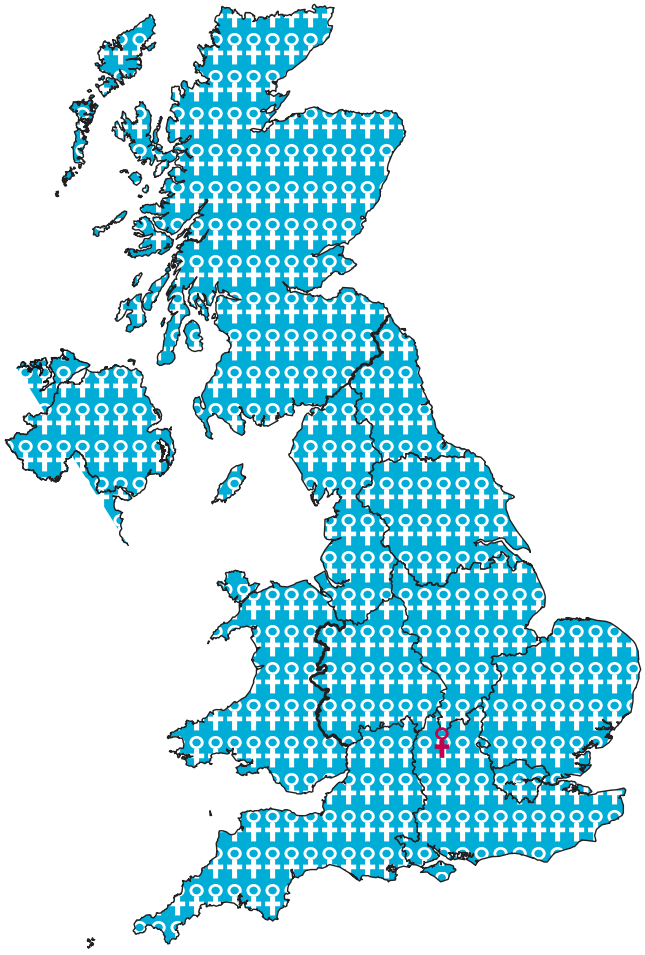
UKOSS

UK Obstetric Surveillance System

Annual Report 2008

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



Royal College of Obstetricians and Gynaecologists

npeu 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 and the Royal College of Obstetricians and Gynaecologists, was launched in February 2005. The system is designed to be used to survey a range of rare conditions in pregnancy. The system is also supported by the Royal College of Midwives, the Obstetric Anaesthetists Association, the National Childbirth Trust, the Faculty of Public Health, the Confidential Enquiry into Maternal and Child Health, the Department of Health, the Health Protection Agency and the National Patient Safety Agency.

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

Studies using UKOSS may be undertaken by any investigator who identifies a suitable topic[1]. 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 which can be suitably addressed using the UKOSS methodology (prospective descriptive, cohort or case-control studies). This report outlines the studies undertaken during the third year of surveillance using UKOSS.

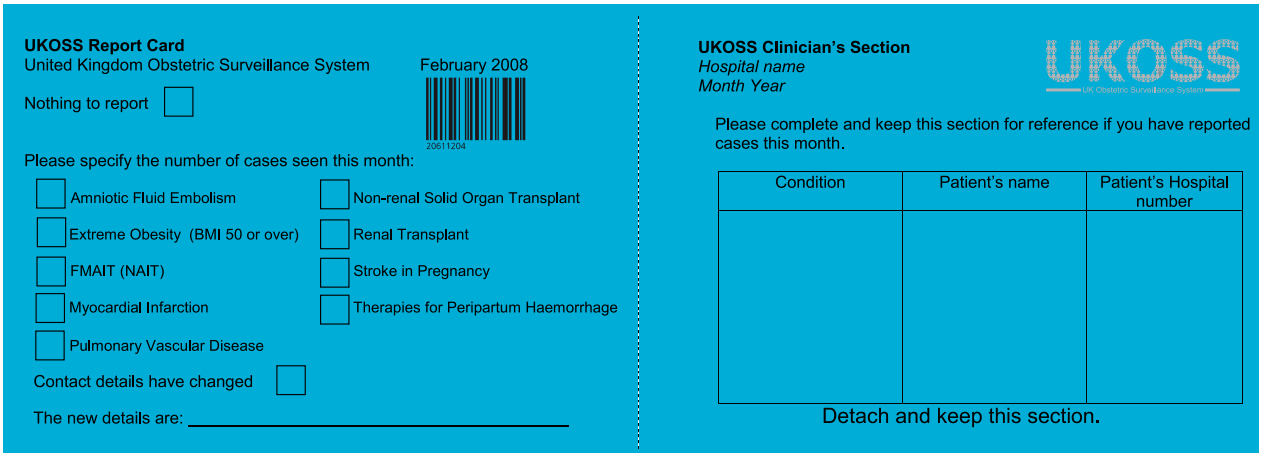
2. Methods

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

On receiving a case report (return of the monthly card mailing), the UKOSS central team dispatches a data collection form to collect more detailed information about each case. The data collection forms are developed individually for each condition and are designed to be short and easily completed from a woman's case notes without requiring reference to any other sources of information. The data collection forms seek confirmation of the appropriate case definition and additional information on risk factors, management and outcomes according to the protocol relating to each condition. UKOSS does not collect any personally identifiable information, including women's names, addresses, dates of birth or hospital numbers. Reporting clinicians are asked to keep their own record of the names of women they have reported, in order that they can retrieve the woman's case notes to complete the data collection form. The Patient Information Advisory Group (PIAG) and the Confidentiality and Security Advisory Group for Scotland (CSAGS) have judged that collection of information only, for the purpose of studying incidence and identifying means to improve patient care, which is not individually identifiable and does not lead to any change in management for the individual patient is acceptable without requiring individual patient consent[2 3]. The UKOSS methodology and that of each individual study have been approved by the London Multi-centre Research Ethics Committee (Study ref 04/MRE02/45).

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

Figure 1: UKOSS Report Card



UKOSS Report Card
United Kingdom Obstetric Surveillance System
February 2008
20511204

Nothing to report ☐

Please specify the number of cases seen this month:

☐ Amniotic Fluid Embolism
☐ Extreme Obesity (BMI 50 or over)
☐ FMAIT (NAIT)
☐ Myocardial Infarction
☐ Pulmonary Vascular Disease
☐ Non-renal Solid Organ Transplant
☐ Renal Transplant
☐ Stroke in Pregnancy
☐ Therapies for Peripartum Haemorrhage

Contact details have changed ☐

The new details are: _____

UKOSS Clinician's Section
Hospital name
Month Year

UKOSS
UK Obstetric Surveillance System

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

Condition	Patient's name	Patient's Hospital number

Detach and keep this section.

