Maternal, Newborn and Infant Clinical Outcome Review Programme

MBRRACE-UK
Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK

Saving Lives, Improving Mothers' Care

Lessons learned to inform future maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2009-2012

December 2014

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December 2014

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Foreword

This report continues the longest running programme of Confidential Enquiries into maternal deaths worldwide, and shows a welcome decrease in the overall rate of maternal death across the United Kingdom. In addition, it includes, for the first time, Confidential Enquiries into maternal deaths occurring in Ireland. The importance of this report lies in going "beyond the numbers" and recognising the death of every woman during or after pregnancy as a tragedy from which it is incumbent upon us, as health professionals, service planners or policy-makers to learn lessons to improve future care. We must recognise that each woman included in this report leaves behind a bereaved family on whom the impact of her death will be lifelong. We owe it to those left behind to learn from the death of their mother, partner, daughter or friend and to make changes for the future to prevent other women from dying.

The focus of this report is therefore clearly to the future, on the actions, small and large, that we as a community or an individual can make to continue to improve the quality of maternity care across the UK and Ireland. As such, it is also enhanced by the inclusion, for the first time, of Confidential Enquiries into the care of women with severe complications in pregnancy, but who survived, thus broadening the messages to improve care yet further. As always, the focus is not in attributing blame, but on improving future mothers' care.

Maternal deaths from genital tract sepsis have fallen significantly, but as this report shows, infections from all causes are an important cause of maternal death. This report spans the period of the influenza A/H1N1 pandemic, which severely affected pregnant women in particular. Some women died before immunisation was introduced, but a number of unvaccinated women died after the vaccination programme began, and, more recently, some women died from non-pandemic type seasonal influenza. The compelling message for the future has to be the importance of continuing the programme of vaccination against influenza in pregnancy in the UK and Ireland, working to maximise uptake and hence to ensure we prevent future influenza-related maternal deaths.

At the same time, and as highlighted across many areas of the health service, early identification of pregnant and postpartum women whose medical condition is deteriorating and rapid actions to diagnose and treat pregnant and postpartum women with suspected sepsis will save lives. The importance of routine measurements such as pulse, temperature, respiratory rate and blood pressure in any ill pregnant women cannot be over-emphasised. Pregnant women can appear relatively well and yet become seriously ill with sepsis very quickly. Midwives, doctors and other health professionals need to "think sepsis" and implement sepsis bundles, including giving antibiotics within an hour of the diagnosis being suspected.

The consistent year on year decrease in direct maternal deaths is evidence of commitment to and success in improving the care of women with obstetric complications in pregnancy throughout the health service. However, we still need to plan for the care of women with known co-existing medical complications in pregnancy. The majority of women who die during or after pregnancy in the UK and Ireland die from indirect causes, that is, from an exacerbation of their pre-existing diseases. Commitment to improve care for these women is needed across all professional organisations and groups, working alongside researchers to provide the evidence to ensure that we can provide the best care for women pre-pregnancy, during and after pregnancy. Throughout the report, areas of guidance where care can be improved have been clearly highlighted; an obvious area in which specific guidance is lacking is for the care of women with epilepsy in pregnancy. As Chief Medical and Nursing Officers we are committed to ensuring the development of such guidance and hence optimal care for mothers with epilepsy.

This report would not be possible without the dedication and commitment of health professionals throughout the UK and Ireland. In particular, we would like to thank the dedicated assessors who review each individual woman's death in order to identify actions to improve care in the future. This work is carried out without remuneration and in the assessors own time, because of their commitment to continuous quality improvement. It behoves health service provider organisations including hospitals, health boards, executives and trusts to continue to recognise the importance of this work at both a national and local level and allow assessors dedicated time for it to continue. We therefore welcome the findings in the report that will ultimately help improve outcomes for mothers and their families across the UK and Ireland.

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Key messages from the report

MBRRACE-UK
Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK

Maternal deaths have decreased

from **11** 2006-08 to **10** 2010-12 per 100,000 women giving birth

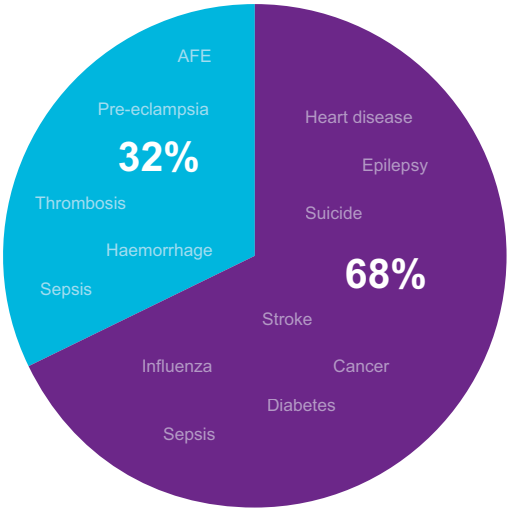
Causes of mothers' deaths

Two thirds of mothers died from medical and mental health problems in pregnancy and **only one third** from direct complications of pregnancy such as bleeding.

Three quarters of women who died had medical or mental health problems before they became pregnant.

Women with pre-existing medical and mental health problems need:

- Pre-pregnancy advice
- Joint specialist and maternity care



Think Sepsis

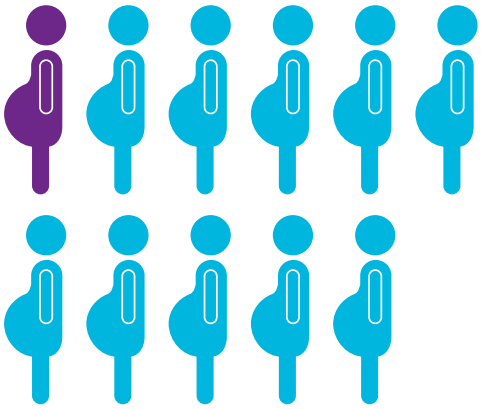
Almost a quarter of women who died had **Sepsis** (severe infection).

Women with sepsis need:

- Early diagnosis
- Rapid antibiotics
- Review by senior doctors and midwives

Prompt treatment and action can make the difference between life and death

Prevent Flu



1 in 11 of the women died from **Flu**

More than half of these women's deaths could have been prevented by a flu jab.

Flu vaccination will save mothers' and babies' lives

Executive Summary

Key areas for action

For Policy-makers, Service Planners and Commissioners, Public Health and Professional Organisations

- Two thirds of women died from indirect causes and almost three quarters of all women who died had co-existing medical complications. High level actions are needed to ensure that physicians are appropriately trained in, and engaged with, the care of pregnant women, and that services are designed for women with medical conditions which provide appropriate and evidence-based care across the entire pathway, including pre-pregnancy, during pregnancy and delivery, and postpartum.
- One in eleven women died from influenza. Increasing immunisation rates in pregnancy against seasonal influenza must remain a public health priority.
- Access to antenatal care remains an issue amongst women who died and ensuring access to appropriate care for all groups must remain part of service planning. More than two thirds of women who died did not receive the nationally recommended level of antenatal care; a quarter did not receive a minimum level of antenatal care.
- Multi-agency evidence based operational guidance is urgently required to standardise and improve the care of pregnant women with epilepsy.

For Medical Directors, Clinical Directors, Heads of Midwifery and Clinical Service Managers

- Women with pre-existing medical conditions should have pre-pregnancy counselling by doctors with experience of managing their disorder in pregnancy.
- Women with medical disorders in pregnancy should have access to a coordinated multidisciplinary obstetric and medical clinic, thereby avoiding the need to attend multiple appointments and poor communication between senior specialists responsible for their care.
- There should be adequate provision of appropriate critical care support for the management of a pregnant woman who becomes unwell. Plans should be in place for provision of critical care on delivery units or maternity care on critical care units, depending on most appropriate setting for a pregnant or postpartum woman to receive care.
- The deaths of all women should undergo multidisciplinary review at a local level.

For Doctors, Midwives and Allied Health Professionals

- All women with any symptoms or signs of ill health, including those who are postnatal, should have a full set of basic observations taken (temperature, pulse rate, respiratory rate and blood pressure), and the results documented and acted upon. Normality cannot be presumed without measurement.
- The key actions for diagnosis and management of sepsis are:
  - Timely recognition
  - Fast administration of intravenous antibiotics
  - Quick involvement of experts - senior review is essential
- Junior staff should not hesitate to seek senior advice.
- Consultant to consultant referral is appropriate when specialist advice is needed.
- All staff should participate in the review of care for the Confidential Enquiry. Individual clinician's perspectives on the care they have provided to women who die or have severe morbidity is invaluable to identify fully the lessons to be learned.

Causes and trends

In 2009-12, 357 women died during, or within six weeks of the end of their pregnancy in the UK. This represents a statistically significant decrease in the maternal mortality rate, which is now 10.12 per 100,000 maternities. The decrease is predominantly due to a reduction in deaths due to direct (obstetric) causes; the mortality rate from hypertensive disorders of pregnancy is now the lowest since the inception of the Confidential Enquiry in 1952. It is clear, however, that maternal deaths from indirect (medical and psychiatric) causes are still not being addressed effectively. Nearly three-quarters of women who died had a co-existing medical complication. There has been no significant change in the rate of indirect maternal death over the last 10 years, a time during which direct maternal deaths have halved; the rate of indirect maternal deaths (6.87 per 100,000 maternities) is now twice that of direct deaths (3.25 per 100,000 maternities). Actions are urgently needed to address deaths from indirect causes.

For the first time this report includes detailed Confidential Enquiries into the care of both women who died during or after pregnancy in the Republic of Ireland as well as the UK, and the review of the care of women with severe morbidity. It also represents a move towards annual reports from the previous triennial reports. Care is reviewed against national guidance, such as from the National Institute of Health and Care Excellence (NICE), where such guidance exists. The messages for care are presented by topic, and each topic will be included once every three years. This report includes topic-specific reviews of deaths and morbidity due to sepsis, and deaths from haemorrhage, amniotic fluid embolism, anaesthetic-related causes, neurological and other indirect causes. For the purposes of this report the care of 237 women was subject to Confidential Enquiry; the 203 women who died from sepsis, haemorrhage, amniotic fluid embolism, anaesthetic-related causes, neurological and other indirect causes between 2009 and 2012 and a sample of 34 women with septic shock who survived.

Influenza was an important cause of death during this period; more than half of the women died after a vaccine became available and their deaths can therefore be considered preventable. The importance of influenza immunisation for pregnant women cannot be over-emphasised.

The maternal mortality rate from genital tract sepsis more than halved between 2006-8 and 2010-12, which is encouraging. However, women dying from genital tract sepsis represented fewer than a quarter of the women who died from infectious causes during or after pregnancy, and detailed review of the care of both women who died from sepsis and women who survived an episode of septic shock showed that there remain a number of key areas in which care can be improved.

Key topic-specific messages for care

Think Sepsis

- ‘Think Sepsis’ at an early stage when presented with an unwell pregnant or recently pregnant woman, take all appropriate observations and act on them.
- The key actions for diagnosis and management of sepsis are:
  - Timely recognition
  - Rapid administration of intravenous antibiotics
  - Quick involvement of experts - senior review is essential
- Repeated presentation to the general practitioner, or community midwife or alternatively repeated self-referral to the obstetric triage or day assessment unit should be considered a ‘red flag’ and warrant a thorough assessment of the woman to investigate for signs of sepsis.
- Early advice from an infectious diseases physician or microbiologist should be sought; this is essential in instances where the woman fails to respond to the first choice antibiotic.
- To avoid preventable deaths, the benefits of influenza vaccination to pregnant women should be promoted and pregnant women at any stage of pregnancy should be offered vaccination.

Prevention and treatment of haemorrhage

- Haemoglobin levels below the normal range for pregnancy should be investigated and iron supplementation considered if indicated to optimise haemoglobin before delivery.
- Stimulating or augmenting uterine contractions should be done in accordance with current guidance and paying particular attention to avoiding uterine tachysystole or hyperstimulation.
- Fluid resuscitation and blood transfusion should not be delayed because of false reassurance from a single haemoglobin result.
- Whilst significant haemorrhage may be apparent from observed physiological disturbances, young fit pregnant women compensate remarkably well. A tachycardia commonly develops but there can be a paradoxical bradycardia. Hypotension is always a very late sign, therefore ongoing bleeding should be acted on without delay.
- In a woman who is bleeding and is likely to develop a coagulopathy or has evidence of a coagulopathy, it is prudent to give blood components before coagulation indices deteriorate.
- Early recourse to hysterectomy is recommended if simpler medical and surgical interventions prove ineffective.

Caring for women with Amniotic Fluid Embolism

- Perimortem caesarean section should be carried out within five minutes or as soon as possible after cardiac arrest and is carried out for the benefit of the woman; there is no need to confirm fetal viability, to do so wastes valuable time.
- It is prudent to trigger the massive obstetric haemorrhage protocol in an undelivered woman at the time the decision to proceed to perimortem caesarean section is made.
- The effectiveness of replacement and supportive therapy should be continuously monitored by the signs and symptoms of adequate oxygen delivery and tissue perfusion.

Lessons for Anaesthesia

- Subdural haematoma and cerebral venous sinus thrombosis are well recognised complications of dural puncture and pregnancy, respectively. Both should always be included in the differential diagnosis of persistent headache after dural tap or post dural puncture headache.
- Anaesthetists should practice drills for managing perioperative airway crises including severe bronchospasm, mechanical obstruction, and difficult intubation/oesophageal intubation.
- Pregnant or postpartum women recovering from anaesthesia require the same standard of postoperative monitoring, including documentation, as non-obstetric patients.
- Anaesthetists must be ready at all times to deal with the adverse effects of local anaesthetics including accidental intrathecal or intravenous injection, and minimise the use of strong concentrations as far as possible.
- All ambulance services should ensure their staff are trained in the relief of aortocaval compression during transfer of all pregnant women. How this was achieved must be routinely documented for each woman.

Learning from neurological complications

- Epilepsy remains a high risk condition in pregnancy and should continue to be managed as such in antenatal and postnatal care. Services should be commissioned and organised to support joint obstetric and neurological care of women with epilepsy during pregnancy.
- Multi-agency evidence-based guidelines are urgently required to standardise and improve the care of pregnant and postpartum women with epilepsy.
- Pre-conception counselling for women with epilepsy is not always provided effectively and should be robustly delivered in all care settings on an opportunistic basis.

- Neurological examination including assessment for neck stiffness is mandatory in all new onset headaches or headache with atypical features, particularly focal symptoms.
- Pregnancy should not alter the standard of care for women with stroke. All women with stroke, pregnant or not, should be admitted to a Hyperacute Stroke Unit.
- Neither pregnancy, caesarean section delivery nor the immediate postpartum state are absolute contraindications to thrombolysis (intravenous or intra-arterial), clot retrieval or craniectomy.

Caring for women with other medical and surgical complications

- A single identified professional should be responsible for co-ordinating the care of women with pre-existing medical conditions.
- Appropriately trained senior physicians should be involved in the care of pregnant and postpartum women with new onset symptoms suggestive of or known underlying medical disorders.
- Routine advice for pregnant women with diabetes mellitus should include the increased risk of hypoglycaemia and education of family members about optimal management of this condition.
- All women with proteinuria should have this quantified and further investigated if found to be significant.
- Senior surgical opinion is essential when dealing with surgical complications in pregnancy or postpartum and should not be delayed by team hierarchy. Early discussion between consultant obstetrician and consultant surgeon is vital.

Conclusions

The decreased maternal mortality rate at a time when maternity services are challenged with greater numbers of women giving birth as well as providing care for women with increasingly complex pregnancies emphasises the importance of continual improvements to care through Confidential Enquiry programmes such as this. This report has identified clear opportunities to improve care in the future. Basic observations and rapid actions have the potential to save women's lives, particularly in relation to sepsis. Events leading to catastrophic haemorrhage can be prevented by cautious and appropriate use of uterotonic drugs. Above all, there is a need for coordinated and concerted action at all levels to improve the care of women with medical complications before, during and after pregnancy. The reviews clearly illustrate that timely recognition of risk, the severity of the condition, accurate diagnosis, involvement of the correct senior staff from multiple disciplines, escalation and prompt treatment and action can make the difference between life and death.

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- Andy Cole, Chief Executive, Bliss (member of the IAG until March 2014)
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- Jenny Mooney, Business Manager, Clinical Outcome Review Programmes (to May 2014), Director of Operations, National Clinical Audit and Patient Outcome Programmes (from May 2014)
- Lorna Pridmore, Clinical Outcome Review Programmes Facilitator

MBRRACE-UK Third Sector Stakeholder Group and Representatives who Attended Meetings:

- Jane Abbott, Bliss
- Beverley Beech, AIMS
- Jenny Chambers, OC Support
- Jane Denton, Multiple Birth Foundation
- Jane Fisher, ARC
- Pauline Hull, electivecesarean.com
- Penny Kerry, Miscarriage Association
- Beckie Lang, Health Campaigns Tommy's
- Neil Long, Sands
- Sarah McMullen, NCT
- Jane Plumb, Group B Strep Support
- Andrea Priest, Best Beginnings
- Gwynne Rayns, NSPCC
- Jean Simons, Lullaby Trust (formerly FSID)
- Cheryl Titherly, ARC
- Maureen Treadwell, Birth Trauma Association

MBRRACE-UK Royal College and Professional Association Stakeholder Group and Representatives who Attended Meetings:

- Carmel Bagness, Royal College of Nursing
- Patrick Cadigan, Royal College of Physicians
- Hilary Cass, Royal College of Paediatrics and Child Health
- Paul Clyburn, Obstetric Anaesthetists Association & Royal College of Anaesthetists
- Sanjeev Deshpande, British Association of Perinatal Medicine
- Denise Evans, Neonatal Nurses Association
- Roshan Fernando, Obstetric Anaesthetists Association & Royal College of Anaesthetists
- Jacque Gerrard, Royal College of Midwives
- Steve Gould, British and Irish Paediatric Pathology Association
- Diane Hulbert, College of Emergency Medicine
- Hannah Knight, Royal College of Obstetricians and Gynaecologists
- Sarah Johnson, Royal College of Obstetricians and Gynaecologists
- Lucy Mackillop, Royal College of Physicians
- Lisa Nandi, British Association of Perinatal Medicine
- Lesley Page, Royal College of Midwives
- David Richmond, Royal College of Obstetricians and Gynaecologists
- Jane Sandall, British Maternal Fetal Medicine Society
- Neil Sebire, Royal College of Pathologists
- Lorraine Tinker, Royal College of Nursing

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For Scotland: Privacy Advisory Committee approval PAC16/14 16th July 2014

For Northern Ireland and Republic of Ireland: Not required as only de-identified data provided

Glossary of terms

AAGBI	Association of Anaesthetists of Great Britain and Ireland
AED	Anti-Epileptic Drug
AFE	Amniotic Fluid Embolism
AFM	Amniotic fluid material
ALS	Advanced life support
APS	Anti-phospholipid syndrome
ARDS	Acute Respiratory Distress Syndrome
BMI	Body mass index
BP	Blood pressure
BTS	British Thoracic Society
CEMD	Confidential Enquiries into Maternal Deaths
CEMM	Confidential Enquiries into Maternal Morbidity
CESDI	Confidential Enquiry into Stillbirth and Deaths in Infancy
CI	Confidence interval
CMACE	Centre for Maternal and Child Enquiries
CNS	Central nervous system
CORPs	Clinical Outcome Review Programmes
CPD	Continuing professional development
CPR	Cardiopulmonary resuscitation
CF	Cystic Fibrosis
CSF	Cerebrospinal fluid
CT	Computerised Tomography
CTD	Connective tissue disorders
DIC	Disseminated intravascular coagulation
ECMO	Extracorporeal membrane oxygenation
EWS	Early warning scores
FFP	Fresh frozen plasma
FIGO	The International Federation of Gynaecology and Obstetrics
GAS	Group A Streptococcus
GP	General Practitioner
HDU	High Dependency Unit
HELLP	Haemolysis, Elevated Liver enzymes, Low Platelets Syndrome
HES	Hospital Episode Statistics
HIV	Human Immunodeficiency Virus
HQIP	Healthcare Quality Improvement Partnership
ICD	International Classification of Diseases
IMD	Index of Multiple Deprivation
ITP	Immune thrombocytopenic purpura
ITU	Intensive Therapy Unit
IUD	Intrauterine death
MBRRACE-UK	Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK
MDE	Maternal Death Enquiry
MEOWS	Modified Early Obstetric Warning Score
MMR	Maternal mortality ratio
MNI-CORP	Maternal Newborn and Infant Clinical Outcome Review Programme
MOH	Massive Obstetric Haemorrhage
MRI	Magnetic Resonance Imaging
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIMACH	Northern Ireland Maternal and Child Health
NSAIDs	Non-steroidal anti-inflammatory drugs
PCR	Protein Creatinine Ratio
PDPH	Post-Dural Puncture Headache
PEA	Pulseless electrical activity
PEFR	Peak expiratory flow rate
PPH	Postpartum Haemorrhage
PPROM	Preterm pre-labour rupture of the membranes
QOF	Quality Outcome Framework
RCOG	Royal College of Obstetricians and Gynaecologists
RR	Risk ratio
SADS	Sudden Adult Death Syndrome
SADS/MNH	Sudden adult death syndrome with a morphologically normal heart
SBAR	Situation Background Assessment Recommendation tool
SIGN	Scottish Intercollegiate Guidelines Network
SIRS	Systemic Inflammatory Response Syndrome
SLE	Systemic lupus erythematosus
SUDEP	Sudden unexpected death in epilepsy
SUI	Serious Untoward Incident
T1DM	Type 1 Diabetes Mellitus
TTP	Thrombotic thrombocytopenic purpura
UKOSS	UK Obstetric Surveillance System
VBAC	Vaginal birth after caesarean section

Contents

1. Introduction and methodology

Marian Knight and Jennifer J Kurinczuk

1.1. Why do we need Confidential Enquiries?

Every maternal death is a tragedy, to the families left behind, to the staff involved, and to the wider communities that the women are a part of. Not to learn lessons for future care from such deaths, with the aim of preventing other mothers from dying and continuously improving our maternity services, would be an even greater tragedy. There are still too many countries in the world where such deaths pass unnoticed. It is a testament to the commitment of doctors, midwives, nurses and Health Departments throughout the UK and Ireland that the death of any woman during or up to one year after pregnancy leads to an in-depth investigation of the cause and circumstances surrounding her death and recommendations for improvements to community, hospital and public health services. The Confidential Enquiries into Maternal Deaths in England and Wales, subsequently the UK, and now also including Ireland, have been conducted continuously since 1952; during this time maternal death rates have fallen from approximately 90 per 100,000 women giving birth (Ministry of Health 1957) to around 10 per 100,000 now.

The UK Confidential Enquiries into Maternal Deaths (CEMD) are held up as a gold standard worldwide and a model for Confidential Enquiries elsewhere (World Health Organisation 2004). Maintaining the continuity of the CEMD in the UK thus impacts not only on maternal health within the UK but also globally. The Confidential Enquiry reports are required reading for midwives and doctors in training not only in obstetrics, but also anaesthetics, psychiatry and obstetric medicine. The reports form a summary of key guidance, implementation of which will lead to improvements in the quality of maternity care, and for many readers will form their first introduction to robust national audit.

Demonstrating the impact of Confidential Enquiries into Maternal Death on numbers and rates of maternal deaths is difficult in countries such as the UK and Ireland where deaths of women during and after pregnancy are rare, since the power of any analysis to demonstrate a statistically significant difference is small. The lack of a statistically significant impact on maternal deaths does not, however, preclude a clinical impact. Maternal deaths form the tip of the iceberg of disease, and recommendations to improve care will thus impact on the care of women with less severe morbidity, potentially preventing the progression of severity. The inclusion of investigations of morbidity topics as a new element in the Confidential Enquiries has the potential to enhance this added value, by specific identification of improvements in care of women who survive as well as those who die.

In addition to numbers, it is important to remember that each woman described in this report was an individual with a life and family. Telling these women's stories not only recognises them and their loss, but has additional power to influence change, and for that reason we have retained the descriptions of individual women's care as vignettes in this report. In the words of Meisel and Karlawish (Meisel and Karlawish 2011):

"Facts and figures are essential, but insufficient, to translate the data and promote the acceptance of evidence-based practices and policies…. narratives, when compared with reporting statistical evidence alone, can have uniquely persuasive effects in overcoming preconceived beliefs.

Stories help the public make sense of population-based evidence. Guideline developers and regulatory scientists must recognize, adapt, and deploy narrative to explain the science of guidelines to women and families, health care professionals, and policy makers to promote their optimal understanding, uptake, and use."

1.2. The Maternal Newborn and Infant Clinical Outcome Review Programme

The UK national surveillance and Confidential Enquiry into Maternal Deaths (CEMD) was established in 1952 and from 1992 until 2011 was led by Professor Gwyneth Lewis, latterly under the auspices of the Centre for Maternal and Child Enquiries (CMACE). Surveillance and national confidential enquires of perinatal deaths have a shorter history with the establishment in 1993 of the Confidential Enquiry into Stillbirth and Deaths in Infancy (CESDI) in response to the relatively high stillbirth and infant mortality rates in the UK in the 1990s. Restructuring and changes to funding led to both sets of enquiries being commissioned from CMACE by the National Patient Safety Agency as one of the three national confidential enquiry programmes along with the confidential enquiries into surgical and medical deaths (NCEPOD) and suicide and homicide by people with a mental health illness who have had contact with mental health services (NCISH).

In 2010 further changes were set in motion with the requirement under European procurement legislation for all three national programmes to be put out for open competitive tenders, now collectively renamed Clinical Outcome Review Programmes (CORPs). The overall budget was reduced and the maternal and infant programme was separated from the child health programme and put out for tender by the commissioners the National Patient Safety Agency (NPSA) as the 'Maternal Newborn and Infant Clinical Outcome Review Programme' (MNI-CORP). The contract for the MNI-CORP was awarded to the MBRRACE-UK collaboration in December 2010 and CMACE closed on 31st March 2011. The closure of CMACE coincided with the decision by the funders (the Departments of Health for England, Scotland, Wales, Northern Ireland and the British Crown Dependencies) to halt the procurement and hold a review of the requirements for the MNI-CORP programme (Shribman 2011). The review was established with a remit to determine the appropriate scope and plan for the future of the MNI-CORP to ensure it met anticipated requirements, and delivered first class output and value for money (Shribman 2011). The review group reported in July 2011 with the recommendation that the surveillance and confidential enquiries should continue and a second procurement exercise commenced in January 2012 run by the new commissioners, the Healthcare Quality Improvement Partnership (HQIP). The MBRRACE-UK collaboration was once again awarded the MNI-CORP contract starting from 1st June 2012.

At the start of the MNI-CORP contract the medical notes which had already been obtained by CMACE for maternal deaths which had occurred since the publication of the last triennial report, that is, from January 2009 onwards, were transferred to MBRRACE-UK. Importantly no reviews of the available notes had been undertaken and only 34% of the notes for maternal deaths in 2009, 2010 and the first quarter of 2011 had been obtained by CMACE and were complete. Thus at the start of the MNI-CORP programme in mid-2012 MBRRACE-UK needed to obtain the outstanding notes and start the process of reviews of deaths from nearly four years earlier. During the interim period, between the closure of CMACE and MBRRACE-UK starting work, maternal deaths in England and Wales were notified by a web-based portal established for this purpose; collection of information about maternal deaths in Scotland and Northern Ireland continued during this period through existing country-specific mechanisms. It is a testament to the dedication of staff from maternity units and elsewhere to the CEMD that MBRRACE-UK has been able to obtain copies of over 99% of the outstanding sets of notes for maternal deaths from 2009 to 2012 reviewed in this report and the team are extremely grateful for the co-operation and support of everyone involved.

This publication in 2014 sees a change to the style of the CEMD report following the introduction of the MNI-CORP. The programme, which includes surveillance and confidential enquiries into maternal deaths and serious morbidity, as well as surveillance and confidential enquiries into stillbirths, infant deaths and serious infant morbidity, requires the production of annual CEMD reports. Reports were previously produced on a triennial basis, because the number of maternal deaths from individual causes is small, and thus three years' worth of data is required to identify consistent lessons learned for future care and to maintain anonymity and confidentiality. Clearly the need to undertake annual reporting does not change this requirement, therefore, each topic-specific chapter which appeared in the previous triennial report will appear in an annual report once every three years on a cyclical basis, alongside a surveillance chapter reporting three years of statistical data. Note that this report contains four years of surveillance data due to the change from CMACE to MBRRACE-UK, new speeded-up processes and the subsequent reduction in the time lag between deaths occurring and report production. The topics to be included in the 2014–16 reports are as follows:

- **2014 (this report):** Surveillance data on maternal deaths from 2009–12. Confidential Enquiry reports on deaths and severe morbidity from sepsis, and deaths from haemorrhage, amniotic fluid embolism (AFE), anaesthesia, neurological, respiratory, endocrine and other indirect causes
- **2015:** Surveillance data on maternal deaths from 2011–13. Confidential Enquiry reports on deaths and severe morbidity from psychiatric causes, deaths due to thrombosis and thromboembolism, malignancy, late and coincidental deaths
- **2016:** Surveillance data on maternal deaths from 20012–14. Confidential Enquiry reports on deaths and severe morbidity from cardiac causes, deaths from pre-eclampsia and eclampsia and related causes and deaths in early pregnancy.

1.3. The MBRRACE-UK Confidential Enquiries into Maternal Deaths Methods

Identifying Maternal Deaths

The deaths of women during or after pregnancy are identified through a variety of sources. The majority are notified to the MBRRACE-UK office directly from the unit in which the maternal death occurred. We request that all such deaths are notified within one week of the death occurring. Others are notified from a variety of individuals such as Coroners/ Procurators Fiscal or pathologists, Local Supervising Authority Midwifery Officers and members of the public. Reports are also identified by the central MBRRACE-UK team from the media, for example, when the results of inquests are reported.

Ascertainment of deaths is cross-checked with records from the Office for National Statistics and National Records of Scotland. Both these sources provide details of registered deaths of any women in which pregnancy, or a pregnancy-specific cause, is listed on the death certificate. In addition, maternal details in birth records are linked to deaths of women of reproductive age occurring over the following 12 months, in order to identify maternal deaths where pregnancy or pregnancy-specific causes are not listed on the death certificate. The deaths identified from these additional sources are then compared with the deaths reported to MBRRACE-UK and when an unreported death is identified, the hospitals where the birth and death occurred are contacted and asked to provide records.

Collecting Information about Maternal Deaths

Following the report of a maternal death, a notification pack is sent to the Unit in which the death has occurred (Figure 1.1). This includes a surveillance form to collect basic demographic and clinical details about the death, together with a form requesting the contact details of the clinicians involved in managing the woman's care. The hospital MBRRACE-UK contact is asked to return the surveillance form together with the details of the local clinicians within one month of the death occurring. The hospital MBRRACE-UK contact is also asked to return a full photocopy of the woman's medical records.

After these documents have been returned, the MBRRACE-UK team send out local clinicians report forms to the clinical staff involved in the woman's care. These ask for the staff perspectives on the care of the woman, and ask them to identify any lessons learned for future care. These documents, together with the woman's medical records, are fully anonymised, scanned and uploaded onto a secure viewing system for independent assessment by MBRRACE-UK trained assessors. Our aim is to have all data complete and ready for assessment by three months from the date of a woman's death.

In addition to case records from the Unit in which the woman died, the MBRRACE-UK team also seek records from other units which cared for her, including units where she delivered and had other antenatal care. In addition, they seek copies of the post-mortem report, either from the hospital pathologist or from the Coroner/Procurator Fiscal. Units are also asked to return a copy of their local review (Serious Untoward Incident review, Root Cause Analysis or similar) where this has been undertaken to provide identified messages for future care at a local level.

Identifiable information about maternal deaths in England, Scotland and Wales is collected directly by the MBRRACE-UK office in Oxford. Privacy issues in Northern Ireland are such that identifiable information about women who have died during or after pregnancy cannot be transferred out of the Province. All the case records and surveillance data are therefore collected by the staff of the Northern Ireland Maternal and Child Health (NIMACH) office of the Public Health Agency of Northern Ireland. Fully anonymised records are then transferred securely to the MBRRACE-UK office in Oxford for analysis and expert review.

