University of Birmingham; Marian Knight, NPEU.

Funding

This study is being funded by a BMFMS (British Maternal Fetal Medicine Society) and TAMBA (Twins and Multiple Births Association) bursary.

4.3.9 Spontaneous Haemoperitoneum in Pregnancy

Key points

- SHiP is the occurrence of sudden haemorrhage intra-abdominally in pregnancy – unrelated to trauma or rupture of the uterus.
- SHiP has been associated with endometriosis, rupture of uterine artery or varicose veins and aneurysms of the splenic artery.
- SHiP is rare but potentially fatal for the mother and the fetus.
- The data from this study will form part of an international collaborative study using the International Network of Obstetric Survey Systems (INOSS).

Background

Spontaneous Haemoperitoneum in Pregnancy (SHiP) is the occurrence of sudden haemorrhage intra-abdominally in pregnancy (unrelated to trauma or rupture of the uterus) and has been associated with endometriosis, rupture of uterine artery or varicose veins and aneurysms of the splenic artery (71).

SHiP is rare but potentially fatal for both mother and baby but it is currently extremely difficult to estimate the incidence of SHiP. Six maternal deaths occurred between 2009 and 2012 in the UK that were attributed to rupture of non-aortic aneurysms. However, little is known about morbidity during that time (37). Anecdotally, some cases have been noted to occur in women undergoing thrombolysis, but the prognostic factors are currently unclear on a population basis. The data from this study will form part of an international collaborative study using the International Network of Obstetric Survey Systems (INOSS).

Case Definition

Any woman 20 weeks or more gestation with sudden intra-abdominal haemorrhage requiring surgery (CS, laparotomy, laparoscopy), without preceding trauma.

EXCLUDE: women with uterine rupture or trauma.

Surveillance Period

January 2016 – December 2017

Interim Results and Conclusions

Up to April 2017 20 cases have been reported. Data for 19 cases have been returned. Of these 5 were reported in error/did not meet the case criteria. The UK data will be combined with data from Denmark and the Netherlands as part of a multi-national INOSS study.

Investigators

Marian Knight, NPEU, UK; Janne Foss Berlac and Jens Langhoff-Roos, University of Copenhagen, Denmark.

Funding

This study is funded by the National Institute for Health Research (NIHR) as part of a Professorship award to Professor Marian Knight.

NHS
National Institute for Health Research

4.3.10 Zika Virus in Pregnancy

Key points

- Zika virus (ZIKV) is an emerging viral infection with increasing transmission in South and Central America.
- Even though not yet scientifically proven, a causal relationship between ZIKV infection in pregnancy and fetal microcephaly is strongly suspected.
- This study will describe the risk of an adverse pregnancy outcome related to infection with ZIKV during pregnancy.

Background

Since early 2015 when Zika virus (ZIKV) infection was first reported in Brazil, ZIKV has rapidly spread over most countries in South and Central America, the Caribbean and countries outside this region. An unusually high number of babies born with microcephaly were reported in Brazil, six months after the rapid increase of cases of ZIKV infection, concentrated particularly in those areas with high rates of the disease. The high numbers of cases are likely to be an overestimate due to case ascertainment; however they are considerable and thus ZIKV was declared as a Public Health Emergency of International Concern by the WHO in February 2016. Even though not yet scientifically proven, a causal relationship between ZIKV infection in pregnancy and microcephaly is strongly suspected. Two babies with microcephaly and confirmed ZIKV infection of mothers resident in countries without active ZIKV but who had travelled to Brazil during their pregnancy have been reported to date (19).

Almost 1.4 million UK residents travelled to South and Central America and the Caribbean on average each year between 2010 and 2014, 25% of those were women of child bearing age.

This study will carry out national surveillance in the UK, to assess the risk of having an adverse pregnancy outcome after travel to a country with active Zika transmission.

Case Definition

Two case definitions are included on the reporting system.

1. Any pregnant woman with a history of travel to a country with active ZIKV transmission during pregnancy or 4 weeks before conception and no adverse pregnancy outcome.
2. Any pregnant woman with a history of travel to a country with active ZIKV transmission during pregnancy or 4 weeks before conception where a fetal abnormality has been detected or miscarriage, stillbirth, neonatal death or termination of pregnancy occurred.

Reporters are requested to report the numbers of women in their unit who fall into either category. Detailed data will only be requested on women with an adverse pregnancy outcome at this stage i.e. UKOSS will only collect numbers of women falling into group 1; reporting clinicians will not be requested to complete a data collection form. Data collection forms will be sent for completion of further details about women in group 2.