3. Participation

All 227 units with consultant-led maternity units in the UK contribute to UKOSS. This represents 100% participation of eligible units and effectively means that the denominator for all UKOSS studies is the entire birth cohort in the UK. The mean monthly card return rate during 2007 was 91% (Figure 2), with regional return rates varying between 87% and 97% (Figure 3). These card return rates continue the high rates obtained during the first two 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 2007

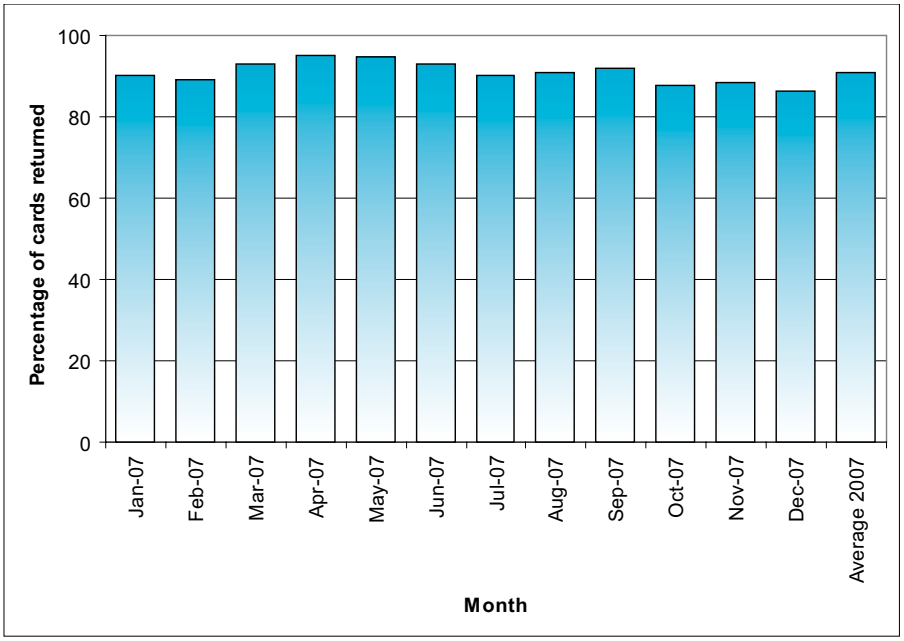
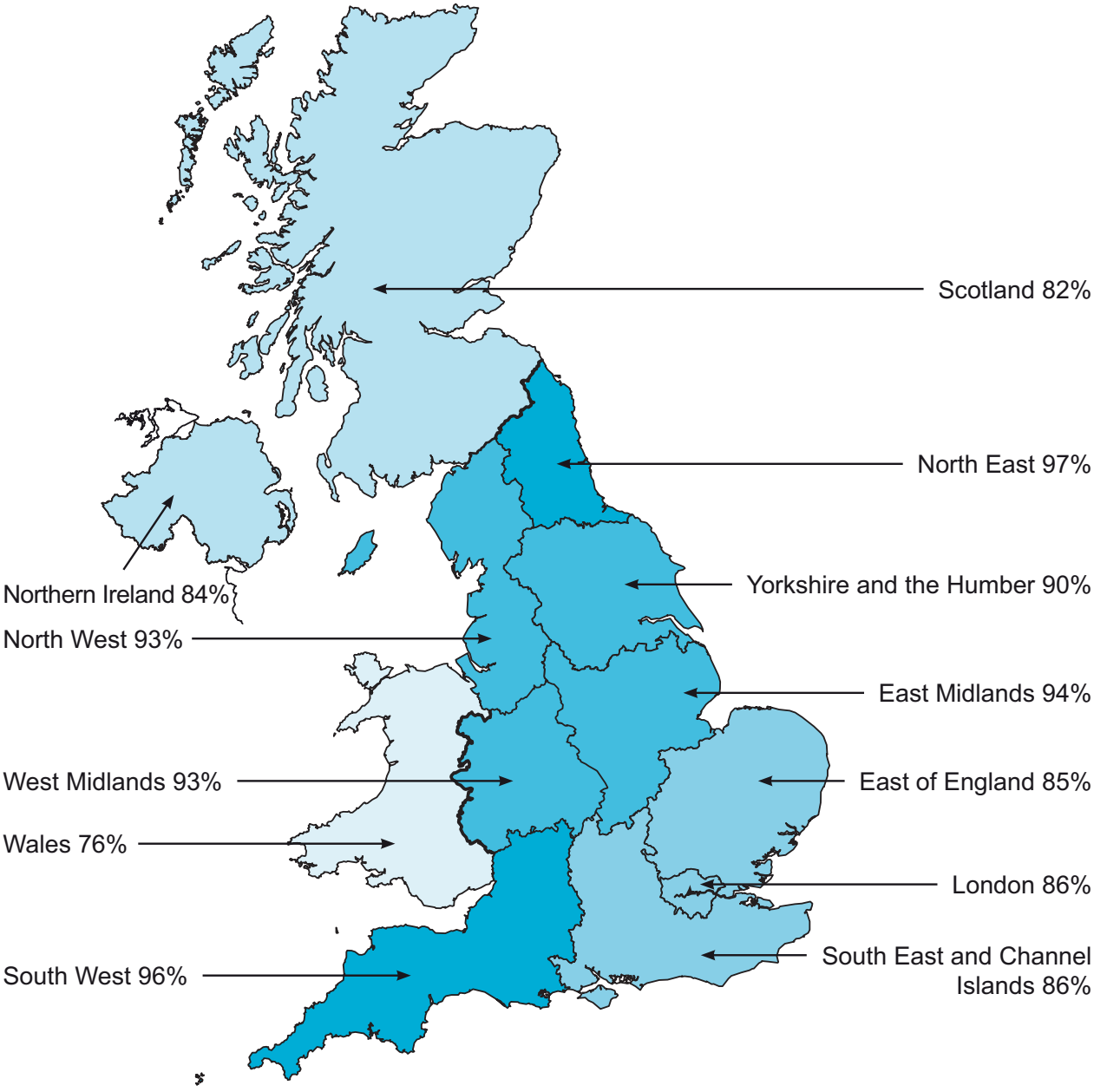


Figure 3: Map showing regional card return rates over the first two years of surveillance

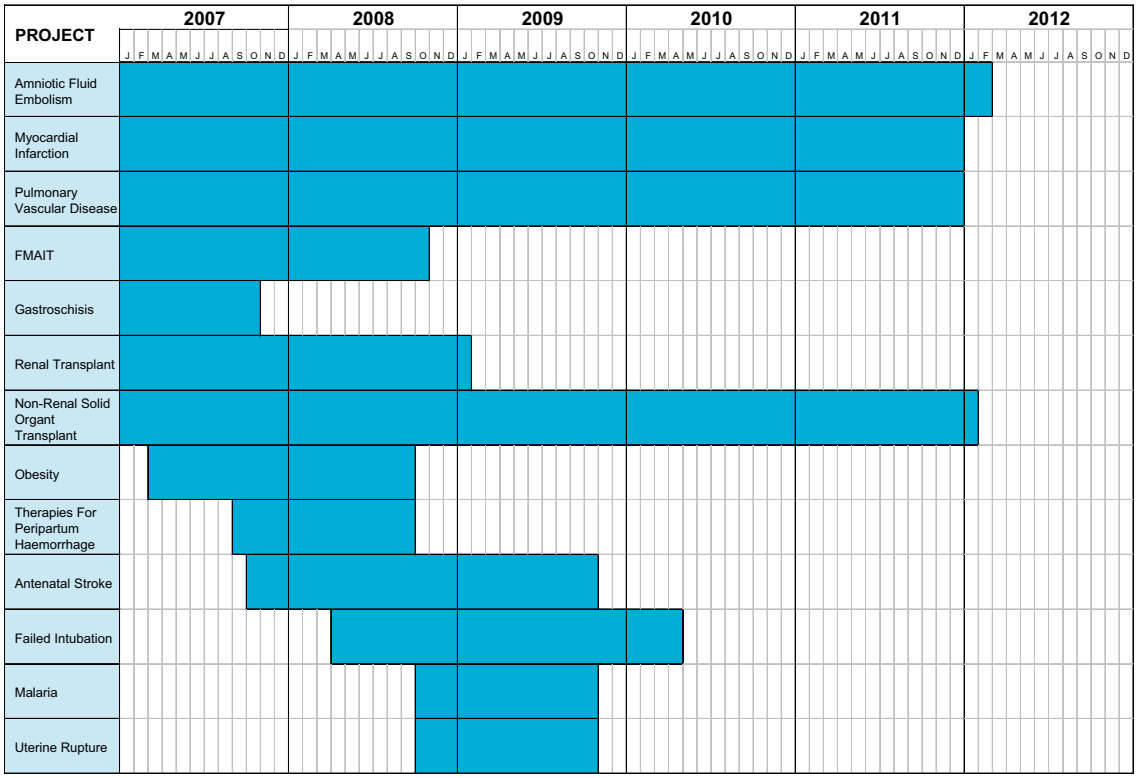


4. Studies

Unless otherwise specified, the results included in this report represent analysis of cases reported and data available up to January 2008. All studies have been funded through a grant to the NPEU from the Department of Health except where indicated. Please note the data presented are provisional, not peer reviewed and definitive conclusions should not be drawn from them.