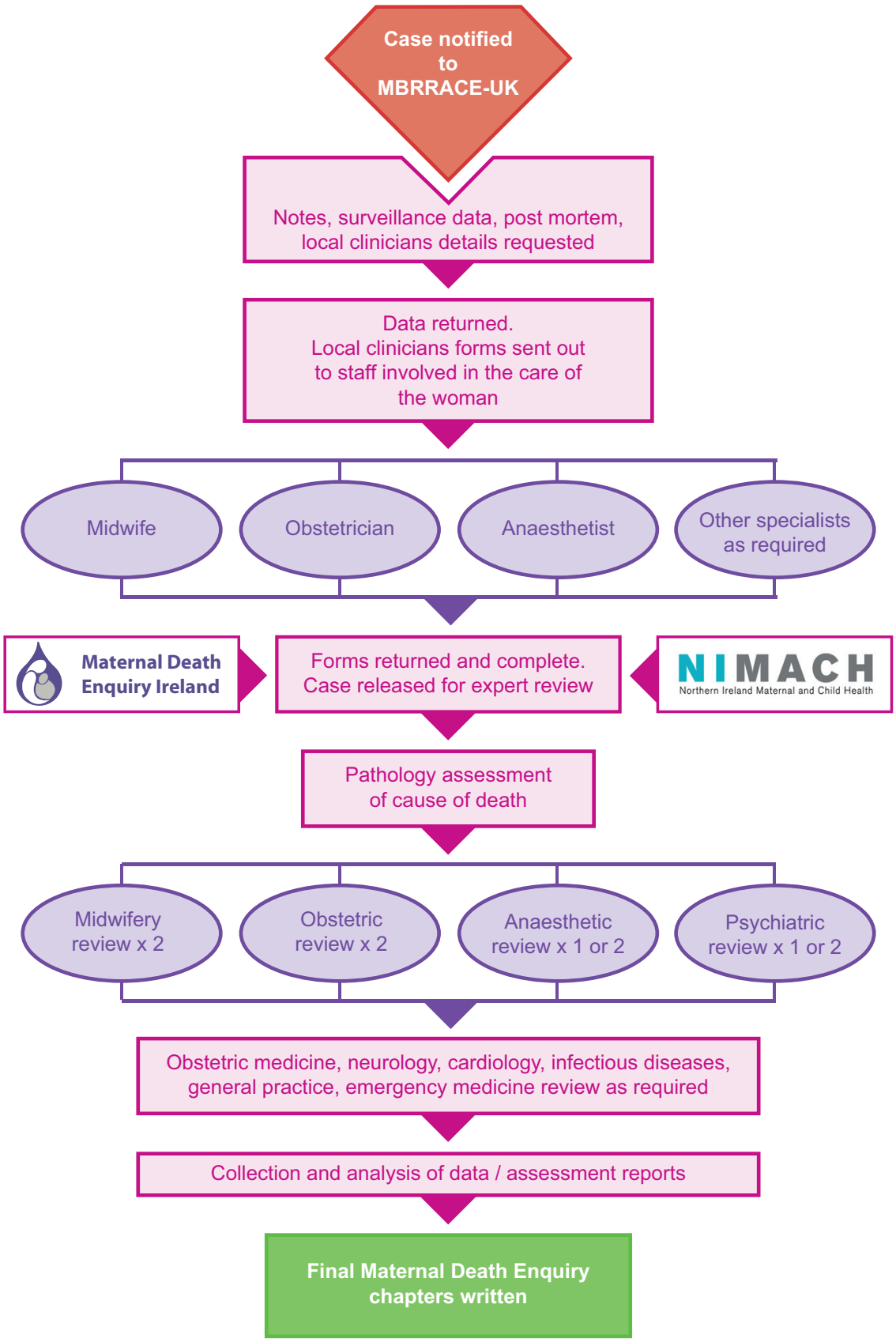
The surveillance information about each death is double-entered into a customised database. Queries about missing or unclear data items are sent back to units to ensure that the data are of high quality. In addition, some data items may be extracted directly from the maternal death records by MBRRACE-UK team staff. Once the data are complete, a dataset is extracted and cleaned prior to analysis by the MBRRACE-UK epidemiology team based in the National Perinatal Epidemiology Unit, University of Oxford.

The Maternal Death Enquiry Ireland

For the first time, deaths from the UK and Ireland are being assessed together in a joint Confidential Enquiry process. The Maternal Death Enquiry (MDE) Ireland was established in 2009 with the remit to carry out surveillance and Confidential Enquiries into maternal deaths in Ireland (Confidential Maternal Death Enquiry in Ireland 2012). In order to enhance the generalisability of the messages for care, whilst maintaining confidentiality and anonymity, maternal deaths occurring in Ireland have been assessed alongside UK deaths using the same processes. Expert assessors from the Irish Republic have joined the pool of UK assessors and contribute to assessment in the same way as UK assessors. Data for Ireland are collected by staff from the MDE

Ireland office in Cork; fully anonymised records are then transferred to the UK MBRRACE-UK office for upload onto the secure viewing system. MDE Ireland continues to analyse and publish surveillance data for Ireland independently (Confidential Maternal Death Enquiry in Ireland 2012); surveillance information for the Republic of Ireland is not included in this report and the trends described in chapter 2 refer only to the UK. The number of deaths reported in each Confidential Enquiry chapter will thus differ from the number recorded in the surveillance chapter due to the inclusion in the Confidential Enquiry of deaths from the Republic of Ireland, as well as selected late maternal deaths.

Figure 1.1: MBRRACE-UK Data Collection and Assessment Processes



Expert Review

MBRRACE-UK has over 80 assessors from various different speciality groups, including anaesthetics, intensive care, obstetrics, midwifery, psychiatry, pathology, general practice, emergency medicine and various medical specialities, including obstetric physicians, cardiologists, infectious diseases physicians and neurologists. Assessors were appointed in a selection process organised by the relevant Royal Colleges or professional organisations, which required specific skills and experience; all are volunteers and do not receive financial remuneration for their work, although they are able to classify their MBRRACE-UK work as part of continuing professional development (CPD). All assessors have undergone a training process and are provided with guidance detailing relevant standards of care against which deaths are assessed. Where possible, the guidance is drawn from national sources such as the National Institute for Health and Care Excellence (NICE), the Scottish Intercollegiate Guidelines Network (SIGN) or professional organisations such as the Royal College of Obstetricians and Gynaecologists (RCOG) and the Association of Anaesthetists of Great Britain and Ireland (AAGBI).

Once the complete records concerning a particular woman have been received, the anonymous records are reviewed by a pathologist and clinical epidemiologist, together with an obstetrician or physician as required. This establishes the most likely cause of the woman's death and allows for her records to be allocated to the appropriate speciality assessors. The care of each woman is then assessed by two obstetricians, two midwives, two pathologists, one or two anaesthetists and other specialist assessors as required, including pairs of psychiatrists, general practitioners, physicians, emergency medicine specialists and intensive care experts. Each woman's care is thus examined by between ten and fifteen expert reviewers. Each primary assessor completes an independent review of the woman's care, highlighting the lessons to be learned to improve care in the future. This is checked by a second assessor in the relevant specialty. Expert assessors are located in all areas of the UK and Ireland; to maintain anonymity, assessors are only asked to review the care of women who have died outside their region or nation. The assessment process and all individual findings are strictly confidential; all assessors are required to sign a confidentiality agreement. Expert assessors give their opinion on the quality of care according to the three criteria given in Box 1.1.

Box 1.1: Assessment of Quality of Care

- Good care; no improvements identified
- Improvements in care* identified which would have made no difference to the outcome
- Improvements in care* identified which may have made a difference to the outcome

*Improvements in care are interpreted to include adherence to guidelines, where these exist and have not been followed, as well as other improvements which would normally be considered part of good care, where no formal guidelines exist.

Assessors are also asked to identify whether any woman's death should be notified to the Healthcare Quality Improvement Partnership (HQIP), which has a standard protocol for all the Clinical Outcome Review Programmes to escalate major concerns about care where it is clear these concerns have not been addressed at a local level. Deaths are notified to HQIP if there is consensus among assessors that they meet one of the following criteria (Box 1.2):

Box 1.2: Concerns escalated to HQIP – standard procedure for all Clinical Outcome Review Programmes

- Death (child or adult) attributable to abuse or neglect, in any setting, but no indication of cross agency involvement (i.e. no mention of safeguarding, social services, police or Local Safeguarding Children Board).
- Staff member displaying:
  - Abusive behaviour (including allegations of sexual assault)
  - Serious professional misconduct
  - Dangerous lack of competency
  - But it is not clear if the incident has been reported to senior staff
- Standards in care that indicate a dysfunctional or dangerous department or organisation, or grossly inadequate service provision.

Reviewing the evidence and reaching conclusions

Once data collection is complete and all women's care has undergone expert assessment, chapter writing groups are convened. These multi-disciplinary groups consist of representatives from all the different relevant specialist assessor groups. Each chapter writing group discusses all of the women who died from a specific cause of death. Initially the cause of death and classification of care is discussed to ensure that all deaths are appropriately classified; subsequently the expert reviews of each woman's care are examined to enable the main themes for learning to be drawn out for the MBRRACE report. Lead members of each chapter-writing group will then draft the initial chapter, which is then edited by Marian Knight and reviewed by all the other group members and editors, prior to reaching a final agreed version. Where possible, recommendations are linked to national guidance from organisations such as NICE.

Definitions and statistical methods

A maternal death is defined internationally as a death of a woman during or up to six weeks (42 days) after the end of pregnancy (whether the pregnancy ended by termination, miscarriage or a birth, or was an ectopic pregnancy) through causes associated with, or exacerbated by, pregnancy (World Health Organisation 2010). A late maternal death is one which occurs more than six weeks but less than one year after the end of pregnancy. Deaths can be further subdivided on the basis of cause into: direct deaths, from pregnancy-specific causes such as pre-eclampsia; indirect deaths, from other medical conditions made worse by pregnancy such as cardiac disease; or coincidental deaths, where the cause is considered to be unrelated to pregnancy, such as road traffic accidents. These definitions are summarised in Box 1.3.

Box 1.3. Definitions of maternal deaths (World Health Organisation 2010)

Maternal death	Death of a women while pregnant or within 42 days of the end of the pregnancy* from any cause related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes.
Direct	Deaths resulting from obstetric complications of the pregnant state (pregnancy, labour and puerperium), from interventions, omissions, incorrect treatment or from a chain of events resulting from any of the above.
Indirect	Deaths resulting from previous existing disease, or disease that developed during pregnancy and which was not the result of direct obstetric causes, but which was aggravated by the physiological effects of pregnancy.
Late	Deaths occurring between 42 days and 1 year after the end of pregnancy* that are the result of Direct or Indirect maternal causes.
Coincidental†	Deaths from unrelated causes which happen to occur in pregnancy or the puerperium.

*Includes giving birth, ectopic pregnancy, miscarriage or termination of pregnancy.

†Termed "Fortuitous" in the International Classification of Diseases (ICD)

For the purposes of MBRRACE-UK and preceding UK Confidential Enquiries, maternal mortality rates with 95% confidence intervals are calculated using national data on the number of maternities (women giving birth at or beyond 24 weeks gestation) as the denominator. This differs from quoted standard international maternal mortality ratios (MMR) which use live births as the denominator; a calculated MMR is provided for comparison purposes. Total maternities for the UK for the period 2009 to 2012 were obtained from the annually reported birth data for England and Wales (Office for National Statistics), Scotland (General Register Office for Scotland) and Northern Ireland (Northern Ireland Statistics and Research Agency). These data were used to calculate age specific and country of birth specific mortality rates and relative risks. Denominator data on place of delivery and multiple pregnancies for the maternities in England and Wales (Office for National Statistics) were used to calculate maternal mortality rates and relative risks by place of delivery and plurality. As previously (Lewis, Cantwell et al. 2011), Hospital Episode Statistics (HES) maternity data for England were used to estimate the denominators for ethnic groups and quintiles of deprivation, and hence to derive estimated mortality rates and relative risks by ethnic and socioeconomic groups in England. Maternities for which ethnicity was not stated were included in the 'white European' group because the re-distributed proportions matched with the estimated ethnic profiles in the UK population census (Health & Social Care Information Centre 2006). Denominator data on maternities by level of deprivation were available for only the financial year 2012–13; hence the calculated proportion of maternities for each quintile for the financial year was applied to the aggregate of 2009–12 to estimate proxy denominators for quintiles of deprivation.

The characteristics of women who die are tabulated and compared where possible with national population data. Characteristics are also compared with other population based data sources, such as from existing UK Obstetric Surveillance System (UKOSS) studies (Knight and Lindquist 2013) if there are no other possible sources of comparative data.

Variance-weighted least squares regression was used to investigate the change in three-yearly maternal mortality rates over time. Risk ratios with 95% confidence intervals were calculated to compare maternal death rates between groups of women. The data were analysed in STATA version 13 (Statacorp).

1.4. The new Confidential Enquiries into Maternal Morbidities

Maternal deaths in the UK are, fortunately, rare. However, a much larger number of women, estimated to be up to 100 times as many as those who die (Waterstone, Bewley et al. 2001), suffer from severe pregnancy complications which can leave them with lifelong disability. There is thus an increasing recognition that we can learn lessons for future care from investigating women with severe morbidity as well as maternal deaths. A new component of the UK Confidential Enquiry programme is therefore the Confidential Enquiries into Maternal Morbidity (CEMM). CEMM topics are chosen by the MBRRACE-UK Independent Advisory Group from topics proposed by clinicians, policy-makers, third sector organisations and members of the public in an annual open application process. The topic chosen for inclusion in the 2014 report is maternal sepsis.

Women are identified for the CEMM in different ways according to the topic. The women with sepsis morbidity were identified from an existing UKOSS study of severe sepsis in pregnancy which identified women with severe sepsis fulfilling the criteria in Box 1.4 between June 2011 and May 2012 (Acosta, Kurinczuk et al. 2014).

All 69 surviving women with septic shock notified nationally were used as the sampling frame. A geographically representative sample of 34 women was drawn at random from this group. A full set of medical records was requested from each hospital concerned. The records then underwent expert assessment in exactly the same way as the records of the women who died.

Box 1.4: Definition of severe sepsis morbidity used in the UKOSS study 2011–12 (Acosta, Kurinczuk et al. 2014)

1. Any women requiring level 2 or level 3 critical care (or obstetric HDU type care) with severe sepsis or suspected severe sepsis
2. A clinical diagnosis of severe sepsis:
   a) Temperature >38°C or <36°C, measured on two occasions at least 4 hours apart
   b) Heart rate >100 beats/minute, measured on two occasions at least 4 hours apart
   c) Respiratory rate >20/minute, measured on two occasions at least 4 hours apart
   d) White cell count >17x10^9/L or <4x10^9/L or with >10% immature band forms, measured on two occasions

2. Maternal Mortality and Morbidity in the UK 2009–12: Surveillance and Epidemiology

Marian Knight, Manisha Nair, Anjali Shah, Nudrat Noor and Collen Acosta

2.1. Key points

Overall there has been a statistically significant decrease in the maternal death rate between 2006-8 and 2009-12 in the UK.

This decrease is predominantly due to a decrease in direct maternal deaths; death rates from hypertensive disorders of pregnancy are now at the lowest rate since the inception of the Enquiry in 1952.

Maternal deaths from indirect causes are still not being addressed. There has been no significant change in the rate of indirect maternal death over the last 10 years, a time during which direct maternal deaths have halved. This needs action across a wide range of health services and not just maternity services, including public health, primary and secondary care. There is a need to train physicians in pregnancy medicine and to recognise obstetric medicine as an essential specialty.

The number of women dying from genital tract sepsis has significantly decreased since 2006-8.

Thrombosis and thromboembolism is once again the leading cause of direct maternal death.

Influenza was an important cause of death during this period; half of the associated deaths occurred after a vaccine became available and can therefore be considered preventable. The importance of seasonal influenza immunisation for pregnant women cannot be over-emphasised; increasing immunisation rates in pregnancy against seasonal influenza must remain a public health priority.

Access to antenatal care remains an issue amongst women who died. More than two thirds of women who died did not receive the nationally recommended level of antenatal care; a quarter did not receive a minimum level of antenatal care.

2.2. Causes and trends

Marian Knight, Anjali Shah, Manisha Nair and Nudrat Noor

Overall in 2009-12, 357 women died in the UK during or in the 42 days following the end of their pregnancy. The deaths of 36 women (10%) were classified as coincidental. There were thus 321 maternal deaths from direct or indirect causes in 2009-12 in the UK. Information on deaths from the Republic of Ireland is not included in this chapter and therefore rates and numbers presented here are comparable with all previous UK reports.

For consistency and comparability with previous triennial reports, all rates are presented over three year periods: 2009–11 and 2010–12. In 2009–11 there were 253 deaths from direct or indirect causes amongst 2,379,014 maternities, a maternal death rate of 10.63 per 100,000 maternities (95% CI 9.36–12.03). In 2010–12 there were 243 deaths from direct or indirect causes amongst 2,401,624 maternities, a maternal death rate of 10.12 per 100,000 maternities (95% CI 8.89–11.47). Table 2.1 and Figure 2.1 show rolling three-yearly maternal death rates since 2003. There was a statistically significant decrease in maternal death rates between 2003–05 and 2010–12 (risk ratio (RR) 0.73; 95% CI 0.61–0.86; $p<0.001$ for trend over time). This is accounted for primarily by a statistically significant halving in the direct maternal death rate over this period (RR 0.52; 95% CI 0.39–0.69; $p<0.001$ for trend over time). In contrast there was no statistically significant change in the rate of indirect death over this period (RR 0.90, 95% CI 0.72–1.11; $p=0.73$ for trend over time).

It is important to note that this decrease in maternal death rates has occurred in the context of an increase in the number of maternities in the UK, with over 110,000 more women giving birth annually in 2012 compared with 2003. Additionally, the population of women giving birth is likely to have higher care needs on the basis of demographic and other trends, including older maternal age (Office for National Statistics 2013), higher rates of obesity (Heslehurst, Rankin et al. 2010) and a greater proportion of births to women born outside the UK. These factors are all associated with a higher risk of maternal death (Nair, Kurinczuk et al. 2014), thus decreasing rates of death suggest that maternity services are

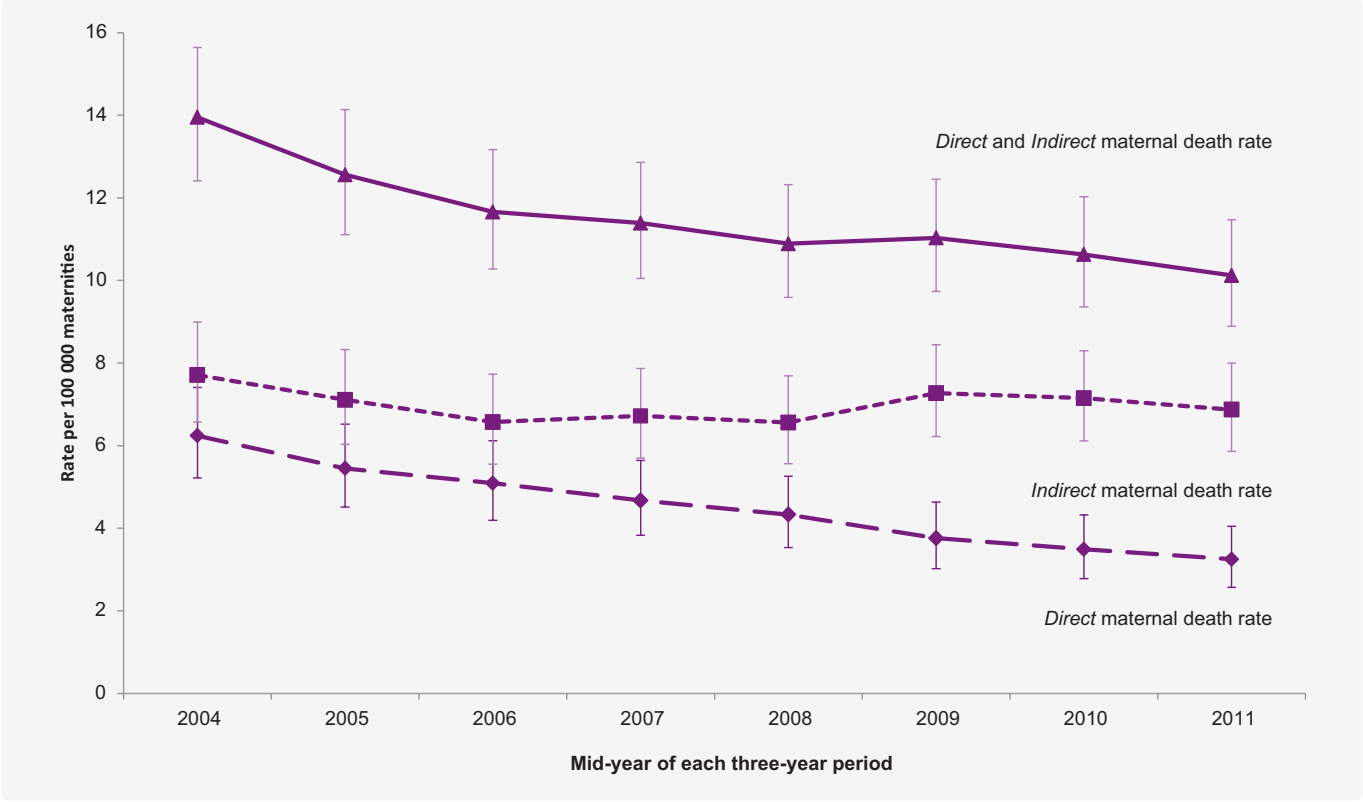
responding appropriately to the challenge of a more complex and numerous maternity population. Neither definitions nor coding practices have changed over this time and thus would not be an explanation for the observed decrease.

Table 2.1: Rolling three year average Direct and Indirect maternal mortality rates per 100,000 maternities; UK 2003–12

3-year period	Total UK maternities	Direct deaths			Indirect deaths			Total Direct and Indirect deaths		
		n	Rate	95% CI	n	Rate	95% CI	n	Rate	95% CI
2003–05	2 114 004	132	6.24	5.26–7.41	163	7.71	6.61–8.99	295	13.95	12.45–15.64
2004–06	2 165 909	118	5.45	4.55–6.53	154	7.11	6.07–8.33	272	12.56	11.15–14.14
2005–07	2 220 979	113	5.09	4.23–6.12	146	6.57	5.59–7.73	259	11.66	10.32–13.17
2006–08	2 291 493	107	4.67	3.86–5.64	154	6.72	5.74–7.87	261	11.39	10.09–12.86
2007–09	2 331 835	101	4.33	3.53–5.26	153	6.56	5.56–7.69	254	10.89	9.59–12.32
2008–10	2 366 082	89	3.76	3.02–4.63	172	7.27	6.22–8.44	261	11.03	9.73–12.45
2009–11	2 379 014	83	3.49	2.78–4.32	170	7.15	6.11–8.30	253	10.63	9.36–12.03
2010–12	2 401 624	78	3.25	2.57–4.05	165	6.87	5.86–8.00	243	10.12	8.89–11.47

Source: CMACE, MBRRACE-UK, Office for National Statistics, National Records Scotland, Northern Ireland Statistics and Research Agency

Figure 2.1: *Direct* and *Indirect* maternal mortality rates per 100 000 maternities; rolling three year average rates 2003–12



Source: CMACE, MBRRACE-UK

The trends in triennial rates since 1985–87 are shown in Table 2.2 and Figures 2.2–2.4. Note that only rates for 2009–11 are included for consistency with previous reports which included triennial rates. This longer term view highlights the difference between direct and indirect maternal death rates; whilst the longer term trend is towards a decrease in direct maternal deaths, indirect maternal deaths have increased. Tackling indirect maternal deaths remains a major challenge for UK health services. This needs action across a wide range of health

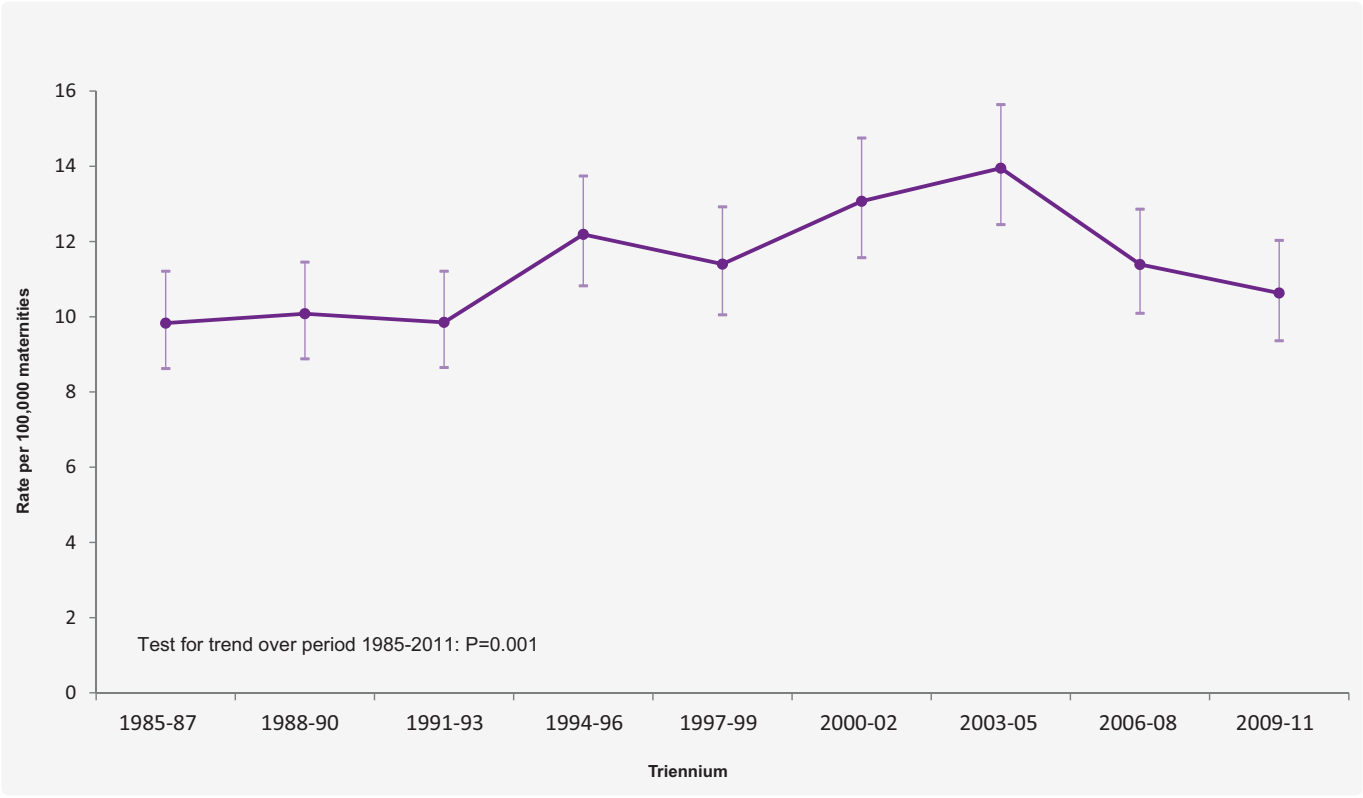
services and not just maternity services, including public health, primary and secondary care. There is a need to train physicians in pregnancy medicine and to recognise obstetric medicine as an essential specialty.

Table 2.2: *Direct* and *Indirect* maternal deaths and mortality rates per 100,000 maternities by triennium, UK 1985–2011.

Triennium	Direct deaths recorded			Indirect deaths recorded			Total Direct and Indirect deaths recorded		
	n	Rate	95% CI	n	Rate	95% CI	n	Rate	95% CI
1985–87	139	6.13	5.19–7.23	84	3.70	2.99–4.58	223	9.83	8.62–11.21
1988–90	145	6.14	5.22–7.23	93	3.94	3.22–4.83	238	10.08	8.88–11.45
1991–93	128	5.53	4.65–6.57	100	4.32	3.55–5.25	228	9.85	8.65–11.21
1994–96	134	6.10	5.15–7.22	134	6.10	5.15–7.22	268	12.19	10.82–13.74
1997–99	106	4.99	4.13–6.04	136	6.40	5.41–7.57	242	11.40	10.05–12.92
2000–02	106	5.31	4.39–6.42	155	7.76	6.63–9.08	261	13.07	11.57–14.75
2003–05	132	6.24	5.27–7.40	163	7.71	6.61–8.99	295	13.95	12.45–15.64
2006–08	107	4.67	3.86–5.64	154	6.72	5.74–7.87	261	11.39	10.09–12.86
2009–11	83	3.49	2.78–4.32	170	7.15	6.11–8.30	253	10.63	9.36–12.03

Source: CMACE, MBRRACE-UK

Figure 2.2: *Direct* and *Indirect* maternal mortality rates per 100,000 maternities; UK: 1985–2011

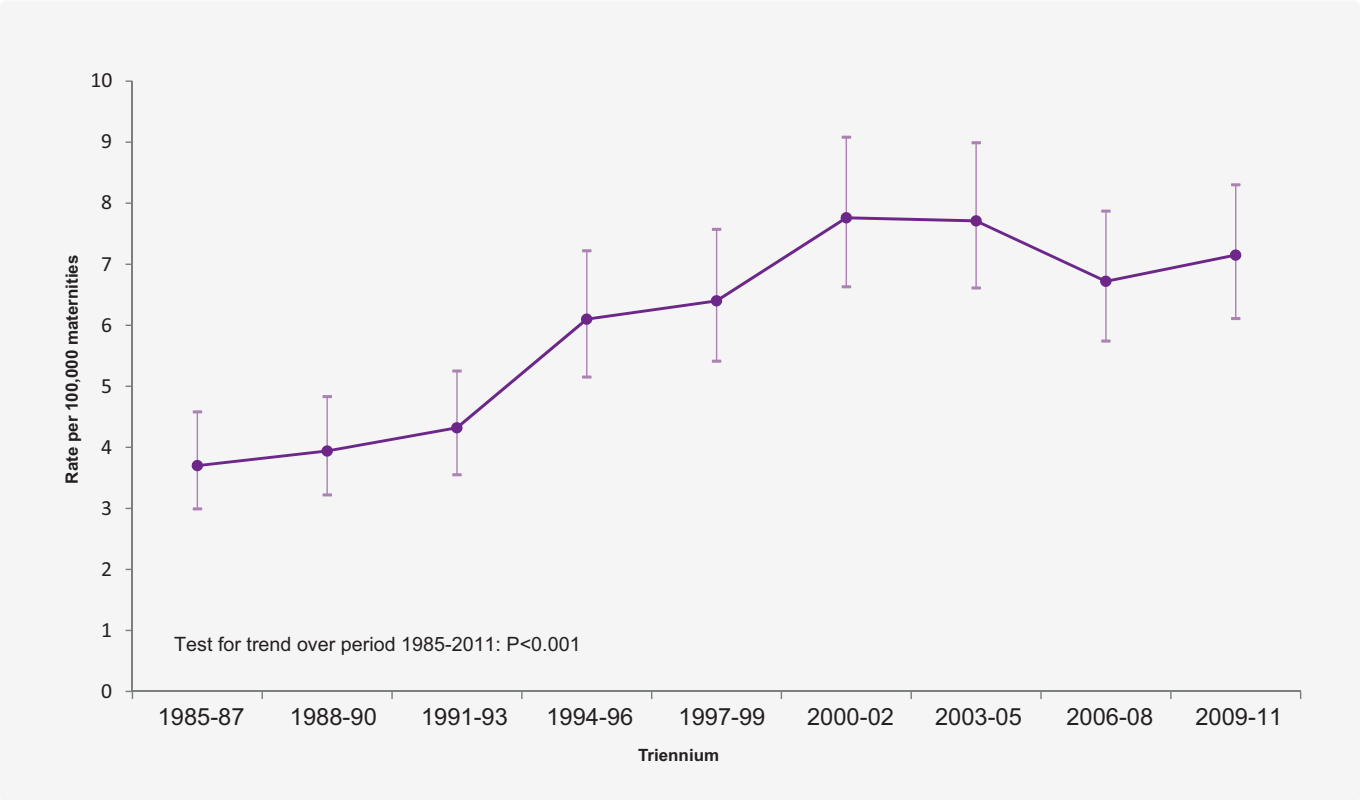


Source: CMACE, MBRRACE-UK

Figure 2.3: *Direct* maternal mortality rate per 100,000 maternities; UK: 1985–2011

Source: CMACE, MBRRACE-UK

Figure 2.4: *Indirect* maternal mortality rates per 100,000 maternities; UK: 1985–2011



Source: CMACE, MBRRACE-UK

International comparison

The UK CEMD, due to multiple sources of death identification, and the commitment of maternity staff, Coroners/Procurators Fiscal, pathologists and others to reporting deaths, has a very high rate of ascertainment. The rate of maternal death may thus appear to be considerably higher than comparable nations which do not undertake such detailed death finding. Many nations simply identify maternal deaths through routine death registration, which can significantly underestimate the number and thus rate of maternal deaths. Table 2.3 illustrates the UK maternal death rates estimated using routine death registration alone to allow for comparison with published international rates. Note that almost half of the deaths identified by the CEMD would not have been identified by the use of routine death registration data alone.

It is international practice to use the number of live births as the denominator for maternal mortality ratios (MMR), whereas the number of maternities is used in the UK to calculate rates, as this represents a figure closer to the true denominator number of women at risk. By applying the number of live births as a denominator to the routine data collected through death certificates, the UK MMR used for international comparisons is 5.57 per 100,000 live births (95% CI 4.67- 6.60).

Table 2.3: Maternal mortality ratios*, UK: 1985–2011

Triennium	No. of deaths identified through death certificates	Rate	95% CI	Denominator number of live births
1985–87	174	7.67	6.61–8.90	2,268,766
1988–90	171	7.24	6.24–8.42	2,360,309
1991–93	150	6.48	5.52–7.60	2,315,204
1994–96	158	7.19	6.15–8.40	2,197,640
1997–99	128	6.03	5.70–7.17	2,123,614
2000–02	136	6.81	5.76–8.05	1,997,472
2003–05	149	7.05	6.00–8.27	2,114,004
2006–08	155	6.76	5.78–7.92	2,291,493
2009–11	134	5.57	4.67–6.60	2,405,251

Source: CMACE, MBRRACE-UK, Office for National Statistics, National Records Scotland, Northern Ireland Statistics and Research Agency.