Surveillance Period

March 2016 – February 2017

Interim Results and Conclusions

Up to February 2017 17 adverse outcomes have been reported amongst 771 women with a history of travel to a Zika-affected area. Data have been received for 14 (82%) cases with adverse outcomes. Four were reported in error. None report microcephaly in the infant. Adverse outcomes directly attributable to Zika virus appear rare in the UK.

Investigators

Richard Pebody, Clarissa Oeser, Public Health England; Asma Khalil, St. George's Hospital, University of London; Patrick O'Brien, University College London Hospitals; Marian Knight, NPEU.

Funding

This study is being funded by Public Health England.

Public Health England

4.4 Future Studies

These studies have been approved by the UKOSS Steering Committee to commence in 2017.

4.4.1 Cirrhosis in Pregnancy

Key points

- Cirrhosis is defined as permanent scarring of the liver as a result of continuous long term damage.
- There are few reports of pregnancy in women with cirrhosis although some small studies have suggested that there is an increased incidence of adverse maternal and perinatal outcomes in women with cirrhosis.
- This study will establish the incidence of cirrhosis in pregnancy women in the UK and describe the management and perinatal outcomes of pregnancies affected by cirrhosis.

Background

Cirrhosis is defined as permanent scarring of the liver as a result of continuous long term damage and it is estimated to affect 45/100,000 women of child-bearing age (72). There are few reports of pregnancy in women with cirrhosis, and therefore data regarding pregnancy outcomes and optimal management are sparse. Several studies have suggested that there are higher rates of both maternal and neonatal mortality in women with cirrhosis (72-77), and women with portal hypertension and oesophageal varices appear to be at higher risk; however none have been large enough to accurately quantify the risks. Other maternal complications include higher rates of anaemia, post-partum haemorrhage, pre-eclampsia, placental abruption and maternal death (75, 77). Fetal complications are reported to include miscarriage, pre-term delivery and intrauterine growth restriction (73-75, 77).

Management of cirrhosis largely relates to treatment of the underlying pathology. There is no consensus on the optimal treatment for variceal bleeding and there are concerns over the use of injection sclerotherapy and octreotide (72). Endoscopy and ligation banding appears to be safe but there are no randomised controlled trials. Furthermore, there are limited data regarding the best way to deliver women with cirrhosis. There are concerns over women labouring as the process involves repeated Valsalva manoeuvres which raises intra-abdominal pressure and therefore increases the risk of variceal rupture (72).

This study will also aim to establish the maternal outcomes associated with cirrhosis, and to determine the effect of pregnancy on disease progression.

Case Definition

All pregnant women with an established history of cirrhosis defined by either confirmation by liver biopsy OR on the basis of radiological findings (nodular liver with enlarged spleen) with either a history of complications of liver disease (ascites, variceal bleeding, encephalopathy, pervious bacterial peritonitis) or supportive laboratory findings (low platelets, low albumin, prolonged prothrombin time or INR).

Main research questions

- What is the incidence of cirrhosis in pregnant women in the UK?
- What are the current management strategies used to treat cirrhosis in pregnancy?
- What is the incidence of co-existent pre-eclampsia, gestational diabetes and pregnancy specific liver disease (Acute Fatty Liver of Pregnancy and Intrahepatic Cholestasis of Pregnancy) in pregnant women with cirrhosis)?
- What are the perinatal outcomes of pregnancies affected by cirrhosis?

Investigators

Catherine Williamson, Victoria Geenes, Michael Heneghan, Leonie Penna, King's College London; Marian Knight, NPEU.

Funding

The Lauren Page Trust

4.4.2 High Neuraxial Block

Key points

- High (complete or total) spinal block is a known complication of epidural or spinal anaesthesia.
- Incidence estimates very widely.
- The recent UKOSS Cardiac Arrest in Pregnancy study identified anaesthetic causes, including high spinal, as the leading cause of maternal cardiac arrest in the UK.
- This study aims to identify the risk factors for the development of high spinal block associated with obstetric anaesthesia in the UK.

Background

High (complete or total) spinal block is a known complication of central neuraxial blockade (epidural or spinal anaesthesia). The terms high, total or complete are used interchangeably to describe a sensorimotor block above that which is required for the surgery and which is associated with significant cardiovascular /respiratory compromise, sometimes culminating in cardiorespiratory arrest.

