UKOSS

UK Obstetric Surveillance System

Twelfth Annual Report 2018

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 & Gynaecologists

NPEU

UNIVERSITY OF OXFORD

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This report should be cited as: O'Connor M, Kurinczuk JJ, Knight M. UKOSS Annual Report 2018. Oxford: National Perinatal Epidemiology Unit 2018

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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 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). A project in Assam, India, became the first to adapt the methodology in a Low and Middle Income Country (LMIC) setting (9).

Studies using UKOSS may be undertaken by any investigator who identifies a suitable topic and secures funding (10). 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 thirteenth year of surveillance using UKOSS.

2. Methods

Case notification is now maintained through online report submission requested monthly from all consultant-led obstetric units in the UK 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 (11, 12). The UKOSS methodology has Research Ethics Committee approval.

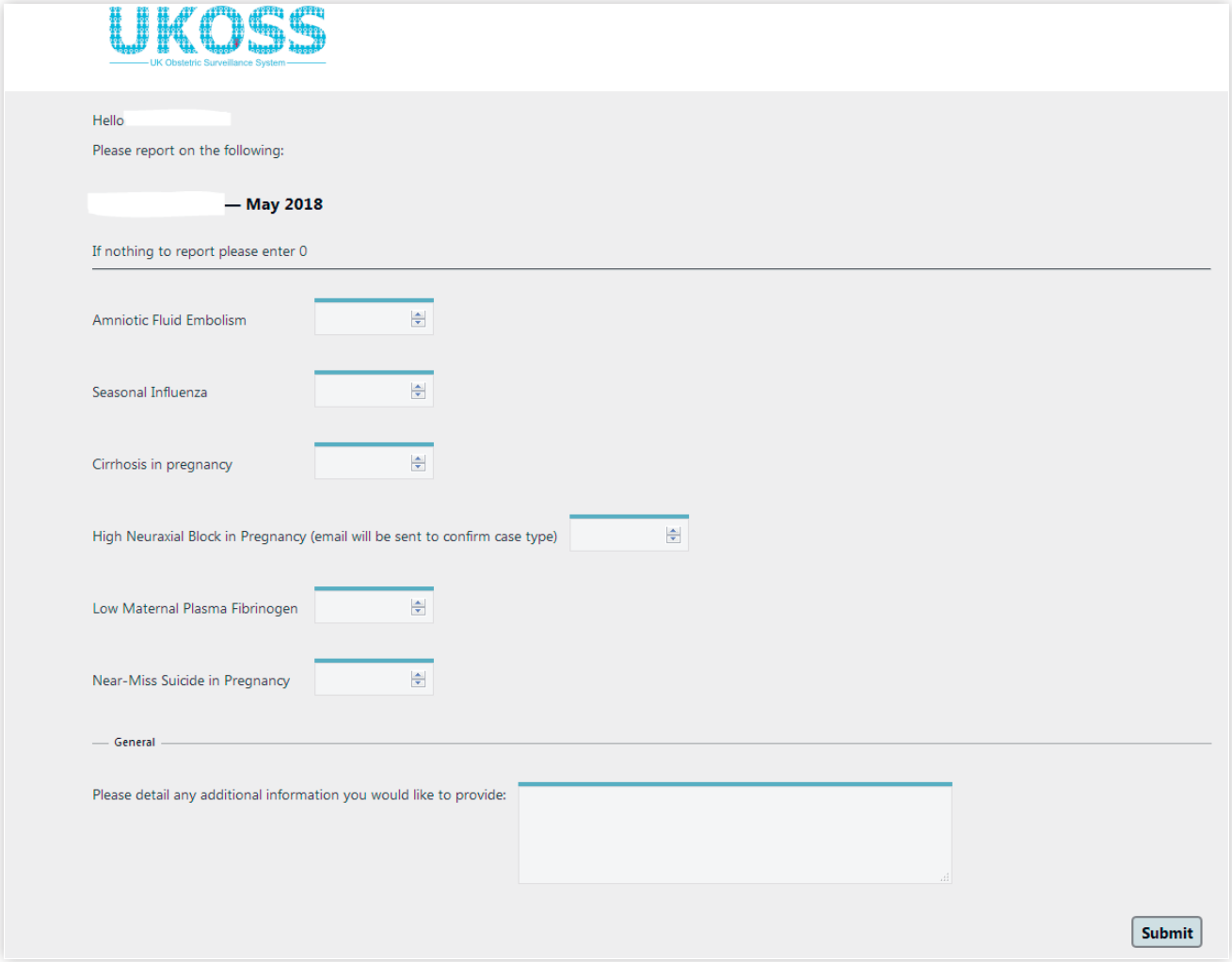
In order to perform case-control or cohort studies, information is also collected about control or comparison women for some studies. For these studies only, clinicians who report a case are asked to follow specific instructions to identify appropriate comparison women and complete a similar data collection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

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(13).
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) (14).
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 (15).
    - UKOSS surveillance of 2009/H1N1 influenza showed a significant association with poor pregnancy outcomes (16).
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(17).
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 (18, 19).
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 (20).
8. Informing public health policy
    - A UKOSS study showing poor perinatal outcomes in pregnant women with 2009/H1N1 influenza (16) was used as evidence to recommend universal immunisation of pregnant women against seasonal influenza (21).
9. Investigating a clinical decision rule
    - A UKOSS study of pulmonary embolism was used to investigate the development of a clinical decision rule about imaging amongst woman with suspected PE (22).

Figure 1: Sample UKOSS Electronic Report Submission Page

(This replaced the original postcard notification system in 2017)



3. Participation

All 198 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 2017 was 97% (Figure 2), the highest since UKOSS began in 2005 which can largely be attributed to the new online reporting system. Regional return rates vary between 85% and 100% (Figure 3). These continued high report return rates are a testament to the support and dedication of reporting clinicians throughout the UK.