*Note that this table reports the Maternal Mortality Ratio and not the rate as elsewhere in the report

Deaths due to individual causes

Maternal deaths by cause, 2006–12 are shown in Table 2.4. Rates for 2009–11 and 2010–12 are presented for consistency and comparison with previous triennial reporting. Table 2.5 shows the death rates by cause between 1985 and 2011.

Table 2.4: Maternal mortality rates by cause, per 100,000 maternities, 2006 to 2012

Cause of death	2006–08			2009–11			2010–12		
	n	Rate	95% CI	n	Rate	95% CI	n	Rate	95% CI
All Direct and Indirect deaths†	261	11.39	10.09–12.86	253	10.63	9.36–12.03	243	10.12	8.89–11.47
Direct deaths									
*Genital tract sepsis**	26	1.13	0.77–1.67	15	0.63	0.35–1.04	12	0.50	0.26–0.87
Pre–eclampsia and eclampsia	19	0.83	0.53–1.30	10	0.42	0.20–0.77	9	0.38	0.18–0.71
Thrombosis and thromboembolism	18	0.79	0.49–1.25	30	1.26	0.85–1.80	26	1.08	0.71–1.59
Amniotic fluid embolism	13	0.57	0.33–0.98	7	0.29	0.12–0.61	8	0.33	0.14–0.66
Early pregnancy deaths	11	0.48	0.27–0.87	4	0.17	0.05–0.43	8	0.33	0.14–0.66
Haemorrhage	9	0.39	0.20–0.75	14	0.59	0.32–0.99	11	0.46	0.23–0.82
Anaesthesia	7	0.31	0.15–0.64	3	0.12	0.03–0.37	4	0.17	0.05–0.43
Other Direct‡	4	0.17	0.07–0.47	‡	‡	‡	‡	‡	‡
All Direct	107	4.67	3.86–5.64	83	3.49	2.78–4.32	78	3.25	2.57–4.05
Indirect									
Cardiac disease	53	2.31	1.77–3.03	51	2.14	1.60–2.82	54	2.25	1.69–2.93
Other Indirect causes	49	2.14	1.62–2.83	72	3.03	2.37–3.81	61	2.54	1.94–3.26
Indirect neurological conditions	36	1.57	1.13–2.18	30	1.26	0.85–1.80	31	1.29	0.88–1.83
Psychiatric causes	13	0.57	0.33–0.98	13	0.55	0.29–0.93	16	0.67	0.38–1.08
Indirect malignancies	3	0.13	0.04–0.41	4	0.17	0.05–0.45	3	0.13	0.03–0.37
All Indirect	154	6.72	5.74–7.87	170	7.15	6.11 –8.30	165	6.87	5.86–8.00
Coincidental	50	2.18	1.65–2.88	23	0.98	0.61–1.45	26	1.08	0.71–1.59
Late deaths	33†	†	†	325	13.66	12.22–15.33	313	13.03	11.63–14.56

*Genital tract sepsis deaths only, including early pregnancy deaths as the result of genital tract sepsis. Other deaths from infectious causes are classified under other indirect causes.

‡Acute fatty liver and genital tract trauma; included with pre-eclampsia and eclampsia and haemorrhage respectively from 2009 onwards.

† Figures on late deaths for 2006–08 include only cases reported to CMACE and not all deaths, therefore rates are not calculated. Cases from 2009–12 identified through direct report and linked national birth and death data and include late direct, late indirect and late coincidental deaths. These deaths will be described fully in the 2015 report.

Sources: CMACE, MBRRACE-UK, Office for National Statistics, National Records Scotland, Northern Ireland Statistics and Research Agency.

Table 2.5: UK Maternal deaths and mortality rates by cause 1985–2011

Cause of death	Numbers									Rates per 100,000 maternities								
	1985–87	1988–90	1991–93	1994–96	1997–99	2000–02	2003–05	2006–08	2009–11	1985–87	1988–90	1991–93	1994–96	1997–99	2000–02	2003–05	2006–08	2009–11
All Direct and Indirect deaths	223	238	228	268	242	261	295	261	252	9.83	10.08	9.85	12.19	11.4	13.07	13.95	11.39	10.63
Direct deaths																		
Genital tract sepsis*	9	17	15	16	18	13	18	26	14	0.40	0.72	0.65	0.73	0.85	0.65	0.85	1.13	0.63
Pre-eclampsia and eclampsia	27	27	20	20	16	14	18	19	10	1.19	1.14	0.86	0.91	0.75	0.70	0.85	0.83	0.42
Thrombosis and thromboembolism	32	33	35	48	35	30	41	18	30	1.41	1.40	1.51	2.18	1.65	1.50	1.94	0.79	1.26
Amniotic fluid embolism	9	11	10	17	8	5	17	13	7	0.40	0.47	0.43	0.77	0.38	0.25	0.80	0.57	0.29
Early pregnancy deaths	16	24	17	15	17	15	14	11	4	0.71	1.02	0.73	0.68	0.80	0.75	0.66	0.48	0.17
Haemorrhage	10	22	15	12	7	17	14	9	14	0.44	0.93	0.65	0.55	0.33	0.85	0.66	0.39	0.59
Anaesthesia	6	4	8	1	3	6	6	7	3	0.26	0.17	0.35	0.05	0.14	0.30	0.28	0.31	0.12
Other Direct‡	27	17	14	7	7	8	4	4	0	1.19	0.72	0.60	0.32	0.33	0.40	0.19	0.17	–
All direct	139	145	128	134	106	106	132	107	82	6.13	6.14	5.53	6.10	4.99	5.31	6.24	4.67	3.49
Indirect deaths																		
Cardiac disease	23	18	37	39	35	44	48	53	51	1.01	0.76	1.60	1.77	1.65	2.20	2.27	2.31	2.14
Other Indirect causes	43	45	38	39	41	50	50	49	72	1.90	1.91	1.64	1.77	1.93	2.50	2.37	2.14	3.03
Indirect neurological conditions	19	30	25	47	34	40	37	36	30	0.84	1.27	1.08	2.14	1.60	2.00	1.75	1.57	1.26
Psychiatric causes	†	†	†	9	15	16	18	13	13	†	†	†	0.41	0.71	0.80	0.85	0.57	0.55
Indirect malignancies	†	†	†	†	11	5	10	3	4	†	†	†	†	0.52	0.25	0.47	0.13	0.17
All Indirect	84	93	100	134	136	155	163	154	170	3.70	3.94	4.32	6.10	6.40	7.76	7.71	6.59	7.15
Coincidental	26	39	46	36	29	36	55	50	22	1.15	1.65	1.99	1.64	1.37	1.80	2.60	2.18	0.98

*Including early pregnancy deaths as a result of sepsis

‡Acute fatty liver and genital tract trauma; included with pre-eclampsia and eclampsia and haemorrhage respectively from 2009 onwards

†Deaths from these causes not included in reports from earlier years

Source: CMACE, MBRRACE-UK

Direct deaths

The mortality rate from genital tract sepsis has more than halved between 2006–08 and 2010–12; a statistically significant decrease (RR 0.44; 95% CI 0.22–0.87, p=0.016) (Table 2.4, Figure 2.5). A number of initiatives have been put in place recently to tackle sepsis as a whole; the international Surviving Sepsis Campaign (Surviving Sepsis Campaign 2014) first highlighted sepsis as a concern in 2002 and subsequently produced management guidelines in 2004, updated in 2008 and 2012 (Dellinger, Levy et al. 2008, Dellinger, Levy et al. 2013). A CMACE emergent theme briefing on genital tract sepsis was issued in September 2010 (CMACE 2010), with the subsequent triennial report highlighting genital tract sepsis further in March 2011 (Lewis, Cantwell et al. 2011). Health Protection Agency guidelines for prevention and control of Group A Streptococcal infection in acute healthcare and maternity settings in the UK were issued in January 2012 (Steer, Lamagni et al. 2012) and RCOG guidelines on bacterial sepsis in pregnancy and bacterial sepsis following pregnancy were issued in April 2012 (Royal College of Obstetricians and Gynaecologists 2012a, Royal College of Obstetricians and Gynaecologists 2012b). It is clear from the Confidential Enquiry into maternal sepsis morbidity (chapter 3) that there are a number of examples of timely recognition and good care of women with Group A Streptococcal genital tract infection who subsequently recovered well.

It is not clear whether any or all of these initiatives can be directly linked to the decrease in mortality rates; cyclical increases in puerperal sepsis have also been linked to increases in population rates of other streptococcal diseases such as scarlet fever, thought to be associated with changes in the circulating phage types of Group A Streptococcus (Acosta and Knight 2013). Scarlet fever resurgences tend to occur on average every four years, with the latest occurring in 2008–09 (Public Health England 2014a). On the basis of a possible resurgence of strains of Group A Streptococcus associated with more severe disease, the Public Health England suggests a need for ongoing vigilance (Public Health England 2014a).

Figure 2.5: Maternal mortality rates from genital tract sepsis 1985–2011

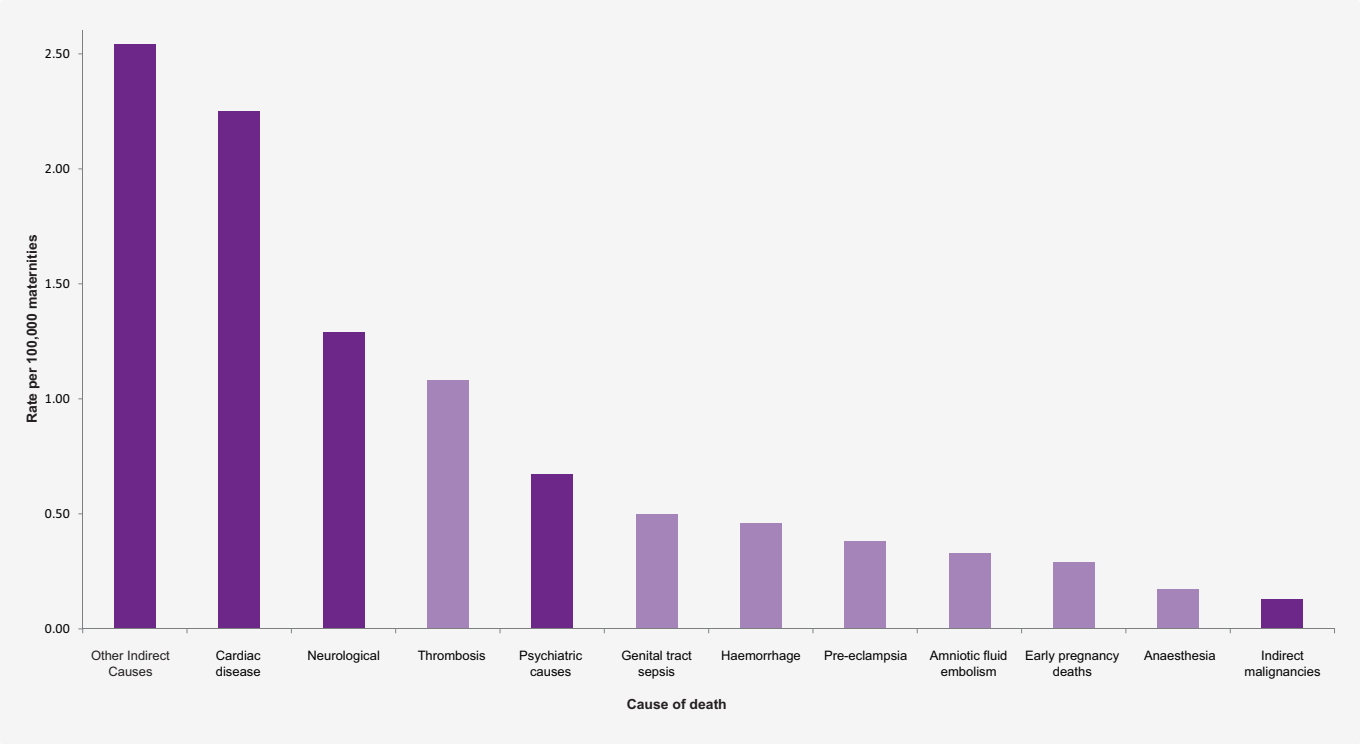
Source: CMACE, MBRRACE-UK

The pattern of direct maternal deaths has thus reverted to that seen in triennia prior to 2006–08, i.e. with thrombosis and thromboembolism as the leading cause of direct deaths (Figure 2.6). It is perhaps unsurprising that maternal deaths from thrombosis and thromboembolism remain the major cause of direct maternal deaths, given the known association with maternal obesity (Knight 2008), and rising rates of obesity in the pregnant population (Heslehurst, Rankin et al. 2010). Deaths specifically attributed to thrombosis and thromboembolism will be reviewed in depth in the 2015 report. It is important to note

that the change in death rate from thrombosis and thromboembolism between 2006–08 and 2010–12 is not statistically significant.

Deaths from pre-eclampsia and eclampsia, including deaths associated with HELLP syndrome and acute fatty liver of pregnancy, are now at the lowest ever recorded rate; the rate decreased significantly between 2006–08 and 2010–12. The incidence of eclampsia has previously been shown to have decreased significantly between 1992 and 2005–06 (Knight 2007a). Changes to the management of eclampsia and pre-eclampsia in the UK followed several large randomised controlled trials, subsequent systematic reviews (Duley, Gulmezoglu et al. 2010a, Duley, Gulmezoglu et al. 2010b, Duley, Henderson-Smart et al. 2010a, Duley, Henderson-Smart et al. 2010b) and the introduction of NICE guidance on Hypertension in Pregnancy in August 2010 (National Institute for Health and Care Excellence 2010).

Figure 2.6: Maternal mortality by cause 2010–12



Solid bars indicate indirect causes of death, half tone bars show direct causes of death

Indirect deaths

As highlighted above, addressing indirect maternal deaths remains a major challenge to UK health services. In 2009–11 and 2010–12, the 'other indirect' group represents the most numerous group, principally due to a major contribution from influenza and other non-genital tract sepsis deaths, discussed further in chapter 3. There were 29 deaths of pregnant women and women up to six weeks postpartum in association with influenza in the UK in 2009–12; more than half of these deaths occurred after a vaccine became available. Pregnant women continue to die in the UK from this preventable cause; increasing immunisation rates in pregnancy against seasonal influenza must remain a public health priority.

As in previous reports, cardiac disease remains the largest single cause of indirect maternal deaths. There was no significant change in the maternal mortality rate from cardiac disease between 2006–08 and 2010–12; the rate remains significantly higher than the rate in 1985–87 (Table 2.5) (RR 2.22, 95% CI 1.36–3.61, p=0.001). More women also died from neurological causes in 2010–12 than from any single *direct* cause of maternal death. The rate of deaths from neurological causes has remained essentially unchanged with no clear trend over time since 1985–87; these deaths are discussed in depth in chapter 7. Indirect deaths from other medical conditions are discussed in detail in chapter 8.

Whilst it might appear that a relatively small number of women died from psychiatric causes in the triennia 2009–11 and 2010–12, it must be remembered that deaths from psychiatric causes make a significant contribution to late maternal deaths (those occurring more than six weeks and up to one year after the end of pregnancy); 95 of the 419 late maternal deaths which occurred between 2009–12 were due to psychiatric causes. Maternal deaths, including

late deaths, from psychiatric causes will be a major focus of the 2015 report. The 2015 report will also include a detailed examination of the women who died between six weeks and one year after the end of their pregnancy, in order to identify deaths which may have been related to or exacerbated by pregnancy, and to identify messages for future care. A further 55 late maternal deaths were from cardiac causes; cardiac disease will be the major focus of the 2016 report.

2.3. The characteristics of women who died 2009–12

Manisha Nair, Anjali Shah, Nudrat Noor and Marian Knight

The mothers and babies

Thirty percent of the 321 women who died were still pregnant at the time of their deaths (Table 2.6); one third of these women were less than 20 weeks gestation. The women who died gave birth to a total of 235 infants; 173 (74%) were known to have survived, 49 were stillborn and 13 died in the neonatal period. The women who died left behind a further 408 surviving children, thus altogether a total of 581 motherless children remain. The majority of women who gave birth did so in hospital (82%); 13% of women gave birth in an accident and emergency department or an ambulance, and 3% of women who died gave birth at home (Table 2.7). The planned place of birth for these women is not known; this information was not collected systematically prior to MBRRACE-UK taking over the CEMD but has been collected for 2013 onwards. One hundred and fifty-two women were delivered by caesarean section; 30% of these by perimortem caesarean section. Of the 46 babies delivered by perimortem caesarean section, 23 (50%) were stillborn and 9 (20%) died in the neonatal period. Of the babies born by perimortem CS at less than 37 weeks gestation, 75% died. Only 5 babies born by perimortem CS at 32 weeks or less survived.

Table 2.6: Timing of maternal deaths in relation to pregnancy 2009–12

Time period of deaths in the pregnancy care pathway	Direct (n=106) Frequency (%)	Indirect (n=215) Frequency (%)	Total (n=321) Frequency (%)
Antenatal period ≤ 20 weeks	13 (12.3)	19 (8.8)	32 (10.0)
Antenatal period >20 weeks	16 (15.1)	47 (21.9)	63 (19.6)
Postnatal on day of delivery	25 (23.6)	33 (15.3)	58 (18.1)
Postnatal 1–41 days after delivery	51 (48.1)	115 (53.5)	166 (51.7)
Not known	1 (0.9)	1 (0.5)	2 (0.6)

Table 2.7: Place of delivery amongst women who died 2009–12

Place of delivery	Direct (n=89) Frequency (%)	Indirect (n=168) Frequency (%)	Total (n=257) Frequency (%)
Home	4 (4.5)	4 (2.4)	8 (3.1)
Hospital (except A&E)	77 (86.5)	133 (79.2)	210 (81.7)
Emergency Department or ambulance	7 (7.9)	26 (15.5)	33 (12.8)
Not known	1 (1.1)	5 (2.9)	6 (2.3)

Socio-demographic characteristics

Table 2.8 shows the socio-demographic characteristics of the women who died between 2009 and 2012.

As has been noted in previous CEMD reports, the rates of maternal mortality are different amongst women from different age, socioeconomic and ethnic minority groups (Table 2.9). Maternal mortality rates are higher amongst older women, women living in the most deprived areas and women from some ethnic minority groups. Note that from these data it is not clear to what extent these characteristics overlap and so these figures do not represent independent risks associated with these factors; however, a detailed comparison of women who died from specific severe morbidities with those who survived suggest these characteristics are independently associated with a higher odds of dying (Nair, Kurinczuk et al. 2014).

Although the minority of women who died (8%) were not UK citizens, over a third (34%) of women were born outside the UK. These women had arrived in the UK a median of 4 years (range 1 month to 21

years) before they died. More than 70% of them were from Asia (mainly India, Pakistan, Bangladesh and Sri Lanka) and Africa (mainly Nigeria, Somalia and Ghana). Thirteen percent of the women born abroad were from Eastern Europe (primarily from Poland) and the remainder were from other parts of Europe and North America. Table 2.10 shows the rates of death amongst women born in selected countries with the highest number of deaths. Women born outside the UK were significantly more likely to die than those born in the UK (RR 1.77, 95% CI 1.39-2.24). Women born in Nigeria had the highest maternal mortality rate (34.2 per 100,000 maternities, 95% CI 16.4-62.9). Three of the ten women from Nigeria who died, died from cardiac disease (30%). Most (70%) were long-term migrants (>5 years of residence). Nine of the ten women received antenatal care, but only one of them received the NICE recommended level of care (booking at less than 10 weeks and no antenatal appointments missed).

Medical and pregnancy-related characteristics

Almost three-quarters (74%) of the women who died were known to have pre-existing medical complications (Table 2.11). Seventeen percent were known to have pre-existing mental health problems. Fifteen percent of women who died were known to have asthma, similar to estimates of prevalence within the population as a whole (Simpson and Sheikh 2010). The other most prevalent disorders were inflammatory/atopic and haematological (including iron deficiency anaemia and sickle cell disease).

Over 22% of women were overweight and 27% obese (Table 2.11), consistent with estimates of obesity prevalence amongst women of reproductive age reported by the Health Survey for England (Health & Social Care Information Centre 2013), but higher than previous estimates of obesity prevalence amongst the pregnant population (Heslehurst, Rankin et al. 2010). This is similar to the figure noted in previous CEMD reports. Obesity has been shown to be independently associated with higher odds of dying from specific pregnancy complications (Nair, Kurinczuk et al. 2014).

Pregnancy-related characteristics are shown in Table 2.12.

Table 2.8: The socio-demographic characteristics of women who died 2009–12

Characteristics	Direct (n=106) Frequency (%)	Indirect (n=215) Frequency (%)	Total (n=321) Frequency (%)
Socio-demographic			
Age			
<20	4 (3.8)	11 (5.1)	15 (4.7)
20 – 24	9 (8.5)	32 (14.9)	41 (12.8)
25 – 29	22 (20.8)	51 (23.7)	73 (22.7)
30 – 34	33 (31.1)	54 (25.1)	87 (27.1)
35 – 39	28 (26.4)	49 (22.8)	77 (24.0)
≥ 40	10 (9.4)	18 (8.4)	28 (8.7)
Parity			
0	39 (36.8)	75 (34.9)	114 (35.5)
1 to 2	44 (41.5)	102 (47.4)	146 (45.5)
≥3	18 (17.0)	35 (16.3)	53 (16.5)
Missing	5 (4.7)	3 (1.4)	8 (2.5)
UK citizen			
Yes	88 (83.0)	186 (86.5)	274 (85.4)
No	10 (9.4)	16 (7.4)	26 (8.1)
Missing	8 (7.6)	13 (6.1)	21 (6.5)
Ethnicity			
White European	66 (62.3)	157 (73.0)	223 (69.5)
Indian	4 (3.8)	13 (6.1)	17 (5.3)
Pakistani	6 (5.7)	9 (4.2)	15 (4.7)
Bangladeshi	1 (0.9)	3 (1.4)	4 (1.2)
Other Asian	4 (3.8)	2 (0.9)	6 (1.9)
Black Caribbean	3 (2.8)	2 (0.9)	5 (1.5)
Black African	12 (11.3)	16 (7.4)	28 (8.7)
Others/ Mixed	7 (6.6)	8 (3.7)	15 (4.7)
Missing	3 (2.8)	5 (2.3)	8 (2.5)
Woman's region of birth			
United Kingdom	66 (62.3)	145 (67.4)	211 (65.7)
Eastern Europe	4 (3.8)	7 (3.3)	11 (3.4)
Western Europe	3 (2.8)	6 (2.8)	9 (2.8)
Asia	11 (10.4)	19 8.8	30 (9.4)
Africa	13 (12.3)	15 (7.0)	28 (8.7)
Australia and North America	1 (0.9)	2 (0.9)	3 (0.9)
Missing	8 (7.5)	21 (9.8)	29 (9.0)
Socioeconomic status (Index of Multiple Deprivation (IMD) of postcode of residence)			
First quintile (Least deprived)	16 (15.1)	22 (10.2)	38 (11.8)
Second quintile	13 (12.3)	29 (13.5)	42 (13.1)
Third quintile	18 (17.0)	30 (13.9)	48 (14.9)
Fourth quintile	30 (28.3)	50 (23.3)	80 (24.9)
Fifth quintile (Most deprived)	24 (22.6)	71 (33.0)	95 (29.6)
Missing	5 (4.7)	13 (6.1)	18 (5.6)
Socioeconomic status (Occupational classification)			
Employed (Either woman or partner)	71 (67.0)	130 (60.5)	201 (62.6)
Unemployed (Both)	11 (10.4)	35 (16.3)	46 (14.3)
Missing	24 (22.6)	50 (23.2)	74 (23.1)
Able to speak/understand English			
Yes	102 (96.2)	203 (94.4)	305 (95.0)
No	2 (1.9)	10 (4.7)	12 (3.7)
Missing	2 (1.9)	2 (0.9)	4 (1.3)
Living arrangements			
With partner	87 (82.1)	157 (73.0)	244 (76.0)
Living alone	3 (2.8)	12 (5.6)	15 (4.7)
With parents/extended family	5 (4.7)	23 (10.7)	28 (8.8)
In social care	0	2 (0.9)	2 (0.6)
Homeless/No fixed abode	0	3 (1.4)	3 (0.9)
Missing	11 (10.4)	18 (8.4)	29 (9.0)
Domestic abuse (prior to pregnancy/ during pregnancy)			
Yes	1 (0.9)	12 (5.6)	13 (4.1)
No	45 (42.5)	68 (31.6)	113 (35.2)
Missing	60 (56.6)	135 (62.8)	195 (60.7)
Known to social services			
Yes	5 (4.7)	37 (17.2)	42 (13.1)
No	95 (89.6)	174 (80.9)	269 (83.8)
Missing	6 (5.7)	4 (1.9)	10 (3.1)

Table 2.9: Maternal mortality rates amongst different population groups 2009–12

	Total maternities 2009–12	Total deaths	Rate per 100,000 maternities	95% CI	Relative risk (RR)	95% CI
Age						
<20	173118	15	8.7	4.9 to 14.3	1.26	0.65 to 2.33
20 – 24	596897	41	6.9	4.9 to 9.3	1 (Ref)	
25 – 29	881544	73	8.3	6.5 to 10.4	1.21	0. 81 to 1.81
30 – 34	902098	87	9.6	7.7 to 11.9	1.40	0.96 to 2.09
35 – 39	505656	77	15.2	12.0 to 19.0	2.22	1.50 to 3.32
≥ 40	123560	28	22.7	15.1 to 32.8	3.30	1.96 to 5.47
IMD Quintiles (England only)						
I (Least deprived/ highest 20%)	391174	32	8.2	5.6 to 11.6	1 (Ref)	-
II	417304	34	8.2	5.6 to 11.4	1.00	0.60 to 1.67
III	483853	43	8.9	6.4 to 12.0	1.09	0.67 to 1.77
IV	592720	66	11.0	8.5 to 14.0	1.34	0.87 to 2.12
V (Most deprived/ lowest 20%)	726457	88	12.1	9.7 to 14.9	1.48	1.00 to 2.29
Ethnicity (England only)						
White (inc. not known)	2084171	188	9.0	7.8 to 10.4	1 (Ref)	
Indian	82877	17	20.5	11.9 to 32.8	2.27	1.30 to 3.74
Pakistani	108341	15	13.9	7.8 to 22.8	1.53	0.84 to 2.60
Bangladeshi	36096	4	11.1	3.0 to 28.4	1.23	0.33 to 3.20
Other Asian	74220	6	8.1	2.9 to 17.6	0.90	0.32 to 1.99
Caribbean	27028	5	18.5	6.0 to 43.2	2.05	0.66 to 4.87
African	96580	26	26.9	17.6 to 39.4	2.98	1.90 to 4.51
Others/ mixed	137432	14	10.2	5.6 to 17.1	1.13	0.61 to 1.94

Table 2.10: Maternal mortality rates according to mother's country of birth (selected countries)

Woman's country of birth	Maternities 2009–2012	Total Deaths	Rate per 100,000 maternities	95% CI	Relative risk (RR)	95% CI
UK	2458671	211	8.6	7.5 to 9.8	1 (Ref)	-
Outside UK	724229	110	15.2	12.5 to 18.3	1.77	1.39 to 2.24
Specific countries						
Bangladesh	33299	3	9.0	1.9 to 26.3	1.05	0.21 to 3.11
India	55203	8	14.5	6.3 to 28.6	1.69	0.72 to 3.39
Pakistan	73523	8	10.9	4.7 to 21.4	1.27	0.54 to 2.54
Sri Lanka	13630	4	29.4	8.0 to 75.1	3.42	0.92 to 8.89
Ghana	13650	3	22.0	4.5 to 64.2	2.56	0.52 to 7.59
Nigeria	29235	10	34.2	16.4 to 62.9	3.99	1.88 to 7.48
Somalia	22512	4	17.8	4.8 to 45.5	2.07	0.56 to 5.38
Poland	78889	7	8.9	3.6 to 18.3	1.03	0.41 to 2.17

Table 2.11: Selected medical conditions and characteristics identified amongst women who died 2009–12

Medical condition/characteristic	Direct (n=106) Frequency (%)	Indirect (n=215) Frequency (%)	Total (n=321) Frequency (%)
Body mass index (BMI)			
<18	1 (0.9)	5 (2.3)	6 (1.9)
18 – 24	35 (33.0)	89 (41.4)	124 (38.6)
25 – 29	28 (26.4)	44 (20.5)	72 (22.4)
≥ 30	31 (29.3)	56 (26.0)	87 (27.1)
Missing	11 (10.4)	21 (9.8)	31 (10.0)
Mental health problems or psychiatric disorders			
Yes	12 (11.3)	42 (19.5)	54 (16.8)
No	87 (82.1)	165 (76.7)	252 (78.5)
Any pre-existing medical problem (excluding obesity)			
Yes	74 (69.8)	163 (75.8)	237 (73.8)
No	25 (23.6)	44 (20.5)	69 (21.5)
Missing	7 (6.6)	8 (3.7)	15 (4.7)
Selected medical conditions (not mutually exclusive)			
Asthma			
Yes	15 (14.2)	33 (15.3)	48 (15.0)
No	84 (79.2)	174 (81.0)	258 (80.4)
Autoimmune diseases			
Yes	3 (2.8)	7 (3.3)	10 (3.1)
No	96 (90.6)	200 (93.0)	296 (92.2)
Cardiac disease (congenital or acquired)			
Yes	2 (1.9)	17 (7.9)	19 (5.9)
No	97 (91.5)	190 (88.4)	287 (89.4)
Diabetes mellitus			
Yes	3 (2.8)	8 (3.7)	11 (3.4)
No	96 (90.6)	199 (92.6)	295 (91.9)
Epilepsy			
Yes	0 (0.0)	17 (7.8)	17 (5.3)
No	99 (93.4)	190 (88.4)	289 (90.0)
Endocrine disorders			
Yes	3 (2.8)	9 (4.2)	12 (3.7)
No	96 (90.6)	199 (92.1)	294 (91.6)
Essential hypertension			
Yes	7 (6.6)	10 (4.7)	17 (5.3)
No	92 (86.8)	197 (91.6)	289 (90.0)
Haematological disorders			
Yes	13 (12.3)	15 (7.0)	28 (8.7)
No	86 (81.1)	192 (89.3)	279 (86.6)
Blood borne viruses			
Yes	2 (1.9)	11 (5.1)	13 (4.0)
No	97 (91.5)	196 (91.2)	293 (91.3)
Inflammatory disorders and allergic /atopic conditions (excluding asthma)			
Yes	10 (9.4)	29 (13.5)	39 (12.1)
No	89 (84.0)	178 (82.8)	267 (83.2)
Other infection			
Yes	4 (3.8)	16 (7.4)	20 (6.2)
No	95 (89.6)	191 (88.8)	286 (89.1)
Renal problems			
Yes	2 (1.9)	9 (4.2)	11 (3.4)
No	97 (91.5)	198 (92.1)	295 (91.9)
Previous thrombotic event			
Yes	3 (2.8)	4 (1.9)	7 (2.2)
No	96 (90.6)	203 (94.4)	299 (93.1)
Neurological disorders			
Yes	3 (2.8)	10 (4.7)	13 (4.0)
No	96 (90.6)	197 (91.6)	293 (91.3)
Musculoskeletal disorders			
Yes	6 (5.7)	15 (7.0)	21 (6.5)
No	93 (87.7)	192 (89.3)	285 (88.8)

Note: The number of women with missing information for all pre-existing medical conditions is 15 (4.7%); 7 (6.6%) for direct deaths and 8 (3.7%) for indirect deaths.

Table 2.12: Pregnancy-related characteristics of the women who died 2009–12

Characteristics	Direct (n=106) Frequency (%)	Indirect (n=215) Frequency (%)	Total (n=321) Frequency (%)
Pregnancy known to be as a result of assisted reproductive technologies			
Yes	4 (3.8)	6 (2.8)	10 (3.1)
No	97 (91.5)	198 (92.1)	295 (91.9)
Missing	5 (4.7)	11 (5.1)	16 (5.0)
Multiple pregnancy			
Yes	3 (2.8)	6 (2.8)	9 (2.8)
No	100 (94.3)	204 (94.9)	304 (94.7)
Missing	3 (2.8)	5 (2.3)	8 (2.5)
Previous caesarean section			
Yes	22 (20.7)	39 (18.1)	61 (19.0)
No	78 (73.6)	172 (80.0)	250 (77.0)
Missing	6 (5.7)	4 (1.9)	10 (3.1)
Number of previous caesarean sections (among women who had a previous caesarean section)			
1	16 (72.7)	33 (84.6)	49 (80.3)
≥*2*	6 (27.3)	6 (15.4)	12 (19.7)

Other characteristics of women who died

Almost a quarter of women who died smoked during pregnancy (Table 2.13); this was particularly prevalent amongst women who died from indirect causes, where the prevalence was close to one third. Eight percent of women who died were known substance users, again, these women were more frequently represented amongst the women who died from indirect causes.

Access to antenatal care remains an issue amongst women who died, although it is not clear whether this is due to lack of availability of appropriate services or other factors precluding their use. Almost one in ten women did not receive any antenatal care, however, five of these women died in early pregnancy (≤10 weeks). Only 29% of women who had antenatal care received the recommended level of care according to NICE antenatal care guidelines (booking at 10 weeks or less and no routine antenatal visits missed) (National Institute for Health and Care Excellence 2008a). Almost two thirds received a minimum level of antenatal care (booking at less than 13 weeks and three or fewer antenatal visits missed); 25% did not receive even this minimum level of care.