4.1. Study Timetable

Figure 4: Provisional UKOSS Study Data Collection Timetable 2007-2012



4.2 Studies completed in 2007

4.2.1 Gastroschisis

Key points

- The birth prevalence of gastroschisis as estimated by this study is in line with the estimate from existing regional congenital anomaly registers, but nearly double the estimate from the National Congenital Anomaly System (NCAS).
- The majority of cases are diagnosed antenatally.
- The majority of cases occurred in mothers aged under 25; known recreational drug use in early pregnancy was a feature in only a small minority of cases.
- Further analysis will be undertaken to assess regional variations in birth prevalence.

Background

Gastroschisis is a congenital anomaly of the anterior abdominal wall, in which gut and other abdominal contents are herniated through a defect in the wall to one side of the umbilicus[4]. The condition has been noted to be increasing worldwide, although the reasons for this rise remain obscure[5]. A number of reports, predominantly from regional congenital anomaly registers, have provided evidence that this increase is also occurring in the UK[4 6-8], leading to a call for further research on the condition by the Chief Medical Officer for England[9]. This increase in birth prevalence of gastroschisis has been noted to occur particularly in infants of younger mothers[9]. Additionally a North-South gradient in birth prevalence has been noted in the UK, although incomplete geographical coverage by regional congenital anomaly registers makes this difficult to study[6]. Currently regional congenital anomaly registers cover only 50% of the UK population and ascertainment through the National Congenital Anomaly System (NCAS) is known to be poor[10]. The

objective of this study was to combine the use of UKOSS, the British Association of Paediatric Surgeons Congenital Anomalies Surveillance System (BAPS-CASS) and the British Isles Network of Congenital Anomaly Registers (BINOCAR) to more completely assess the birth prevalence of gastroschisis in the UK.

Case definition

All pregnant women with a fetus affected by gastroschisis.

Excluded: Aplasia or hypoplasia of abdominal muscles, skin-covered umbilical hernia or omphalocele.

Surveillance Period

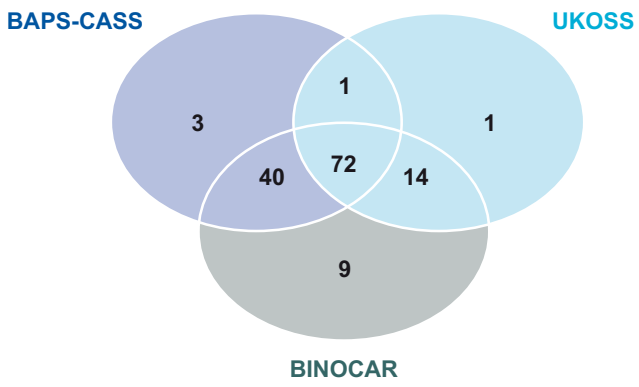
September 2006 – October 2007

Interim Results

Although data collection through UKOSS is complete, data collection for the parallel study through BAPS-CASS (www.npeu.ox.ac.uk/BAPS-CASS), and for the comparison with reporting to congenital anomaly registers (BINOCAR) is still underway. These figures therefore represent interim results which may be modified when all data are complete.

There were 303 cases of gastroschisis identified through UKOSS & BAPS-CASS in an estimated 726,517 total births; 285 (94%) infants were live born. Simple capture-recapture analysis suggests 38 cases nationally were not identified through these two sources. Twenty-four further cases have been identified through BINOCAR to date, representing an estimated total prevalence of 5.0 cases/10,000 total births (95%CI 4.5 - 5.5/10,000) (finguere 5). Two hundred and ninety-eight cases (99%) were diagnosed antenatally; 17 (6%) had additional non-bowel anomalies. The median age of mothers was 21 years (range 16-45). Five percent of women were reported to have used recreational drugs in early pregnancy. Thirty-five percent had suspected intrauterine growth restriction antenatally, 20% had oligohydramnios and 3% had polyhydramnios. Outcomes are known for 327 pregnancies. Sixteen were terminated (seven fetuses with additional anomalies); eight miscarried; there were nine intrauterine deaths (Stillbirth rate 30 per 1000 total births) and 12 infant deaths (infant mortality rate 41 per 1000 live births).

Figure 5: Live born cases reported through UKOSS and BAPS-CASS



Note that BINOCAR covers only half of all births in England and Wales and these figures therefore represent the number of infants born with gastroschisis in an estimated denominator of 300,000 total births.

Interim Conclusions

The national prevalence of gastroschisis estimated from this study is almost double the most recent figure from the National Congenital Anomaly System (NCAS), corroborating reports of under-ascertainment through NCAS. This study suggests the national prevalence of gastroschisis is in line with estimates from BINOCAR[11]. Further information on regional variations, prognostic factors and outcomes will be available at the end of the study.

Funding

This study is part funded by a small grant from BDF Newlife.

4.3 Studies in progress

4.3.1 Amniotic Fluid Embolism

Key points

- Amniotic fluid embolism is a leading cause of maternal mortality in the UK today.
- Estimates of incidence and mortality vary widely.
- This study incorporates the previous UK voluntary amniotic fluid embolism register.
- Preliminary analysis shows the estimated incidence using active surveillance through UKOSS is more than twice that obtained through passive registration.

Background

Amniotic fluid embolism (AFE) has been identified by the UK Confidential Enquiry into Maternal Deaths as a leading cause of maternal mortality[12] with some evidence that fatality is decreasing in the UK. Estimates of incidence vary tenfold between 1.3 and 12.5 per 100,000 pregnancies[13]. Estimates of the mortality rate from this condition also vary widely[14], from as much as 86% to more recent estimates of 16-30%. No clear risk factors are identifiable from previous case series, but some preliminary evidence suggests that earlier diagnosis may lead to better outcomes. A wide range of treatments have been described in case reports[14], but there has been no comprehensive study of the epidemiology and management of this condition in the UK. A database of voluntary notifications was established in the UK to collect information on epidemiology and management[15]; this register was incorporated into UKOSS to improve ascertainment and allow a comprehensive study of the epidemiology and current management.

Case definition

EITHER A clinical diagnosis of AFE (acute hypotension or cardiac arrest, acute hypoxia or coagulopathy in the absence of any other potential explanation for the symptoms and signs observed)

OR A pathological diagnosis (presence of fetal squames or hair in the lungs).