Figure 2:UKOSS national monthly report return rates January-December 2017

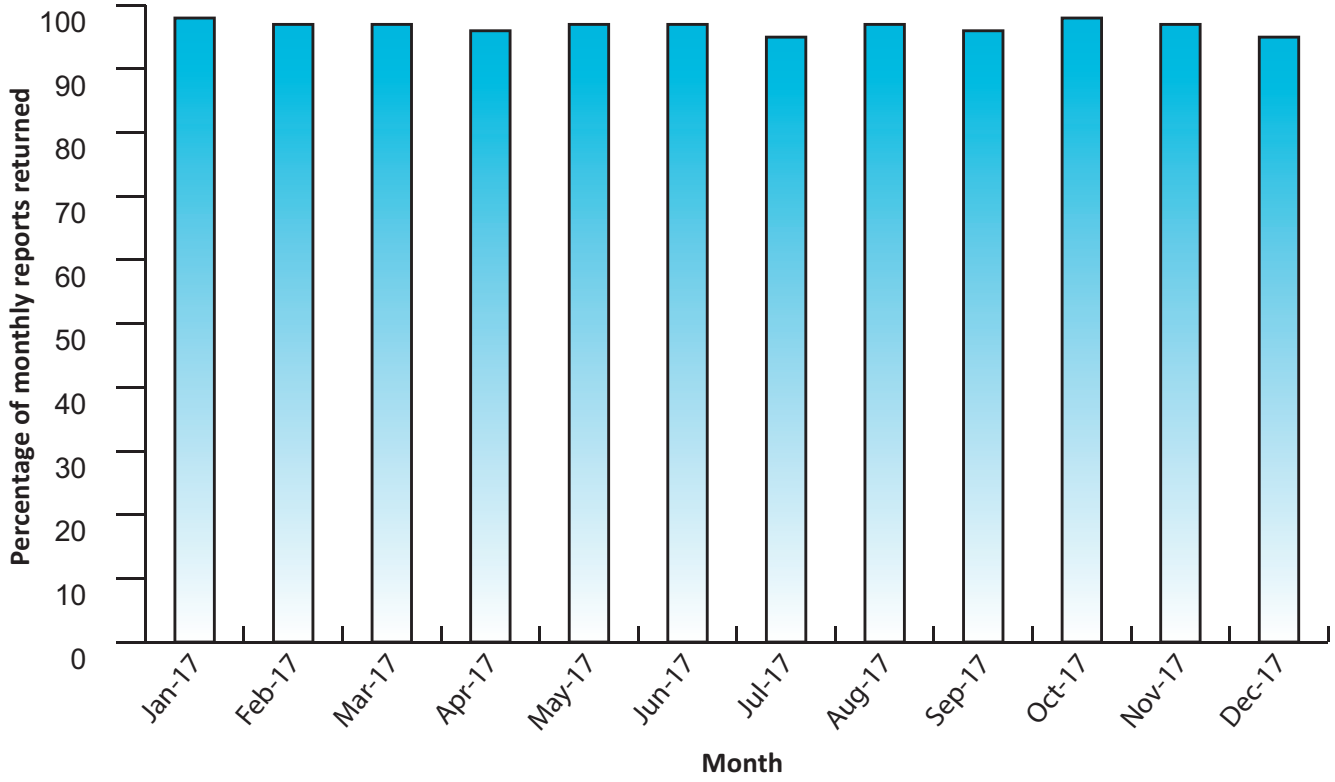
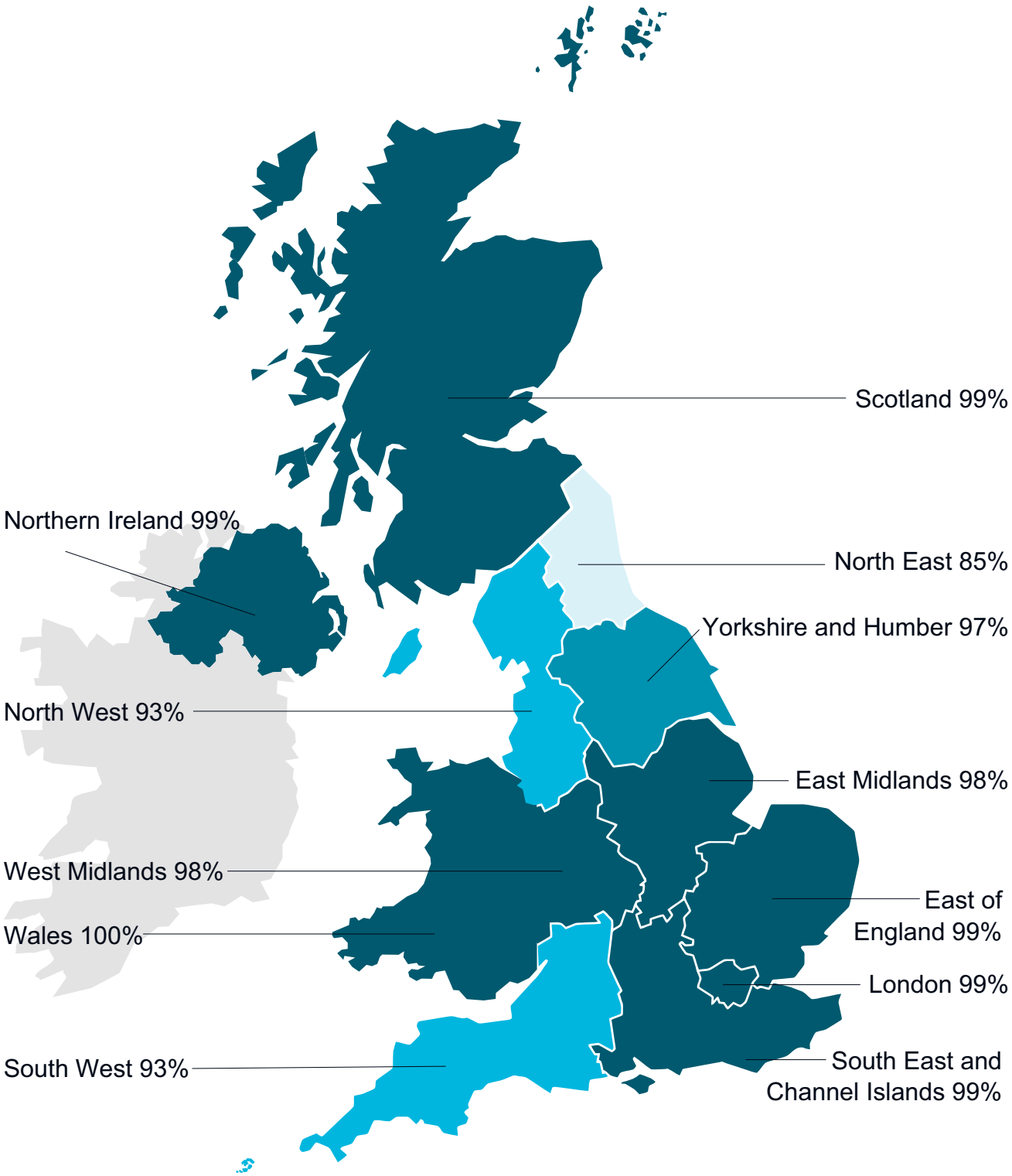