Table 2.13: Other characteristics of women who died, 2009–12

Characteristics	Direct (n=106) Frequency (%)	Indirect (n=215) Frequency (%)	Total (n=321) Frequency (%)
Smoking			
Smoker	15 (14.2)	66 (30.7)	81 (25.2)
Non-smoker	72 (67.9)	122 (56.7)	194 (60.4)
Missing	19 (17.9)	27 (12.6)	46 (14.3)
Substance user			
Yes	3 (2.8)	21 (9.8)	24 (7.5)
No	99 (93.4)	193 (89.8)	292 (91.0)
Missing	4 (3.8)	1 (0.4)	5 (1.5)
Received any antenatal care*			
Yes	90 (84.9)	194 (90.2)	284 (88.5)
No	14 (13.2)	21 (9.8)	35 (10.9)
Missing	2 (1.9)	0	2 (0.6)
Gestational age at booking (among women who received any antenatal care)			
≤10	29 (32.2)	78 (40.2)	107 (37.7)
11 – 12	35 (38.9)	52 (26.8)	87 (30.6)
>12	21 (23.3)	43 (22.2)	64 (22.5)
Missing	5 (5.6)	21 (10.8)	26 (9.2)
Received NICE recommended antenatal care† (among women who received any antenatal care)			
Yes	24 (26.6)	58 (29.9)	82 (28.9)
No	59 (65.6)	113 (58.2)	172 (60.6)
Missing	7 (7.8)	23 (11.9)	30 (10.5)
Received a minimum level of antenatal care† (among women who received any antenatal care)			
Yes	59 (65.6)	117 (60.3)	176 (61.9)
No	22 (24.4)	48 (24.7)	70 (24.7)
Missing	9 (10.0)	29 (15.0)	38 (13.4)

*includes 5 women who died in early pregnancy

†NICE recommended antenatal care: booked at 10 weeks or less and no antenatal visits missed. Minimum level of care: booked at less than 13 weeks and 3 or fewer antenatal visits missed.

Quality of care received

Note that the information in this section is only for the 203 women who died and are included in the confidential enquiry chapters of the report, and includes women from the Republic of Ireland and some women who died more than 42 days after the end of pregnancy. Table 2.14 shows the classification of care as agreed by the assessors. Twenty-nine percent of women were assessed to have received good care which could not have been improved.

We are unable to comment in a robust way on the lessons learned locally by the clinicians in the hospitals managing these women, as reports from local clinicians were received for only a very small proportion of the deaths undergoing confidential enquiry (Table 2.15). Whilst the length of time that had elapsed since some of these deaths occurred might account for some difficulty in completion of the local report on the woman's death, it is concerning that evidence of local reflection was missing for such a high proportion of deaths.

Table 2.14 Classification of care received for women who died and are included in the confidential enquiry chapters (n=203)

	Number of women (%) (n=203)
Classification of care received	
Good care	58 (29)
Improvements to care which would have made no difference to outcome	39 (19)
Improvements to care which may have made a difference to outcome	106 (52)

Table 2.15. Local clinicians' reports received

Specialist group	Number of reports returned N (%) (n=203)
Obstetrics	33 (16)
Anaesthetics/critical care	27 (13)
Midwifery	33 (16)
General practice	36 (18)
Medical specialties	15 (*)
Emergency medicine	8 (*)

*Not required for all deaths, therefore percentage not calculated

2.4. Women who survived: the epidemiology of septic shock in pregnancy

Manisha Nair, Colleen Acosta and Marian Knight

A national case-control study undertaken through the UK Obstetric Surveillance System (UKOSS) showed that for every woman who dies from maternal sepsis, there are fourteen women who survive life-threatening septic shock (Acosta, Kurinczuk et al. 2014). The UKOSS study, conducted between June 2011 and May 2012, reported a total of 365 confirmed cases of severe sepsis giving an estimated incidence of 47 cases per 100,000 maternities (95% CI 42 to 52) in the UK. Of these 365 women, 71 developed septic shock representing an incidence of 9.1 per 100,000 maternities (95% CI 7.1 to 11.5). Infection with Group A Streptococcus was the single most important factor associated with increased odds of progression from severe sepsis to septic shock after accounting for socio-demographic characteristics and mode of delivery (adjusted odds ratio 4.84; 95% CI 2.17 to 10.78) (Acosta, Kurinczuk et al. 2014). The characteristics of the 69 women with septic shock associated with pregnancy who survived are shown in Table 2.16. As noted in section 1.4, a stratified random sample of 34 of these women was selected for inclusion in the Confidential Enquiry into Maternal Morbidity, and the results of this Confidential Enquiry are included in Chapter 3.

Table 2.16: The characteristics of women who survived septic shock in association with pregnancy in the UK, June 2011-May 2012 (Acosta, Kurinczuk et al. 2014)

Characteristics	Total (n=69) Frequency (%)
Socio-demographic	
Age	
<25	16 (23)
25 – 34	33 (48)
≥ 35	20 (29)
Parity	
0	25 (36)
≥1	43 (63)
Missing	1 (1)
Ethnicity	
White European	44 (64)
Other	25 (36)
Missing	0 (0)
Socioeconomic status (Occupational classification)	
Employed (Either woman or partner)	44 (64)
Unemployed (Both)	12 (17)
Missing	23 (33)
Smoking	
Smoker	21 (30)
Non-smoker	46 (67)
Missing	2 (3)
Body mass index (BMI)	
<18	1 (1)
18 – 24	38 (55)
25 – 29	18 (26)
≥ 30	9 (13)
Missing	3 (4)
Medical and pregnancy characteristics	
Any pre-existing medical problem (excluding obesity)	
Yes	18 (26)
No	51 (74)
Missing	0 (0)
Multiple pregnancy	
Yes	5 (7)
No	64 (93)
Missing	
Previous caesarean section	
Yes	10 (14)
No	59 (86)
Missing	

3. Think Sepsis

David Churchill, Alison Rodger, John Clift and Derek Tuffnell on behalf of the MBRRACE-UK sepsis chapter writing group

Chapter writing group members: David Churchill, John Clift, Lisa Elliott, Sara Kenyon, Marian Knight, Jenny Kurinczuk, Sebastian Lucas, James Neilson, Catherine Nelson-Piercy, Sue Orchard, Alison Rodger, Judy Shakespeare, Derek Tuffnell, Steve Yentis.

3.1. Key messages

'Think Sepsis' at an early stage when presented with an unwell pregnant or recently pregnant woman, take all appropriate observations and act on them.

The key actions for diagnosis and management of sepsis are:

- Timely recognition
- Fast administration of intravenous antibiotics
- Quick involvement of experts - senior review is essential

Repeated presentation to the general practitioner, or community midwife or alternatively repeated self-referral to the obstetric triage or day assessment unit should be considered a 'red flag' and warrant a thorough assessment of the woman to investigate for signs of sepsis.

Early advice from an infectious diseases physician or microbiologist should be sought; this is essential in instances where the woman fails to respond to the first choice antibiotic.

There should be adequate provision of appropriate critical care support for the management of a pregnant woman who becomes unwell. Plans should be in place for provision of critical care on delivery units if this is the most appropriate setting for a woman with sepsis to receive care.

To avoid preventable deaths, the benefits of influenza vaccination to pregnant women should be promoted and pregnant women at any stage of pregnancy should be offered vaccination against seasonal and pandemic flu with inactivated vaccine.

3.2. Background

This report sees an encouraging decrease in the UK mortality rate from genital tract sepsis, which had risen in 2006–08 to the highest rate in the previous 20 years. Nevertheless, sepsis in its widest sense, including deaths from all infectious causes, remains a leading contributor to maternal mortality and particularly morbidity in both high income countries (including the UK and Ireland) and low income countries. Alongside this is the background of general concern over "superbugs" and antibiotic resistance, periodic influenza pandemics and the decade long "Surviving Sepsis Campaign". Sepsis has been highlighted as a concern in several recent reports, including the Parliamentary and Health Service Ombudsman (Parliamentary and Health Service Ombudsman 2013) and in a Patient Safety Alert from NHS England (NHS England 2014a) Therefore sepsis should remain at the forefront of every clinician's mind.

Pregnant women are uniquely at risk from sepsis. Their immune system is modulated to accept foreign proteins from the feto-placental unit and usually they are young and fit, and able to withstand the physiological insults of widespread inflammation for long periods of time. Pregnant or postpartum women can appear well until the point of collapse, which can occur with little warning. However, more often than not a woman's physiological vital signs, the pulse, blood pressure, temperature and respiratory rate, will give an indication of the early stages of sepsis.

Included in this chapter are maternal deaths occurring more than 42 days after the end of pregnancy, where assessors considered there were important lessons to be learned, as well as deaths from the Republic of Ireland. The number of women described does not therefore match exactly with the number of women reported in chapter 2, which includes surveillance data only on women in the UK who died during pregnancy or within 42 days of the end of their

pregnancy. To further enhance the lessons learned to improve future care, the mortality reviews have also been supplemented by reviews of the care of women who survived severe sepsis.

Overall, and reassuringly, the standard of care was better in the women who survived than those who died. However, the same themes emerged, with respect to the clinical and organisational improvements that can be made when caring for these women, as were found in the mortality reviews. The messages for care identified from both women who died from sepsis and women with septic shock have therefore been integrated throughout the chapter. This is reflected in the use of vignettes from both women who survived (coloured purple) and women who died (coloured blue) to illustrate the lessons learned for future care. Hence the recommendations found in this report, if implemented, will have a positive benefit for all women in pregnancy and postpartum who experience sepsis.

Definitions of Sepsis

Sepsis has been defined as the presence of an infection along with the manifestations of a systemic inflammatory response (SIRS). The features of SIRS were initially defined as a combination of two or more of the following; hyper or hypothermia, tachycardia, tachypnoea and a raised white cell count. These criteria were initially drawn up for the non-pregnant population, but modifications have been suggested to account for the altered physiology of pregnancy (Waterstone, Bewley et al. 2001). A diagnosis of sepsis is made when there is a systemic inflammatory response in the presence of an infection or when an infection is strongly suspected. However in a pregnant or recently pregnant woman, a single abnormal finding can be significant and warrants a thorough clinical assessment looking for signs of an infection.

'Severe sepsis' is sepsis associated with one of the following; organ dysfunction, for example acute renal failure, tissue hypo-perfusion causing lactic acidosis or hypotension.

'Septic shock' is a vasodilatory or distributive form of shock and is defined as persisting hypotension despite adequate fluid resuscitation in the presence of sepsis.

3.3. Summary of the key findings 2009–12

Eighty-three women died from sepsis between 2009 and 2012, defined in its widest sense as a death from a primarily infective cause. Twenty women died as a result of genital tract sepsis and are hence classified as direct maternal deaths, 63 died from other infections and are hence classified as indirect deaths. This latter group comprised 36 women who died from influenza, and 27 from other causes. Twelve women included in this chapter died more than 42 days beyond the end of their pregnancy (late deaths), but as there were messages to be learned for future care in relation to pregnancy, they are reviewed here.

As noted above and in Chapter 2, this represents a significant decrease in the mortality rate from genital tract sepsis in the UK since 2006–08 when there were 1.13 maternal deaths per 100,000 maternities; the rate of maternal mortality from genital tract sepsis in 2010–12 was 0.50 per 100,000 maternities. This is a more than halving of the death rate from genital tract sepsis in the UK. However, as these numbers show, genital tract sepsis deaths represent less than a quarter of all the maternal deaths from infections; the overall rate of maternal mortality from infectious causes in the UK and Ireland (excluding late deaths) in 2009–12 was 2.04 per 100,000 maternities (95% CI 1.60–2.58).

The women who died

Genital tract sepsis

A total of 20 women died from genital tract sepsis. In general, the organism Group A Streptococcus (GAS) was associated with genital tract infections in early pregnancy and peripartum, whereas coliforms were associated with second trimester ascending infections. The women with genital tract sepsis included seven women in the second trimester; five women died following preterm pre-labour rupture of the membranes in the second trimester, including one in which an emergency cervical suture was placed, and a further two following an emergency cervical suture in the second trimester. Culture results were available for six of these seven women; in all six women the organisms cultured were coliforms. Two women died from Group A Streptococcus following first trimester miscarriage. Two women died antenatally due to Group A Streptococcus. There were nine women who died following term birth, eight due to Group A streptococcus. Six of these term Group A Streptococcus deaths were following vaginal births, one of which was a planned home birth, and two followed caesarean section. The other death after term birth followed a caesarean delivery. All women who died after caesarean section were given prophylactic antibiotics. This represents a total of 12 women who died from Group A Streptococcus, 6 from infection with coliforms and 2 unknown. Additionally three women died from Group A Streptococcus with no clear genital tract focus (see below).

Sepsis due to other causes

Influenza

This report covers the period in 2009–12 when there was an H1N1 influenza pandemic. Thirty-six women died from influenza, accounting for 43% of all deaths in this chapter. Twenty-seven had confirmed H1N1, five had probable (though unconfirmed) H1N1, one had influenza A (not specified whether H1N1 variant or not) and three had influenza B. This contrasts with 2006–08, when one influenza-related death was reported, and 2003–05 when there were none.

Pneumococcal disease

Nine women died from pneumococcal disease. Five women died of pneumococcal meningitis and one from a pneumococcal brain abscess. One woman died from pneumococcal pneumonia and invasive pneumococcal infection and another two of pneumonia of unclear cause. None of these deaths were influenza associated.

Other causes

Of the remaining 18 deaths, three women had fulminating Group A Streptococcus infections in the third trimester, with no obvious evidence of a genital tract focus of infection. Three women died from overwhelming sepsis (two of uncertain origin), and two from appendicitis. There were two deaths from streptococcal (non-pneumococcal) meningitis, thus a total of seven deaths with evidence of meningitis. The other sepsis deaths were subsequent to a urinary tract infection, a complex sinus infection, a quinsy, fulminant herpes simplex (2 deaths), a breast abscess, miliary tuberculosis and a pelvic abscess.

The pathological features of sepsis deaths are discussed in appendix A1.

Women's characteristics

For the total group of women who died from sepsis the median age at time of death was 30 years with a range of 17 to 45. Data from the 2012 census shows that the average age of mothers in the general population was 29.8 years and that the total fertility rate rose more in the over 35 years age groups (Office for National Statistics 2012). In the group of women who died from genital tract sepsis over one third (35%, n=7) were over the age of 35, compared to 22% and 26% in the influenza and other groups.

Thirty-three percent of women (n=27) were primiparous and 33% (n=27) were from minority ethnic groups. The proportion of women who were born outside of the UK was 24%, which again reflects the general population; in 2012, 26% of live births were to women born outside the UK (Office for National Statistics 2012). There were a number of women from ethnic minority groups (40%, n=8) who died from genital tract sepsis.

The majority of women (82%) died in the postnatal period, which is perhaps to be expected, as delivery will frequently form part of any management plan for a critically ill pregnant woman.

Over a fifth (24%, n=20) of the women who died smoked, and the majority of these women (65%, n=13) died from a respiratory cause. Twenty-two percent of women (n=18) were obese.

The women who survived – septic shock in association with pregnancy

Confidential case reviews of the 34 women who survived septic shock are included in this chapter. Twenty four of the women had genital tract sepsis, including six with Group A Streptococcus infection. Of note, three women had septic shock in association with genital tract sepsis following second trimester membrane rupture and one following a second trimester cervical rescue suture. Ten women had septic shock from other causes, including two women with Group A Streptococcal infection but no evidence of genital tract infection.

3.4. Messages for future care

Delay in diagnosis

The symptoms of sepsis may be non-specific and can occur in a range of conditions some of which are minor and self-limiting. Many pregnant women present either to their GP or community midwife or to the local hospital's triage or day unit with vague symptoms seeking reassurance and help, therefore doctors and midwives will frequently encounter women complaining of malaise, non-specific pain, loose stools or diarrhoea and occasional vomiting, without there being any serious organic disease.

Nevertheless a small number of women will have sepsis and clinicians must remain alert to this possibility. The quality of initial assessment should not be dependent on the hospital department through which a woman first accesses services. For example: when admitted to an obstetric ward, women should have a full medical history and examination undertaken; a pregnant or postpartum woman who presents to A&E should be assessed in a standard way before referral to the obstetric team. A thorough clinical history should be taken and any possible source of infection should be explored through a systems review and examination. This includes looking for signs of otitis media or sinusitis; both of which can lead to invasive CNS infections including meningitis, and where pelvic sepsis is

suspected a rectal and vaginal examination looking for pain or purulent discharge. Pain, particularly disproportionate pain such as abdominal pain requiring opioid analgesia after vaginal delivery, can be a symptom of sepsis. It is also important to take a history of symptoms in close contacts.

The presence of upper respiratory tract symptoms should alert the clinician to the possibility of Group A Streptococcus or influenza as a possible diagnosis. If a woman has a sore throat, the Centor criteria are useful to predict bacterial infection (Office for National Statistics 2013). The presence of three or four of the following signs suggests that a woman may have a bacterial infection and would benefit from antibiotics: tonsillar exudate, tender anterior cervical lymphadenopathy or lymphadenitis, fever, an absence of cough.

A woman went to her GP in the first trimester with a sore throat. She had lymphadenopathy but no other assessment was made. She presented to the gynaecology department 24 hours later with diarrhoea and vomiting and feeling unwell. She was hypotensive and tachycardic. She was reviewed by a junior doctor almost three hours after admission who did not recognise the seriousness of her condition. The obstetric registrar reviewed her 6 hours following admission and prescribed antibiotics, which were not given for over an hour. When the seriousness of her condition was recognised she was transferred to another hospital for intensive care. Despite emergency surgery she died from overwhelming Group A Streptococcal sepsis.

The reviews identified several women who were seen by healthcare professionals in the community on several occasions with symptoms and physical signs of infection. Unfortunately, either their infection was not diagnosed until a late stage or a deteriorating clinical situation went unrecognised. When a woman is being managed in the community it is important to arrange a follow up, or to use “safety-netting”: giving the woman clear guidance to return in the absence of improvement, or if she has symptoms which might suggest SIRS. Although not specific for pregnancy, the UK Sepsis Trust Primary Care Toolkit provides criteria for screening patients with suspected sepsis for SIRS and “Red Flag Sepsis” (UK Sepsis Trust 2014) (Box 3.1). Any pregnant or postpartum woman whose condition is worsening or who has “Red Flag Sepsis” should be transferred immediately for hospital assessment.

A woman who was seven days post spontaneous vaginal delivery became unwell at home with a fever. She was advised to attend the maternity unit immediately. On admission she was noted to be tachycardic, tachypnoeic and febrile. She was prioritised for urgent medical review. A diagnosis of acute sepsis from retained products was made and fluid resuscitation started immediately. Intravenous antibiotics were started within one hour of the diagnosis and she was transferred to the high dependency unit. The retained products of conception were removed promptly and she made a full recovery. Blood culture subsequently grew Klebsiella. Early recognition, clear advice and prompt treatment led to a good outcome without any further complications.

In one woman the diagnosis of sepsis was never considered although she was acutely shocked. Haemorrhage is the most common cause of shock in pregnancy and naturally considered first by obstetricians. But when haemorrhage has been ruled out or the treatment for haemorrhage is failing to improve the woman’s condition, sepsis must be seriously considered as a potential cause. As noted in the anaesthesia chapter, clinicians must be aware of the risk of ‘fixation error’ and always consider other possible diagnoses in the event of failure to respond to treatment of the initial presumed cause of illness.

Two hours after delivery a woman became unwell on the postnatal ward feeling faint. Her oxygen saturation was 65%. She was reviewed by junior staff and found to be shocked, with moderate PV bleeding. Her temperature was never measured. A diagnosis of haemorrhage was made and she was treated with fluids. She failed to improve and was taken to theatre where she had a cardiac arrest. A laparotomy and hysterectomy were carried out but resuscitation failed. The postmortem found an extensive blistering skin rash, swollen labia and disseminated intravascular coagulation all as a result of overwhelming Group A Streptococcal sepsis.

"Think Sepsis" at an early stage when presented with an unwell pregnant or recently pregnant woman, take the appropriate observations and act on them.

The key actions for diagnosis and management of sepsis are:

- **Timely recognition**
- **Fast administration of intravenous antibiotics**
- **Quick involvement of experts - senior review is essential**

NHS England Patient Safety Alert NHS/PSA/R/2014/015 (NHS England 2014a)

Box 3.1: SIRS screening and evaluation for Red Flag Sepsis (UK Sepsis Trust Primary Care Toolkit) (UK Sepsis Trust 2014)

a. Screening for SIRS

SIRS is confirmed if ANY TWO of the following are present:

Immediate

- New onset of confusion or altered mental state
- Temperature >38.3°C or <36°C
- Heart Rate >90 beats per minute*
- Respiratory Rate (counted over 60 seconds) >20 breaths per minute

Point of Care Test (commonly available)

- Blood Glucose >7.7mmol/L in the absence of known diabetes

Point of Care Test (not yet widely available)

- White cell count >12 or <4 x10^9/L

b. Evaluation for Red Flag Sepsis

Act immediately if ANY ONE of the following are present:

- Systolic BP <90mmHg (or >40mmHg fall from baseline)
- Heart rate >130 per minute
- Oxygen saturations <91%
- Respiratory rate >25 per minute
- Responds only to voice or pain/unresponsive

Point of Care test (not yet widely available)

- Lactate >2.0mmol/L

*Note the guidelines are not specific for pregnancy and these observations should be interpreted in the context of the normal physiology for the pregnant woman. RCOG guidance suggests using a threshold of 100 beats per minute in pregnancy (RCOG Green-top Guideline 64a) (Royal College of Obstetricians and Gynaecologists 2012a).

Incomplete Assessment

Throughout this report the absence or incomplete recording of observations was a recurring theme. It was in the postnatal period where the absence of vital sign readings was most obvious. It cannot be over-stressed that all four of the physiological vital signs are as important as each other and an abnormality in any one should be taken seriously.

A woman presented to her GP with a flu-like illness in the third trimester. She was prescribed an antiviral which she did not take. Three days later she was referred to the hospital with a productive cough, rigors and vomiting. She was tachycardic but her respiratory rate was not taken. She was prescribed amoxicillin and told to report to her GP the following week if she was no better. Two days later she re-presented with respiratory failure. Despite treatment and delivery her respiratory condition worsened and she died from multi-organ failure three weeks later. Swabs taken at the second admission found H1N1 influenza.

The reviewers frequently found that the respiratory rate was not measured. This is as important a physiological measure as the pulse rate, blood pressure and temperature. Sepsis causes an increased respiratory rate to meet an increased oxygen demand of the tissues, as well as in possible compensation for metabolic acidosis or due to the presence of acute respiratory distress syndrome (ARDS). The threshold for the upper limit of normal in pregnancy is 20 breaths per minute.

A woman was admitted in preterm labour and delivered rapidly. Three hours after delivery she was noted to be tachycardic and had a low blood pressure. These observations were not plotted on a MEOWS or similar chart. She was not reviewed by an obstetrician and was discharged for low risk postnatal care. Her community midwife saw her 24 hours later. No observations were taken. On day 4 she was admitted to the A&E as an emergency but found to be dead on arrival. A post mortem revealed Group A Streptococcal sepsis. Further enquiries revealed that investigations taken in the hospital during her labour were abnormal. Blood results indicated sepsis and a high vaginal swab cultured Group A Streptococcus.

Postnatally the potential for infection may be higher, especially for genital tract sepsis. The raw placental bed presents a ready site for ascending and blood borne infections. This is an issue of importance and midwives must remain vigilant. When there is an indication for the vital signs to be recorded a full set must be taken (National Institute for Health and Care Excellence 2006). Several women did not have a complete set of observations postnatally, and this was considered a lost opportunity for earlier diagnosis.

A woman was visited by her community midwife postnatally, following a spontaneous vaginal delivery. On day 5 she was noted to have a temperature of over 41°C. No other observations were taken. The community midwife discussed the woman with her GP who considered that it was likely to be due to a viral illness and advised that the midwife visit the following day. The following day the woman was apyrexial, but she was tachycardic and had a low blood pressure. She had been taking paracetamol for her fever. The next day the woman was “very sleepy”, she remained apyrexial, but was more tachycardic with a blood pressure of 80/40mmHg. The midwife requested a home visit but the woman was advised to visit the surgery. She was found to be severely septic and was admitted to intensive care with septic shock. She was found to have retained products and Group A Streptococcus infection. Her uterus was evacuated and she eventually recovered.

In the postnatal period health professionals must perform and record a full set of physiological vital signs, pulse, blood pressure, temperature and respiratory rate, in any woman with symptoms or signs of ill health.

NICE Postnatal Care Guideline CG37 & RCOG green-top guideline 64a

(National Institute for Health and Care Excellence 2006, Royal College of Obstetricians and Gynaecologists 2012a)

Immediate management of a woman with sepsis

Once the diagnosis of sepsis is suspected or recognised, if the woman is not already in hospital, she should be admitted as an emergency via a blue light ambulance. Once in hospital, a sepsis care bundle must be utilised immediately. Examples include the Surviving Sepsis Campaign Resuscitation Care

Bundle, the Institute for Healthcare Improvement severe sepsis bundles (Institute for Healthcare Improvement 2013) and the UK Sepsis Trust 'Sepsis Six Care Bundle' (The UK Sepsis Trust 2013); other local versions exist. The components of the 'Sepsis Six' bundle are shown in Box 3.2.

Box 3.2: The "Sepsis Six" care bundle to be undertaken within one hour of sepsis diagnosis (The UK Sepsis Trust 2013)

- Take an arterial blood gas and give high flow oxygen if required
- Take blood cultures
- Commence intravenous antibiotics
- Start intravenous fluid resuscitation
- Take blood for haemoglobin and lactate levels
- Measure the urine output hourly

Several of the assessments identified that the elements of these bundles were incompletely applied. Prospective observational data have shown that use of the sepsis six bundle is associated with a reduction in mortality (Daniels, Nutbeam et al. 2011); other basic care bundles have been shown to improve survival (Miller, Dong et al. 2013). Although the reviewers found that in general the bundles were poorly applied, the specific components that were most frequently neglected were: administration of timely and appropriate antibiotics (within 1 hour of suspected sepsis), measurement of serum lactate and adequate fluid resuscitation.

a) Administration of timely antibiotics

Antibiotic administration is a key part of the immediate management. Time to administration of antibiotics is a strong predictor of mortality (Gaieski, Mikkelsen et al. 2010). From the recognition of signs of sepsis, each hour's delay in administering antibiotic therapy increases the chance of mortality by 8% (Kumar, Roberts et al. 2006). Thus the concept of the 'Golden Hour' has been developed to ensure that antibiotics are administered within the first hour from diagnosis or suspected diagnosis (Dellinger, Levy et al. 2008, Dellinger, Levy et al. 2013).

In several instances there was a considerable delay in administering antibiotics to women who were clearly septic. Often the reasons were unclear but many were due a lack of understanding of the seriousness of the woman's condition. The importance of early antibiotic administration must be emphasised to all healthcare professionals. It is the responsibility of the prescriber to ensure that cultures are taken and antibiotics are given, even if this means prescribers administering the antibiotics themselves.

b) Choice of antibiotic

The choice of antibiotic is as important as timely administration. The most commonly identified bacterial organisms in women dying of sepsis were Group A Streptococcus, Escherichia coli, and Streptococcus pneumoniae. In most women with sepsis, antibiotics will be started prior to culture of the infecting organism. Antibiotic choice should therefore be based on the suspected site of infection with the antibiotics chosen to have an appropriate spectrum of activity based on local prescribing guidelines. If the source of sepsis is unknown then antibiotics covering a broad range of possible organisms should be used and later the spectrum can be narrowed or targeted based on the culture results, radiological imaging or the development of specific signs or symptoms. It should be remembered also that resistance patterns differ by hospital and local antibiotic guidance should be consulted. For women with penicillin allergy the exact nature of the allergy should be confirmed and antibiotic choice discussed with either an infectious diseases physician or microbiologist. The responsibility for checking doses, interactions and contraindications for a given woman rests with the prescriber.

Women who have arrived in the UK from other parts of the world may be more likely to be colonised with antibiotic resistant gram negative organisms (van der Bij and Pitout 2012). This is especially likely if they have been in contact with healthcare facilities in other countries. Specialist advice should be sought from infectious disease physicians or clinical microbiologists if the woman is thought to be at risk of antibiotic resistant organisms and empirical therapy is being considered. An Intensive Care Society core standard is that there should be a daily microbiology ward round on intensive care units, and this is particularly important for pregnant or postpartum women. Note that this standard applies equally to pregnant or postpartum women who are receiving critical care on the labour ward or other obstetric setting.

Early advice from an infectious diseases physician or microbiologist should be sought; this is essential in instances where the woman fails to respond to the first choice antibiotic. The choice of antibiotic may need to be adjusted to widen the spectrum of organisms being covered and/or in light of the suspected source of infection.

c) Measurement of serum lactate

Lactic acid is an important marker of tissue hypoxia and a strong indicator of the potential for multi-organ failure and mortality (Trzeciak, Chansky et al. 2006, Mikkelsen, Miltiades et al. 2009). Serum lactate was measured inconsistently in the records reviewed. In normal women lactate levels can be transiently raised post-delivery, but if a raised lactate is discovered in conjunction with the signs of infection it must not be dismissed. A serum lactate measurement of >2mmol/L indicates severe sepsis and >4mmol/L indicates septic shock.

d) Fluid resuscitation

Fluid resuscitation was often late and inadequate. The effects of fluid boluses on blood pressure were seldom monitored; serial measurements of vital signs along with hourly assessment of urine output must be made. A woman who fails to show a sustained response to fluid resuscitation may need vasopressor support to correct hypotension and restore organ perfusion.

In one woman repeated boluses of crystalloid were given without proper monitoring. The systemic inflammation of sepsis can cause lung damage and ARDS that will be worsened by iatrogenic fluid overload. Therefore if there is a failure to achieve a sustained response to a fluid challenge, additional monitoring will be necessary before administering more fluid.

Where sepsis is suspected a sepsis care bundle must be applied in a structured and systematic way with urgency. Each maternity unit must have a protocol for which bundle to use and audit its implementation.

RCOG Green-top guidelines 64a & 64b

(Royal College of Obstetricians and Gynaecologists 2012a, Royal College of Obstetricians and Gynaecologists 2012b)

Two women presented in early pregnancy with sepsis following miscarriage. In both women the sepsis was diagnosed early and the sepsis resuscitation bundle applied with speed. Both women had short periods of level 2/3 care and made complete recoveries.

Failure to assess severity and detect deterioration

In several of the reviews it was apparent that once treatment with antibiotics had been initiated, those looking after the women relaxed, expecting a good response, and on-going monitoring was inadequate.

Once immediate resuscitation has been implemented using a sepsis care bundle, each woman will need a rational management plan to be drawn up. An accurate assessment must be made of the woman's clinical condition by a consultant. The plan should be made to include the frequency of physiological measurements, further investigations to identify the source of infection, baseline swabs and blood tests, and appropriate further referral to consultants from other specialties. These results then need reviewing to ensure the plan is appropriate for the woman's clinical situation.

The required baseline tests include: a C reactive protein, a full haematological profile including the differential white cell count and clotting studies, biochemistry measurements, blood cultures, microbiological swabs or samples from any candidate site for infection including a throat swab and a urine specimen. A nasopharyngeal aspirate should also be taken for respiratory viruses in someone presenting with upper or lower respiratory tract infection symptoms. Biochemistry measurements (urea and electrolytes and liver function tests) are important not only as a baseline but also to identify any signs of renal or hepatic dysfunction.

Sepsis is a progressive condition. Results within the "normal range" on one occasion can rapidly become abnormal. Trends in the values of the indicators are often more important than the thresholds themselves and will help to decide how rapidly the disease is progressing or alternatively, the woman's response to treatment. If the response fails to materialise in a timely way, or an initial response is not sustained a senior obstetrician should undertake a further review of the woman. It may be that the woman is further along the sepsis sequence than originally anticipated. More intensive support such as inotropes or ventilation may be necessary.

Clinicians should not only document an action plan in the case record but initiate the actions required such as the administration of antibiotics and the commencement of fluids.

A consistent theme in many of the women who died, was that the oversight of their care was left to junior doctors for far too long and that senior consultant involvement from all involved specialties, including obstetrics, anaesthetics, general medicine, infectious diseases, and intensive care was sought or delivered far too late.

A woman was admitted in the second trimester with vomiting and preterm pre-labour rupture of the membranes. She was found to be septic with chorioamnionitis that had caused an intrauterine death of the fetus. The sepsis resuscitation bundle was promptly applied and following blood cultures and a discussion with the consultant microbiologist, antibiotics were commenced within one hour of diagnosis. Despite resuscitation with fluids for her hypotension she failed to improve. The team proceeded to hysterotomy to remove the source of the sepsis. After two days of supportive care on the intensive care unit she made a full and complete recovery. Her treatment was prompt and effective with rapid source control when she failed to respond to more conservative treatments. The time from admission to control of the sepsis was 18 hours.

The Care Setting

All women deserve high quality care at all times. It is important that women with sepsis are cared for in an appropriate setting. Some women were cared for on medical wards, and, as a consequence, did not receive appropriate obstetric or midwifery review. Other women were incorrectly risk assessed at booking which resulted in them being cared for in units that were neither equipped nor staffed to provide the necessary level of care required. The risk assessment process should be continual throughout pregnancy and when risk factors are identified, women should be advised appropriately about the required level of care to ensure their and their baby's safety.