Surveillance Period

February 2005 – ongoing

Interim Results

In the first three years of the study 67 cases of amniotic fluid embolism were reported. Information has been received for 59 of these cases (88%). There were 12 cases which were subsequently reported by clinicians as not cases and two duplicate reports. Seven further cases did not meet the case definition. There were thus 38 confirmed cases in an estimated 2,147,000 maternities. This gives an incidence estimate in the UK of 1.8 cases per 100,000 maternities (95% CI 1.3 to 2.4 per 100,000). There were nine deaths reported to UKOSS among the 38 cases, giving an estimated case fatality rate of 24% (95% CI 11-40%).

Interim Conclusions

The estimated incidence using active surveillance is more than twice that obtained by passive registration[15]. The study is ongoing and the results will be analysed further when sufficient cases have been collected to generate robust results.

4.3.2 Antenatal Stroke

Key points

- Stroke is an important cause of severe maternal morbidity and mortality in the UK.
- The increasing age of women at childbirth, along with other risk factors, may lead to an increase in the incidence of stroke associated with pregnancy.
- There have been no prospective national studies to estimate the incidence or outcomes of this condition.
- This study will investigate the incidence, risk factors, management and outcomes of stroke in pregnancy in the UK in order to inform future guidelines for prevention and treatment.

Background

The decreasing incidence of direct causes of maternal death over the past half century has led to a heightened awareness of non-obstetric factors responsible for maternal mortality[16]. While stroke associated with pregnancy is rare (estimates of incidence from retrospective studies vary from 3 to 30 per 100,000 pregnancies), the last seven Confidential Enquiries into Maternal Deaths report 144 deaths from stroke associated with pregnancy. In addition to premature death, stroke associated with pregnancy causes ongoing disability in many survivors, which has a serious impact for mother and infant, and on families, caregivers, and health services. Several population based studies suggest that there is an increase in the rate of all forms of stroke during the puerperium, but not during pregnancy itself[17], however the estimates of incidence from different studies vary widely. The larger studies, based on administrative datasets are subject to coding errors, and can not collect information on individual cases, whilst the smaller studies are based on very few cases, and often recruit from specialist referral centres where the incidence may be higher, and estimates of the denominator population may be inaccurate.

As the age of women childbearing increases, alongside an increase in other vascular risk factors, the incidence of stroke pregnancy may be increasing. By prospectively collecting data on maternal stroke this study will provide valuable information into the epidemiology of stroke associated with pregnancy.

Case definition

All women in the UK identified as having a stroke during pregnancy.

To be included as a case the stroke must

EITHER Be confirmed at postmortem

OR Be confirmed by a consultant neurologist or physician

OR Be confirmed by diagnostic testing (e.g. MRI/CT)

Surveillance Period

October 2007 – October 2009

Interim Results

Eleven cases were reported up to January 2008 and data returned about six of them (55%). One did not meet the case definition. There were thus five confirmed cases.

Interim Conclusions

This study is currently at an early stage. These interim results suggest that the incidence of antenatal stroke is similar to that estimated from the literature. Risk factor and outcome information will be assessed once data collection is complete.

Investigators

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Marian Knight, NPEU

Funding

This study is funded by Wellbeing of Women.

Wellbeing of Women

Charity Registration No: 239281

4.3.3 Fetomaternal Alloimmune Thrombocytopenia (FMAIT/NAIT)

Key points

- FMAIT is associated with significant fetal and infant morbidity and mortality, first pregnancies are often severely affected and the diagnosis is usually made with the birth of a first affected infant.
- There is a debate about the utility of antenatal screening for the condition.
- Parallel descriptive studies using the British Paediatric Surveillance Unit and the National Blood Service database as well as UKOSS, suggest that the incidence of clinically detected FMAIT is less than one third of that estimated from prospective screening studies.
- Background

FMAIT, also known as neonatal alloimmune thrombocytopenia or NAIT, is the most common cause of severe neonatal thrombocytopenia in otherwise well term infants[18], and is analogous to the fetal/neonatal anaemia caused by haemolytic disease of the newborn (HDN). The condition results from a fetomaternal incompatibility in platelet alloantigen, most commonly HPA-1a, and can lead to serious bleeding, intracranial haemorrhage and sometimes death of the fetus or infant[19]. In contrast to HDN, first pregnancies are often severely affected and the diagnosis is usually made with the birth of a first affected infant. There is therefore a current debate about the utility of screening for the condition. A recent evaluation has identified a number of deficiencies in basic epidemiological information needed to assess the utility of antenatal screening[20]. This study aims to address some of these deficiencies.

Case definition

All pregnant women with a previous child affected by fetomaternal alloimmune thrombocytopenia or pregnant women otherwise known to be alloimmunised with a platelet-incompatible fetus.

Surveillance Period

August 2006 – September 2008

Interim Results

There were 79 cases reported through the three reporting systems over the period October 2006 to September 2007, in an estimated 726,517 births, representing an estimated incidence of 1.1 cases per 10,000 total births (95% CI 0.9-1.4). Capture-recapture analysis suggests there are unlikely to be any missed cases. We have received further information on 77 confirmed cases, including 17 infants born before 01/10/06 or after 30/09/07. Fifty-five cases (71%) were identified postnatally and 22 (29%) antenatally. The management of the 22 antenatal cases is illustrated in Table 1. There were two intrauterine deaths, one infant death and seven infants had an intracranial haemorrhage. Seven of these ten cases with serious clinical problems occurred in women without a history of FMAIT.

Table 1: Management of antenatally diagnosed cases of FMAIT

Antenatal treatment	Number of infants (%)
Steroids, intravenous immunoglobulin (IVIg) + intrauterine platelet transfusion (IUT)	9 (41)
IVIg alone	8 (36)
Steroids + IVIg	2 (9)
IVIg + IUT	2 (9)
IUT alone	1 (5)

Interim Conclusions

The incidence of clinically detected FMAIT estimated from this national study is less than one third of that estimated from prospective screening studies[19]. More than two thirds of cases with serious clinical problems were diagnosed postnatally, highlighting the importance of appropriate assessment of the case for antenatal screening.

Funding

This study is funded by Wellbeing of Women.

Wellbeing of Women WOW
Charity Registration No: 239281

4.3.4 Myocardial Infarction

Key points

- Myocardial infarction in pregnancy is known to be associated with significant maternal and fetal mortality.
- The current incidence estimate is based on a study from 1970.
- Current trends in lifestyle factors and increasing age at childbirth are likely to be leading to an increase in incidence.
- This study will provide a national picture of the incidence of the disease, its epidemiology and management

Background

Myocardial infarction in pregnancy is known to be associated with significant maternal and fetal mortality[21]. The widely quoted incidence estimate of 1 in 10,000 births is based on a study conducted in 1970[22]. However, with current trends in lifestyle factors associated with cardiovascular disease risk and increasing age at childbirth, the incidence of MI during pregnancy can be expected to have increased. A recent retrospective database analysis from the USA[23] provided evidence that this may be the case, identifying an increase in incidence of myocardial infarction in pregnancy from 1 in 73,400 pregnancies in 1991 to 1 in 24,600 in 2000. To date this is the only recent population study of this condition, although there are more than 150 individual case reports in the world literature[24]. A systematic review of the case reports in 1996 identified a number of features of MI during pregnancy which differed from MI outside of pregnancy, and reported a case fatality rate of 21% and a fetal mortality rate of 13%[21]. Normal coronary artery morphology was noted in 29% of women; MI in pregnancy may be caused by coronary artery dissection, embolus without atheroma in addition to atherosclerosis[21 25]. Classic coronary risk factors appear to be the exception rather than the rule: 19% of patients had hypertension, 26% were smokers and only 2% had hyperlipidaemia. The authors of this review acknowledge the possible biases in favour of reporting of cases which are in some way unusual; a systematic prospective study on a population basis is thus clearly needed. This study will provide a national picture of the incidence of the disease, its epidemiology and management.