The incidence of high spinal block associated with obstetric anaesthesia is not known. Estimates vary between 1:2,971 (78) and 1:16,200 (79) anaesthetics. More recently a retrospective study in the USA suggested an incidence of high spinal block of 1:4336 anaesthetics (80). However the majority of the studies that include high spinal as a complication of central neuraxial block, come from the era before the widespread use of low dose techniques in obstetric anaesthesia ('mobile epidurals'). Importantly, the recent UKOSS Cardiac Arrest in Pregnancy study identified anaesthetic causes, including high spinal, as the leading cause of maternal cardiac arrest in the UK (81). While the outcomes for cardiac arrest in this setting were good, it behooves obstetric anaesthesia to identify the potential risk factors and causes of high spinal block in obstetrics to reduce this complication. This study will provide the most accurate description of the incidence of high spinal block in obstetric patients to date, with implications for improved safety.

Case definition

Any pregnant or postpartum woman who develops a high block in association with spinal and or epidural anaesthesia /analgesia that requires ventilatory support* and /or cardiopulmonary resuscitation**.

*Ventilatory support includes the additional use of 'bag/mask' ventilation, or ventilation assisted by the use of a supraglottic airway device or endotracheal tube.

**Cardiopulmonary resuscitation includes the use of basic and advanced life support.

Main research Questions

- What is the current incidence of high spinal associated with obstetric anaesthesia in the UK?
- What are the risk factors for the development of high spinal associated with obstetric anaesthesia?
- How is high spinal associated with obstetric anaesthesia managed?
- What are the outcomes for the mother and baby in a woman who develops a high spinal associated with obstetric anaesthesia?

Investigators

Gary Stocks, Imperial College Hospitals
Nuala Lucas, Northwick Park Hospital
Marian Knight, NPEU
Paul Sharpe, University Hospitals of Leicester NHS Trust

Funding

This study is funded by a grant from the Obstetric Anaesthetists Association (OAA).

4.4.3 WHO Global Obstetric Sepsis Study (GLOSS)

Key points

- Globally sepsis is a major cause of both maternal and newborn deaths, but the exact burden of disease is unknown.
- This study will form part of a one week WHO multi-country global study of women with suspected or confirmed sepsis.
- This study aims to test new WHO criteria for identification of maternal sepsis across both low and high resource settings, describe the outcomes of suspected or confirmed maternal sepsis for mothers and infants, and additionally, in the UK and other European participating countries, describe on a national basis the patterns of anti-microbial usage amongst women with suspected maternal.

Background

The latest estimates suggest that infections are the underlying cause of 11% of maternal deaths (82) and about 25% of newborn deaths (83), but the true burden of maternal infection and its complications is not well known. As is the case for other maternal conditions, the main reason for this uncertainty is the absence of standard definitions, identification criteria and measurement tools. In order to reduce the burden of maternal and neonatal infections it is necessary to have actionable identification criteria and optimize prevention and treatment of these conditions; improving our understanding of epidemiological and contextual factors will also contribute to that.

This UKOSS study will be part of a global multi-country study across 58 countries, one workstream of the World Health Organisation “Global Maternal and Neonatal Sepsis Initiative” which has the overall goal of accelerating reduction of preventable maternal and newborn deaths related to sepsis.

Study duration

In contrast to other UKOSS studies, this study will take place over ONE WEEK only, following any women or their infants who remain in hospital for up to six weeks or until discharge, whichever is sooner.

Case definition

Any pregnant woman or recently pregnant woman (up to 42 days after the end of pregnancy) who has received any investigation or treatment for presumed infection between 00.00 28/11/2017 and 24.00 04/12/2017 and who has been admitted for at least 12 hours.

The following are examples of women who would be expected to be included:

- Those with clinical signs suggestive of infection
- Those with a sample sent for culture for presumed infection
- Those prescribed antibiotics or other antimicrobial at admission or during hospital stay EXCEPT for prophylaxis at e.g. caesarean section or for GBS or 3rd or 4th degree tear or PROM.

AND/OR Any woman whose death is caused or aggravated by a suspected or confirmed infection.