In one instance where a woman was on a midwifery-led unit, the abnormal clinical signs of sepsis were not recognised, which led to a delay of 6 hours in transferring her to the consultant delivery unit.

It is recommended that education on the recognition and treatment of sepsis is integrated into the annual training already taking place for all staff caring for pregnant women, especially for those practicing in 'low risk' settings.

Another dilemma is where to care for pregnant women who need intensive care, but also need to labour and deliver. Critical care units are not appropriate places to deliver babies. Their staff do not have the skills to deal with obstetric complications. However delivery units are inappropriate places to manage women with multi-organ failure or in need of ventilation. Nevertheless the overriding principle is that a woman with sepsis must receive the level of care she needs regardless of where she is situated, and critical care should be provided on the delivery unit if this is the most appropriate setting. Alternatively, maternity care should be provided on the critical care unit if this is the most appropriate setting. Most women will only require high dependency care and many delivery units will have the necessary facilities and multi-disciplinary teams in place to provide this level of care. Once a woman is delivered a multi-disciplinary review can take place to decide the best location to continue with her care.

There should be adequate provision of appropriate critical care support for the management of a pregnant woman who becomes unwell. All consultant led delivery suites must have access to level 2 high dependency unit facilities that are appropriately equipped and staffed by teams of senior obstetricians, anaesthetists and midwives, skilled in looking after seriously ill women especially those with sepsis. Plans should be in place for provision of critical care on delivery units or maternity care on critical care units, depending on most appropriate setting for a woman with sepsis to receive care.

Communication

The reviews raised issues concerning communication between professionals, maternity units, and also with women. The reviewers noted advice on infection prevention and symptom identification in situations where women were prone to sepsis such as premature rupture of membranes was inadequate. It was not clear that women were made aware of the

gravity of the risks they may encounter when refusing to take the advised course of action recommended by their doctor or midwife.

A woman early in the second trimester had preterm pre-labour rupture of the membranes. She was prescribed erythromycin, but declined admission and took her own discharge. No discussion took place about the prognosis for the pregnancy or the option of termination. She developed a vaginal discharge two days later but despite medical review no swabs were taken and no change in management was discussed. The next day she became unwell and her GP considered that her symptoms were a side effect of the erythromycin and so reduced the dose. Later that day she was admitted with what proved to be irreversible septic shock and died.

Professionals must be clear and spell out the potential consequences of failing to detect and manage sepsis in a timely manner, including the possibility of long-term morbidity from multi-organ failure and even death. Trying to minimise the risks can ultimately fail the woman and her family. Early preterm pre-labour rupture of the membranes (PPROM) has a very poor prognosis for the baby and carries a significant risk for the woman. Realistic advice needs to be given including the option of termination of pregnancy. Any signs of infection should be treated seriously and intervention by emptying the uterus should be strongly recommended. This is the only way to remove the source of infection. Clinicians need to be aware that the prophylactic dose of erythromycin for PPROM should not be considered effective for the treatment of established infection. In view of the high risk of complications, PPROM should be managed in secondary care; it is not appropriate for care to be handed over to the general practitioner. Women discharged with PPROM should always be advised to contact their obstetrician in the event of any concerns.

Communication between professionals has been highlighted as an issue elsewhere in this report and previous reports. There was a widespread tendency for trainee doctors not to inform their consultants about these women in a timely way. A consultant obstetrician should review all women with sepsis immediately. Women with sepsis warrant close consultant obstetrician involvement and coordination of care plus the involvement of other relevant consultants as appropriate including infectious diseases, microbiology, anaesthetics and critical care.

Seven hours following a caesarean section at term a woman complained of offensive lochia. Twenty-four hours later she became unwell with a tachycardia and unstable blood pressure. No other observations were recorded. An obstetrician was not asked to review her for a further hour. Following that review it was requested that the woman be transferred to the delivery suite. The transfer did not take place for another 4 hours. Despite treatment she deteriorated and was transferred to ITU where she stayed for 8 days before recovering. Incomplete observations, poor communication, including with consultant staff, and a lack of prioritisation were all thought to have contributed to this woman's deterioration and prolonged stay on ITU.

Similarly, it was clear from some reviews that the staff caring for the women were unaware of the seriousness of the women's condition. The obstetric team must ensure that midwifery and anaesthetic colleagues are made aware if women have severe sepsis or suspected sepsis, and that women with sepsis receive appropriate attention from midwives trained in caring for seriously ill women.

A woman was admitted to hospital in the second trimester of pregnancy with chorioamnionitis one week after the insertion of a cervical suture for a threatened miscarriage. An intrauterine fetal death was diagnosed and the suture removed. A necrotic placenta was removed two hours after delivery of the fetus, following which the woman had a massive postpartum haemorrhage. She was later transferred to ITU but died from multi-organ failure due to sepsis. Workload on the delivery suite was high and this woman was not prioritised as high risk. Inexperienced junior midwives who did not recognise the severity of the woman's condition looked after her. There was also a lack of senior oversight from the obstetric team.

The responsible consultant obstetrician must show clear leadership and be responsible for liaising with anaesthetists, midwives, infectious diseases physicians/ microbiologists and all other professionals who need to be involved in the care of these women. When a woman is transferred to level 3 critical care, daily consultant obstetric involvement must remain, even if only in a supportive role, until such time that the woman is ready to be repatriated to the maternity unit.

RCOG Green-top guideline 64b

(Royal College of Obstetricians and Gynaecologists 2012b)

Governance

Serious incident reviews or root cause analyses were not carried out to review the care received by all women who died. Even fewer of the morbidity cases of women who recovered from septic shock underwent a local review. In other instances, where a review was carried out, the quality was poor. This is a lost opportunity, reducing the capability of the host organisation and the wider NHS to learn from these tragic and serious events. When a thorough serious incident review was carried out it was clear that maternity units learned valuable lessons and in turn that enabled them to improve their systems and processes.

A high quality multi-disciplinary serious incident review / root cause analysis should be carried out on all maternal deaths and all women with severe sepsis by the unit in which the woman was cared for, or when women die in the community, by the institution responsible for community services.

3.5. Lessons for care of specific infectious morbidities

Genital Tract Sepsis

In several of the women with genital tract sepsis, there was a delay in identifying the source of the sepsis and dealing with it surgically. This could have been avoided had a clear plan for monitoring the woman been in place and a senior obstetrician taken responsibility for the woman's care.

A woman presented in labour and was noted to have genital tract sepsis. She was delivered by caesarean section. The operation was complicated by a lateral tear and atony with an estimated blood loss of 1500mls. She was given intravenous antibiotics for 48 hours after delivery but her sepsis did not improve. There were several changes of antibiotics. On day 5 postpartum a CT scan was performed and found what was thought to be an area of sepsis in the wound communicating with the uterine cavity. On day 6 she worsened and a laparotomy was performed. The uterus was necrotic and the abdomen contained a great deal of pus. She had a sub-total hysterectomy and wound debridement. Despite intensive care she developed acute respiratory distress syndrome, deteriorated and died.

The reviewers noted that frequently symptoms and signs clearly indicated infection in the genital tract but further investigations were not undertaken or carried out until it was too late in the clinical course. When there is an established focus of infection reliance on antibiotics alone to bring about a cure can be dangerous. Where the tissue is already necrotic the blood supply is poor and so is the delivery of antibiotic to the affected area. Consequently the tissue concentration of antibiotics will be inadequate. Obstetricians must be aggressive in investigating any clinical evidence of genital tract sepsis to locate the source. Imaging should be performed early with either magnetic resonance (MRI) or computed tomography (CT) scans and acted on with appropriate drainage of any collections or surgical excision of infected tissue. If a conservative approach is attempted it may be necessary to repeat the imaging in order to assess the effectiveness of drug therapy. However, when imaging identifies that conservative treatment is failing, it will be necessary to remove the source of the infection to improve the woman's chances of recovery. It must be remembered that, just as with haemorrhage, a hysterectomy for women with severe genital tract sepsis can be life-saving.

When sepsis is present the source should actively be sought with appropriate imaging and consideration given to whether surgical or radiologically-guided drainage is required.

RCOG Green-top guideline 64b

(Royal College of Obstetricians and Gynaecologists 2012b)

Influenza

Influenza is a highly infectious acute viral infection of the respiratory tract caused mainly by influenza A and influenza B infections, which usually occurs in a seasonal pattern with epidemics in the winter months (Public Health England 2014b). In April 2009 a novel strain of influenza A virus subtype H1N1 ('swine flu') was identified in Mexico and rapidly spread globally (McLean and Pebody 2010). The virus was termed pandemic A/H1N1/09 virus by WHO (for brevity referred to as H1N1 hereafter) and a global pandemic declared from June 2009 to August 2010. The first UK cases were reported on 27 April 2009 and two waves of pandemic activity were seen in the UK, the first wave peaking in mid/late-July 2009, with the second wave starting with the return to school in the autumn and peaking in mid-October 2009 (McLean and Pebody 2010). Complications of H1N1 in the general population appeared similar to seasonal influenza with the majority experiencing mild symptoms. However those with asthma, diabetes, heart disease or who were pregnant were at higher risk of complications. In the 2009 pandemic, there was a four times higher rate of hospital admission in pregnant women compared to the general population, and a seven times higher risk of admission to an intensive care unit (Lapinsky 2010, McLean and Pebody 2010, Siston, Rasmussen et al. 2010, Pierce, Kurinczuk et al. 2011).

As noted above, 36 pregnant or recently pregnant women died from influenza, 32 thought to be due to H1N1. In 33% (n=12) of women presentation was initially to primary care, 36% (n=13) to obstetric services, 28% (n=10) to A&E or urgent care services and one woman did not have any contact with medical services prior to her death at home.

Influenza was not even considered as a possible diagnosis in the vast majority (n=34, 94%) of women at their initial presentation with respiratory illness whether to primary or secondary care, even at the height of the H1N1 pandemic. This led to delays in appropriate referral, testing and treatment. All women who died had delays in appropriate testing; a naso-pharyngeal aspirate for respiratory viruses should have been performed on admission to hospital as per guidelines at the time (Lim, Baudouin et al. 2009).

A woman presented to her GP during the second wave of the H1N1 pandemic at term with symptoms suggestive of a chest infection and was treated with amoxicillin. Shortly afterwards, she was admitted in labour and had a delivery by caesarean section. She was febrile post-operatively with worsening dyspnoea, desaturation and a productive cough. Over the following two days her respiratory symptoms deteriorated so she was started on antibiotics. She was transferred to ITU where H1N1 testing was finally done, but anti-viral treatment was started only when a positive result was obtained. She continued to deteriorate and died.

Department of Health/RCOG Guideline on the investigation and management of pregnant women with seasonal or pandemic flu should be followed

(Department of Health and the Royal College of Obstetricians and Gynaecologists 2009)

Vaccination

Vaccination is the main public health response to influenza in general, as well as to the 2009 A/H1N1 influenza pandemic. Influenza vaccination in pregnancy reduces maternal morbidity and mortality, improves fetal outcomes including reduced likelihood of perinatal death, prematurity and low birth weight, prevents influenza in the infant up to 6 months of age through transfer of maternal antibodies and potentially improves long-term adult outcomes for the infant (Tamma, Ault et al. 2009, Naleway, Irving et al. 2014). In view of this, pregnancy was added as a clinical risk category for routine influenza immunisation in 2010. Current guidance from the Department of Health recommends that all women who are pregnant during the influenza season, regardless of stage of pregnancy, should be offered the inactivated influenza vaccine (Public Health England 2014b). Multiple studies have demonstrated that these vaccines can safely be given to pregnant women (Tamma, Ault et al. 2009, Naleway, Irving et al. 2014, Public Health England 2014b).

Despite this recommendation and strong support from professional bodies, seasonal influenza vaccination coverage rates during pregnancy in the UK are generally low at around 25% if the only indication for immunisation is pregnancy (Public Health England 2014c). This is despite the 2009 pandemic resulting in increased attention to the importance of vaccination during pregnancy. This compares to rates of 74% in those aged >65 years and 52% in those in a clinical risk group (Public Health England 2014c). H1N1 vaccine uptake amongst pregnant women in the UK at the time of the pandemic was low at 14.9% (Sethi and Pebody 2010).

None of the women who died had been documented to have received seasonal flu vaccine or H1N1 vaccination in those who presented after 21st October 2009 (when the UK A/H1N1 vaccination programme commenced). Of the deaths from confirmed or probable H1N1, 38% were prior to vaccine availability in the UK and 62% after a vaccine was available, and could thus be regarded as preventable. Of those who could have been vaccinated against H1N1, it was documented that three women had refused vaccination. It was not clear how many of the others had been actively offered vaccination through primary care or obstetric services.

A pregnant woman who smoked refused vaccination offered by her GP for seasonal influenza or H1N1. She presented in the third trimester with flu-like symptoms including fever, cough and dyspnoea. Rapid deterioration led to her requiring ventilation in ITU, but she died within 24 hours of admission.

The benefits of influenza vaccination to pregnant women should be promoted and pregnant women at any stage of pregnancy should be offered vaccination against seasonal and pandemic influenza with inactivated vaccine.

Immunisation against Infectious Disease – "The Green Book"

(Public Health England 2014b)

Use of neuraminidase inhibitors

A recently published systematic review by the Cochrane Collaboration on the efficacy of neuraminidase inhibitors for influenza found little evidence of benefit in the general adult population (Jefferson, Jones et al. 2014). However most patients in the treatment studies included in the review were not at high risk of severe complications and pregnant women were specifically excluded from most trials. Observational data continues to show significant benefit with the use of neuraminidase inhibitors in pregnant women with seasonal and pandemic influenza from early treatment with antiviral agents (Siston, Rasmussen et al. 2010, Pierce, Kurinczuk et al. 2011, Muthuri, Venkatesan et al. 2014, Nguyen-Van-Tam, Openshaw et al. 2014). Department of Health/RCOG guidelines recommend that antiviral treatment should be commenced as early as possible in pregnant women with signs of influenza, particularly within the first 48 hours of onset of symptoms (Department of Health and the Royal College of Obstetricians and Gynaecologists 2009). Benefits were also seen if antiviral drugs were commenced up to 7 days after onset of symptoms in the H1N1 2009 influenza pandemic. Relenza (zanamivir) is the recommended antiviral treatment in pregnancy though Tamiflu (oseltamivir) is recommended for women with asthma or chronic pulmonary disease; or severe, systemic or complicated H1N1 influenza (Department of Health and the Royal College of Obstetricians and Gynaecologists 2009). Data on the safety of antiviral drugs in pregnancy is reassuring; there have been no increased risks of adverse outcomes, including congenital anomalies, preterm birth, low birth weight, neonatal seizures, stillbirth or neonatal death, associated with in utero exposure to antiviral drugs (Yudkin 2014).

Four women had a known contact with H1N1 or flu-like illness in family members and two women had been prescribed prophylactic antivirals, though these were not taken by either woman. Reasons for not taking prescribed antivirals were not clear.

A woman presented to her GP in the second trimester with fever, cough and flu like symptoms. Her husband had suspected H1N1 and was taking oseltamivir. The GP prescribed antibiotics and zanamivir, which the woman did not subsequently take. She was admitted one week later with lobar pneumonia and required immediate admission to ITU and subsequent ECMO. H1N1 was diagnosed after 24 hours of admission but despite subsequent anti-viral treatment she deteriorated and died.

In this review, all but two women with H1N1 who accessed clinical services had delayed diagnosis and initiation of appropriate antiviral therapy. This was because, in the vast majority of deaths, influenza or a respiratory virus was not considered as a diagnosis at initial presentation, even in the

height of the H1N1 pandemic. This led to delays in testing for H1N1. When appropriate testing for H1N1 was eventually requested, in 75% of women tested antiviral treatment was not commenced until after a positive H1N1 result was received, even though this was thought the most likely underlying aetiology in a clinically deteriorating woman. The majority had antibiotic therapy commenced at the time of admission to hospital with respiratory symptoms though this was generally with amoxicillin only, as appropriate for adults hospitalised with low severity pneumonia, rather than both amoxicillin and clarithromycin as standard treatment for adults hospitalised with moderate severity community acquired pneumonia (Lim, Baudouin et al. 2009).

A pregnant woman presented to A&E and was admitted overnight with a cough, fever and dyspnoea. All members of her family had influenza-like illness. She was discharged home the next day with no relevant investigations performed and no antibiotic or antiviral treatment initiated. Her condition deteriorated and when reviewed by her GP the next day, emergency readmission was arranged. Testing for H1N1 was conducted which was positive and antiviral treatment commenced, however the woman rapidly deteriorated and died 3 days later.

Early neuraminidase inhibitor treatment should be instigated for pregnant women with symptoms consistent with influenza, in line with national guidance.

(Department of Health and the Royal College of Obstetricians and Gynaecologists 2009)

Ventilation and extra-corporeal membrane oxygenation (ECMO)

Several women with H1N1 influenza were managed with ECMO; for others it was not clear whether management with ECMO was ever discussed or considered. In patients with severe but potentially reversible respiratory failure early referral to an ECMO-capable facility has been shown to improve 6 month survival (Peek, Mugford et al. 2009). Early referral to an expert regional centre showed clear benefits for the individuals who were referred, irrespective of whether they actually received ECMO. The National Specialised Commissioning Team has commissioned five providers of this service in England, all of which should provide a retrieval service.

The Acute Respiratory Distress Syndrome Network (ARDSnet) published their results in 2000 for patients with acute respiratory distress syndrome (ARDS) and acute lung injury (The Acute Respiratory Distress Syndrome Network 2000). The findings demonstrated a reduction in mortality rate from 39.8% in the traditional ventilation group (tidal volumes 12ml/kg predicted body weight and plateau pressures <50cm H_2O) to 31.0% in the protective lung ventilation group (tidal volumes 6ml/kg and plateau pressures <30cm H_2O). It is now considered best practice to ventilate patients in this manner to reduce lung damage due to barotrauma and volutrauma. Lower oxygenation levels are acceptable with protective lung ventilation (SaO_2 > 88%). A mechanical ventilation protocol summary can be found on the ARDSnet website (NIH NHLBI ARDS Clinical Network 2006). Compliance to such protocols should be regularly audited.

Not all ECMO units provide onsite obstetric care, therefore it is important when considering and communicating with a referral centre that obstetric management is considered, particularly in the antenatal woman.

Early advice should be sought from a respiratory centre if a woman is failing to respond to standard respiratory support.

Pneumococcal infection in pregnancy

Five women died of pneumococcal meningitis and one from a pneumococcal brain abscess. One woman died from pneumococcal pneumonia and invasive pneumococcal infection and another two from pneumonia of unclear cause. Streptococcus pneumoniae is the commonest cause of community acquired pneumonia (Bartlett and Mundy 1995, Public Health England 2014b). Pneumococcal pneumonia can also lead to invasive pneumococcal bacteraemia with complications such as pneumococcal meningitis, which has a mortality rate of 20–30%. Invasive pneumococcal infection occurs in both immunocompetent and immunosuppressed individuals but it is unclear whether pregnant women per se are a higher risk group. Pneumococcal vaccine is recommended in the UK for those in high risk groups, but pregnant women with no additional risk factors are not considered a high risk group in this context.

Surveillance in the UK has shown a large reduction in both invasive and non-invasive pneumococcal disease incidence due to vaccine serotypes in both vaccinated and to a smaller degree in older unvaccinated populations. However during the same period, the UK has seen an increase in invasive disease due to non-vaccine serotypes ('serotype replacement') (Public Health England 2014b). Continued surveillance and identification of factors associated with invasive pneumococcal infection and serotype distribution are important to inform vaccination programmes in the UK, and to further assess the risk of invasive pneumococcal disease amongst pregnant women.

A woman in the second trimester collapsed at work with headache. The woman spoke to NHS 24 twice and was advised to take paracetamol. The woman also saw her GP and was given the same advice. Her symptoms deteriorated and she was taken again to see the GP by her family with a temperature, severe headaches and poor balance. The GP's advice was to increase analgesia. Her conscious level deteriorated over the following few hours and the family called an ambulance. On arrival at A&E she was intubated and a CT scan demonstrated meningoencephalitis. She died 24 hours later from an invasive pneumococcal infection.

Bacterial meningitis in pregnancy

Few publications describe bacterial meningitis during pregnancy. In one literature review a total of 42 women with bacterial meningitis during pregnancy were described; 60% had meningitis due to Streptococcus pneumoniae (25 women) and 17% to Listeria monocytogenes (seven women) (Adriani, Brouwer et al. 2012). A review from the Netherlands of 15 deaths from meningitis during pregnancy, of which 10 were due to S. pneumoniae, reported that in two thirds of the deaths otolaryngological infections were the site of origin of the infection (Schaap, Schutte et al. 2012). However there did not seem to be a higher incidence of pneumococcal meningitis in pregnancy compared to the background population on the limited evidence available, though this needs to be monitored nationally to assess if incidence is increasing. In 2006–08, three women died of central nervous system infection of whom two had pneumococcal meningitis (Lewis, Cantwell et al. 2011).

In this review five women died of pneumococcal meningitis, one from a pneumococcal brain abscess and two from other streptococcal meningitis, making a total of seven with evidence of bacterial meningitis. Two women had evidence of direct extension of S. pneumoniae from the nasopharynx due to untreated infection of the middle ear and one had untreated frontal sinusitis with subsequent development of osteomyelitis of the frontal bone and a cerebral abscess. Four had contact with primary care services and two women had attended primary care several times with symptoms suggestive of early CNS infection including very severe headache with no investigations or antibiotic treatment initiated. Two had evidence of lobar pneumonia at post-mortem, in addition to pneumococcal meningitis, and had attended primary care with respiratory symptoms, which were not treated with antibiotics, prior to haematogenous spread of S. pneumoniae to the meninges. It must be remembered that otitis media and sinusitis can result in meningitis if not treated and followed up effectively.

A woman had a three month history of left frontal headache during the second and third trimester. She saw her GP multiple times about this complaint but she was not given any antibiotic therapy. Four weeks before her death she was also reviewed by a doctor in the antenatal unit who did not refer for further investigations despite localising features and a prolonged history of pain. She presented again three days before her eventual death when her CNS infection was finally diagnosed.

Repeated presentation to the general practitioner or community midwife or alternatively repeated self-referral to the obstetric triage or day assessment unit should be considered a 'red flag' and warrant a thorough assessment of the woman to investigate for signs of sepsis.

3.6. Local review and recognition in women who died and women who survived

Sara Kenyon, Lisa Elliot and Sue Orchard

Table 3.1 shows the care provided to women who died from sepsis and women with septic shock. Assessors noted improvements that could be made in the care of both women who died and women who survived. As highlighted throughout this chapter, in many instances observations (temperature, pulse rate, respiratory rate, blood pressure) were either only partially done or not undertaken at all and then not charted on a MEWS or similar chart; there was a lack of recognition of the severity of the woman's condition and of the need to refer to more senior staff. Importantly, for both women who died and women who survived, the most common place for this to happen in was the obstetric unit, with neither midwives nor doctors undertaking observations or referring women. The reasons behind this are clearly complex but taking a set of standard observations is a core nursing/midwifery task. It is possible that the focus on 'normality' within maternity has had entirely unintended consequences with these core tasks not being undertaken rigorously.

Despite the fact that MBRRACE-UK assessors identified clear improvements that could be made to care in more than two thirds of women, internal reviews were only undertaken for half the women who died, and just over a third of the women with septic shock. Few of those reviews that were undertaken included root cause analysis or similar. In a number of instances information was lacking as to whether the review was multidisciplinary or a root cause analysis undertaken.

CONCLUSIONS

This information thus highlights further these clear messages for clinical staff in relation to the care of women with severe sepsis:

- A complete set of observations should be undertaken, as required by NICE guidance, or if there is concern in any way. This will ensure confirmation of normality rather than presumption.
- If observations are abnormal they should be responded to and referral made to more senior staff.
- Multidisciplinary internal reviews should be undertaken to ensure any improvements in care are identified and lessons learned to prevent sepsis deaths or severe morbidity in the future.

Table 3.1: Local review and recognition in women with sepsis

	Maternal sepsis deaths N (%) (n=83)	Women with septic shock N (%) (n=34)
Classification of care received		
Good care	19 (23)	9 (26)
Improvements to care which would have made no difference to outcome	12 (14)	18 (53)
Improvements to care which may have made a difference to outcome	52 (63)	7 (21)
Delay in recognition or management	58 (70)	24 (71)
Locations of delays*		
Community midwife	7 (12)	6 (25)
Primary care	14 (24)	2 (8)
Accident and Emergency	6 (10)	0 (0)
Obstetric unit	38 (66)	18 (75)
Gynaecology/early pregnancy unit	4 (7)	0 (0)
Private care	2 (3)	0 (0)
Internal review undertaken	44 (53)	12 (35)
Staff involved in internal review		
Obstetrician	28 (64)	12 (100)
Midwife	28 (64)	5 (42)
Anaesthetist	19 (43)	2 (17)
Other	23 (52)	3 (25)
External reviewer	2 (5)	0 (0)
Root Cause Analysis undertaken	17 (39)	4 (33)

* Delays may occur in more than one location therefore figures do not add up to 100%

4. Prevention and treatment of haemorrhage

Sara Paterson-Brown and James Bamber on behalf of the MBRRACE-UK haemorrhage chapter writing group

Chapter writing group members: James Bamber, Geraldine Butcher, Sara Kenyon, Marian Knight, Jenny Kurinczuk, Annette Lobo, Lucy MacKillop, Elizabeth Mcgrady, James Neilson, Sara Paterson-Brown.

4.1. Key messages

Haemoglobin levels below the normal UK range for pregnancy should be investigated and iron supplementation considered if indicated to optimise haemoglobin before delivery.

Physiological observations including the respiratory rate recorded within a trigger system such as the MEOWS chart should be used to monitor all antenatal and postnatal admissions. However, it is the response to the abnormal score that will affect outcome not simply its documentation.

Concerns should be escalated to a senior doctor or midwife if a woman deteriorates, and there should be a named senior doctor in charge of ongoing care.

Fluid resuscitation and blood transfusion should not be delayed because of false reassurance from a single haemoglobin result; consider the whole clinical picture.

Whilst significant haemorrhage may be apparent from observed physiological disturbances, young fit pregnant women compensate remarkably well. Whilst a tachycardia commonly develops there can be a paradoxical bradycardia and hypotension is always a very late sign, therefore ongoing bleeding should be acted on without delay.

In a woman who is bleeding and is likely to develop a coagulopathy or has evidence of a coagulopathy, it is prudent to give blood components before coagulation indices deteriorate and worsen the bleeding.

If pharmacological measures fail to control the haemorrhage, initiate surgical haemostasis sooner rather than later.

Early recourse to hysterectomy is recommended if simpler medical and surgical interventions prove ineffective.

Stimulating or augmenting uterine contractions should be done in accordance with current guidance and paying particular attention to avoiding uterine tachysystole or hyperstimulation.

4.2. Background

Obstetric haemorrhage is a leading cause of maternal mortality worldwide accounting for up to 50% of maternal deaths in some countries, while in the UK it accounts for approximately 10% of all direct maternal deaths. It is also a significant cause of maternal morbidity. Postpartum haemorrhage (blood loss ≥500ml) affected 13% of all maternities in England in 2011–12 (Health & Social Care Information Centre 2012) and major obstetric haemorrhage (blood loss ≥2500ml, or blood transfusion ≥5 units red cells, or treatment for coagulopathy) affected 0.6% of maternities in Scotland in 2011 (Lennox and Marr 2013). Both in the UK and internationally the incidence of recorded postpartum haemorrhage is increasing. In England the recorded incidence of postpartum haemorrhage has nearly doubled from 7% of all maternities in 2004/5 to 13% in 2011/2012 (Health & Social Care Information Centre 2012).

In writing this report the authors have been mindful of the many recommendations and guidelines for good practice for the management of obstetric haemorrhage published by previous Confidential Enquiries into Maternal Deaths, NICE, the Royal Colleges and other national organisations. The review of these maternal deaths due to haemorrhage focused on recommendations which could be implemented better to improve outcomes in the future.

4.3. Summary of the key findings 2009–12

In the UK and Ireland there were 17 direct deaths due to obstetric haemorrhage in this four year period. This gives an overall mortality rate of 0.49 per 100,000 maternities (CI 0.29-0.78) and a case fatality rate for massive haemorrhage of approximately 1 per 1200 women, on the basis of an estimated rate of massive obstetric haemorrhage of 6 per 1000 (Lennox and Marr 2013). The absolute numbers are expected to be higher than previously as this report covers four years and includes Ireland, and this does not represent a significant increase in mortality which was previously 0.39 per 100,000 maternities (table 4.1). However, it still places obstetric haemorrhage as the third leading cause of direct maternal deaths. The number of direct deaths by type of obstetric haemorrhage is shown in table 4.1.

Table 4.1 Direct deaths by type of obstetric haemorrhage 1994–2012

Time period	Placental Abruption	Placenta praevia	Postpartum haemorrhage		Total deaths from haemorrhage	Direct haemorrhage death rate per 100,000 maternities	
			Atony	Genital Tract Trauma		rate	CI
1994–06	4	3	5	5	17	0.77	0.45–1.24
1997–99	3	3	1	2	9	0.42	0.19–0.80
2000–02	3	4	10	1	18	0.9	0.53–1.42
2003–05	2	3	9	3	17	0.8	0.47–1.29
2006–08	2	2	3 +2	(0/2)	9	0.39	0.18–0.75
2009–12†	2	1*	7**	7***	17	0.49	0.29–0.78

†Figures for UK and Ireland. All other figures are UK only.

*One placenta praevia percreta

**Includes one woman who had a portion of retained placenta which contributed to the bleeding, and one who also sustained vaginal tears.

***there were four ruptured uteri, two others were lower genital tract trauma, and one had trauma sustained in the form of angle extensions at caesarean section

In addition to these deaths there are other deaths with associated haemorrhage counted in other chapters. One woman is included in the anaesthetic chapter who had a haemorrhage after a caesarean section and returned to theatre for evacuation of some retained placenta sustaining a larger bleed, several women died of catastrophic haemorrhage after amniotic fluid embolisms and another woman classified as an early pregnancy death had a uterine rupture after a termination of pregnancy.

The mothers who died

The age range of the 17 women who died was 25 to 47 years with a median age of 33 years old. Six were nulliparous, and three of the eleven multiparous women had at least one previous caesarean section (range 1-2). The number of previous deliveries for the multiparous women ranged from one to five. The BMI of the women ranged from 18-40 kg/m^2 (median 25 kg/m^2) and weight ranged from 45 – 116kg (mean 69kg). Eight women were of normal BMI (20-25 kg/m^2), three were underweight (BMI <20 kg/m^2) and five were obese (BMI >30 kg/m^2). Nine women weighed less than 60kg. One woman was unbooked and not weighed. All but one spoke English. Two women were Jehovah's witnesses. Nine women were delivered by caesarean section (two of these were perimortem), six had spontaneous vaginal deliveries and two had instrumental deliveries. All except one delivered at term.

There were seven deaths associated with uterine atony

Four deaths with atony were after caesarean delivery and these women weighed less than 60kg with normal BMI. One of these deaths followed an elective caesarean delivery; the other three deaths occurred after emergency caesarean sections in young nulliparous women. One woman had twins, and one had a prolonged labour as risk factors for haemorrhage. Two women had an intrauterine balloon placed, of whom one went on to have a hysterectomy.

Three women had problems with uterine atony after spontaneous vaginal deliveries. One of these women had a successful vaginal birth after previous caesarean section, one had one previous vaginal delivery and one had five previous deliveries. None of the women had a prolonged labour but one woman was induced. An intrauterine balloon was placed in two of these women, one of whom also had a Brace suture and she went on to have a hysterectomy. Another woman who is included in the amniotic fluid embolism chapter also had haemorrhage associated with atony.

Seven deaths were associated with genital tract trauma

Four women had a uterine rupture; none of these women had a previous caesarean section. Three women were multiparous and one was nulliparous but had had a previous molar pregnancy. Three women had inductions including two with misoprostol following intrauterine deaths (IUD). The woman who laboured spontaneously was augmented with syntocinon.

Two women bled from lower genital tract trauma: both were nulliparous and had double instrumentation at operative vaginal delivery. Another woman sustained trauma at the time of her caesarean section with extensions of the uterine incision into the angle and also into the cervix

Two deaths followed placental abruption

One woman was nulliparous whilst the other had four previous deliveries. In one woman the delivery was by caesarean section whilst the other woman delivered vaginally following an induction of labour. Both died of catastrophic haemorrhage associated with postpartum disseminated intravascular coagulopathy.

One death from placenta percreta

This woman had an antenatal diagnosis of placenta percreta and was delivered by elective caesarean section.

Nine women were delivered by caesarean section

Two deaths involved perimortem caesarean sections. In another death the woman had a severe abruption and was in extremis on arrival in hospital before her category 1 caesarean section. Three women had caesarean sections during labour and three followed elective caesarean sections: involving twins in two deaths (both Never Events (NHS England Patient Safety Domain Team 2013)) and for placenta accreta in the third woman.

Four of the deaths were due to uterine atony and another woman sustained trauma at the time of surgery in the form of angle extensions. A woman who died after a postpartum haemorrhage due to retained placenta tissue following an emergency caesarean is included in the anaesthetic chapter.