Figure 3: Map showing regional return rates during 2017

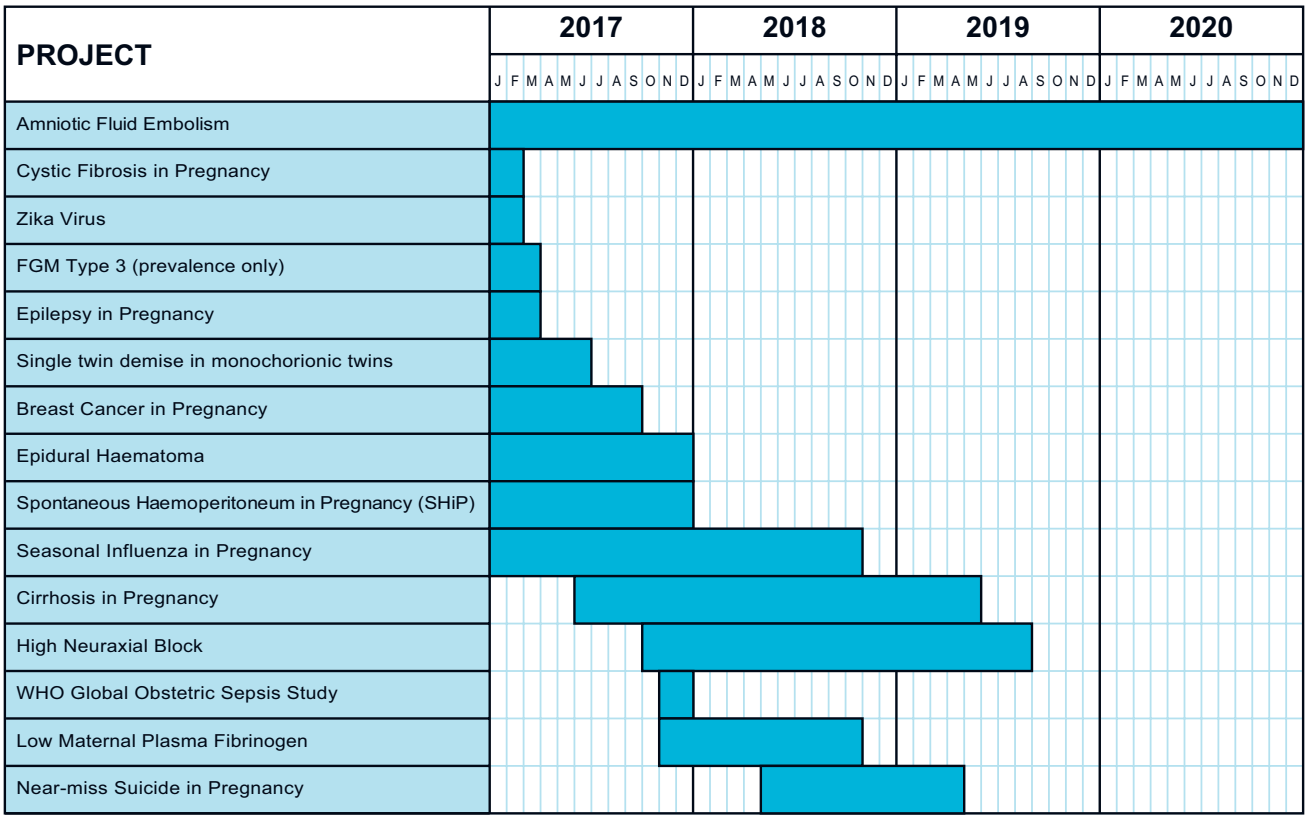


4. Studies

Unless otherwise specified, the results included in this report represent analysis of cases reported and data available up to April 2018. 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 2016-2020



4.2 Studies completed in 2017

4.2.1 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. 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 (23) 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 (24) and UK specific advice from the RCOG about the timing of interventions and delivery (25). A group in Australia and New Zealand are conducting a similar study, which will make comparisons hugely informative (26).

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 HER2 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

Up to June 2018, 132 cases of newly diagnosed breast cancer in pregnancy were reported. So far information has been received for 120 (91%) cases. Of these 28 were reported in error or were found not to meet the case criteria, seven were found to be duplicates and three data collection forms could not be completed due to lost hospital notes. This leaves 82 cases for this interim report.

With an estimate of 1,532,187 maternities during the two years of the study, this currently gives an estimated incidence of primary breast cancer diagnosed in pregnancy of 5.3 /100,000 maternities.