Exclusion criteria. Women presenting the following conditions will be excluded, unless they present with systemic repercussions due to infection:

- Any non-severe, localised, uncomplicated infection
    - Vaginosis, candidiasis
    - Lower tract urinary infection
    - Fungal infections of the skin (athlete’s foot, jock itch, ringworm, and yeast infections)
    - Otitis
    - Pharyngitis
    - Herpes simplex, Herpes Zoster (Shingles)

- Any uncomplicated chronic infection without evidence of another acute infection
    - Sexually transmitted infections (Gonorrhea, Syphilis, Trichomonas,Chlamydia, Hepatitis, HIV)
    - Tuberculosis
- Any colonisation (presence of microorganisms without clinical signs/symptoms)
    - Known GBS vaginal, urethral and/or rectal colonization
    - Asymptomatic bacteriuria
    - Known oropharyngeal colonization
- Any iatrogenic hypothermia/hyperthermia (e.g. related to epidural, thyroid storm, prostaglandin administration) during hospital stay;
- Use of any prescription of prophylactic antibiotics (e.g. for GBS colonization, after caesarean section, manual removal of the placenta, vaginal delivery);

Primary Objectives

1. To develop and validate a set of criteria for identification of possible severe maternal infection (presumed maternal sepsis);
2. To develop and validate a set of criteria for identification maternal sepsis (confirmed sepsis);
3. To assess the frequency and the outcomes of maternal sepsis in developing and developed countries;
4. To assess the frequency of use of a core set of practices recommended for prevention, early identification and management of maternal sepsis.

Secondary Objectives

5. To contribute to the understanding of vertical transmission of bacterial infection by assessing outcomes and management of neonates born to women with suspected or confirmed peripartum infection;
6. To raise awareness about maternal and neonatal sepsis among health care providers, policy makers and the general public, including pregnant women, mothers and their families;
7. To build a network of health facilities to implement quality improvement strategies for better identification and management of maternal and early neonatal sepsis.

Additional objectives for European countries

8. To describe antimicrobial usage amongst women with possible severe maternal infection.
9. To explore migration status and internal displacement status amongst women with possible severe maternal infection and describe any variations in their management.

Investigators

Mercedes Bonet, Joao-Paulo Dias de Souza, WHO
Marian Knight, NPEU
David Lissauer, Univeristy of Birmingham

World Health Organization

human reproduction programme hrp

research for impact

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5. Publications

5.1 Pregnancy outcomes in women with myeloproliferative disorders: a UK prospective cohort study

Published Article

Alimam S, Bewley S, Chappell LC, Knight M, Seed P, Gray G, Harrison C, Robinson S. Pregnancy outcomes in myeloproliferative neoplasms: UK prospective cohort study. Br J Haematol. 2016 Oct;175(1):31-6. doi: 10.1111/bjh.14289.

Key points

- Myeloproloferative disorders (MPD) including primary myelofibrosis, essential thrombocythaemia and polycythaemia vera are uncommon in pregnancy, and guidelines for management are largely based on extrapolation from experience of managing women with acquired thrombophilia.
- The aim of this study was to estimate the incidence of MPD in pregnancy in the UK and report maternal and perinatal outcomes using contemporary management.
- Between January 2010 and December 2012 58 women with MPD in pregnancy were identified; 47 (81%) with essential thrombocythaemia, five (9%) polycythaemia vera, five (9%) myelofibrosis and one (2%) MPD-unclassified.
- Maternal complications included 9% (5/57) pre-eclampsia, 9% (5/57) post-partum haemorrhage and 3·5% (2/57) post-partum haematoma. There were no maternal deaths or thrombotic events.
- The overall incidence of miscarriage was 1·7/100 (95% confidence interval [CI] 0·04–9·2) and the perinatal mortality rate was 17/1000 births (95% CI 0·44–92).
- The majority of women (85%, 45/53) delivered at term (≥37 weeks gestation). Delivery was induced in 45% (24/53) and 45% (24/53) were delivered by caesarean section.
- 22% (12/54) of neonates were small for gestational age and 13% (7/54) were admitted to a neonatal unit.
- The findings of this large, UK prospective study suggests women with MPN appear to have largely successful pregnancies with better outcomes than would be anticipated from the literature.

5.2 Macroprolactinomas and non-functioning pituitary adenomas and pregnancy outcomes: a UK national cohort study

Published Articles

Lambert K, Rees K, Seed PT, Dhanjal MK, Knight M, McCance DR, Williamson C. Macroprolactinomas and Nonfunctioning Pituitary Adenomas and Pregnancy Outcomes. Obstet Gynecol. 2017 Jan;129(1):185-194. doi: 10.1097/AOG.0000000000001747