Six women had a hysterectomy

The rate of peripartum hysterectomy in the UK is approximately 40 per 100,000 maternities and the case fatality is less than 1% (Knight 2007b) so in this time period we would have expected approximately 1300 women to have had a peripartum hysterectomy in the UK and Ireland, therefore these 6 deaths represent a case fatality from peripartum hysterectomy of approximately 0.4%.

4.4. Overview of care and lessons to be learned

Improvements in care which may have made a difference to outcome were noted in all deaths.

Over the years recommendations regarding policies, procedures and guidelines have been repeated in successive Confidential Enquiry reports. **These recommendations emphasise the importance of focusing attention on basic clinical acumen and skills**. In all of the maternal deaths due to haemorrhage reviewed, potential improvements in care were identified which may have made a difference to the outcome. Improvements are most needed in clinical recognition of the severity of the problems and in resuscitation techniques. In five deaths (28%) the administration of excessive uterotonics was identified as a key contributory factor.

Antenatal care and abnormal results

Most women had good antenatal care and only one woman was unbooked. Three women were anaemic in the antenatal period only one of whom received oral iron. Iron deficiency anaemia not only reduces the tolerance to acute haemorrhage but may also contribute to uterine atony because of depleted uterine myoglobin levels necessary for muscle action.

Haemoglobin levels below the normal UK range for pregnancy (that is, 110g/l at first contact and 105 g/l at 28 weeks) should be investigated and iron supplementation considered if indicated to optimise haemoglobin before delivery

NICE Antenatal care guideline CG62 and RCOG green-top guideline 52

(National Institute for Health and Care Excellence 2008a, Royal College of Obstetricians and Gynaecologists 2011b)

One woman also had thrombocytopenia which was not explored further whilst another woman who was anaemic also had atypical blood antibodies which delayed transfusion when she haemorrhaged.

Pregnant women with atypical red cell alloantibodies that could potentially cause problems with cross-matching or issues with the availability of appropriate blood at short notice should be discussed with the blood transfusion service regarding the frequency of antenatal testing and whether referral to a specialist centre for further investigation and advice on subsequent antenatal management is needed

NICE Antenatal care guideline CG62 and RCOG green-top guideline 65

(National Institute for Health and Care Excellence 2008a, Royal College of Obstetricians and Gynaecologists 2014)

Communication, Ownership, Leadership and Teamwork

Communication, ownership, clinical leadership and teamwork emerged once more as problematic areas in this review period. The main problems identified with communication involved

- disagreements in estimated blood loss in three women
- lack of communication of concerns regarding blood loss in five women
- not escalating to a senior when their condition deteriorated in two women

Lack of leadership was a feature in *three deaths*

- It appears that this was exacerbated by changing shifts with lack of continuity of care at a senior level, and lack of over-riding responsibility and ownership;
- Co-ordination of care following multidisciplinary specialist reviews did not always occur. Follow up discussions and records of clinical decisions after different specialists have reviewed a woman were sometimes missing;
- Effective communication between clinical staff is essential particularly in situations which require prompt decision making and action, such as a woman who is haemorrhaging. The use of a structured communication tool, such as the Situation - Background - Assessment - Recommendation (SBAR) tool, may be very useful and effective in such situations and should be encouraged (National Institute for Health and Care Excellence 2007a).

Concerns should be escalated to a senior doctor or midwife if a woman deteriorates, and there should be a named senior doctor in charge of ongoing care

Anticipation

An anaemic woman had a caesarean section after a very prolonged labour. She was of small stature and lost almost 1000mls at surgery. No blood was ordered. Three hours later when she then bled 2500mls vaginally from an atonic uterus she was initially resuscitated with fluids, receiving 8 litres of crystalloid and 2 litres of colloid before blood was available for her. She developed pulmonary oedema and was intubated ventilated and transferred to ITU where she died from ARDS, sepsis and multi-organ failure a month later.

This woman was at risk of PPH due to her prolonged labour and her tolerance to it was reduced by being anaemic and yet blood was not cross-matched, either prior to surgery or when she had bled almost a litre at caesarean section. Given her risk for uterine atony following such a long augmented labour it would have been a sensible added precaution to have given her prophylactic uterotonics. Her subsequent bleed comprised almost 50% of her circulating volume and it is not surprising that she decompensated rapidly.

Underestimation of blood loss in smaller women

Nine women in this series weighed less than 60kg

The circulating blood volume increases in pregnancy to approximately 100ml/kg and so responses to the estimated blood loss should take the woman's stature into account. For example a woman of 70kg who loses 1500mls of blood has lost about 20% of her circulating volume, whilst in a woman who weighs 55kg this would comprise almost 30% (Table 4.2). The classic teaching of clinical signs and symptoms to expect from different blood loss values of 15%, 30% and 40% help to target resuscitation and treatment (Paterson-Brown and Howell 2014).

Recognition of haemorrhage and the deteriorating woman

The severity of the situation was not recognised in 11 women (61%).

Inadequate observations were a feature in seven deaths

Inadequate observation suggesting systemic failures in either staffing or routine tasks was a common finding in these deaths, as illustrated by the following vignette:

A woman had labour induced on the antenatal ward where she received uterotonic agents. She did not have observations done on arrival and subsequent observations were extremely limited, inadequate and infrequent (at best at 9 hourly intervals). This failure to record observations continued even when the woman's condition was deteriorating and the woman was becoming increasingly distressed. A further uterotonic was administered without any recorded observations or examination. Staff handover was mentioned as a reason for the delay in attending to the woman who was becoming increasingly unwell. Her condition continued to deteriorate until she collapsed and had a cardiac arrest. She had a perimortem caesarean section on the antenatal ward where a large haemoperitoneum was discovered secondary to a uterine rupture. She had not had a previous caesarean section.

In this woman there was a complete lack of midwifery care. The observations that had occurred were undertaken by healthcare assistants, but the lack of clinical overview not only failed to support these very junior staff, but removed any opportunity for picking up warning signs and symptoms had they been present. Very similar themes were observed in the care of other women with a similar clinical course.

Table 4.2 Estimated blood volumes and proportionate losses according to body weight

Weight	Total blood volume*	15% blood volume loss	30% blood volume loss	40% blood volume loss
50kg	5000mls	750mls	1500mls	2000mls
55kg	5500mls	825mls	1650mls	2200mls
60kg	6000mls	900mls	1800mls	2400mls
65kg	6500mls	975mls	1950mls	2600mls
70kg	7000mls	1050mls	2100mls	2800mls

*Based on 100mls/kg blood volume in pregnancy (Royal College of Obstetricians and Gynaecologists 2011b) but may overestimate blood volume in obese women (Lemmens, Bernstein et al. 2006)

Abnormal observations were not escalated in five women

A woman had an elective caesarean section with cumulative blood loss of 2000mls. She had a rising respiratory rate, a tachycardia and a falling blood pressure. There was no escalation of care despite very worrying and deteriorating observations. She was eventually found to have had a serious concealed haemorrhage.

Whilst the value of MEOWS charts remains unproven they do provide a framework not only to encourage observations to be carried out and recorded but most importantly to recognise abnormalities and facilitate escalation of care. For MEOWS charts to operate successfully it is important that they are completed correctly and results are acted upon.

Physiological observations including the respiratory rate recorded within a trigger system such as the MEOWS chart should be used to monitor all antenatal and postnatal admissions. However, it is the response to the abnormal score that will affect outcome, not simply its documentation.

(Lewis 2007, Maternal Critical Care Working Group 2011)

Estimating blood loss was a problem in eight women

While bleeding after delivery is inevitable 'heavy lochia' should ring alarm bells and attempts should be made to tally up accumulated losses. The following vignette illustrates this important point:

A woman delivered spontaneously vaginally but then proceeded to 'trickle'. The observation of a tachycardia and hypotension was only made three hours post-delivery when she was reviewed by the in-coming night duty obstetric registrar and just before she collapsed with DIC and a haemoglobin count of less than 50g/l.

There were many deaths where there were inconsistencies in documented loss between different care givers suggesting lack of both teamwork and communication and resulting in delayed recognition of massive haemorrhage and inevitably delayed treatment.

A woman with a previous caesarean section had a ventouse delivery after the forceps blades had failed to lock. She immediately bled torrentially from vaginal tears and was taken to theatre. The extent of the bleeding in the room (2500ml) was not conveyed to the anaesthetist in theatre. After a further 2500ml of blood loss by the end of the repair in theatre she had only had one unit of blood as the anaesthetist had been reassured by a result from an acute point of care haemoglobin measurement which recorded a haemoglobin concentration of 110g/l.

There were at least three deaths where an acute point of care haemoglobin measurement result falsely reassured staff. If fluid resuscitation has not occurred then neither has haemodilution and therefore haemoglobin measurements in this context show the starting position for a woman's haemoglobin measurement and do not help with estimating either the blood loss or the need for blood. The decision to transfuse a woman should be based on regular observations of her condition combined with the estimated blood loss and anticipated clinical course. Delaying the transfusion of blood and its products in the presence of haemorrhage can lead to sudden deterioration of the woman's condition and possibly death.

Fluid resuscitation and blood transfusion should not be delayed because of false reassurance from single haemoglobin results when there is evidence of considerable blood loss and fluid resuscitation has not been commenced or is inadequate. Haemoglobin measurements should be repeated regularly during the transfusion process.

Handbook of Transfusion Medicine (United Kingdom Blood Services 2013)

Resuscitation

Achieving intravascular access quickly is the pre-requisite for commencing prompt and appropriate volume resuscitation and there was one death in which this was particularly difficult and a surgical venous cut down was attempted. In this instance the difficulty was due to severe haemorrhage and peripheral vascular shut down, but difficulties can also occur in obese women. Interosseous technology is being introduced in trauma care and in paediatrics with a growing evidence base in resuscitation medicine, and is now also taught on obstetric emergency training courses (Paterson-Brown and Howell 2014).

Maternity units should have as part of their major obstetric haemorrhage protocol guidance for achieving intravascular access when access is particularly difficult. The use of interosseous technology and appropriate staff training should be considered.

As discussed previously a haemoglobin measurement taken before adequate fluid resuscitation should not be used as the sole determinant to guide transfusion and resuscitation decisions. Blood gas acid base (HCO_3 and base deficit) and lactate measurements on the other hand are important measures of significant hypovolaemia and inadequate tissue perfusion due to blood loss. Repeated measurements of serum lactate, base deficit and haematocrit/haemoglobin are recommended to monitor tissue perfusion and oxygenation during haemorrhage and resuscitation (Kozek-Langenecker, Afshari et al. 2013).

Serial blood lactate and base deficit measurements, alongside serial haemoglobin measurements, should be made during the evaluation and resuscitation of women who have obstetric haemorrhage.

ESA Guideline 2013, Management of severe perioperative bleeding

(Kozek-Langenecker, Afshari et al. 2013)

Whilst significant haemorrhage may be apparent from observed physiological disturbances young fit pregnant women compensate remarkably well. Whilst a tachycardia commonly develops there can be a paradoxical bradycardia and hypotension is always a very late sign, therefore ongoing bleeding should be acted upon quickly (Thomas and Dixon 2004).

The aim of resuscitation is to maintain an effective circulating volume, adequate tissue perfusion and oxygenation and to minimise coagulopathy until the bleeding stops. Unfortunately this was not achieved in many of the deaths reviewed. Variable combinations of fluids, blood and blood components were given and at variable times and rates. In five deaths there were delays in getting blood and blood products and in another five deaths the resuscitation was inadequate. Effective resuscitation for massive haemorrhage requires blood and blood components to be replaced rapidly and in the appropriate ratios. In many instances the women who died were given too little blood too late and the blood was often not accompanied by adequate and timely replacement coagulation products. It was not apparent that cell salvage was used in any of these women, but neither was it apparent that cell salvage might have altered the outcome.

In a woman who is bleeding and is likely to develop a coagulopathy or has evidence of a coagulopathy, it is sensible to give blood components before coagulation deteriorates and worsens the bleeding.

Handbook of Transfusion Medicine (United Kingdom Blood Services 2013)

Although it is unclear whether it is applicable in obstetric haemorrhage, there is increasing evidence from trauma and military medicine that when replacement blood transfusion exceeds 50% of the blood volume the provision of plasma in approximate 1:1 ratios with blood may reduce overall transfusion requirements. The provision of plasma (and platelets) in fixed amounts with blood as packs ('major haemorrhage packs') by the transfusion laboratory as part of a major haemorrhage protocol activation may help ensure adequate and timely replacement (Royal College of Obstetricians and Gynaecologists 2011b, United Kingdom Blood Services 2013).

Each maternity unit should review its major haemorrhage protocol and assess it in accordance with current guidance which suggests that while acknowledging the general principle that results of coagulation studies and the advice of a haematologist should be used to guide transfusion of coagulation factors, up to 1 litre (equivalent to 4 units) of FFP and 10 units of cryoprecipitate (two packs) may be given empirically in the face of relentless bleeding, while awaiting the results of coagulation studies.

RCOG Green-top guideline 52, Handbook of Transfusion Medicine 2013

(Royal College of Obstetricians and Gynaecologists 2011b, United Kingdom Blood Services 2013)

Rapid infusion of cold fluids (> 100 ml/minute) has been reported to cause potentially lethal cardiac arrhythmias and hypothermia impairs clotting (United Kingdom Blood Services 2013). There was one death due to a pulseless electrical activity (PEA) cardiac arrest which followed the rapid transfusion of 5 units of blood with no indication that a rapid warmer infusion device was used. The need to administer blood through blood warming equipment has been highlighted in previous CEMD reports and in RCOG GT52.

All maternity units should have rapid access to rapid fluid infusers which incorporate a blood warming device and are CE marked.

RCOG Green-top guideline 52

(Royal College of Obstetricians and Gynaecologists 2011b)

Haemostasis: Stopping the bleeding

However prompt the diagnosis and resuscitation following massive haemorrhage the outcome will be poor and the condition of the woman will continue to deteriorate if the source of bleeding is not stopped ("turning off the tap"). Consumptive coagulopathy can develop very rapidly and it is imperative to retain awareness of the original pathology while managing the woman.

A nulliparous woman had labour induced following a concealed abruption with a fetal death at term. Her condition deteriorated dramatically over 14 hours but she was allowed to eventually deliver vaginally on the intensive care ward where she died.

At no point during this woman's deterioration was consideration given to changing the plan of care (and to consider caesarean section despite the fetal death) and to try to 'turn off the tap'.

Intrauterine balloon tamponade was attempted in eight women

In three women there were several hours delay between delivery and balloon insertion due to failure to recognise severity of haemorrhage and two of these women went on to have a hysterectomy (one of whom had also had a compression suture).

Of the five women who had an intrauterine balloon inserted in a timely fashion two were Jehovah's Witnesses but despite ongoing bleeding neither had a hysterectomy. One other woman did have a hysterectomy eventually for ongoing bleeding seven hours later but this was too late to reverse the catastrophic course. In two other deaths the problem was uterine rupture and the balloons were unhelpful and potentially dangerous.

These deaths highlight the apparent tendency to try an intrauterine balloon even when the situation is extreme. Whilst conservative measures to preserve the uterus in the face of postpartum haemorrhage are to be commended, sometimes definitive treatment in the form of a hysterectomy is required to stop the bleeding promptly as the speed of deterioration in massive haemorrhage can be very rapid. Such decisions should be made promptly at a senior level.

If pharmacological measures fail to control the haemorrhage, initiate surgical haemostasis sooner rather than later. Intrauterine balloon tamponade is an appropriate first- line 'surgical' intervention for most women where uterine atony is the only or main cause of haemorrhage. A 'positive test' (control of PPH following inflation of the balloon) indicates that laparotomy is not required, whereas a 'negative test' (continued PPH following inflation of the balloon) is an indication to proceed to laparotomy. Hysterectomy should not be delayed until the woman is in extremis.

RCOG Green-top guideline 52

(Royal College of Obstetricians and Gynaecologists 2011b)

Important factors when considering intrauterine balloon tamponade (Royal College of Obstetricians and Gynaecologists 2011b)

- be sure it is uterine atony or the placental bed that are causing the bleeding;
- it is not suitable in cases of uterine trauma;
- it needs to be inserted early in the proceedings;
- be ready to proceed to definitive surgery if it is unsuccessful in staunching the flow (sometimes described as the 'tamponade test').

Early recourse to hysterectomy is recommended when:

- blood is unavailable or refused;
- when there has been delayed recognition or delayed diagnosis of the severity of the situation;
- when conservative measures are unsuccessful.

Hysterectomy was performed in six women

Three of these were performed promptly at the time of caesarean section: one in quick sequence after an emergency caesarean section for an abruption, one following a perimortem caesarean section for a ruptured uterus, and the third was at caesarean section for placenta percreta. This latter pathology requires a total hysterectomy, as the subtotal procedure leaves the cervical stump which is often involved in the pathology and continues to bleed. Furthermore at caesarean hysterectomy the caesarean incision should be quickly closed to limit blood loss during the hysterectomy (Royal College of Obstetricians and Gynaecologists 2011a) and in one woman this was not done exacerbating the ongoing heavy bleeding.

Three women had delayed hysterectomies after continued bleeding following unsuccessful tamponade by intra-uterine balloons. Two of these women had uterine atony, and one had sustained uterine trauma.

Early recourse to hysterectomy is recommended, especially where bleeding is associated with placenta accreta or uterine rupture or when bleeding continues after a trial with an intrauterine balloon. Hysterectomy should not be delayed until the woman is in extremis or while less definitive procedures with which the surgeon has little experience are attempted.

RCOG Green-top guideline 52

(Royal College of Obstetricians and Gynaecologists 2011b)

Placental pathology:

Despite increasing numbers of women at risk from abnormally adherent placenta following previous caesarean sections, only one death was due to placenta praevia percreta in a woman with two previous caesarean sections. There were no other deaths from placenta praevia or placenta accreta, although one woman who died from genital tract trauma after a successful VBAC (vaginal birth after caesarean section) did have a small area of accreta identified at post-mortem. There were no deaths from unexpected placenta praevia accreta found at caesarean section, suggesting that previous recommendations regarding imaging and preparations for women with placenta praevia and a previous caesarean section have been followed (Paterson-Brown and Singh 2010, Royal College of Obstetricians and Gynaecologists 2011a).

The Care Bundle for placenta praevia after caesarean section devised by RCOG and the National Patient Safety Agency requires:

- Consultant Obstetrician planned and is directly supervising delivery
- Consultant Obstetric Anaesthetist planned and is directly supervising anaesthetic at delivery
- Blood and blood products available on site
- Multidisciplinary involvement in pre-operative planning

- Discussion and consent should include possible interventions (hysterectomy, leaving the placenta in situ, cell salvage, interventional radiology)
- Local availability of a level 2 critical care bed

Robust and detailed planning in high risk cases such as placenta percreta, need to be made and documented, with that plan anticipating the worst case 'what if' scenario and preparing accordingly. Maternity units who undertake to deliver women with placenta accreta should have the relevant specialist facilities and skills to safely manage the care of these women. These facilities and skills include adequate blood bank resources, interventional radiology access and intensive care facilities as well as experienced anaesthetists and surgeons.

Table 4.3: Recommended misoprostol doses (Weeks and Faundes 2007, National Institute for Health and Care Excellence 2008d, Royal College of Obstetricians and Gynaecologists 2010)

Use	Dose and frequency	Maximum
Intrauterine fetal death from 18–26 weeks	100 micrograms 6 hourly	Maximum of 4 doses
Intrauterine death after 26 weeks	25–50 micrograms 4 hourly	Maximum 6 doses

The misuse of uterotonics

A multiparous woman with no previous caesarean deliveries was induced for an intrauterine fetal death in the third trimester. She received excessively high and frequent doses of misoprostol and sustained a uterine rupture. She had a spontaneous delivery but then bled torrentially and arrested. She had a large haemoperitoneum at laparotomy.

This was not an isolated incident. Misoprostol is not licensed for use in pregnancy, and is an extremely strong uterotonic. It must be used with extreme caution in the second and third trimester. One death occurred before the RCOG guidelines were published (Royal College of Obstetricians and Gynaecologists 2010) but there had been FIGO recommendations regarding recommended doses since 2007 as listed in Table 4.3. There are difficulties with these small doses as the tablet needs to be halved or quartered making for potentially imprecise doses, therefore dissolving in water has also been suggested.

There were three deaths following hyperstimulation with syntocinon.

Syntocinon was given to a multiparous woman in spontaneous labour in order to expedite delivery when there was fetal distress at 9cm cervical dilatation and she was already contracting strongly. The uterus ruptured with bleeding occurring before and then torrentially after, spontaneous delivery.

Stimulating or augmenting uterine contractions should be done in accordance with current guidance and paying particular attention to avoiding uterine tachysystole or hyperstimulation

SUMMARY RECOMMENDATIONS:

1. Communication, ownership and teamwork

With reduced doctor hours and shift patterns of working there can be difficulties with continuity of care. It is nevertheless crucial that a sense of ownership and responsibility exists and a consultant should take responsibility for liaising and co-ordinating care rather than leaving this responsibility to changing shifts of junior staff.

Joint communication and agreement between attending midwives, obstetricians and anaesthetists regarding the estimated blood loss in any particular woman should be formulated together with an ongoing plan including:

- where the woman should be recovered
- what observations are needed and how often
- encouraging and facilitating escalation if the woman deteriorates
- having a named senior doctor in charge of ongoing care
- having a plan for alternative management in the event that her haemorrhage is not controlled

2. Attention to detail regarding maternal observations:

Observations should be

- Carried out in a timely fashion
- Thorough and complete including respiratory rate
- Documented carefully
- If abnormal their importance should be recognised and escalated

3. Maintaining a high index of suspicion:

Keeping a critical mind, anticipating risk factors and explaining observations rather than accepting them, should aid earlier recognition of a problem. Taking the woman's weight into account will also help highlight those small women who may decompensate more quickly. Delay in recognition of massive haemorrhage can be fatal because when this delay is accompanied by metabolic acidosis, hypothermia, coagulopathy and anaemia, it can become impossible to recover the clinical situation as is starkly demonstrated by some of the deaths in this report.

4. Resuscitation:

- Early IV access with rapid warm volume replacement
- Once it is recognised that a massive haemorrhage has occurred and especially if bleeding is ongoing it is recommended that one unit of FFP is given for every one unit of blood, and that the sooner this starts the better the outcome. As bleeding continues additional blood products such as platelets and cryoprecipitate will be required together with specialist haematological advice.
- All units should keep a supply of O negative blood on the labour ward
- Hypotension occurs late in hypovolaemia and a normal blood pressure should not be taken as a reassuring sign
- A haemoglobin measurement during the early acute phase of haemorrhage before adequate fluid resuscitation is not helpful in guiding transfusion requirements except to reflect what the situation was before the bleeding commenced

5. 'Turning off the tap'

Whatever the cause (for example atony, vaginal tears, concealed haemorrhage) the priority is to control the haemorrhage. Delaying this can be dangerous. If the first approach doesn't work then asking for help and going on to an alternative management plan in a timely fashion is imperative, whether this be 'bailing out' and performing a caesarean section or a hysterectomy depending on the pathology.

6. The dangers of uterotonics

Uterotonics are lifesaving in postpartum haemorrhage, but they can be dangerous in the pregnant woman and should be used with care and respect:

- Syntocinon should always be used carefully but this is especially true in spontaneously labouring multiparous women where extreme caution is needed
- Misoprostol should only be given according to current recommendations

7. Human factors

The main human factor highlighted from review of these deaths is lack of 'Situation Awareness', most particularly delays in recognising the severity of the problem. While guidelines, protocols and proformas are necessary and helpful they need to be supported and interpreted by ongoing ***clinical scrutiny of the woman.*** Rather than failing to see the wood for the trees we risk the reverse in failing to give attention to detail:

- Maintain a high index of clinical suspicion in each individual
- Take, document and then ***explain*** observations
- Communicating and escalating concerns early
- *Understand and explain* the underlying cause of the problem i.e. make a diagnosis
- *Tailor the treatment according to the diagnosis and continually re-evaluate the woman and her treatment* rather than persisting with ineffective or inappropriate care

CONCLUSIONS

Obstetric haemorrhage is common and familiar to all obstetricians, anaesthetists and midwives who have to manage it on a regular and frequent basis. This should not make us casual in our vigilance to recognise and respond to it. We must continue to scrutinise the care of women who have this complication to identify failings in systems processes or individuals in order to learn from them and avoid deaths such as these reviewed here which may have been preventable.

5. Caring for women with Amniotic Fluid Embolism

Ann Harper and Rowan Wilson on behalf of the MBRRACE-UK AFE chapter writing group

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5.1. Key messages

Perimortem caesarean section should be carried out within five minutes or as soon as possible after cardiac arrest and is carried out for the benefit of the woman; there is no need to confirm fetal viability, to do so wastes valuable time. Emergency Departments, Ambulance Services and crews need to recognise this element of resuscitation in pregnant women.

It is prudent to trigger the massive obstetric haemorrhage protocol in an undelivered woman at the time the decision to proceed to peri-mortem caesarean section is made.

Hysterectomy should not be delayed until the woman is in extremis or while less definitive procedures with which the surgeon has little experience are attempted.

It is important to replace major blood loss with red cells, plasma and platelets as soon as possible to avoid the dilutional effects of volume expanders.

The effectiveness of replacement and supportive therapy should be continuously monitored by the signs and symptoms of adequate oxygen delivery and tissue perfusion.

5.2. Background

Amniotic Fluid Embolism (AFE) affects in an estimated 1 in every 50,000 women giving birth (Knight, Tuffnell et al. 2010). Case fatality estimates range from 11%-61% and although the definition and incidence of AFE varies considerably, the more recent series report a lower fatality rate than 30 years ago (McDonnell, Percival et al. 2013). The apparent improved survival may be in part due to better identification of women who survive AFE and different study methodology (Knight, Berg et al. 2012) as well as improvements in care.

One of the difficulties studying the condition is that clinical diagnosis is generally a best guess, retrospective and by exclusion of other causes, with no specific investigations for confirmation. Proposed pathogenic mechanisms involving antigenic insult and host susceptibility may help explain why some women have a less severe response. There are no denominator data for the presence of fetal squames in the maternal circulation because that is difficult evidence to confirm even in women who die. It is known that fetal squames can be found in the circulation of women that do not die and do not have a clinical diagnosis of AFE; conversely women that do die from clinical AFE may not have evidence of fetal squames identified. Diagnosis on clinical grounds has therefore been accepted from the time of the 1991–1993 CEMD Report (Department of Health 1995). Both the UK Amniotic Fluid Embolism Register (1997–2004) (Tuffnell 2005) and the subsequent UKOSS national prospective study (2005-ongoing) (Knight, Tuffnell et al. 2010) have defined AFE clinically (Box 5.1).

5.3. Summary of key findings for 2009–12

During the four year period 2009–12, 11 women who died from amniotic fluid embolism (AFE) in the UK and Ireland were reported to the Enquiry. The mortality rate due to AFE in the UK in 2009–11 was 0.29 per 100,000 maternities (95% CI 0.12–0.61) and in 2010–12 was 0.33 per 100,000 maternities (95% CI 0.14–0.66). AFE also contributed to the death of one other woman who is discussed but not counted in this chapter as the principal cause of her demise was uterine rupture. Amniotic fluid embolism ranks as the 5th leading cause of *direct* maternal death in the most recent triennium (2010–12). Although the numbers and mortality rates have fallen from the previous two triennia, this decline is not statistically significant and the number and rate of deaths from this condition fluctuate over the years (Table 5.1).

Box 5.1: Diagnostic criteria for Amniotic Fluid Embolism used by the UK Obstetric Surveillance System (UKOSS) (Knight, Tuffnell et al. 2010)

In the absence of any other clear cause

EITHER

Acute maternal collapse with one or more of the following features:
- Acute fetal compromise
- Cardiac arrest
- Cardiac rhythm problems
- Coagulopathy
- Hypotension
- Maternal haemorrhage
- Premonitory symptoms, eg, restlessness, numbness, agitation, tingling
- Seizure
- Shortness of breath

Excluding women with maternal haemorrhage as the first presenting feature in whom there was no evidence of early coagulopathy or cardio-respiratory compromise

OR

Women in whom the diagnosis was made at postmortem examination with the finding of fetal squames or hair in the lungs

All deaths of AFE, whether or not the woman has survived, should continue to be reported to UKOSS (ukoss@npeu.ox.ac.uk) or to:
UKOSS
National Perinatal Epidemiology Unit
Nuffield Department of Population Health
University of Oxford
Old Road Campus
Oxford
OX3 7LF

Table 5.1: Direct deaths attributed to amniotic fluid embolism and rate per 100 000 maternities, UK, 1985–2012

Triennium	Number of women	Rate	95% CI
1985–87	9	0.40	0.21–0.75
1988–90	11	0.47	0.26–0.83
1991–93	10	0.43	023–0.80
1994–96	17	0.77	0.48–1.24
1997–99	8	0.38	0.19–0.74
2000–02	5	0.25	0.11–0.59
2003–05	17	0.80	0.50–1.29
2006–08	13	0.57	0.33–0.98
2009–11*	7	0.29	0.12–0.61
2010–12*	8	0.33	0.14–0.66

*2009–12 data from overlapping triennia, excludes women from the Republic of Ireland

The women who died

Eleven women were considered to have died from AFE. Another woman had features of AFE but died primarily from uterine rupture and her care is considered elsewhere. Their ages ranged between 25–42 years (median 30 years); five were multiparous. All of the women had appropriate antenatal care and most had uncomplicated pregnancies; one woman had a twin pregnancy and two women had a uterine scar. The majority of women had singleton pregnancies and delivered at term (range: 30 – 41 weeks; median: 39 weeks). All of the women collapsed either before or within minutes of delivery; seven suffered acute collapse during labour; three during caesarean section, and one just after vaginal delivery. The perinatal mortality rate associated with AFE is estimated to be 135 per 1000 total births (UKOSS) (Knight, Tuffnell et al. 2010). In this series, there were two intra-uterine deaths; as far as is known all of the other ten babies survived.

The BMIs of the eleven women ranged from 22 to 47kg/m^2 (median 26kg/m^2); only two had a BMI>30kg/m^2. There was no significant history of allergy or atopy. Three women were smokers, and none had any known history of substance misuse. All eleven women were UK or Irish citizens, all spoke English, and only two (19%) came from ethnic minority groups.

5.4. Messages for care

UKOSS data indicate that in optimal circumstances with excellent resuscitation and ongoing care and support, many women with AFE do survive (Knight, Tuffnell et al. 2010). Several of the deaths described here occurred in labour wards or obstetric theatres with senior trainees or consultant obstetricians and anaesthetists present or immediately available and with exemplary resuscitation; however, their presentations were so sudden and catastrophic that they could not be saved. As one consultant anaesthetist commented: *"the lesson that I have learned is that even the most straightforward of cases can result in disaster, from unforeseeable events".* Hospital Root Cause Analysis was undertaken in ten of the eleven deaths; one death was also subjected to an external review. Nevertheless, three of the reviews were incomplete with no recommendations or conclusions made available to the Confidential Enquiry. There was no indication that any local review had taken place for one woman.

Induction of labour

Induction of labour is a known risk factor for AFE (Knight, Berg et al. 2012). Labour was induced or augmented in six of the women who died, and the reviewers considered that different choices around induction might have led to a different outcome for several women. In some instances, inappropriate uterotonics were used to induce labour, including dinoprostone (Propess) in women of high parity; the manufacturers state that it should not be used in women who have had three or more full term deliveries. AFE contributed to the death of another woman who was induced with mifepristone and misoprostol following late fetal death:

> A woman who had an intrauterine death discovered in late pregnancy had labour induced with mifepristone followed by misoprostol in a dosage regimen that was not uncommon at the time but, as described in the haemorrhage chapter, is more suitable for early pregnancy. She laboured rapidly and collapsed after a difficult delivery. Although the main cause of her death was massive haemorrhage due to uterine rupture, fetal squames were present in her lungs and AFE considered to be a contributory factor.

Although induction of labour is a common intervention serious complications including uterine rupture and AFE do sometimes occur. Units should ensure that their protocols follow the guidance set out in the NICE Clinical Guideline No. 70 on Induction of Labour and the RCOG Green-top Guideline No. 55 on Late Intrauterine Fetal Death and Stillbirth

(National Institute for Health and Care Excellence 2008d, Royal College of Obstetricians and Gynaecologists 2010).

Uterine hyperstimulation

Three of the women who died developed uterine hyperstimulation after induction of labour. One woman who presented with spontaneous rupture of membranes and meconium staining of the liquor developed strong contractions with fetal bradycardia and collapsed less than one hour after syntocinon was commenced to induce labour. Two women who were given a single vaginal prostaglandin pessary developed uterine hyperstimulation; one collapsed immediately after spontaneous rupture of membranes; the second woman collapsed as the placenta was delivered vaginally.

Avoid uterine hyperstimulation as it is a risk factor for AFE as well as fetal asphyxia; if it does occur, if possible remove the stimulus (e.g. stop syntocinon infusion, remove Propess) and consider using a tocolytic agent such as terbutaline.