The maternal age at diagnosis ranged from 26 to 42 years with a median of 35. The median gestational age at diagnosis was 28 weeks. The gestation at delivery ranged from 28 to 41 weeks with a median of 37 weeks. There were 77 live-births, 1 stillbirth, and two miscarriages. Two women underwent termination of pregnancy. One woman died 4 days postpartum and one died 3 months after miscarriage.

Interim Conclusions

This study is complex because maternity and oncology care has frequently been undertaken on separate sites. We are very grateful for the extra effort that clinical teams are going to in order to search out missing data. As this is on-going, we would not wish draw 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)

4.2.2 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 aimed 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 (27), 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 (28, 29). Based on the limited published evidence, a guideline was published in 2008 for the management of pregnant women with CF (30) 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 (28), 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.

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 booked for antenatal care in a UK obstetric unit.

Surveillance Period

March 2015 – February 2017

Interim Results

During the two-year study period, 102 cases of cystic fibrosis in pregnancy were reported. Information has been received for 94 cases (92%). Of these, 15 were reported in error, five cases were duplicates and one case could not be completed due to lost hospital notes. Of the remaining cases, 8 were excluded on account of not having genetically confirmed CF.

There were 65 pregnancies meeting the case description. These included 4 women who underwent termination of pregnancy and one woman who miscarried. There were 60 liveborn infants as the cohort included two sets of twins.

The median age of women was 24 years (range 19-39 years) with a median BMI of 23 (range 14.6 - 39.2). The mean baseline FEV_1 was 72% predicted (range 18 - 116). 70% of the women were primiparous. 29% of the women had pre-existing CF-related diabetes, 13% had pre-existing liver disease and 51% had pancreatic insufficiency.

None of the women died during the study period. 10 women were admitted to HDU, with no admissions to ITU. Two women developed pancreatitis in pregnancy, 21 developed gestational diabetes, one developed obstetric cholestasis and three developed pre-eclampsia.

The median gestation at delivery was 37.5 weeks (range 28-41). 60% of infants were delivered after 37 weeks. Of the 21 pre-term deliveries, 5 followed spontaneous onset of labour, 16 were iatrogenic pre-term delivery, 5 of which were directly attributed to CF. 33% of deliveries were by caesarean section.

Of the 60 infants born, one died in the early postnatal period. 16 infants were admitted to NICU.

Interim Conclusions

Successful pregnancy in women with CF is reported across a wide range of lung functions. Subgroup analysis of outcomes in those with the poorest lung function is ongoing.

Investigators

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

Funding

This study has been funded by Wellbeing of Women.

WELLBEING OF WOMEN

4.2.3 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 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 management (31). 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 (32). 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 2018, 26 cases of epidural haematoma or abscess have been reported. Information has been received for 24 cases (92%) of which four were reported in error, two were duplicates and one data collection form could not be completed due to lost hospital notes.

Interim Conclusions

Data analysis for this study is still underway 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.

4.2.4 Epilepsy in Pregnancy

Key points

- Epilepsy is the most common neurological disorder encountered in pregnancy and affects one percent of the UK population (33, 34).
- The majority of women with epilepsy can expect a normal pregnancy, however epilepsy continues to be an important indirect cause of death for a minority of women.
- It is clear from successive confidential enquiries the management of women with epilepsy who die can be improved(35).
- There have been repeated calls amongst the research community for high-quality, prospective data enabling the value of current policy recommendations to be assessed (36-38).

Background

Amongst women presenting for maternity care, approximately 1 in 200 are receiving treatment for epilepsy, with a mortality risk that is reported to be up to 10 times greater than that of the general maternity population (39-41).

Between 2013 and 2015, 8 maternal deaths were attributed to epilepsy (maternal mortality rate =0.03/100,000). All were classified as cases of 'Sudden Unexplained Death in Epilepsy' (SUDEP)(35). 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 (36, 42). 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 (37, 40, 43). 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 (44). 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 (45). 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 woman in the UK who fulfilled 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

Over the course of the study 94 women with severe uncontrolled epilepsy were identified and they were compared with 186 control women with epilepsy. Women with uncontrolled epilepsy were younger and more likely to be unemployed than control women. In the year preceding pregnancy, women with uncontrolled epilepsy were more likely to be admitted to hospital to manage their epilepsy (OR 7.95, 95%CI 3.52-18.1) than controls, and more likely to have been seen by epilepsy specialist services (OR 2.06, 95%CI 1.23-3.44). Three women with severe uncontrolled epilepsy died (case fatality 3.2%, 95%CI 0.7-9.0%).

Interim Conclusions

There are significant opportunities to optimise pre-pregnancy epilepsy control in this population, which may have an impact on pregnancy outcomes.

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

NHS
National Institute for Health Research

NPEU
PRU-MHC

4.2.5 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"(46). 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(47). Psychological harm and post-traumatic stress disorder have also been described(48). Despite widespread practice and misconceptions about FGM there are no identified health benefits associated with FGM(46, 47).

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(49). 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(50). 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 case-control study of FGM.

Mandatory data collection of FGM is already underway in England. However, this data collection requires submission of patient-identifiable data, a cause of concern for some clinicians(51). With only 50% of eligible acute Trusts currently returning data centrally, under-ascertainment remains problematic.

Case definition

Any pregnant woman in the UK who fulfilled 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

October 2016 – March 2017

Interim results and conclusions

Over the six month period 141 cases of FGM were reported. Using an estimate of total births from 2015 (782,674) this gives a prevalence of 3.60 per 10,000 or 1 in 2,800, however as anticipated there was considerable clustering of cases across centres. Overall 11 hospitals reported 111 of the 141 cases (79%) and the remaining 30 cases were reported by 20 different hospitals. The majority of hospitals, as anticipated, reported no cases. Of note, we were informed that some centres struggled to identify the type of FGM from hospital notes or case records. From this we can conclude that any estimate of prevalence is likely to be an underestimate. The bigger issue is one of capacity of the units with large numbers of cases and whether they could cope providing the data for all these cases together with control data.