Key points

- Most women with microprolactinomas (diameter <10mm) will have uncomplicated pregnancies. However, macroprolactinomas (diameter 10mm or more) or non-functioning pituitary adenomas may undergo symptomatic enlargement. The incidence of this in pregnancy in the UK is unknown.
- The aim of this study was to describe the incidence, characteristics, management and outcomes of pregnancy in women with pituitary tumours.
- Between March 2010 and Febuary 2013 71 women with pituitary tumours in pregnancy were identified (49 with macrolactinomas, 16 with nonfunctioning adenomas, three with acromegaly, three with Cushing's disease).
- Symptomatic tumor expansion occurred in 10 women, 6 with a macroprolactinoma and 4 with a non-functioning adenoma.
- None of the 9 women treated with surgery or radiotherapy before pregnancy had symptomatic tumor expansion.
- 7/51 (14%) women with known tumours who had not had surgery or radiotherapy before pregnancy had tumor expansion; 6 of these women had symptoms.
- There was no evidence that pituitary tumors were associated with adverse pregnancy outcomes (pregnancy-induced hypertension, preeclampsia, preterm labour, stillbirth).
- This study showed that nonfunctioning pituitary adenomas occur more commonly in pregnancy than previously thought and can present with symptoms of pituitary expansion. The majority of women have good pregnancy outcomes.

5.3 Pregnancy at very advanced maternal age: a UK population-based cohort study

Published Article

Fitzpatrick KE, Tuffnell D, Kurinczuk JJ, Knight M. Pregnancy at very advanced maternal age: a UK population-based cohort study. BJOG. 2016 Sep 1. doi:10.1111/1471-0528.14269. [Epub ahead of print]

Key points

- Childbearing at advanced maternal age is becoming increasingly common in high income countries, however most studies investigate women giving birth at 35 or 40 years and over.
- The aim of this study was to describe the characteristics, management and outcomes of women giving birth at very advanced maternal age (48 years and over) in the UK and to estimate the risk of adverse outcomes attributable to very advanced maternal age.
- 233 women age 48 years and over and 454 comparison women were identified between 1st July 2013 and 30th June 2014.
- Older women were more likely than comparison women to be overweight or obese, nulliparous, have pre-existing medical conditions, a multiple pregnancy, and to have conceived following assisted conception.
- After adjustment for demographic and medical factors older women appeared more likely than comparison women to have pregnancy complications including gestational hypertensive disorders, gestational diabetes, postpartum haemorrhage, caesarean delivery, iatrogenic and spontaneous preterm delivery.
- After adjustment for multiple pregnancy or use of assisted conception, significant associations remained only with gestational diabetes (aOR 4.8, 95%CI 1.9-12.0), caesarean delivery (aOR 2.8, 95%CI 1.4-5.4) and admission to an intensive care unit (aOR 33.5, 95%CI 2.7-412.2).
- Since many of the increased risks appear to be explained by multiple pregnancy or use of assisted conception, recommendations regarding assisted conception, including egg donation in older mothers as well as single embryo transfer, should take these findings into account.

5.4 Pregnancy outcomes in women with mechanical prosthetic heart valves: a prospective descriptive population based study

Published Article

Vause S, Clarke B, Tower CL, Hay C, Knight M; (on behalf of UKOSS). Pregnancy outcomes in women with mechanical prosthetic heart valves: a prospective descriptive population based study using the United Kingdom Obstetric Surveillance System (UKOSS) data collection system. BJOG. 2016 Dec 26. doi:10.1111/1471-0528.14478. [Epub ahead of print]

Key points

- Women with mechanical prosthetic heart valves need lifelong anticoagulation to prevent valve thrombosis, but there is currently little evidence to guide the choice of anticoagulant regimen in pregnancy.
- The aim of this study was to describe the incidence of mechanical prosthetic heart valves in pregnancy in the UK, rates of maternal and fetal complications in this group of women, and to identify whether these vary with the anticoagulation used during pregnancy.
- 58 women were identified between February 2013 and January 2015, giving an estimated incidence of 3.7 (95% CI 2.7–4.7) per 100 000 maternities.
- Five women died (9%) and a further 24 (41%) had serious maternal morbidities including 4 with a cerebrovascular accident (7%) and 5 with a thrombosed valve (9%).
- There was a poor fetal outcome in 26 (47%) pregnancies. Only 16 (28%) women had both a good maternal and a good fetal outcome.
- Low-molecular-weight heparin was used throughout pregnancy by 71% of women. Of these, 83% required rapid dose escalation in the first trimester. Monitoring regimens lacked consistency.
- This study shows that women with mechanical prosthetic heart valves are at extremely high risk, and should be referred to specialist centres at the earliest opportunity, preferably prior to conception. Once pregnant they need expert obstetric, haematology, cardiology and anaesthetic input.