NICE Induction of labour guideline CG70

(National Institute for Health and Care Excellence 2008d)

Differential diagnosis

Maternal collapse is a rare event but it has many different causes that are often not immediately obvious. Although immediate resuscitation is the first concern, early systematic consideration of all possible causes can help to improve survival as some are reversible with appropriate treatment. The common causes of maternal collapse are outlined in **Box 5.2** and discussed in the RCOG Green-top Guideline on Maternal Collapse in Pregnancy and the Puerperium (Royal College of Obstetricians and Gynaecologists 2011c). Not all of the eleven women with AFE had a typical presentation, as indicated in Box 5.1 and Appendix A2, and in some the diagnosis was only confirmed at post mortem:

A woman was induced at term. Shortly after an epidural top-up she became hypotensive, breathless and dizzy, then cyanosed and arrested. Intralipid was given to counteract possible local anaesthetic toxicity. She was delivered by caesarean section in the delivery room whilst CPR continued. She developed pulmonary oedema and disseminated intravascular coagulation. She had intensive surgical and medical management of haemorrhage. She was transferred to ITU for multi-organ failure support until care was withdrawn after confirmation of irrecoverable brain injury. The absence of seizure or ventricular arrhythmia, coupled with the nature of her clinical presentation followed by the onset of massive haemorrhage and DIC, and the post-mortem finding of fetal squames in the pulmonary circulation were in keeping with the final diagnosis of AFE.

Box 5.2: Causes of maternal collapse

Consider:

Reversible Causes of Collapse (4H's and 4T's) (Resuscitation Council (UK) 2010) *and examples*

Hypoxia	*Eclampsia, sepsis, intracranial haemorrhage, AFE*
Hypovolaemia	*Obstetric haemorrhage*
Hypo/hyperkalaemia/metabolic	*Sepsis*
Hypothermia	
Tension pneumothorax	
Tamponade, cardiac	
Toxins	*Drug toxicity/overdose, AFE, anaphylaxis*
Thrombosis (coronary or pulmonary)	

Cardiopulmonary Resuscitation

When faced with sudden unexpected collapse in a previously well woman, prompt action is vital as there is often little time to salvage the situation. The cornerstone of treatment is immediate advanced life support (ALS), noting the importance of left lateral tilt or uterine displacement in pregnant women. This is discussed further in the anaesthetic chapter.

Cardiopulmonary resuscitation (CPR) after collapse was begun after <1 to 23 minutes in ten women and nearly 2 hours after other resuscitative efforts in one.

It is important that all obstetricians and midwives maintain and regularly update their skills in immediate life support, that all equipment (oxygen, resuscitation trolley etc.) is regularly checked and maintained in good working order, accessible and ready for immediate use, and that senior staff are called to the scene immediately and attend promptly.

It is recommended that pregnant women (>20 weeks gestation) that collapse and are still pulseless with no return of spontaneous circulation after 4 minutes of CPR have an immediate caesarean section (Box 5.3) (Royal College of Obstetricians and Gynaecologists 2011c).

None of the seven women who had a perimortem caesarean section were delivered within five minutes of their cardiac arrest. In five, delivery occurred between 15–30 minutes after collapse, in one after 45 minutes, and in one woman, who had collapsed at home, substantially later. Five perimortem caesarean sections were carried out in an operating theatre after transfer with limited general anaesthesia, one was undertaken in the emergency department with no anaesthetic and one was performed in a delivery room with an epidural already in place and with subsequent transfer to theatre after delivery.

A woman was admitted for induction of labour for postmaturity. Shortly after a vaginal examination to confirm spontaneous rupture of membranes she complained of feeling unwell and collapsed. Full CPR was not initiated for over 20 minutes; she was delivered by caesarean section in theatre after a further 20 minutes. Resuscitation, involving a hysterectomy for major obstetric haemorrhage and subsequent further exploratory laparotomy, continued for several hours. Fetal squames were found in the lung, heart and kidneys at postmortem as well as extensive cerebral infarction.

Box 5.3 Perimortem caesarean section

Rationale:

Pregnant women become hypoxic more quickly than non-pregnant women and irreversible brain damage can ensue after 4–6 minutes. Delivery of the fetus and placenta facilitates resuscitation; the procedure is performed primarily in the interests of maternal, not fetal, survival (Royal College of Obstetricians and Gynaecologists 2011c).

The basic principles are:

Take the decision to perform a caesarean section if there is no cardiac output after 4 minutes of collapse.
When resuscitation is ongoing, the uterus should be emptied even if there has been delay.
Aim to deliver the fetus and placenta within 1 minute.
Do it on the spot – do not move to theatre.
No anaesthetic is necessary.
A scalpel is the only essential equipment*.
Use the incision that will give most rapid access** .
If resuscitation is successful following delivery, the uterus and abdomen can be closed in the usual manner and the woman transferred to a more appropriate environment.

*A pre-mounted scalpel blade and two cord clamps should be kept available on the resuscitation trolley to ensure that there are no delays if perimortem caesarean section is necessary.
**A midline abdominal incision and a classical uterine incision will give the most rapid access, but a transverse approach can be used if the operator is more comfortable with that incision.

Perimortem caesarean section should be carried out within five minutes or as soon as possible after cardiac arrest; there is no need to confirm fetal life, to do so wastes valuable time.

This requirement has implications for Emergency Departments and their staff, especially those not co-located with an obstetric unit. Non-obstetricians with some surgical training should be aware of how and when to conduct perimortem caesarean section.

Ambulance Services and crews need to recognise this element of resuscitation in pregnant women. Unless the arrest occurs in a location remote from secondary care basic life support should be commenced and rapid transfer to hospital arranged.

RCOG Green-top guideline 56

(Royal College of Obstetricians and Gynaecologists 2011c)

The primary cardiac rhythm disturbance was pulseless electrical activity (PEA) in all of the women who collapsed in hospital, although six women were subsequently defibrillated, some repeatedly, during their resuscitation. The early administration of epinephrine (ideally within 3 minutes) is independently associated with improved outcomes, including neurologically intact survival, in women with non-shockable rhythms at cardiac arrest, with a stepwise decrease in survival with increasing delay (Donnino, Salciccioli et al. 2014).

Two women were recorded as spontaneously breathing supplemental oxygen through an Ambu bag at the beginning of their resuscitation despite hypoxia demonstrated on pulse oximetry. The junior doctors involved in these deaths seemed not to have realised that the one way valve in an Ambu bag only allows for positive pressure ventilation and so these women did not receive supplemental oxygen and were inadequately ventilating against a closed valve. In another death, portable oxygen equipment was not immediately available and caused a short delay in transfer to theatre.

A multiparous woman was admitted post term with spontaneous rupture of membranes and meconium stained liquor. A syntocinon infusion was started as she was in early labour. Within an hour she was contracting strongly and began involuntary pushing. The fetal heart rate dropped, she became distressed and breathless, then cyanosed and unresponsive with seizure activity. She had an emergency caesarean section under general anaesthesia. Although records did not identify cardiac or respiratory arrest during the acute collapse, she died several days later after brain stem death was confirmed.

Sudden unexplained loss of consciousness is a good indication of inadequate cardiac output, especially coupled with cyanosis and a profound fetal bradycardia and should mandate immediate CPR. Measurements of blood pressure and pulse, intermittently taken during a rapid transfer to theatre are likely to be misleading either because they are unreliable, spurious or falsely reassure as the significant physiological reserve of pregnant women can disguise the warning signs of illness up until the point of total collapse.

Of the eleven women who died, only four (36%) survived long enough to be transferred to ITU; all four had extensive fatal neurological damage. In the seven women who did not reach ITU, resuscitation continued for between 70 and 300 minutes. In the UKOSS population-based study, 7% of survivors had serious permanent neurological damage.

Management of bleeding

Many of the lessons for future care identified in the haemorrhage chapter apply equally in the situation of amniotic fluid embolism. In a previous Report (2003–05) (Lewis 2007) it was commented that AFE has in some instances provided a useful scapegoat for poor care and this is particularly true in relation to haemorrhage. Some maternal deaths reported to MBRRACE-UK and considered in this period were reclassified by the assessors from AFE to other causes; one of these was a woman who died from unrecognised haemorrhage.

None of the women with AFE had evidence of bleeding prior to their collapse; in one bleeding with severe hypotension was the first recognised manifestation of a problem. All but two women had rapid onset of massive obstetric haemorrhage and coagulopathy within an hour or so of their initial collapse. Estimated blood losses ranging from 2

to over 12 litres were recorded, and one woman received 34 units of red cells as well as many other fluids and blood products. It is thus prudent to assume that *any* cause of major maternal collapse in the peripartum period will involve significant blood loss at some stage. Obstetric units need to have guidelines defining massive obstetric haemorrhage (MOH) and its management, placing emphasis on trigger phrases, nominated staff for communication, collection, recording and equipment gathering as well as physical resuscitation efforts. There is inherent delay in waiting to meet exact criteria for the triggering of an MOH management protocol (for example blood loss >2L, >50% estimated blood volume in 3hrs, >150mls/min ongoing loss) as the limited and distracted personnel present at the time of first collapse who need to make that call, are frequently busy providing ALS.

It is prudent to trigger the massive obstetric haemorrhage protocol in an undelivered woman at the time the decision to proceed to peri-mortem caesarean section is made, and within the same time frame for a delivered woman in whom there is also no return of spontaneous circulation at four minutes after advanced life support commences.

All but one of the women who died had a caesarean section, three had hysterectomies and six had exploratory laparotomies, two of whom had already had hysterectomies. Early resort to hysterectomy in massive haemorrhage may, by removing the main source of blood loss, buy time to replace red cells and clotting factors and so improve the chances of survival.

Hysterectomy should not be delayed until the woman is in extremis or while less definitive procedures with which the surgeon has little experience are attempted.

RCOG Green-top guideline 52

(Royal College of Obstetricians and Gynaecologists 2011b)

Guidelines from the European Society of Anaesthesiology provide a recent summary of current evidence on coagulation monitoring and management in postpartum haemorrhage (Kozek-Langenecker, Afshari et al. 2013). Low fibrinogen levels have been associated with severity of PPH (Charbit, Mandelbrot et al. 2007) but further research is needed to establish a relationship with the haemorrhage of AFE. Both the RCOG and the European Society of Anaesthesiology recommend fibrinogen measurement as part of the assessment of any postpartum bleeding (Royal College of Obstetricians and Gynaecologists 2011b, Kozek-Langenecker, Afshari et al. 2013). It is important to replace major blood loss with red cells, plasma and platelets as soon as possible to avoid the dilutional effects of volume expanders.

The effectiveness of replacement and supportive therapy should be continuously monitored by the signs and symptoms of adequate oxygen delivery and tissue perfusion.

Additional management

A variety of other treatments and monitoring have been used for AFE (Kissko JMIII 2013, Tuffnell and Slemeck 2014): pulmonary vasodilators (inhaled nitric oxide, aerosolised prostacyclin); trans-oesophageal echocardiography; pulmonary artery catheter; plasma exchange transfusion; uterine artery embolisation; intralipid; strategies aimed at the inhibition of coagulation activation (antithrombin III concentrate, (activated) protein C, (recombinant) thrombomodulin, serine protease inhibitor FOY-305); cardiopulmonary bypass; extracorporeal membrane oxygenation; intra-aortic balloon counterpulsation. The majority of these are not routinely available on obstetric units, and none were used in any of the women who died. Most lack robust evidence and ongoing data collection about both women who die and women who survive AFE will be important to investigate their utility.

CONCLUSIONS

The majority of women who died from AFE collapsed suddenly and were not able to be resuscitated from their initial collapse. Care was considered exemplary in two cases, and in five cases, although improvements to care were noted, it was not felt that this would have made a difference to outcome. In four women improvements were noted which may have made a difference to outcome. The majority of key actions relate to management of sudden unexpected collapse and haemorrhage and maintaining skills in immediate life support is important in order to be prepared for treating women with this rare but extremely severe condition.

6. Lessons for Anaesthesia

Steve Yentis and Paul Clyburn on behalf of the MBRRACE-UK Anaesthetic chapter writing group

Chapter writing group members: Paul Clyburn, Diana Fothergill, Linda Ibbetson, Mike Kinsella, Marian Knight, Jenny Kurinczuk, Pamela Redmond, Steve Yentis

6.1. Key points

Subdural haematoma and cerebral venous sinus thrombosis are well recognised complications of dural puncture and pregnancy, respectively. Both should always be included in the differential diagnosis of persistent headache after dural tap or post-dural puncture headache.

Anaesthetists should practice drills for managing peri-operative airway crises including severe bronchospasm, mechanical obstruction, and difficult intubation/oesophageal intubation.

Pregnant or postpartum women recovering from anaesthesia require the same standard of postoperative monitoring, including documentation, as non-obstetric patients.

Anaesthetists must be ready at all times to deal with the adverse effects of local anaesthetics including accidental intrathecal or intravenous injection, and minimise the use of strong concentrations as far as possible.

Prompt action and good communication within and between teams are crucial when dealing with sudden unexpected catastrophes, especially when the diagnosis is not immediately clear.

All ambulance services should ensure their staff are trained in the relief of aortocaval compression during transfer of all pregnant women. How this was achieved must be routinely documented for each woman.

Units should ensure appropriate observations on all women. If an Early Warning Score system is in place, units should regularly audit their completion and ensure that abnormal results trigger the locally determined action.

All Serious Untoward Incident investigations of pregnant or postpartum women should include an obstetric anaesthetist.

6.2. Messages for anaesthetic care

Background

The reduction in deaths due to anaesthesia over the last 30 years is rightly seen as one of the successes of the Confidential Enquiry into Maternal Deaths. In the 1970s–1980s, the number of deaths directly due to anaesthesia fell from 30–50 in each triennium to 10–20, and since 2000 this figure has been 6–7. Along with the reduction in 'direct anaesthetic deaths' has come the difficulty in drawing wider lessons from examining the details of a small number of deaths, together with a realisation that focusing mainly on direct anaesthetic deaths risks missing important lessons highlighted in anaesthetic involvement in other deaths, both indirect and direct. Such lessons continue to be pertinent today: the importance of good communication amongst and between teams; the need to involve senior clinicians early; the provision of 'intensive care' beyond the intensive care unit; the difficulty (especially for junior staff) of recognising 'sick' women; the importance of involving clinicians with expertise in anaesthesia/critical care early; and the risks associated with an ageing and more obese obstetric population.

Obstetric anaesthetists who remember reports from the last 10 years and before will notice a change of emphasis in this chapter compared with previous ones. This change is reflected in the whole of the current programme of the Confidential Enquiry into Maternal Deaths, in which the focus is on preventable factors and lessons to be learned. For anaesthesia, this is particularly pertinent: first, there is now a relatively small number of deaths 'caused' by anaesthesia as discussed above; and second, deaths involving anaesthesia are almost invariably multifactorial and complex, and may even be impossible to categorise as an 'anaesthetic death' or one due to another cause. Thus this chapter is entitled *Lessons for*

Anaesthesia, and not *Anaesthetic Deaths* as in previous reports. It is important to appreciate that whilst a precise diagnosis and aetiology is useful in terms of epidemiological surveys and counselling of relatives and pregnant women, in practical terms the implications of a catastrophic event such as maternal death on the unit and staff, and the lessons that can be learnt from such events, are often generic.

There are several deaths discussed in this chapter, although only four have been defined as 'anaesthetic deaths' according to the criteria used in previous reports. The deaths discussed followed accidental dural puncture during neuraxial block or postoperative hypoventilation, were temporally linked to anaesthesia or concerned critical care. These are discussed further, below.

The women who died

Complications after post-dural puncture headache

Two women died who had experienced accidental dural taps while undergoing epidural cannula placement. One underwent a blood patch; the other was treated conservatively. Neither had hospital follow up or GP referral after discharge. Both women experienced headaches for some weeks before emergency presentations with what turned out to be cerebral vein thrombosis in one case and subdural haematomata in the other.

'Best practice' for the management of dural tap and post-dural puncture headache should include outpatient follow-up and notification of the woman's GP, in case subsequent complications occur (St George's Hospital 2014). The association between post-dural puncture headache and subdural haematoma is well described, even after intentional dural puncture e.g. spinal anaesthesia (Zeidan, Farhat et al. 2006), and subdural haematoma should always be amongst the differential diagnoses of postpartum headache. Cerebral venous sinus thrombosis occurring postpartum is also well described (Lockhart and Baysinger 2007). In both deaths, the key factor that might have saved these women's lives was prompt and appropriate imaging and transfer to a neurosurgical unit when they first presented; in the event this was arranged late, even with symptoms and signs suggesting their condition was very serious, and one woman was transferred to another centre with an inadequately skilled escort despite being semi-comatose.

The second death also raises the issue of who is responsible for prescribing postoperative heparin. The woman concerned did not receive thromboprophylaxis as per guidance despite recognised risk factors. Since the introduction of Royal College of Obstetricians and Gynaecologists guidelines on thromboprophylaxis following operative delivery (Royal College of Obstetricians and Gynaecologists 2009), use of such prophylactic measures are thought to be more widespread (Lewis, Cantwell et al. 2011). It is often the anaesthetist who prescribes postoperative heparin (or even gives the first dose) and so anaesthetists have a role in at least initiating appropriate preventative measures. Each unit must develop its own local protocols to ensure that all women in need of postoperative heparin do actually receive it, and any failure to achieve this must be seen as representing a failure in communication between the staff responsible for her postoperative care – including anaesthetists – and should be investigated.

Subdural haematoma and cerebral venous sinus thrombosis are well recognised complications of dural puncture and pregnancy, respectively. Both should always be included in the differential diagnosis of persistent headache after dural tap or after post-dural puncture headache.

Any woman who suffers a dural tap or post-dural puncture headache must be notified to her GP and routine follow-up arranged.

Any pregnant or recently pregnant woman with serious neurological symptoms/signs requires urgent appropriate early referral/imaging.

Inter-hospital transfer of a high-risk and/or a woman with a reduced level of consciousness requires appropriate medical (usually anaesthetic) involvement (Association of Anaesthetists of Great Britain and Ireland 2009).

The Obstetric Anaesthetists' Association website has a sample woman information sheet that can be given to women who suffer dural tap and/or PDPH, and their GPs (Obstetric Anaesthetists' Association 2011).

Hypoventilation during or after general anaesthesia

Two women experienced prolonged hypoventilation during or following general anaesthesia for treatment of postpartum haemorrhage. Both women were overweight. In one case, hypoventilation occurred during anaesthesia and may have resulted from undiagnosed bronchospasm. The tracheal tube was removed and replaced more than once. In another case, hypoventilation occurred after extubation and may have occurred for a prolonged period of time before re-intubation took place. Monitoring throughout this period was inadequate.

One death was initially attributed to anaphylaxis; however, during review for the Enquiry this was felt to be unlikely because peri-arrest (especially if defibrillation is used) or postmortem tryptase levels may be raised in the absence of anaphylaxis, such that values > 50–100 µg/l are required before a diagnosis of anaphylaxis is supported (Mayer, Krauskopf et al. 2011, McLean-Tooke, Goulding et al. 2014); the presence of low titres of specific IgE does not necessarily indicate anaphylaxis. Further aspects of the post-mortem examination of anaesthetic-related deaths are discussed in Appendix A3.

The evidence for bronchospasm, whatever the cause, was felt to be strong on clinical grounds, and yet this does not appear to have been considered. When tracheal intubation is followed by difficulty or failure to ventilate the lungs, it is important to consider accidental oesophageal intubation and/or a mechanical problem with the anaesthetic breathing system and tracheal tube; to this end, it is reasonable to remove the tracheal tube and replace it, since even with a good laryngoscopic view of the vocal cords, it is possible to take one's eye off the cords at the moment the tube is passed and for it to pass posteriorly into the oesophagus. However, repeated removals and replacements suggest that all attention was fixed on the tracheal tube, without consideration of first, the interruption of oxygen delivery that repeated airway manoeuvres cause, and second, other courses of action, in particular treating bronchospasm – which in a situation of near-impossible ventilation, must be very severe – with β-adrenergic agents and/or other drugs. The tube itself can be checked by passing a suction catheter down it and the anaesthetic breathing system itself can be the cause of obstruction in the absence of bronchospasm (Carter 2004) (best excluded by changing the breathing system e.g. using a self-inflating bag). It is also important to appreciate that in severe, life-threatening bronchospasm, ventilation may be inadequate to the point where no carbon dioxide is detectable in expired gases.

Fixation error, that is, remaining focussed on one initial diagnosis without considering others when treatment appears to be failing, is an ever-present danger in managing complications and crises (Yentis 2010) and has been commented on before in the context of the Confidential Enquiry into Maternal Deaths (Lewis, Cantwell et al. 2011). It is best avoided by repeated instances of 'standing back', during the event, and reviewing and recapping critical incidents including deaths, especially with other team members. Simulation, either in simple 'drills and skills' or formal simulation settings, may be helpful in reinforcing these aspects of management.

The end of anaesthesia and transfer to recovery and handover to nursing/midwifery staff is often a period when monitoring and documentation may be lacking. However, if the anaesthetist is involved for a prolonged period in the recovery of a woman, e.g. when she is monitored for ongoing blood loss after a postpartum haemorrhage or if there are concerns over immediate recovery or ventilation/oxygenation, then intra-operative standards of monitoring (including documentation) must be continued. It is particularly important to use pulse oximetry in any woman for whom there are concerns around respiratory function.

Capnography to measure carbon dioxide levels is easy if the trachea is intubated, but can also be used to monitor respiratory rate and also (though less accurately) end-tidal carbon dioxide, without intubation. Arterial blood gas analysis should be readily available in delivery suites and should be made use of in women with respiratory insufficiency; an indwelling arterial cannula is useful if repeated sampling is required.

When multiple problems happen together, it is all too easy to focus on one at the expense of the other(s), a further example of fixation error. Haemorrhage and hypovolaemia are still common causes of morbidity and death (see Chapter 4) and may additionally have contributed to the demise of this woman following bronchospasm.

All team members, including anaesthetists, must be aware of the risk of fixation error and teams must practise recapping and reviewing critical incidents, e.g. using simulation.

Anaesthetists should practise drills for peri-operative airway crises including severe bronchospasm, mechanical obstruction, and difficult intubation/oesophageal intubation (Henderson, Popat et al. 2004, Pratt 2012, Obstetric Anaesthetists' Association/Association of Anaesthetists of Great Britain and Ireland 2013).

All staff should be aware that peri- and post-mortem tryptase levels may be raised considerably above 'normal' without necessarily indicating anaphylaxis.

Pregnant or postpartum women recovering from anaesthesia require the same standard of postoperative monitoring, including documentation, as non-obstetric patients (Association of Anaesthetists of Great Britain and Ireland 2010, Association of Anaesthetists of Great Britain and Ireland 2013).

Anaesthetists must be able to recognise hypoventilation through a combination of clinical features and appropriate monitoring/ investigations.

Adequate volume must be given to replace previous and ongoing losses in women with haemorrhage.

Collapse after anaesthesia

Two women collapsed after anaesthesia; one following an epidural top-up and one following wound infiltration with 20 ml bupivacaine 0.5% at the end of a caesarean section. In both cases there was careful consideration of the possible differential diagnosis including early administration of Intralipid to counteract possible intravenous local anaesthetic, even though the role of local anaesthetic in the sequence of events was uncertain. There was prompt recognition and management of collapse, involvement of senior staff, and appropriate uterine displacement during CPR and peri-mortem caesarean section in the woman who collapsed before delivery. Ultimately the deaths were not attributed to anaesthesia.

The temporal association of these deaths with anaesthesia cannot be ignored, even if the anaesthetic was appropriate and competently administered. Every epidural top-up is potentially a dangerous one if local anaesthetic concentrations stronger than the ~0.1% in common current use are given. In these cases there was no evidence of drug error, though as is so often the case, this cannot be excluded completely. The likelihood of local anaesthetic toxicity was felt to be very low, both by the clinicians at the time (but who gave Intralipid anyway, which was considered reasonable by the reviewers) and the Enquiry reviewers. The clinical team exercised prompt management for both women and undertook a careful analysis of the possible differential diagnosis.

Anaesthetists must be ready at all times to deal with the adverse effects of local anaesthetics including accidental intrathecal or intravenous injection, and minimise the use of strong concentrations as far as possible.

Prompt action and good communication within and between teams are crucial when dealing with sudden unexpected catastrophes, especially when the diagnosis is not immediately clear.

All maternity units must have Intralipid available for treatment of accidental intravenous administration of local anaesthetic, and a protocol for its administration (Association of Anaesthetists of Great Britain and Ireland 2010).

Sudden collapse can occur at any time and the cause may not always be apparent.

Hyperkalaemia

A previously healthy woman developed pre-eclampsia and mild renal impairment and underwent uncomplicated elective caesarean section under spinal anaesthesia. Diclofenac was given rectally for postoperative analgesia. She was found to be hyperkalaemic several hours postoperatively but despite referral to critical care, no treatment was instituted despite a second test result confirming severe hyperkalaemia, with worsening renal function. She suffered a cardiac arrest a few hours later, from which she could not be resuscitated.

As this woman's death illustrates, once a seriously high potassium concentration has been detected, urgent treatment is required, with involvement of senior staff including anaesthetic/critical care.

Overall, this woman's antenatal care was good, with close monitoring and treatment of her hypertensive problems. However, what might pass as a normal creatinine concentration in a non-pregnant woman can indicate renal dysfunction in a pregnant woman, especially if it has increased significantly from previous values. Non-steroidal anti-inflammatory drugs (NSAIDs) can cause significant renal problems and are contraindicated in women known to have impaired renal function; it is not clear whether this woman's renal problems were exacerbated by use of NSAIDs.

Hyperkalaemia is a medical emergency and requires immediate treatment, ideally monitored in a critical care area.

Non-steroidal anti-inflammatory drugs are contra-indicated in impaired renal function.

Other anaesthetic lessons

Anaesthetic reviews were provided for all 203 deaths which underwent confidential enquiry for this report. A number of common themes emerged from the comments made during review, and these are summarised below.

Teamworking and crisis management

As in previous reports, there were several instances of issues related to human factors such as communication within/between teams, leadership and fixation error, though there were many instances where the evidence suggested excellent communication and teamwork, and of impressive reflection after the event at both individual and unit levels. The reviewers remain convinced that ongoing training in such issues, for example using simulation, is vital to further a culture of good teamwork within units, and that all units should facilitate such training within their staff.

Uterine displacement

In a number of deaths, there was no mention of either lateral maternal tilt or manual displacement of the uterus, to prevent or reduce aortocaval compression. This is a basic consideration in the management of all pregnant women especially those requiring resuscitation. It is likely that in some deaths, such manoeuvres were done but not recorded in the notes, but in other deaths, uterine displacement was specifically mentioned as instituted only midway through women's acute management. In particular, some women arriving at emergency departments having collapsed or become unwell out of hospital were specifically recorded as having been 'wedged' on arrival, the implication being that this had not been the case during transfer (transfer notes, when they referred to positioning, recording nothing or 'supine'). A very strong recommendation from this Enquiry is that all ambulance services must ensure training of their staff in the importance and relief of aortocaval compression during transfer of all pregnant women in the third trimester (Association of Ambulance Chief Executives 2013), and that documentation relating to transfer of pregnant women must specify the woman's position including whether she was tilted laterally, and the method used. This should be the focus of ongoing audit within ambulance services.

Use of early warning scores (EWS)

In several deaths, there was poor recording of basic observations that might have alerted staff earlier to women developing critical conditions, or a poor/inadequate response when parameters should have triggered further action but didn't. A major deficiency with regards to obstetric EWS systems in particular is the lack of direct evidence that they improve actual outcome, though a number of recent studies have attempted to investigate their usefulness and applicability (Singh, McGlennan et al. 2012, Carle, Alexander et al. 2013, Isaacs, Wee et al. 2014). Whilst accepting that the amount of high-level evidence supporting the use of obstetric EWS is limited, the reviewers agreed that it is important to ensure that women are appropriately monitored and their observations are recorded, and that having an EWS in place does at least require women to be monitored clinically. Further, if an EWS chart is being used, units must ensure through regular audit that

abnormal results do trigger the action that has been locally determined. The importance of observations is a recurring theme throughout this report.

Doses of intravenous induction agents

In a number of deaths, comment was made on the seemingly excessive dose of thiopental (and occasionally, propofol) used as anaesthetic induction agents in severely ill women, for example with septic or haemorrhagic shock. This might represent poor recognition of women's critical status or perhaps a relative unfamiliarity of anaesthetists (especially trainees) with thiopental, as a result of its greater cost and relatively short supply in recent years, and the current widespread use of propofol as the standard anaesthetic induction agent in most settings. Thus, the situation now exists whereby some trainees' only exposure to the use of thiopental is in the obstetric unit (Walker, Vaughton et al. 2012). This begs the question as to whether thiopental should continue as the drug of choice for obstetric anaesthesia (Rucklidge 2013).

Intra-operative temperature management

A number of deaths involving prolonged anaesthesia, especially when haemorrhage was a factor, caused reviewers to comment on the apparent lack of temperature measurement and any evidence of attempts to warm women. Recent guidance has stressed the importance of warming patients during surgery (National Institute for Health and Care Excellence 2008b) and this is especially important during prolonged surgery and haemorrhage.

Other anaesthetic management issues

Although overall, the standard of anaesthetic management was considered acceptable and in many deaths, exemplary, there were some deaths in which the reviewers commented on glaring deficiencies. Examples include prolonged postoperative hypoventilation noted above, and inadequate preparation for, and management of, massive blood loss in known high-risk women (including the lack of appropriate monitoring such as arterial/central venous cannulation and urine output measurement, and inadequate volume replacement). Such decision-making and skills should be core competencies of all anaesthetists managing such women.

Abdominal pain

Severe pain was a feature of several deaths from sepsis. It is worth noting here that anaesthetists may be requested to see/advise on pregnant women specifically to help with pain management, without necessarily being aware that abdominal pain in a pregnant woman (excluding labour pain or acute postoperative pain), that is severe enough to require parenteral opioids, may herald a serious underlying condition that may require senior input and/or escalation of care.

Serious Untoward Incident (SUI) investigations

It is notable that in some deaths, internal hospital enquiries were conducted that were felt by the reviewers to be inadequate in both scope and process. Of particular relevance to this chapter is the fact that many of these enquiries did not include an anaesthetist on the panel, even when the death concerned clearly involved anaesthetic management issues. Even if not considered an 'anaesthetic-related' death, anaesthetists are key members of such panels through their close involvement in the day-to-day running of maternity units, their expertise in critical illness and resuscitation, and their training in teamworking and human factors as a necessary part of anaesthetic practice. The exclusion of anaesthetists from such enquiries was judged to be totally unacceptable to the reviewers, who strongly recommend that all hospital SUI investigations of pregnant and postpartum women must include an obstetric anaesthetist as a matter of course, even when the cause of death is not thought to be centred around anaesthetic issues. External anaesthetic input may be required in deaths where this is thought to be the case, to ensure an independent opinion.

All units should maintain or initiate ongoing multi-disciplinary team training for their maternity staff.

All ambulance services should ensure their staff are trained in the relief of aortocaval compression during transfer of all pregnant women in the third trimester. How this was achieved must be routinely documented for each woman.

Units should ensure appropriate observations on all women. If an Early Warning Score system is in place, units should regularly audit their completion and ensure that abnormal results trigger the locally determined action.

Anaesthetists should be trained in the use of anaesthetic induction agents in critically ill women. Anaesthetic departments should consider whether thiopental should continue to be used in their maternity unit, and have written policies accordingly.

Normal maternal body temperature should be maintained during massive obstetric haemorrhage.

Pregnant women with abdominal pain severe enough to require parenteral opioids should be reviewed by senior medical staff including an anaesthetist.

All Serious Untoward Incident investigations of pregnant and postpartum women should include an obstetric anaesthetist.

CONCLUSIONS

The number of deaths identified as being directly due to anaesthesia remains low, and there were very many examples of good practice, as well as thoughtful and detailed reflection, exhibited by the anaesthetic teams involved in the women who are described in this report. However, there were also deaths in which the assessors considered that improvements to care might have reduced the severity of the women's condition, and in some instances, prevented the death. These improvements to care were not always in specific 'anaesthetic' management per se. As integral members of a multidisciplinary team, anaesthetists must continue to be involved in critical periods of peripartum care in high-risk women, and this requires them to be proactive rather than only reactive. The importance of human factors continues to be highlighted and anaesthetists must continue to support efforts to maintain or improve multidisciplinary team training in this regard. Finally, it behoves all hospitals to include anaesthetists in the review of serious incidents involving pregnant women.

7. Learning from neurological complications

Andrew Kelso and Adrian Wills on behalf of the MBRRACE-UK neurology chapter writing group

Chapter writing group members: Philippa Cox, Malcolm Griffiths, Vijay Jagannathan, Andrew Kelso, Marian Knight, Jenny Kurinczuk, Lucy MacKillop, Cathy Nelson-Piercy, Catherine Williamson, Adrian Wills, Debra Young.

7.1. Key messages

Epilepsy remains a high risk condition in pregnancy and should continue to be managed as such in antenatal and postnatal care.

Multi-agency evidence based operational guidance is urgently required to standardise and improve the care of pregnant women with epilepsy.

Services should be commissioned and organised to support joint obstetric and neurological care of women with epilepsy during pregnancy.

Pre-conception counselling for women with epilepsy is not always provided effectively and should be robustly delivered in all care settings on an opportunistic basis.

Sudden Unexpected Death in Epilepsy (SUDEP) remains the major cause of death in pregnant or postpartum women with epilepsy, and further research is required to inform risk reduction strategies.

Pregnancy should not alter the standard of care for women with stroke.