Case definition

All women in the UK identified as having acute myocardial infarction during pregnancy using the joint European Society of Cardiology/American College of Cardiology criteria[26]:

EITHER A typical rise and gradual fall (troponin) or more rapid rise and fall (CK-MB) of biochemical markers of myocardial necrosis with at least one of the following: (a) schaemic symptoms, (b) development of pathologic Q waves on the ECG, (c) ECG changes indicative of ischaemia (ST segment elevation or depression), or (d) coronary artery intervention (e.g. coronary angioplasty)

OR Pathological findings of an acute MI.

Surveillance Period

August 2005 – ongoing

Interim Results

Thirty-one cases were reported up to January 2008 and data returned about 26 of them (84%). Six were returned as non-cases and seven did not meet the case definition. This leaves 13 confirmed cases, representing an estimated incidence of 7 cases per million maternities (95% CI 4-12) or 1 in 143,000 maternities.

Interim Conclusions

There have been substantially fewer cases than the expected number reported. This may be due to under-reporting, to a genuinely lower incidence or due to previous incidence estimates including postnatal cases, which are not usually identified through UKOSS. We will be investigating other sources of case ascertainment and comparing fatal cases reported to UKOSS with those reported to CEMACH. We have also extended the study period from two to five years in order to allow us to generate a robust estimate of incidence at the end of the study.

4.3.5 Extreme Obesity

Key points

- Obesity is an important and growing public health problem.
- Preliminary results from this study suggest that nearly one in every thousand women delivering in the UK is extremely obese (BMI ≥ 50).
- These women have significantly more pregnancy complications and poorer outcomes than comparison women.
- Full analysis at the end of the study will determine whether these results are confirmed and provide additional information to guide counselling and management of this group of women.
- Background

Obesity is now recognised to be an important public health problem throughout the developed world[27]. The prevalence of obesity is rising rapidly in the UK in all age groups, including women of reproductive age[28]. Recent reports of the UK Confidential Enquiry into Maternal Deaths[12] have highlighted obesity as a factor in increasing numbers of maternal deaths in the UK. Retrospective database analyses in Canada, Australia and the UK have identified particular disease risks associated with pregnancy among obese women[29-31], including pre-eclampsia, venous thromboembolism and gestational diabetes, and higher rates of labour induction, delivery by caesarean section, general anaesthesia and anaesthetic complications[32.] Obese women are also at increased risk of poor perinatal outcomes, including stillbirth and neonatal death[33]. The majority of these studies focus on women with moderate obesity (BMI greater than 30). The studies therefore include only a very few women who are extremely obese and have not specifically addressed the risks in the extremely obese group. The risk of pregnancy complications in extremely obese women is potentially even higher than among moderately obese women. However, because of the relatively small numbers of women with this degree of obesity, a national study is needed to investigate this further. The objective of this study is to investigate the prevalence and outcomes of pregnancy in women with extreme obesity in the UK, and assess the risk of adverse outcomes attributable to obesity.

Case definition

EITHER Any woman weighing over 140Kg at any point during pregnancy

OR Any woman with a Body Mass Index (BMI) greater than 50 at any point during pregnancy

OR Any woman estimated to be in either of the previous categories but whose weight exceeds the capacity of hospital scales.

Reporting clinicians are also asked to collect information about one comparison woman for each case, identified as the woman delivering immediately before the case in the same hospital.

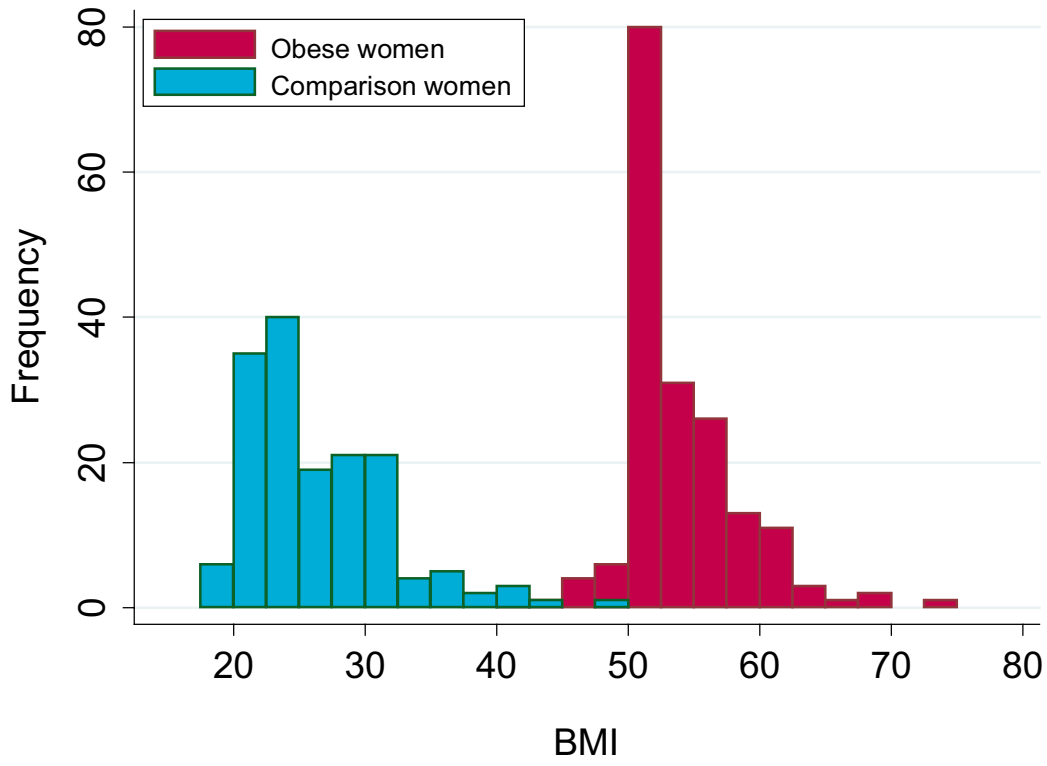
Surveillance Period

March 2007 – September 2008

Interim Results

One thousand and nineteen (1019) cases of extreme obesity in pregnancy were reported up to January 2008. We have received further information about 724 women (71%); 126 women did not meet the case definition and there were 22 duplicate reports, leaving 575 confirmed cases (392 with incidence only information and 183 with detailed information). Three hundred and twenty-four cases delivered or had estimated dates of delivery within the first six months of the study, giving an estimated incidence of 9.1 cases per 10,000 or 1 in 1100 maternities (95% CI 8.1-10.1 per 10,000). The median BMI of these women is 52.6 (range 37.2-77) (Figure 6), compared with a median BMI of 25 (range 18-48) in comparison women. Obese women were of a similar age, but more likely to be multiparous and more likely to be of white ethnicity than comparison women. Outcomes are known for 160 cases and 167 comparison women (Table 2).

Figure 6: Body Mass Index (BMI) in pregnant women in the UKOSS extreme obesity study*



*Includes obese women with a weight of 140Kg or over whose BMI was below 50Kg/m^2. None of the comparison group had either a BMI of ≥ 50Kg/m^2 or a weight of over 140Kg.