The UKOSS Steering Committee reviewed the prevalence study results and felt that although a full study into the management of FGM Type 3 should be undertaken, it would not fit within the current UKOSS methodology and would therefore benefit from being run as a separate research project independent of UKOSS.

Investigators

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

Funding

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

4.2.6 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(52). Fetal morbid sequelae may include prematurity, death of the surviving fetus or survival with perinatal morbidity(53). In addition, maternal morbidity has been reported as increased with higher (than background) rates of pre-eclampsia, coagulopathy and sepsis (54, 55). 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 woman 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).

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

Pregnancies in which both twins died should be included if the death of at least one twin occured antenatally and pre-dated the death of the secon twin.

Surveillance Period

July 2016 – June 2017

Interim Results

Up to April 2018, 137 cases were reported. Data have been received for 126 (92%) cases. Of these 44 (35%) were reported in error/did not meet the case criteria and 12 were duplicate reports. Case ascertainment is currently being cross-checked with MBRRACE-UK and has suggested underascertainment particularly in pregnancies where both twins died. We are currently in the process of contacting units to assess whether these are confirmed cases.

Interim Conclusions

Once case ascertainment is complete, full analysis will be undertaken. However interim data suggest single twin demise is less common than previously estimated.

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.

4.2.7 Spontaneous Haemoperitoneum in Pregnancy

Key points

- Spontaneous Haemoperitoneum in Pregnancy (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

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(56).

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 and 10 women died between 2013 and 2015(41). However, little is known about morbidity

during that time(35). 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.

EXCLUDED: women with uterine rupture or trauma.

Surveillance Period

January 2016 – December 2017

Interim Results

Twenty-six cases have been reported. Data for 25 (96%) cases have been returned. Of these, 5 were reported in error/did not meet the case criteria.

Interim Conclusions

The UK data are being analysed in combination with data from Belgium, Denmark and the Netherlands as part of a multi-national INOSS study. Analysis will be undertaken once data collection is completed in the Netherlands later in 2018.

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

4.2.8 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 formed part of a one week WHO multi-country global study of women with suspected or confirmed sepsis.
- This study aimed 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 sepsis.

Background

The latest estimates suggest that infections are the underlying cause of 11% of maternal deaths (57) and about 25% of newborn deaths (58), 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 took place over **ONE WEEK** only, following any women or their infants who remained in hospital for up to six weeks or until discharge, whichever was sooner.

Case definition

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

Surveillance Period

28th November 2017 – 4th December 2017

Interim Results and Conclusions

Up to April 2018, 588 cases of maternal sepsis were reported in the UK. Data have been received for 392 (67%) cases. Of these, 37 were reported in error and 5 were duplicate cases. Several thousand cases have been identified globally across 58 countries and data are currently being analysed by the WHO with the aim for results to be published early next year.

Investigators

Mercedes Bonet, Joao-Paolo Souza, WHO; Marian Knight, NPEU

World Health Organization

human reproduction programme hrp

research for impact

UNDP·UNFPA·UNICEF·WHO·WORLD BANK

4.2.9 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(20).

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 carried 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 were added to the reporting card/electronic submission page

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 were requested to report the numbers of women in their unit who fell into either category. Detailed data was only requested on women with an adverse pregnancy outcome i.e. UKOSS only collected numbers of women falling into group 1; reporting clinicians were not requested to complete a data collection form. Data collection forms were sent for completion of further details about women in group 2.

Surveillance Period

March 2016 – February 2017

Interim Results

726 pregnant women with a relevant travel history were recorded. In 12 of these, an adverse pregnancy outcome was reported, an observed proportion of 1.7% (95 CI 0.9% to 2.9%). This proportion does not exceed the expected level of any of the specified outcomes.

Interim Conclusions

These results suggest that in the UK the number of adverse pregnancy outcomes does not exceed expected levels. This study showed how rapid surveillance using UKOSS could be used in an emerging situation.

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 was funded by Public Health England.

Public Health England

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 2018, 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 and data are currently being assembled.

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 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(59). 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(59-64), 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(62, 64). Fetal complications are reported to include miscarriage, pre-term delivery and intrauterine growth restriction(60-62, 64).

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(59). 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(59).

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, previous bacterial peritonitis) or supportive laboratory findings (low platelets, low albumin, prolonged prothrombin time or INR).

Surveillance Period

June 2017 – May 2019

Interim Results and Conclusions

Up to April 2018, 25 cases of cirrhosis were reported with data received for 16 (64%) cases. Of these, one case was a duplicate.

Investigators

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

Funding

The Lauren Page Trust

4.3.3 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(65) and 1:16,200(66) anaesthetics. More recently a retrospective study in the USA suggested an incidence of high spinal block of 1:4336 anaesthetics(67). 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(68). While the outcomes for cardiac arrest in this setting were good, it behoves 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.

Surveillance Period

September 2017 – August 2019

Interim Results and Conclusions

Up to April 2018, 33 cases of high neuraxial block have been reported. So far information has been received for 24 (73%) cases. Of these, 3 were reported in error/did not meet the case criteria.

Investigators

Gary Stocks, Imperial College Hospitals; Nuala Lucas, Northwick Park Hospital; Marian Knight, NPEU

Funding

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

4.3.4 Low Maternal Plasma Fibrinogen

Key Points

- Obstetric haemorrhage remains an important cause of maternal mortality in the UK.
- Evidence suggests the incidence of obstetric haemorrhage in high-resource settings is increasing.
- It is unclear whether fibrinogen replacement at or below a level of 2g/L affects blood loss.
- Further observational evidence is required before potentially developing a randomised controlled trial of coagulation management.

Background

Obstetric haemorrhage is an important cause of maternal mortality in the UK. In the 2012-2014 Confidential Enquiry thirteen women died as a direct consequence of haemorrhage; a number that is unchanged from the previous report (35). With evidence suggesting that the incidence of obstetric haemorrhage is increasing in high-resource settings, a better understanding of the mechanisms of injury and, more importantly, the clinical sequelae in obstetric patients is needed (69-71).