5.5 The CAPS Study: incidence, management and outcomes of cardiac arrest in pregnancy in the UK: a prospective, descriptive study

Published Article

Beckett VA, Knight M, Sharpe P. The CAPS Study: incidence, management and outcomes of cardiac arrest in pregnancy in the UK: a prospective, descriptive study. BJOG. 2017 Feb 24. doi: 10.1111/1471-0528.14521. [Epub ahead of print].

Key points

- The importance of rapid delivery for maternal benefit after cardiac arrest (perimortem caesarean section) is becoming a widely accepted practice.
- There are no prospective data, however, to assess the timing with which this intervention is performed in practice and the relationship to outcomes.
- The objectives of this study were to describe the incidence, risks, management and outcomes of cardiac arrest in pregnancy in the UK population, with specific focus on the use of perimortem caesarean section (PMCS).
- Between July 2011 and June 2014 there were 66 cardiac arrests in pregnancy, an estimated incidence of 2.8 per 100 000 maternities (95% CI 2.2–3.6).
- 16 women arrested solely as a consequence of obstetric anaesthesia, 12 of whom were obese.
- 28 women died (42%); those who died were more likely to have collapsed at home.
- Perimortem caesarean section was performed in 49 women, 11 in the emergency department. The time from collapse to PMCS was significantly shorter in women who survived (median interval 3 versus 12 minutes, p=0.001).
- Forty-six of 58 babies were born alive; 32 babies to surviving mothers and 14 to women who died.
- This study showed that although cardiac arrest is rare in the pregnant UK population, nearly a quarter of arrests were associated with obstetric anaesthesia, suggesting an opportunity to reduce the incidence further. High maternal survival rates were achieved with timely resuscitation, including PMCS.

5.6 Severe Primary Autoimmune Thrombocytopenia (ITP) in Pregnancy: a National Cohort Study

Published Article

Care A, Pavord S, Knight M, Alfirevic Z. Severe Primary Autoimmune Thrombocytopenia (ITP) in Pregnancy: a National Cohort Study. BJOG. 2017 Apr 22. doi: 10.1111/1471-0528.14697. [Epub ahead of print].

Key points

- Primary autoimmune Thrombocytopenia (ITP) is a haemorrhagic disorder characterised by transient or persistent decrease in platelet count and, depending on the degree of thrombocytopenia, an increased risk of bleeding. Historically fears of bleeding risk have dominated management of ITP.
- The aim of this study was to quantify UK incidence of severe ITP in pregnancy, determine current treatment strategies and describe maternal and neonatal morbidity and mortality associated with severe ITP in pregnancy.
- 107 pregnancies in women with severe ITP were reported to UKOSS between June 2013 and January 2015, an estimated 8.3 per 100,000 maternities (95% CI 6.8 - 100).
- 22 women (21%) did not receive any antenatal therapy, 85 (79%) had therapy. There was no difference between asymptomatic treated and untreated cohorts in severity of disease or outcome.
- Postpartum haemorrhage (51%) and severe postpartum haemorrhage (21%) was reported more frequently than the reported rate in the general pregnant population (5-10%).
- No neonates required treatment for thrombocytopenia and there were no cases of neonatal intracranial bleeding.
- This study shows that women with severe ITP in pregnancy remain at risk of severe postpartum haemorrhage, but neonatal morbidity and mortality is low. Whilst balancing risks for pregnancy of prophylactic antenatal treatment in asymptomatic women against observed low disease morbidity, we may be over treating asymptomatic patients.

5.7 Abstracts

The following abstracts were presented at meetings in 2016/2017:

2017

- Dipep: Diagnosis of Pulmonary Embolism in Pregnancy. Presented at the British Maternal Fetal Medicine Society Annual Meeting March 2017 and British Congress of Obstetrics and Gynaecology, March 2017
- Stephen McCall: Maternal super obesity: an international collaborative population-based cohort study. Poster presented at the British Maternal Fetal Medicine Society Annual Meeting March 2017 and the Medical Research Council DTP Symposium 2017
- George Attilakos: Vasa praevia: A national UK study using the UK Obstetric Surveillance System (UKOSS). Presented at the British Maternal Fetal Medicine Society Annual Meeting March 2017

- Stephen McCall: Unifying data - INOSS collaborative studies of extreme obesity and anaphylaxis in pregnancy. Presented at INOSS Annual Meeting 2017

5.8 UKOSS Publications to date

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