Table 2: Outcomes of women in the UKOSS Extreme Obesity study

Outcome	Number of extremely obese women n(%)	Number of comparison women n(%)	Unadjusted Odds Ratio (95% CI)
Gestational diabetes	24 (15)	4 (2)	7.33 (2.19-24.5)
Gestational hypertensive disorder	36 (22)	9 (5)	5.33 (2.23-12.8)
Thrombotic event	1 (1)	0 (0)	Unstable estimate
Shoulder dystocia	3 (2)	2 (1)	1.50 (0.25-9.00)
Delivery <37 weeks	24 (15)	8 (5)	3.33 (1.34-8.30)
Caesarean delivery	82 (51)	36 (21)	3.87 (2.19-6.82)
Maternal death	0 (0)	0 (0)	Not calculable
Perinatal death	6/164 (4)	2/169 (1)	3.00 (0.61-14.9)

Conclusions

These preliminary results suggest that nearly one in every thousand women delivering in the UK has a BMI of 50Kg/m^2 or over, or weighs more than 140Kg. Even at this early stage of the study, it appears that these women have significantly more pregnancy complications and poorer outcomes than comparison women. Full analysis at the end of the study will determine whether these results are confirmed and will provide additional information to guide counselling and management of this group of women.

4.3.6 Pregnancy in Transplant Recipients

Key points

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

Background

Despite initial concerns about the advisability of pregnancy in solid-organ transplant recipients, there have now been reports of over 14,000 births to women with transplanted organs[34]. Most studies are centre-based and retrospective[35]. Three voluntary registers have collected data at various times: the US National Transplantation Pregnancy Register (1991-present)[36], the UK Transplant Pregnancy Register (1994-2001)[35] and the European Dialysis and Transplant Association Registry (1960-1992)[37]. Recent analysis of data from the UK Transplant Pregnancy Register identified high rates of preterm delivery (50%) and delivery by caesarean section (72%) in pregnant renal transplant recipients. Worse outcomes were associated with poorer pre-pregnancy graft function and drug-treated hypertension during pregnancy. This UK register, however, no longer collects information. Immunosuppressive regimens are continually developing, and more information is needed about the intrauterine effects and neonatal consequences of immunosuppressive drugs. The objective of this project is to collect information about pregnancy outcomes amongst current solid organ transplant recipients in the UK and describe the outcomes for women and their infants. This information is important to inform future management and counselling of these women. The project is divided into two studies: the first to investigate outcomes in women with renal transplants and the second to investigate outcomes in women with other solid organ transplants.

Case definitions

Renal transplant study:
All pregnant women with a transplanted kidney, with or without other transplanted organs.

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

Surveillance Period

January 2007 - ongoing

Interim Results

Fifty-nine cases of pregnancy in renal transplant recipients were reported, and data collection forms returned for 40 (68%). There were two duplicate cases and two which did not meet the case definition, leaving 36 confirmed cases. Five women are not yet delivered and four pregnancies miscarried. There have been no maternal deaths and no perinatal deaths among 30 infants (including three sets of twins).

Eighteen cases of pregnancy in non-renal solid organ transplant recipients were reported, and data collection forms returned for 15 (83%). There were 15 confirmed cases and no duplicates. Thirteen women had received liver transplants, one a lung transplant and one a heart transplant. The recipient of the heart transplant died; there were no other maternal deaths. One woman had a miscarriage and one infant died among twelve for whom outcomes are known.

Interim Conclusions

These studies are still at an early stage. The outcomes for women and their infants appear largely good, but more definitive conclusions will be drawn at the end of the studies. The study of renal transplant recipients is planned for completion in 2009 and the study of other solid organ transplant recipients will run until 2012.

4.3.7 Pulmonary Vascular Disease

Key points

- Pulmonary vascular disease in pregnancy is widely considered to pose an extreme risk of maternal death.
- There have been no recent prospective case series to assess this risk.
- Novel methods of management may impact on case outcomes.
- This study will provide a national picture of the incidence of the disease, its epidemiology and management.

Background

Pre-existing or gestational occurrence of pulmonary vascular disease, including Eisenmenger's syndrome, primary and secondary pulmonary hypertension, is one of the rare conditions widely considered to pose an extreme risk of maternal death[38]. Three of the six maternal deaths in women with congenital heart disease reported in the UK in the last triennium were associated with pulmonary vascular disease[12]; since 1991 there have been 25 maternal deaths in the UK associated with this condition. Eisenmenger's syndrome is estimated to carry a maternal mortality rate of 40% per pregnancy[16], with an infant mortality rate of 10-15%[38]. A systematic review of the literature in 1998 suggested that the maternal mortality rate had remained unchanged over the previous 20 years[38]. However, the authors of this review recognise that there may be inherent biases in published reports of pregnancy in women with pulmonary vascular disease in pregnancy and call for more information from detailed prospective case series in order to differentiate the risks of pregnancy and eventually provide an optimal plan of management. Cases in the UK were collected prospectively on a voluntary basis by the UK Registry of High Risk Obstetric Anaesthesia[39], however, problems with ascertainment caused the register to cease to collect data. The objective of this prospective study through UKOSS is to provide an appropriate national case series with good ascertainment to allow comprehensive study of the epidemiology and current management of Eisenmenger's syndrome and pulmonary hypertension.

Case definition

EITHER Pulmonary hypertension: defined as 1) a mean (not systolic) pulmonary artery pressure equal to or greater than 25mmHg at rest or 30 mmHg on exercise in the absence of a left-to-right shunt or 2) a pulmonary artery systolic pressure greater than 36mmHg[40]. Pulmonary hypertension may be primary (no cause identified) or secondary (known cause identified, for example, vasculitis, connective tissue disease, chronic pulmonary thromboembolism, sickle cell disease, drug use),

OR Eisenmenger's syndrome: defined as pulmonary hypertension secondary to an uncorrected left-to-right shunt from a ventricular septal defect, atrial septal defect or patent ductus arteriosus[41].

Surveillance Period

March 2006 – ongoing

Interim Results

To date 33 cases of pulmonary vascular disease have been reported, with further information available for 27 (82%). Two duplicate cases were reported and there were nine reported cases which did not meet the case definition (the majority being cases of pulmonary embolism), leaving 16 confirmed cases in an estimated 1,370,000 maternities (incidence 12 cases per million maternities; 95% CI 7-19; 1 in 83,000 maternities). Twelve of these cases were known prior to pregnancy and four were diagnosed during pregnancy or immediately postnatally. Two pregnancies were terminated. One woman died (case fatality 7%; 95% CI 0.2-34%). There were no perinatal deaths among 15 infants.

Interim Conclusions

Pulmonary vascular disease in pregnancy is extremely rare in the UK. However, the early results from this study suggest that mortality may not be as high as previously reported. This study will continue for a further three years in order to identify a larger population-based series of cases.

4.3.8 Therapies for Peripartum Haemorrhage

Key points

- Haemorrhage remains an important cause of maternal mortality in the UK.
- B-Lynch or brace sutures, recombinant factor VIIa and arterial embolisation or ligation are now being used more commonly to treat severe peripartum haemorrhage.
- There are no systematically collected data available at a population level to assess the clinical outcomes following use of these therapies.
- This study will describe the use of these specific therapies for treatment or prophylaxis for peripartum haemorrhage in the UK and assess the outcomes following their use.

Background

Haemorrhage is the second most common cause of direct maternal death in the UK as identified in the most recent report of the Confidential Enquiry into Maternal Deaths[12]. However, deaths from haemorrhage represent only the tip of the iceberg of disease; severe haemorrhage has been included in the definition of 'near-miss' maternal morbidity in several studies[42 43].