Women with a plasma fibrinogen <2g/L and continuing bleeding represent a high-risk group that is associated with both progressive haemorrhage and the increased use of blood products and invasive procedures (69, 70). Two double-blind RCTs have investigated the role of fibrinogen replacement in PPH. Pre-specified subgroup analysis of the second RCT showed that, if the fibrinogen level was >2g/L during severe PPH, fibrinogen replacement did not affect blood loss or the need for transfusion but that an effect below 2g/L could not be excluded (72). This supports a RCOG recommendation that fibrinogen replacement is not necessary if plasma fibrinogen is above 2g/L (69). However, a possible effect of fibrinogen replacement at fibrinogen levels of below 2g/L cannot be excluded on the basis of the trial data (72, 73).

It is clear from the previous UKOSS study of massive transfusion (71) that the haematological parameters observed amongst groups of women with different causes for their obstetric haemorrhage are very variable, and hence differences in the underlying cases of haemorrhage in the trial participants may have had a substantial impact. The aim of this study is to obtain further observational evidence before potentially developing a randomised controlled trial of coagulation management.

Case Definition

Any woman with either a laboratory Clauss fibrinogen <2g/L OR Fibtem <10mm OR TEG functional fibrinogen <200mg/dL at any time during pregnancy or postpartum before first discharge, irrespective of cause.

Surveillance Period

November 2017 – October 2018

Interim Results and Conclusions

Up to April 2018, 54 cases of low maternal plasma fibrinogen were reported. So far information has been received for 29 (54%) cases. Of these, 3 were reported in error/did not meet the case criteria.

Investigators

Marian Knight, NPEU; Simon Stanworth, NHSBT; Rachel Collis, Cardiff and Vale UHB; Peter Collins, Cardiff and Vale UHB

Funding

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

4.3.5 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, and a group of control women, in order to investigate risk 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, and a group of control women, in order to investigate risk 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 2018

Interim Results

Up to April 2018, 450 cases of seasonal influenza have been reported. Data have been received for 237 (53%) cases. Of these 17 were reported in error/did not meet the case criteria, one was a duplicate and one data collection form could not be completed due to lost hospital notes. We began requesting two control forms with each case from November 2017 onwards and to date we have requested 688 controls and received data for 172 (25%).

Interim Conclusions

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

Investigators

Marian Knight, NPEU

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.

NHS
National Institute for Health Research

NPEU
PRU-MHC

4.4 Future Studies

These studies have been approved by the UKOSS Steering Committee to commence in 2018.

4.4.1 Hyponatraemia

Key points

- Little is known about hyponatraemia in pregnancy but it can have major consequences for both woman and neonate.
- There have been a growing number of case reports of women who have been unwell around the time of labour and delivery and consequently been found to have hyponatraemia.
- Very few studies into hyponatraemia in pregnancy have been conducted so it is hoped this study will establish the incidence of hyponatraemia in pregnant women in the UK and describe the management and perinatal outcomes of pregnancies and births affected by hyponatraemia.

Background

Knowledge on hyponatraemia in pregnancy is limited to a growing number of case reports of women and neonates who have had seizures or confusion around the time of labour and delivery. These women were otherwise well and excessive drinking and oxytocin infusion diluted in 5% dextrose has been implicated (74-76). There have been some concerns regarding whether birthing pools have a link to hyponatraemia (77).

A prospective observational cohort study from Sweden showed that the incidence of hyponatraemia immediately post-delivery is 26% in women who have had more than a total of 2.5L fluid intake both orally and intravenously (78). They showed that women had a lower sodium when the labour was longer. They also showed that babies' cord sodium was lower when women had a higher fluid intake in labour. This study was limited by the fact that oxytocin was diluted in 5% dextrose and that a proportion of women also were given 5% dextrose intravenously for calorific purposes. This study showed an 8% incidence of hyponatraemia overall, though none of these women had severe symptoms.

A guideline has been developed after multiple severe cases of peri-partum hyponatraemia in Northern Ireland. There is no strong evidence base to inform this guideline but it was developed via consensus of senior clinicians from the 5 acute Healthcare trusts in Northern Ireland (79). This study will provide further information to inform future guidelines.

Case Definition

Any woman with hyponatraemia (Na<125mmol/l) presumed in retrospect to be due to water intoxication, excluding sepsis and pre-eclampsia.

Main research questions

- What is the current incidence of symptomatic peripartum hyponatraemia in the UK?
- What are the risk factors for the development of peripartum hyponatraemia?
- How is peripartum hyponatraemia managed?
- What are the delivery and postpartum outcomes for the mother and baby in a woman who develops a peri-partum hyonatraemia?

Investigators

Arani Pillai, Nottingham University Hospital NHS Trust; Nuala Lucas, Northwick Park Hospital; Cathy Nelson-Piercy, Guy's & St Thomas' Foundation Trust and Imperial College Healthcare Trust

Funding

This study is currently pending, subject to funding.

4.4.2 Near Miss Suicide in Pregnancy

Key points

- Mental illness is a leading cause of maternal mortality in the UK.
- The largest proportion of maternal deaths result from suicide.
- Antenatal suicide attempts occur less frequently than postnatal attempts although they clearly increase risk of harm to the fetus.
- There are currently no studies that have explored near miss suicides during pregnancy despite it becoming increasingly recognised that studying near miss events can provide important additional information to guide prevention strategies of rare events.

Background

Mental illness is estimated to affect one in ten pregnancies and, in the UK, has persistently been found to be a leading cause of maternal mortality (35, 80). Although maternal deaths are rare (8.8 per 100,000 maternities) (35, 81), recent confidential enquiries into maternal mortality found that almost one in five women who died during birth had a mental illness and almost a quarter of those who died in the postnatal period died from mental health related causes (81). Among this group of women the largest proportion of deaths resulted from suicide (2.3 deaths by suicide during or up to one year after the end of pregnancy per 100,000 maternities between 2009-13 (81).

It is becoming increasingly recognised that studying near miss events (or life-threatening situations) can provide important additional information to guide prevention strategies of rare events (82), however no previous studies have explored near miss suicides during pregnancy. Three quarters of maternal suicides occur during the postnatal period, making suicides during the antenatal period a rare event (81). There is also evidence to suggest that suicide attempts may occur less frequently during pregnancy than following birth, although robust incident figures are not currently available.

Antenatal suicide attempts also increase the risk of potential harm to fetal development, particularly in the case of drug overdoses during pregnancy which can have teratogenic or fetotoxic effects (83). However, no national data on near miss suicides during pregnancy exists (83), and very little is known about the epidemiology, neonatal outcomes, warning signs or clinical management proceeding and following a near miss suicide event during pregnancy with the UK. Finding ways to recognise and respond appropriately to women at particular risk signifies a key public health goal. Current insufficient research in this area is likely to limit efforts to effectively identify women at high risk of suicide and prevent further tragedies in the future.

Case definition

Any woman with self-inflicted injury or poisoning, during pregnancy, requiring an admission to a general hospital for:

Either Level 2 critical care (i.e. patient requiring more detailed observation or intervention including support for a single failing organ system or post-operative care and those 'stepping down' from higher levels of care)

Or Level 3 critical care (i.e. patients requiring advanced respiratory support alone or monitoring and support for two or more organ systems. This level includes all complex patients requiring support for multi-organ failure)

Or A liver unit

Main research Questions

- What is the incidence of near miss suicides during pregnancy in the UK?
- What are the circumstances of the near miss suicide events (e.g. methods, timing and nature) and individuals' characteristics (i.e. socio-demographic, diagnostic status, prescribed medication and prior contact with maternity and mental health services) during pregnancy in the UK?
- What type antenatal and mental healthcare do women with near miss suicides during pregnancy receive before and following the near miss event? (e.g. what assessments and treatments were offered, how many women were receiving input from specialist psychiatric teams prior to and following the event)
- What are the maternal (i.e. level of injury, care plans and pregnancy and birth outcomes) and neonatal outcomes (i.e. birth outcomes) for women with near miss suicides during pregnancy?
- What are the circumstances and potential warning signs women with a near miss suicide during pregnancy?

Investigators

Abigail Easter and Louise Howard, Institute of Psychiatry, Psychology and Neuroscience, London; Jane Sandall, Department of Women and Children's Health, King's College London; Louise M Howard

Funding

This study is funded as part of a King's Improvement Science Fellowship (funded by King's Health Partners).

5. Publications

5.1 The incidence, characteristics, management and outcomes of anaphylaxis in pregnancy: a population-based descriptive study

Published Article

McCall SJ, Bunch KJ, Brocklehurst P, D'Arcy R, Hinshaw K, Kurinczuk JJ, et al. The incidence, characteristics, management and outcomes of anaphylaxis in pregnancy: a population-based descriptive study. BJOG: An International Journal of Obstetrics and Gynaecology. 2018;125(8):965-971.

Key points

- Anaphylaxis in pregnancy is a potentially fatal systemic hypersensitivity reaction. The incidence in the general population is thought to be increasing, and with greater use of antibiotic prophylaxis, for example for Group B Streptococcal (GBS) carriage, there is the potential for a rising incidence in the pregnant population.
- The aim of this study was to describe the incidence, causative agents, management and associated outcomes of anaphylaxis in association with pregnancy.
- 37 women with anaphylaxis associated with pregnancy were identified between October 2012 and September 2015, giving an estimated incidence of 1.6 (95% CI: 1.1–2.2) per 100 000 maternities.
- Four cases occurred in women with known penicillin allergies: two received co-amoxiclav and two cephalosporins.
- Twelve women had anaphylaxis following prophylactic use of antibiotics at the time of a caesarean delivery. Prophylactic use of antibiotics for Group B streptococcal infection accounted for anaphylaxis in one woman.
- Two women died (5%), 14 (38%) women were admitted to intensive care and seven women (19%) had one or more additional severe maternal morbidities.
- No infants died; however, in those infants whose mother had anaphylaxis before delivery (n=18) there were seven (41%) neonatal intensive care unit admissions, three preterm births and one baby was cooled for neonatal encephalopathy.
- This study highlights the seriousness of the outcomes of this condition for the mother. The low incidence is reassuring given the large proportion of the pregnant population that receive prophylactic antibiotics during delivery.

5.2 Deflation versus maintained inflation of gastric band in pregnancy: A national cohort study

Published Articles

Jefferys A, Lenguerrand E, Cornthwaite K, Johnson A, Lynch M, Hyde J, Draycott T, Siassakos D. Deflation versus maintained inflation of gastric band in pregnancy: A national cohort study. Obstet Med. 2017 Jun;10(2):67-73.

Key points

- As bariatric surgery becomes more common, the number of women undergoing pregnancy after such surgery is also thought to be increasing. Laparoscopic adjustable gastric banding (LAGB) accounts for a third of bariatric procedures, but evidence to guide band management during pregnancy is lacking.

- The aim of this study was to describe the outcomes of pregnancy for women and infants according to band management (deflation versus maintained inflation).
- 107 women with an LAGB in pregnancy were identified in the UK between November 2011 and October 2012; 42 women had the band deflated during pregnancy (39%), in 54 inflation was maintained (50%) and in 11 women band management was unknown (10%).
- There was a greater mean gestational weight gain amongst women who had their band deflated (15.4kg vs 7.6kg in the inflated group, p=0.05), but maternal outcomes were otherwise similar.
- Infants of women whose band was deflated had a higher mean birthweight (3712g vs 3380g in the inflated group, p<0.01, but infants of mothers whose band remained inflated were more likely to be small for gestational age (6/54, 11% vs 0/44, 0% in deflated group, p=0.05). Other perinatal outcomes were similar.
- Most outcomes were worse in both groups in comparison to national data.
- This study suggests that inflation may be associated with better maternal outcomes, but deflation associated with better infant outcomes for women with an LAGB in pregnancy.