The basic treatment of major peripartum haemorrhage consists of surgery and/or medical management with transfusion and uterotonic drugs. However, there are now a number of reports of the use of other therapies, including recombinant factor VIIa[44], B-Lynch or brace sutures[45], ligation[46] and embolisation[47] of major pelvic vessels (internal iliac/uterine arteries) in cases with continued bleeding. None of these therapies have been evaluated in large randomised controlled trials, but all are used widely throughout the UK. There are no systematic data available at a population level to assess the clinical outcomes following use of these therapies. For example, there are only nine reports in the literature of failed B-Lynch sutures[48]. However, in the UKOSS study of peripartum hysterectomy, 50 women who underwent a peripartum hysterectomy to control haemorrhage had had a B-Lynch or Brace suture prior to requiring a hysterectomy. In order to assess the clinical outcomes following these therapies, we need to identify all cases in which they are used. This descriptive study will collect information on the timing of use of these therapies, subsequent haemorrhage and requirement for additional management strategies such as hysterectomy. This will allow us to investigate the outcomes associated with these specific different management strategies depending upon the timing of use in order to inform future guidelines for prevention and management.

Case definition

The cases will be all women in the UK treated for peripartum haemorrhage with:

EITHER Activated factor VIIa

OR B-Lynch or other brace suture

OR Arterial ligation or embolisation.

Surveillance Period

October 2007- October 2008

Interim Results

To date 77 cases who had received the specific therapies for peripartum haemorrhage have been reported, with further information available for 21 (27%). One duplicate case was reported and there was one reported case which did not meet the case definition, leaving 19 confirmed cases. Ten (53%) women were managed with brace sutures, four (21%) with factor VIIa and six (32%) with vessel embolisation or ligation; one woman had two different treatments. None of these women died.

Interim Conclusions

This study is at a very early stage and it is not yet possible to draw any conclusions. The planned completion date for the study is October 2008, following which detailed analysis will be undertaken.

Funding

This study is funded by Wellbeing of Women.

Wellbeing of Women WOW

Charity Registration No: 239281

4.4 Future studies

The following studies have been approved by the UKOSS Steering Committee and are due to commence in 2008/2009.

4.4.1 Failed Intubation

Key points

- Although anaesthetic-related maternal deaths have decreased in number in recent years, hypoxia related to failed intubation remains a consistent cause of mortality.
- The incidence of failed intubation in the obstetric population is thought to be higher than in the non-pregnant population.
- The reasons for this higher incidence in the obstetric population are multiple.
- •his study will investigate the incidence, risk factors, management and outcomes of failed intubation in the obstetric population in the UK in order to inform future guidelines for prevention and treatment.

Background

Reports from the Confidential Enquiries into Maternal Deaths have shown a decrease in the number of anaesthetic related deaths over recent years[12]. However, a consistent cause of death is hypoxia relating to a failure to intubate and ventilate. The incidence of failed intubation among the pregnant population is estimated to be up to 8 times that of the non-pregnant population,[49 50] but as yet, no national data exist.

The reasons for this higher incidence in the obstetric population are several. Anatomical changes in the airway due to physiological changes in pregnancy have been noted[51]. Additionally, the physiological changes of a reduced functional residual capacity and an increased metabolic rate in pregnancy lead to a rapid progression to hypoxia following induction and apnoea. This adds pressure on the anaesthetist to intubate quickly before desaturation occurs. These issues are compounded by the fact that obstetric surgical procedures are now less frequently performed under general anaesthesia, so that training opportunities for junior anaesthetists are increasingly rare[52]. The procedures are also frequently required "out of hours" when the trainee anaesthetist is likely not to be working under direct supervision. Finally, the amount of time spent in training is reduced overall[53].

Case definition

Any woman of over 20 weeks gestation given a general anaesthetic (whether on delivery suite or another hospital department) where a failed intubation has occurred.

Failed intubation is defined as failure to achieve tracheal intubation during a rapid sequence induction for obstetric anaesthesia, thereby initiating a failed intubation drill.

Surveillance Period

April 2008- April 2010

Main Research Questions

- What is the UK incidence of failed intubation for obstetric general anaesthesia?
- What are the risk factors for failed intubation for obstetric surgery?
- How is failed intubation managed?
- What are the maternal outcomes after failed intubation?
- What are the neonatal outcomes after failed intubation?

Investigators

David Milne, Audrey Quinn, Amanda Pinder, Heather Gorton; Leeds General Infirmary.

Funding

This study will be funded by the Obstetric Anaesthetists Association (OAA).

4.4.2 Malaria

Key points

- Malaria is an important cause of maternal and perinatal morbidity and mortality worldwide
- Travel-associated cases in the UK occur most commonly in the 15-44 age group
- There is no national information about the incidence of malaria in pregnancy in the UK, how these women are treated and the outcomes of pregnancy
- This study will describe the epidemiology of malaria in pregnancy in the UK and use the information to inform development and implementation of guidelines for both prevention and management

Background

Worldwide, malaria is the cause of severe maternal and perinatal morbidity and mortality. It is estimated that the population attributable fraction of maternal deaths due to malaria in sub-Saharan Africa is up to 23% and of neonatal deaths 18%[54]. Research in African and Asian populations shows that pregnant women are at higher risk both of acquiring disease and of suffering from more severe disease than non-pregnant women[54]. Malaria can cause severe anaemia, and in semi-immune populations may be associated with few other symptoms prior to the onset of severe complications such as adult respiratory distress syndrome or death, due to the sequestration of malarial parasites within the placenta[55]. In non-immune pregnant women, infection with falciparum malaria is more likely to lead to severe complications such as cerebral malaria than in the non-pregnant population. Infants are similarly severely affected; maternal malaria may lead to stillbirth and also preterm birth or intrauterine growth retardation, with a consequent increase in neonatal mortality.

The majority of information about malaria in pregnancy comes from populations in which malaria is endemic or epidemic. About 1500-2000 travel-associated cases of malaria are reported in the UK annually, with the peak occurring in the population aged 15-44[56]. However, no information exists about the number of women with malaria in the UK who are pregnant, the populations in the UK in which malaria in pregnancy occurs, how these pregnant women with malaria are treated or the consequences of the disease in these women and their infants. This information is important to develop and implement guidelines for both prevention and management. This descriptive study will describe the epidemiology of malaria in pregnancy in the UK and the outcomes for both women and their infants.

Case definition

Any women with a positive blood film for malaria parasites (or confirmed placental malaria) at any time during pregnancy or immediately postpartum (before discharge from hospital after delivery).

Surveillance Period

October 2008- October 2009

Main Research Questions

- What is the incidence of malaria in pregnancy in the UK?
- Does the disease predominantly occur in women from specific ethnic groups?
- Does the disease occur in women who have travelled to specific regions outside the UK?
- How and when does the disease present? How is malaria in pregnancy managed in the UK?
- What are the outcomes of malaria in pregnancy for mother and infant?

4.4.3 Uterine Rupture

Key points

- Uterine rupture is associated with significant maternal and fetal morbidity.
- A decrease in the number of women attempting vaginal birth after caesarean section may be due to concerns about the risk of uterine rupture.
- There are no systematic data available at a population level to quantify the incidence of uterine rupture and to assess the risks associated with induction and augmentation of labour in women who have had a previous caesarean delivery.
- This study will investigate the incidence, risk factors and outcomes of uterine rupture in the UK.
- Background

True uterine rupture is a catastrophic event with significant associated maternal and fetal morbidity and mortality. In the developed world it most commonly occurs in women who have previously delivered by caesarean section[57]. This observation has led to debate about the optimal management of labour and delivery in women who have delivered by caesarean section in previous pregnancies. Women with a previous caesarean delivery have generally been encouraged to attempt a trial of labour in subsequent pregnancies[58], but recent reports of an increased risk of morbidity, particularly due to uterine rupture, are thought to have contributed to a marked decrease in the number of women attempting vaginal birth after caesarean section[59]. The rate of caesarean section delivery in the UK is increasing, with previous caesarean section being the most common primary obstetric indication for repeat caesarean[60]. Two recent systematic reviews have attempted to quantify the incidence of uterine rupture[57 61]. Both these reviews identified a number of deficiencies in the few existing studies in developed countries and suggested that a prospective national study of uterine rupture would offer the best opportunity to guide preventive strategies. They identified only one previous UK population-based study[42], which reported 12 ruptures in 48,865 deliveries, a rate of approximately 1 in 4000 deliveries.