5.3 Neonatal outcomes after failed tracheal intubation during obstetric general anaesthesia for caesarean section: Secondary analysis of a UKOSS case-control study

Published Article

Quinn AC, Kinsella SM, Gorton HJ, Knight M, Columb MO, Robson SC, Mushambi MC. Neonatal outcomes after failed tracheal intubation during obstetric general anaesthesia for caesarean section: Secondary analysis of a UKOSS case-control study. Eur J Obstet Gynecol Reprod Biol. 2017;217:181-182.

Key points

- Poor neonatal outcomes following failed tracheal intubation at caesarean section are frequently described, however, in many instances the operation is performed in the context of fetal distress, thus it is difficult to ascribe causation.
- The aim of this secondary analysis was to examine factors which might influence neonatal outcome after failed endotracheal intubation.
- 50 pregnant women in whom failed tracheal intubation occurred during general anaesthesia for caesarean section were compared with 94 control pregnant women who had uneventful general anaesthesia.
- There were no differences between cases and controls with respect to indication and urgency category of caesarean section. However, significant factors independently associated with neonatal intensive care unit admission were 5 min Apgar score (aOR 0.50 per unit increase, 95%CI 0.36-0.67), birth weight (aOR 0.87 per 100g increase, 95%CI 0.82-0.94), gestation (aOR 0.56 per week increase, 95%CI 0.45-0.71), lowest maternal SpO_2 (aOR 0.96 per 1% increase, 95%CI 0.93-1.00) and failed tracheal intubation (aOR 3.88, 95%CI 1.29-11.65).
- Failed tracheal intubation at caesarean section thus appears to be an independent factor associated with the need for extra neonatal support, and obstetric and neonatal services should be aware of this link.

5.4 Hormone-secreting adrenal tumours cause severe hypertension and high rates of poor pregnancy outcome; a UKOSS study with case control comparisons

Published Article

Quartermaine G, Lambert K, Rees K, Seed PT, Dhanjal MK, Knight M, McCance DR, Williamson C. Hormone-secreting adrenal tumours cause severe hypertension and high rates of poor pregnancy outcome; a UKOSS study with case control comparisons. BJOG. 2018;125(8):719-727.

Key points

- Hormone secreting adrenal tumours, causing phaeochromocytoma, primary aldosteronism and adrenal Cushings syndrome, are rare, but case series have reported significant morbidity and mortality in pregnancy.
- The aim of this study was to undertake a prospective, national cohort study using UKOSS to describe the incidence, monitoring, management and outcomes of hormone-secreting adrenal tumours in pregnant women.
- Between March 2011 and February 2015, 15 pregnant women met the inclusion criteria: ten with phaeochromocytoma, three with primary aldosteronism and two with Cushing's syndrome, representing an overall incidence of 0.5 per 100,000 maternities.
- Clinical symptoms were similar to those in non-pregnant women due to the hormones released.
- All women diagnosed in pregnancy had severe hypertension.
- There was a significantly increased risk of adverse pregnancy outcomes in women with any one of the tumours, with increased rates of stillbirth, preterm birth and operative delivery compared to a control group of pregnant women without tumours.
- This study showed that adrenal tumours are associated with increased risks for pregnant women and their babies. Data on these tumours to inform practice are limited and international collaborative efforts are likely to be needed.

5.5 The DiPEP study: an observational study of the diagnostic accuracy of clinical assessment, D-dimer and chest x-ray for suspected pulmonary embolism in pregnancy and postpartum

Published Article

Goodacre S, Horspool K, Nelson-Piercy C, Knight M, Shephard N, Lecky F, Thomas S, Hunt BJ, Fuller G. The DiPEP study: an observational study of the diagnostic accuracy of clinical assessment, D-dimer and chest x-ray for suspected pulmonary embolism in pregnancy and postpartum. BJOG 2018; [Epub ahead of print].

Key points

- Pulmonary embolism (PE) is the leading direct cause of death in pregnancy and postpartum. However, many pregnant and postpartum women with suspected PE undergo negative investigation. The decision to undertake imaging could be informed by clinical decision rules.

- The aim of this study was to use a UKOSS study of confirmed PE together with a prospective study of women with suspected PE to identify the clinical features associated with pulmonary embolism (PE) diagnosis and determine the accuracy of decision rules and D-dimer for diagnosing suspected PE in pregnant/postpartum women.
- 324 pregnant/postpartum women with suspected PE were compared to 198 pregnant/postpartum women with diagnosed PE.
- The only clinical features associated with PE on multivariate analysis were age (odds ratio 1.06; 95% CI 1.01–1.11), previous thrombosis (3.07; 1.05–8.99), family history of thrombosis (0.35; 0.14–0.90), temperature (2.22; 1.26–3.91), systolic blood pressure (0.96; 0.93–0.99), oxygen saturation (0.87; 0.78–0.97) and PE-related chest x-ray abnormality (13.4; 1.39–130.2).
- Neither clinical decision rules nor D-dimer had clinically useful thresholds for decision-making.
- This study showed that clinical decision rules and D-dimer should not be used to select pregnant or postpartum women with suspected PE for further investigation. Clinical features and chest x-ray appearances may have counter-intuitive associations with PE in this context.

5.6 Abstracts

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

- Severe uncontrolled epilepsy in pregnancy in the UK

5.7 UKOSS Publications to date

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6. Acknowledgements

These studies would not have been possible without the support 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 Betsi Cadwaladr University Health Board (BCUHB), BMFMS, King's Health Partners, National Institute for Health Research, Obstetric Anaesthetists Association (OAA), Public Health England, The Lauren Page Trust, TAMBA and Wellbeing of Women.

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