In addition to difficulties in quantifying the incidence of uterine rupture, Guise et al[61] noted that existing observational studies were insufficient to answer additional questions about the risks of rupture associated with induction and augmentation of labour. The planned case-control study using the UK Obstetric Surveillance System will address these questions and quantify the national incidence of uterine rupture in the UK.

Case definition

The cases will be all women in the UK identified as having a uterine rupture using the following definition[61 62]: a complete separation of the wall of the pregnant uterus, with or without expulsion of the fetus, involving rupture of membranes at the site of the uterine rupture or extension into uterine muscle separate from any previous scar, and endangering the life of the mother or fetus. Any asymptomatic palpable or visualised defect (for example noted incidentally at caesarean delivery) will be excluded.

Surveillance Period

October 2008- October 2009

Main Research Questions

- What is the current incidence of uterine rupture in the UK?
- What are the characteristics of women who suffer from uterine rupture?
- What proportion of ruptures occur in women who have previously delivered by caesarean section?
- What is the risk associated with labour induction or augmentation of labour after prior delivery by caesarean section?
- What are the outcomes for mother and infant?

5. Publications

5.1 Acute Fatty Liver of Pregnancy (AFLP)

Published article

Knight M, Nelson-Piercy C, Kurinczuk JJ, Spark P, and Brocklehurst P. A prospective national study of acute fatty liver of pregnancy in the UK. Gut. Published Online Early 2008 Mar 10; doi:10.1136/gut.2008.148676.[63]

Key points

- Nationally AFLP is rare, with an estimated incidence of 5.0 cases per 100,000 maternities (95%CI 3.8-6.5/100,000) or 1 in 20,000 maternities.
- Diagnostic criteria previously proposed agree substantially with clinical diagnosis[64].
- Eighteen percent of women had twin pregnancies and 20% were underweight (BMI <20). This suggests women with twin pregnancies appear to be at higher risk but further studies are needed to investigate the risk associated with low BMI.
- One woman received a liver transplant. One woman died (case fatality rate 1.8%, 95%CI 0-9.4%). There were seven deaths among 67 infants (perinatal mortality rate 104 per 1000 births, 95%CI 43-203).
- The incidence estimate from this study is lower than documented by earlier hospital-based studies, but maternal and neonatal outcomes are better than previously reported, possibly related to improved ascertainment.

5.2 Antenatal Pulmonary Embolism

Published Article

Knight M on behalf of UKOSS. Antenatal pulmonary embolism: risk factors, management and outcomes. BJOG 2008; 115(4):453-61.[65]

Key points

- A total of 143 antenatal pulmonary embolisms were reported, representing an estimated incidence of 1.3 per 10,000 maternities (95% CI 1.1-1.5).
- There were several cases where thromboprophylaxis was not provided according to national guidelines, and there may be scope for further work on guideline implementation.
- The main risk factors for pulmonary embolism were multiparity (adjusted odds ratio (aOR) 4.03, 95% CI 1.60-9.84) and obesity (body mass index ≥ 30 kg/m^2) (aOR 2.65, 95% CI 1.09-6.45); however, without additional studies of cost-effectiveness, we are unable to recommend any changes to current guidelines which would aid prevention of this serious condition.
- Nearly a third of women with antenatal PE had no classical risk factors and only nine women with classical risk factors were eligible for prophylaxis under current guidelines. Further work is needed to assess how information about these risk factors may be used to guide prophylaxis.
- Two women had recurrent pulmonary emboli (1.4%, 95% CI 0.2-5.1%), and five women died (case fatality 3.5%, 95% CI 1.1-8.0%).
- Thus significant severe morbidity from thromboembolic disease underlies the maternal deaths from antenatal PE reported in the UK, with approximately 30 women diagnosed with the condition for each woman who died.

5.3 Eclampsia

Published Article

Knight M on behalf of UKOSS. Eclampsia in the United Kingdom 2005. BJOG 2007; 114(9):1072-8.[66]

Key points

- The incidence of eclampsia has decreased significantly in the UK from 4.9 per 10,000 maternities in 1992 to 2.7 cases per 10,000 maternities (95%CI 2.4-3.1).
- The majority of women in the UK are managed with magnesium sulphate according to national protocols and maternal morbidity has been significantly reduced as a consequence.

- No women in the study died (case fatality 0%, 95%CI 0-1.7%). Fifty-four (26%) had recurrent fits. Twenty-two women (10%) were reported to have other severe morbidity after the eclamptic episode.
- Outcomes were known for 222 infants (204 singletons, 18 twins). Eight infants were stillborn and five died in the neonatal period (perinatal mortality 59 per 1000 births (95% CI 32-98)).
- This study has revealed the practical benefits of the incorporation of research evidence into practice through the widespread use of evidence-based guidelines.

5.4 Peripartum Hysterectomy

Published Articles

Knight M on behalf of UKOSS. Peripartum hysterectomy in the UK: management and outcomes of the associated haemorrhage. BJOG 2007; 114(11):1380-7.[67]

Knight M, Kurinczuk JJ, Spark P, Brocklehurst P on behalf of UKOSS. Cesarean delivery and peripartum hysterectomy. Obstet Gynecol 2008; 111(1):97-105.[68]

Key points

- The incidence of peripartum hysterectomy in the UK is 4.1 cases per 10,000 maternities (95% CI 3.6-4.5) with a case fatality of 0.6% (95% CI 0-1.5%).
- Peripartum hysterectomy is strongly associated with previous delivery by cesarean section (OR 3.52, 95% CI 2.35-5.26), and the risk rises with increasing number of previous cesarean section deliveries (OR 2.14 with one previous delivery (95% CI 1.37-3.33), 18.6 with two or more (95% CI 7.67-45.4)).
- Maternal age and parity are also important risk factors.
- The majority of cases occur in association with either uterine atony or a morbidly adherent placenta (placenta accreta).
- The associated haemorrhage is managed in a variety of ways and not universally according to existing guidelines.
- Further investigation of the outcomes following some of the more innovative therapies for control of haemorrhage is needed (see section 4.2.8. Therapies for peripartum haemorrhage)

5.5 Saving Mothers' Lives

Information from UKOSS studies has been used to provide denominator morbidity information for the latest report "Saving Mothers' Lives: Reviewing maternal deaths to make motherhood safer – 2003-2005"[12]. UKOSS studies are referenced in the following chapters:

- Chapter 2: Thrombosis and thromboembolism (Antenatal pulmonary embolism study)
- Chapter 3: Pre-eclampsia and eclampsia (Eclampsia study)
- Chapter 4: Haemorrhage (Peripartum hysterectomy study)
- Chapter 5: Amniotic Fluid Embolism (AFE study)
- Chapter 9: Cardiac disease (Pulmonary vascular disease study)
- Chapter 10: Other indirect deaths (TB study)

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