Neurological examination including assessment for neck stiffness is mandatory in all new onset headaches or headache with atypical features, particularly focal symptoms.

All women with stroke, pregnant or not, should be admitted to a Hyperacute Stroke Unit.

Neither pregnancy, caesarean section delivery nor the immediate postpartum state are absolute contraindications to thrombolysis (intravenous or intra-arterial), clot retrieval or craniectomy.

7.2. Caring for women with epilepsy

Andrew Kelso

Background

Epilepsy is the commonest serious neurological disease. One percent of the UK population is affected. Twenty three percent of people with epilepsy are women of child-bearing age (Joint Epilepsy Council of the UK and Ireland 2011). It has been suggested that epilepsy related mortality is increased with pregnancy (Adab, Kini et al. 2004). Previous enquiries into maternal deaths have highlighted the management of epilepsy as an area which should be improved (Lewis, Cantwell et al. 2011). In the CMACE report of 2011, the use of lamotrigine was associated with a number of maternal deaths, and it was recommended that there should be greater awareness of fluctuations in lamotrigine levels during pregnancy (Lewis, Cantwell et al. 2011). Other observations included a lack of pre-pregnancy counselling, delayed or no referral to an epilepsy specialist during pregnancy, lack of specific advice regarding bathing, and a lack of perception of epilepsy as a high-risk condition. The association of difficult social circumstances and epilepsy related deaths was highlighted.

Summary of the key findings 2009–12

In the period 2009–12, 14 maternal deaths during pregnancy or up to 42 days postpartum were attributable to epilepsy or seizures, a rate of 0.40 per 100,000 maternities (95% CI 0.22–0.68). These women are described further in Table 7.1 and their anti-epileptic drug (AED) use is summarised in Figure 7.1. The mortality rate is not statistically significantly different from the rate in 2006–08. It is disturbing that many of the concerns identified previously are still featured in this report. Sudden unexpected death in epilepsy (SUDEP) was the most common cause of death, in 12 women. Three deaths occurred in the immediate postpartum period. Common features of all deaths included:

- Women of child bearing age were not given pre-conception counselling
- Epilepsy nurses and other specialists were not available or used during pregnancy to help care for women with epilepsy
- There was a delay in referring pregnant women with epilepsy or seizures to specialist services, or barriers to them accessing those services
- Pregnant women with epilepsy were still not routinely identified as a high risk group (both in outpatient and inpatient settings), and appropriate precautions such as never placing them in single rooms were not always taken

Figure 7.1: Numbers of women prescribed different anti-epileptic drugs

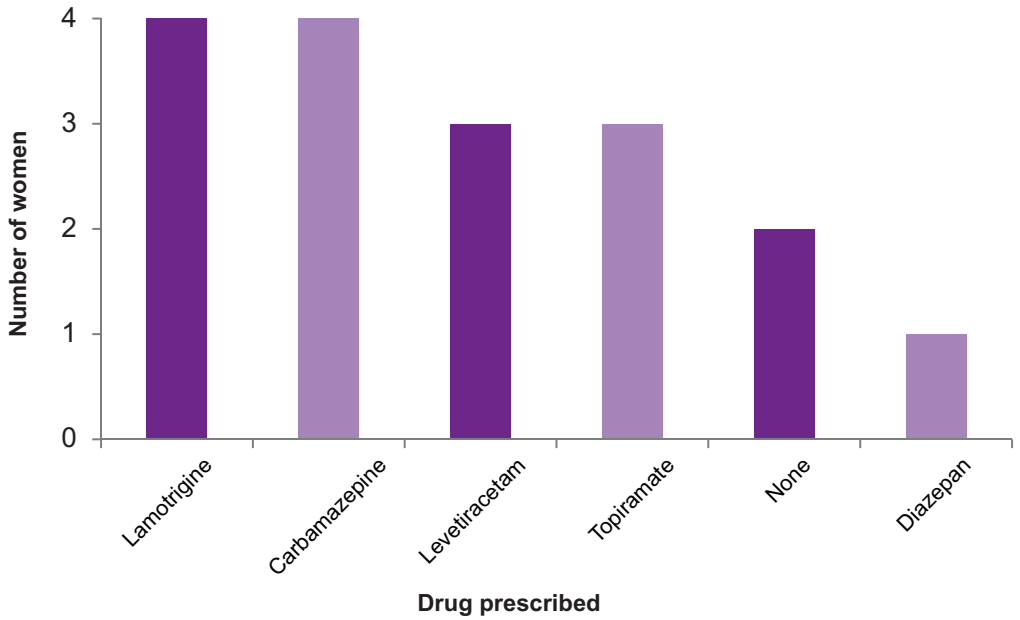

Table 7.1. Summary of the care of women with epilepsy who died

Cause of death	Medications	Pre-conception counselling?	Specialist review during pregnancy?	Was epilepsy controlled pre-pregnancy?	Improvements to care which may have changed outcome?
SUDEP	CBZ; TPM	No	Yes	No	Yes
SUDEP	none	No	No	N/A	Yes
Drowning	none	No	No	No	Yes
SUDEP	CBZ	No	No	No	Yes
Drowning	TPM; CBZ	No	No	Yes	Yes
SUDEP	CBZ	Yes	Yes	No	Yes
SUDEP	LTG	Yes	Yes	No	No
SUDEP	TPM; LEV	No	Yes	No	Yes
SUDEP	LTG	No	Yes	No	Yes
SUDEP	LTG	No	No	No	No
SUDEP	LTG	No	Yes	Yes	No
SUDEP	DZP	No	Yes	No	No
SUDEP	LEV	No	No	No	Yes
SUDEP	LEV	No	No	Yes	Yes

CBZ - Carbamazepine, TPM - Topiramate, LTG - Lamotrigine, LEV - Levetiracetam, DZP - diazepam.

In addition, the deaths of a further 12 women who died between 6 weeks and one year after the end of their pregnancy were attributed to epilepsy. Two women drowned, 6 women had SUDEP and 4 women died following other complications of seizures. Four of the 12 women died within the first six months after giving birth and two of these deaths were thought to be directly causally related to pregnancy.

Overview of care and lessons to be learned

Pre-conception counselling

Pre-conception counselling is recommended in national and international guidance on care of women with epilepsy (Harden, Hopp et al. 2009, National Institute for Health and Care Excellence 2012). Benefits include an analysis of treatment plans based upon most recent evidence, an opportunity to modify AED regimens to the safest possible combinations; for example, avoiding sodium valproate treatment where safely possible, using the lowest effective dose of as few AEDs as possible. Only two women (14%) received pre-conception counselling. Whilst the NHS Quality Outcome Framework (QOF) previously specified that women of childbearing age should receive annual disease specific advice regarding pregnancy, contraception and conception, this has been lacking in these deaths, and the removal of this requirement from the current QOF is of significant concern in light of these observations (BMA, NHS England et al. 2014).

Pre-conception counselling for women with epilepsy is widely advised, but is not always delivered effectively and should be robustly offered in all care settings on an opportunistic basis

NICE Epilepsy guideline CG137

(National Institute for Health and Care Excellence 2012)

Epilepsy nurses

The value of epilepsy nurses in the care of people with epilepsy has been extensively documented elsewhere (Epilepsy Action 2010). In brief, the added value of an epilepsy nurse includes a greater emphasis on psychosocial outcomes, improved treatment compliance, reduced emergency admissions as a result of seizures, better seizure control, and more frequent clinical reviews. It is possible (although unlikely) that epilepsy nurse involvement was not recorded adequately and was invisible to reviewers. However, a continued emphasis on epilepsy nurse involvement is likely to deliver significant health benefits to this group of women, and all antenatal services should identify a liaison epilepsy nurse to integrate into their routine antenatal service.

All antenatal services should identify a liaison epilepsy nurse to integrate into their routine antenatal service

Delays in referral

All women with a possible new diagnosis of epilepsy should be seen promptly by a specialist in epilepsy and the care of pregnant women with epilepsy should be shared between an epilepsy specialist or obstetric physician and an obstetrician

NICE Epilepsy guideline CG137

(National Institute for Health and Care Excellence 2012).

This was lacking in seven women (50%) in this review, and was a prominent missed opportunity to prevent death. One illustrative death is summarised here:

A woman with a diagnosis of childhood epilepsy and several years of seizure freedom off medication had a recurrence of tonic clonic seizures in pregnancy. Referral to an epilepsy specialist was made by her GP but she died from drowning associated with a tonic clonic seizure before she was reviewed, several months after her referral. She was not prescribed AEDs.

The contributing factors in this death are numerous, but a faster referral to, and response from, specialist services is very likely to have prevented her death. A telephone referral to make an appointment is prudent, with provision of an urgent appointment by the specialist service in response, in recognition of the importance of such referrals. Specialist epilepsy services are generally under-resourced nationally, but a focus on high risk groups (including pregnant women) is arguably a service which should be prioritised by commissioners, service planners and providers.

Two women died from drowning, as has been noted in previous reports, and the importance of advice not to bathe alone has to be emphasised again. Shared specialist care would provide an opportunity to reiterate that advice.

In hospital care

There were two unexpected deaths in hospital. One woman was not in hospital for medical reasons, the other was admitted for management of hyperemesis gravidarum. They were both accommodated in single rooms. This placed them at higher risk of unwitnessed seizures (and the associated risk of SUDEP) than if they were at home, when seizures are likely to be witnessed by family members. SUDEP is much more likely to occur when seizures are unwitnessed. A policy of never accommodating pregnant or recently pregnant women with epilepsy in single rooms is implemented in many centres (National Institute for Health and Care Excellence 2012) and national adherence to this advice may be life-saving. The woman with hyperemesis gravidarum did not see a senior doctor for her entire 5 day admission, and worse did not see any doctor for the three days prior to her death. She also had undiagnosed hypokalaemia, which may have been a co-factor in her death. Another factor may have been inability to ingest her drugs due to vomiting. Pregnant women with epilepsy are still not always regarded as being high-risk, and they require diligent medical and nursing support during hospital admissions.

Pregnant or recently pregnant women with epilepsy should never be accommodated in single rooms.

NICE Epilepsy guideline CG137

(National Institute for Health and Care Excellence 2012)

Postpartum care

Three women died in the immediate postpartum period, and it is recognised that mothers with epilepsy are at higher risk of breakthrough seizures at this time (Walker, Permezel et al. 2009). Reasons for this are varied, including sleep deprivation, stress, and altered treatment compliance, and it seems likely that in some women biological changes (e.g. hormonal or neurochemical factors) may also be relevant. Women with epilepsy and their families should be specifically advised of the risks of epilepsy in the postpartum period, and ways to mitigate these risks, including not sleeping or bathing alone.

Sudden unexplained death in epilepsy

Most of the deaths in this series (12/14) (86%) were from sudden unexplained death in epilepsy (SUDEP). SUDEP is recognised as a major cause of death in epilepsy, and whilst epidemiological evidence is lacking, there are significant concerns that SUDEP might be more common in pregnancy (Edey, Moran et al. 2014). Pregnant women with epilepsy and their relatives (as for all patients with epilepsy) should be counselled about SUDEP, and appropriate first aid advice given. Modifiable factors that can mitigate the risk of SUDEP (not sleeping alone, AED compliance, first aid for witnessed seizures) should be addressed robustly, including in the postpartum period. More high quality research is urgently required to address the suggestion that SUDEP is increased in pregnancy, and to inform risk mitigation strategies.

SUDEP remains the major cause of death in pregnant or postpartum women with epilepsy, and further research is required to inform risk reduction strategies

Anti-epileptic drugs and maternal death

There has been a clear association between the use of lamotrigine and maternal death in previous enquiries (Lewis, Cantwell et al. 2011), but is not clear if this is an effect of the drug itself (it is known to have labile metabolism during pregnancy, with large fluctuations in bioavailablility (Pennell, Peng et al. 2008)), the way in which it is used during pregnancy (some mothers will require a dose increase), or the types of epilepsies treated with lamotrigine. Fewer deaths were associated with lamotrigine in this series, but this has not resulted in a reduction in maternal deaths, and indicates that other factors are also important in risk of death in these women. A greater understanding of the metabolism and effects of anti-epileptic drugs during pregnancy is urgently required, and may partly be answered by the current EMPIRE study (EMPIRE 2014), and by further development of pregnancy and epilepsy registries (Meador, Pennell et al. 2008). Women who died clearly still had concerns about taking anti-epileptic drugs in pregnancy because of perceived or actual risks to the baby; this is another area in which the involvement of epilepsy nurses in pregnancy care is likely to prove beneficial.

Socioeconomic factors

Many of these women came from socio-demographic groups known to have access issues with respect to healthcare. These groups include women who speak little or no English, had moved to the UK from

another country, women with drug and addiction problems, or those from chaotic social backgrounds. Management of epilepsy in these populations remains challenging, and they should be identified as requiring particularly intensive support from obstetric services.

The way forward

Improvements in care were noted which may have made a difference to the outcome for ten of these women. Many of the same recommendations for improvements in care made in previous enquiries are still seen. What then is the best course of action from this point? There are several guidelines and a wide range of published evidence and opinion available regarding the care of women of child-bearing potential with epilepsy, but there is a lack of objective and agreed operational guidance on the care of pregnant women with epilepsy. A joint guideline with input from obstetric, midwifery, epilepsy, general practice and third sector stakeholders (including, for example, the Royal College of Obstetricians and Gynaecologists, Royal College of Midwives, Association of British Neurologists, Royal Colleges of Physicians, Royal College of General Practitioners, Epilepsy Action, Epilepsy Society, Epilepsy Bereaved) might go some way to move this forward. Implementation of such a guideline would obviously be a matter for the relevant agencies and hospitals, but the use of a standard and agreed care plan for all pregnant women with epilepsy might standardise and improve the quality of care. That we can provide better care for pregnant women with epilepsy is clear. Translating this need into fewer deaths is the challenge that faces us all.

Multi-agency evidence based operational guidance is urgently required to standardise and improve the care of pregnant women with epilepsy.

7.3. Messages for stroke care

Adrian Wills

Intracerebral and subarachnoid haemorrhage

Twenty-six women died of intracranial haemorrhage in the UK and Ireland between 2009 and 2012, 0.75 per 100 000 maternities overall. Thirteen had subarachnoid haemorrhage and thirteen had intracerebral bleeds. Several of the intracerebral bleeds occurred in association with labour. The majority of women presented with sudden collapse or severe headache with rapid deterioration and subsequent death. In most deaths there were no previous symptoms to alert the healthcare providers that they were at risk of an intracranial haemorrhage. However, neurological examination including assessment for neck stiffness is mandatory in all new onset headaches or headache with atypical features, particularly focal symptoms. Beware of misdiagnosing migraine in these women.

A woman who was a known migraine sufferer was seen on the maternity unit. She was complaining of headache, blurred vision and dizziness. On examination there were no signs of pre-eclampsia. No neurological examination was documented and in particular there was no record of the absence or presence of neck stiffness. She was discharged home. She was re-admitted one week later following a collapse and cardiac arrest. A CT scan showed diffuse subarachnoid haemorrhage. She was transferred to a regional neuroscience centre, but in spite of exemplary supportive care, she died a few days after admission. Her initial headache was probably a first bleed followed by a catastrophic re-bleed one week later.

Close liaison between teams, including obstetric, neurosurgical and neurological, is essential to improve outcomes for women with subarachnoid haemorrhage (National Confidential Enquiry into Patient Outcome and Death 2013). In women with subarachnoid haemorrhage, the neurosurgical team may recommend administration of Nimodipine (to prevent vasospasm), prior to transfer to the Regional Neuroscience Centre.

A woman presented to the emergency department a few days postpartum. She complained of sudden onset headache. In spite of the presence of meningeal irritation she was discharged home following review by a medical SHO (core trainee). She re-presented two days later with continuing severe headache and neck stiffness. A CT scan showed a diffuse subarachnoid bleed from an anterior cerebral artery aneurysm. She experienced a rapid decline in conscious level probably due to vasospasm rather than re-bleeding. In spite of administration of Nimodipine and intracranial pressure monitoring she continued to deteriorate and died.

A hypertensive woman was admitted for induction of labour with dinoprostone gel. After delivery of the baby's anterior shoulder she received an injection of syntometrine, following which she complained of severe headache and then suffered a seizure followed by asystole. After successful resuscitation a CT scan showed massive subarachnoid haemorrhage. She died shortly afterwards.

Whilst it is not clear that administration of syntometrine contributed to the occurrence of subarachnoid haemorrhage in this woman, NICE guidance on Hypertension in Pregnancy and Intrapartum Care recommends that women should receive syntocinon 10 International Units for prophylaxis of the third stage and not syntometrine, because of the association with nausea, vomiting and raised blood pressure with ergometrine (National Institute for Health and Care Excellence 2010).

Neurological examination including assessment for neck stiffness is mandatory in all new onset headaches or headache with atypical features, particularly focal symptoms.

In women with subarachnoid haemorrhage, nimodipine may be recommended to prevent vasospasm and hence the associated neurological deterioration.

Oxytocin alone (without ergometrine) is the drug of choice for the routine active management of the third stage of labour.

NICE Hypertension in pregnancy guideline CG107, NICE Intrapartum Care guideline CG55

(National Institute for Health and Care Excellence 2007b, National Institute for Health and Care Excellence 2010)

Ischaemic stroke

Death from ischaemic stroke in pregnancy in the UK and Ireland between 2009 and 2012 was very uncommon, with a mortality rate of 0.03 per 100 000 maternities. There were a number of recurrent themes identified in common with women who died from cerebral haemorrhage, the majority based around the key premise that pregnancy should not alter the standard of care for women with stroke. Time to treatment is of the essence in achieving good outcomes in stroke care, and thus all women with stroke, pregnant or not, should be admitted to a Hyperacute Stroke Unit. Any neurological disorder in a woman with Glasgow Coma Score of <9/15 mandates airway protection, prior to transfer. Neither pregnancy, caesarean section delivery nor the immediate postpartum state are absolute contraindications to thrombolysis (intravenous or intra-arterial), clot retrieval or craniectomy. The potential risks and benefits need to be assessed as in any other woman, and this is best undertaken in the context of senior level discussion.

A woman developed headache and lower limb weakness several days after delivery. There was no previous history of migraine. In spite of this her GP diagnosed migraine and reassured her. Six hours later she developed an exacerbation of her symptoms. She had a dense right sided weakness and reduced conscious level. A CT scan showed cerebral artery thrombosis. Thrombolysis was withheld because of concerns about bleeding risk related to prior caesarean section. A repeat CT scan showed a large cerebral infarct with sulcal effacement. Craniectomy was not considered until two days later by which time she had developed fixed dilated pupils.

Neurological disorders do cause anxiety in non-neurologists and this may be exacerbated by the additional complication of pregnancy. Midwives should have no hesitation in escalating beyond the obstetric registrar or GP if they are concerned about a particular woman with neurological symptoms. Similarly juniors should not hesitate to seek senior input. As has been discussed in previous chapters, emergency perimortem caesarean section may improve the mother's prognosis following an episode of collapse, and this is also the case following acute stroke.

Pregnancy should not alter the standard of care for stroke.

All women, pregnant or not, should be admitted to a Hyperacute Stroke Unit.

NICE Stroke guideline CG68

(National Institute for Health and Care Excellence 2008c)

Neither pregnancy, caesarean section delivery nor the immediate postpartum state are absolute contraindications to thrombolysis (intravenous or intra-arterial), clot retrieval or craniectomy.

7.4. Women with other neurological complications

Women who died from infections of the nervous system are discussed in chapter 3. Two other women died from rare neurological complications. For one woman there were numerous delays in her care which may have made a difference to outcome, including the availability of a bed at a regional neuroscience centre; themes also observed amongst women with intracranial haemorrhage. Another woman presented several times with neurological symptoms over two to three weeks before undergoing a neurological examination and diagnosis of a demyelinating disorder. Although it is unlikely that earlier intervention in this context would have changed her outcome significantly, there was a small window of opportunity for earlier diagnosis and intervention, and neurological examination should be essential in all women presenting with neurological symptoms during pregnancy.

CONCLUSIONS

Neurological disease remains an important cause of maternal death. A number of important lessons for future care of women with epilepsy were identified; in 10 (71%) of the 14 women whose care was reviewed, improvements in care were noted which may have made a difference to their outcome. In a further 2 women (14%), improvements in care were noted but these were not felt to have made a difference to outcome. In two women (14%) care was thought to be good and no improvements noted. This highlights the urgent need for multidisciplinary guidance on the care of women with epilepsy in pregnancy.

In contrast, the care of 15 women with stroke (56%) the care was felt to be good, with no improvements noted. In five women (19%) improvements in care were noted which may have made a difference to outcome, emphasising the importance of specialist stroke care for pregnant or postpartum women with stroke.

8. Caring for women with other medical complications

Cathy Nelson-Piercy, Lucy MacKillop, Catherine Williamson, Malcolm Griffiths on behalf of the MBRRACE-UK Medical complications chapter writing group

Chapter writing group members: Philippa Cox, William Fawcett, Malcolm Griffiths, Vijay Jagannathan, Marian Knight, Jenny Kurinczuk, Lucy MacKillop, Cathy Nelson-Piercy, Catherine Williamson, Debra Young

8.1. Key messages

Women with pre-existing medical conditions should have pre-pregnancy counselling by doctors with experience of managing their disorder in pregnancy.

Women with medical disorders in pregnancy should have access to a coordinated multidisciplinary obstetric and medical clinic, thereby avoiding the need to attend multiple appointments and poor communication between senior specialists responsible for their care.

Pregnant women with medical conditions require an individualised care plan made together by members of the multidisciplinary team including an obstetrician, obstetric anaesthetist, obstetric or specialty physician, surgeon and members of the allied health professions as appropriate.

Appropriately trained senior physicians should be involved in the care of pregnant and post partum women with new onset symptoms suggestive of or known underlying medical disorders.

All pregnant women presenting with acute respiratory compromise require urgent assessment by a physician and an anaesthetist or intensive care specialist.

Routine advice for pregnant women with diabetes mellitus should include the increased risk of hypoglycaemia and education of family members about optimal management of this condition.

All women with proteinuria should have this quantified and further investigated if found to be significant.

Super morbidly obese pregnant women should be looked after by specialist multidisciplinary teams.

Senior surgical opinion is essential when dealing with surgical complications in pregnancy or postpartum and should not be delayed by team hierarchy. Early discussion between consultant obstetrician and consultant surgeon is vital.

8.2. Respiratory Disease

There were 10 deaths (not including late deaths) attributable to respiratory diseases in this four-year period. This period covers the epidemic of H1N1 influenza; the 36 deaths caused by influenza are discussed separately in the sepsis chapter and are not included here.

Asthma remains the most common respiratory cause of maternal death, present in three deaths (0.1 per 100000 maternities). This is comparable to previous enquiries (0.22 per 100000 maternities 2006–08) (Lewis, Cantwell et al. 2011).

All three women dying from asthma were smokers although two were reported to have given up in the first trimester. Two women died early in pregnancy. It is not known whether these women had pre-pregnancy counselling or were compliant with their medication. Due to unfounded concerns over medication effects on the growing fetus, it has been shown in many studies that a significant proportion of women will cease their regular medications when they find out they are pregnant. It is imperative that women are counselled before pregnancy about the safety of asthma medications, but also the message that active treatment of asthma using pharmacological therapy is safe at any gestation, should be emphasised at every contact with medical professionals. A recent report of the national asthma audit by the Royal College of Physicians highlights the lack of education amongst women and healthcare providers as a key failing and reason for the continued deaths each year from this treatable disease (Royal College of Physicians 2014).

Moreover, special consideration should be given to the unpredictable nature of the effects of pregnancy on asthma. This is highlighted in the BTS/SIGN guidelines which list pregnancy as a criterion for admission to hospital despite good peak expiratory flow rate (PEFR), and early referral to a critical care physician for pregnant women with acute severe asthma (BTS / SIGN 2014).

The third woman had multiple medical issues including hypertension, a high BMI and poorly controlled asthma with a history of poor compliance, and refusal to attend hospital. She continued to smoke and drink alcohol through her pregnancy. She was appropriately seen by her midwife, obstetrician, general practitioner and respiratory physician but there was disjointed care and poor communication between these healthcare professionals. For example, it was noted in the first trimester by her respiratory physician that her asthma had worsened since commencing labetolol (a beta-blocker; a class of drug that is known to cause bronchoconstriction). A letter was sent to the GP requesting it be changed in favour of methyldopa but it was not until well into the second trimester and more than two months after the review that she was switched to methyldopa. This highlights again the importance of multidisciplinary and timely management of pregnant women with dynamic and often unpredictable physiology. It also highlights the need for all physicians to have a working knowledge of the common medical problems in pregnancy so they feel confident to change medications if appropriate immediately. Requests for GPs to instigate or change drug therapy introduce extra steps and delays for the woman, and are not always appropriate.

Women should be advised of the importance of maintaining good control of their asthma during pregnancy to avoid problems for both mother and baby.

Counsel women with asthma regarding the importance and safety of continuing their asthma medications during pregnancy to ensure good asthma control.

SIGN/BTS Asthma Guideline 101 (BTS / SIGN 2014)

Two women died of cystic fibrosis (CF), one in the first trimester and one nine months postpartum. There were no CF deaths between 2006–08 (Lewis, Cantwell et al. 2011) and one in 2003–05 (Lewis 2007). This might be a result of an increase in women with severe CF becoming pregnant due to improved therapies and survival. Awareness of the importance of contraceptive advice in women with severe CF is vital, and there cannot be a reliance on subfertility due to low BMI as a substitute for effective contraception (Edenborough, Borgo et al. 2008).

The other six deaths from predominantly respiratory causes include a number of rare conditions. While three deaths were unheralded and it is likely that little could have been done to prevent them; the recurring theme among the other deaths is that the severity (and by inference, the knowledge) of the disorder and the effect of pregnancy physiology on the condition were under appreciated by both maternity services and the respiratory physicians caring for these women. In several deaths, there were multiple contacts with multiple specialties but all assumed the other had overall management of the woman. There was a lack of multidisciplinary plans of care. Furthermore, there was a failure to appreciate the severity of respiratory failure on admission leading to unacceptable delays in escalating treatment.

In four deaths (including one late death), underlying pulmonary hypertension (secondary to their respiratory disease), known to be associated with a very high mortality rate in pregnancy, was not screened for in early pregnancy despite significant lung disease. While the knowledge of co-existent pulmonary hypertension might not have changed the outcome of the pregnancy; the lack of knowledge prohibited full counselling of the women to explain the significant risks to life in continuing the pregnancy. It is likely that in all these women, pulmonary hypertension contributed to their demise.

Women with severe lung disease require screening for pulmonary hypertension prior to pregnancy.

8.3. Liver disease

There were five deaths attributed to liver disease. Two women had fulminant liver failure.

A previously well woman developed severe hepatic derangement in mid pregnancy, one week following antibiotic treatment. She presented with a two day history of cough, dark urine and headache and was noted to be very sick and febrile. Despite excellent care, timely transfer to high-dependency and then ITU and liver transplant she continued to deteriorate and died.

Unfortunately a postmortem was not performed, but investigations performed prior to death did not provide an explanation for her deterioration. The second woman had liver failure secondary to accidental paracetamol overdose; she did not realise her analgesia contained paracetamol. This death emphasises the importance of informing women about the paracetamol content of combined preparations that are used for analgesia in pregnancy, e.g. co-codamol or co-dydramol.

Features predictive of death or need for transplant are acidosis and encephalopathy (Westbrook, Yeoman et al. 2010). Both women were noted to be acidotic and confused soon after admission. It is essential to recognise the high risk of hepatic deterioration in women with hepatic impairment, confusion and acidosis as rapid transfer to a Liver Unit could be life-saving. Unfortunately the second woman was not transferred to a Liver Unit despite the ITU consultant contacting three separate referral centres. This was due to lack of availability of beds. If she had been transferred to a Liver Unit, this woman who probably took an accidental overdose could have been assessed for liver transplant.

One woman had congenital biliary atresia that had been treated with a Kasai procedure as a baby. She had known splenomegaly with splenic varices and, as noted in the aneurysm section, died in mid pregnancy of a ruptured splenic artery aneurysm, a rare complication of this condition in pregnant women (Selo-Ojeme and Welch 2003). She was well managed by the combined hepatology/high-risk antenatal team, but she did not follow advice to continue taking propranolol during pregnancy. She did not receive pre-pregnancy counselling and there was a nine week delay in haematology review for low platelets. While these omissions did not contribute to her death, increased medical input would have provided the opportunity to emphasise the importance of taking propranolol during pregnancy.

A woman with known cirrhosis had haematemesis secondary to bleeding oesophageal varices. Her care was coordinated between a specialist liver unit, a stand-alone maternity unit and a general hospital. There was good care from the multidisciplinary team of specialists, but it is likely that the need to attend three different hospitals contributed to her failure to attend all appointments. It was not clear whether she was treated with a beta-blocker and her failure to attend hospital appointments may have meant the opportunity to encourage her to take potentially life-saving treatment was missed.

Another woman with cirrhosis was awaiting liver transplant when she became pregnant against medical advice. She had been seen by her hepatologist and maternal medicine specialist during pregnancy and oesophageal varices had been excluded. She died of a ruptured splenic artery aneurysm in mid pregnancy (see aneurysm section).

Women with hepatic failure, encephalopathy and metabolic acidosis in pregnancy should be transferred to a specialist Liver Unit for consideration of liver transplant

Ensure that women taking analgesia are aware that some combined preparations contain paracetamol.

8.4. Endocrine disease

Phaeochromocytoma

There were two deaths in women with phaeochromocytoma. Both had normal blood pressure measurements during pregnancy. One complained of palpitations during pregnancy, but neither had any other clinical features suggestive of phaeochromocytoma earlier in pregnancy. Both women presented with severe back pain and vomiting and were noted to have hypertension, tachycardia, hyperglycaemia and to be very unwell. The obstetric team tried to contact the medical registrar several times to review one woman, and could not do so. The diagnosis of phaeochromocytoma was not considered in either woman, and in one woman there was a significant delay in treating marked hypertension despite pre-eclampsia being mentioned as a possible diagnosis. It is unacceptable for medical staff to be unavailable for acutely unwell pregnant women, and it is surprising that a senior physician was not called when the registrar did not respond to multiple calls. This death emphasises the importance of ensuring that senior medical staff are available to review acutely unwell pregnant women in a timely manner. The fact that both women had hyperglycaemia when they presented is consistent with a recent series in which four out of six women with phaeochromocytoma in pregnancy had raised plasma glucose (Oliva, Angelos et al. 2010).

Consider phaeochromocytoma in women with atypical, severe hypertension in pregnancy.

If a woman with one autoimmune disease becomes unwell in pregnancy, consider another autoimmune condition.

Thyroid disease

Two women that died had severe hyperemesis gravidarum with marked biochemical thyrotoxicosis One woman was well managed in a joint obstetric/endocrine clinic and had been admitted in an attempt to optimise treatment. She died in the course of exemplary treatment, illustrating the difficulty of managing severe thyrotoxicosis in women with hyperemesis gravidarum. The second woman had persistent hypokalaemia, yet the medical staff managing her did not give anti-emetics, nor potassium replacement despite serum levels of 2.6–2.8mmol/L. This woman was also persistently tachycardic, but there was no evidence that the medical team performed appropriate investigations to distinguish between the diagnoses of new-onset thyrotoxicosis or severe dehydration and hypokalaemia secondary to hyperemesis. Both thyroid storm and hypokalaemia are potentially fatal disorders, and establishing the correct diagnosis, and initiating appropriate treatment for hypokalaemia (Marti, Schwarz et al. 2014) represents the basic standard of care. Note that another woman, discussed in chapter 7, died from SUDEP in association with hyperemesis and hypokalaemia.

Hypokalaemia (<3mmol/L) can cause arrhythmia and must be corrected.

Women with hyperemesis gravidarum should be treated with antiemetic therapy, thiamine, low molecular weight heparin and electrolyte disturbance, particularly hypokalaemia, should be corrected. (Jarvis and Nelson-Piercy 2011)

Diabetes

Six women had type 1 diabetes mellitus (T1DM). Five had established T1DM, and another was assumed to have developed a first episode of diabetic ketoacidosis several months after delivery. This woman did not have any clinical features suggestive of diabetes during her pregnancy or in the intervening period. One young woman with T1DM had a history of alcohol dependence and chronic pancreatitis and was not aware that she was pregnant. She died from complications related to her pancreatitis.

The other four women had long-standing T1DM and were managed in joint antenatal diabetic clinics. Two died of ketoacidosis, one drowned as a result of likely hypoglycaemia and one died suddenly of presumed, 'diabetic dead in bed' syndrome. Comments in the notes indicated that all four women had poor control prior to conception and during pregnancy. However, they were all engaging with the antenatal diabetic service, and these deaths reflect the difficulty in achieving good glycaemic control in pregnant women with long-standing diabetes mellitus. The pre-pregnancy HbA1c was >10% in the two women where it was available. The women all had hypoglycaemic episodes during pregnancy, likely due to attempting to optimise their glycaemic control. Three women had such severe hypoglycaemia that they were admitted for optimisation of control.

The woman that drowned, probably due to hypoglycaemia, had suffered several episodes of hypoglycaemia throughout the first trimester and it was not clear whether she had been advised about the risks of bathing alone. This death underlies the importance of emphasising the risks of hypoglycaemia to women with T1DM (CEMACH 2005).

One woman with a strong family history of autoimmune disorders developed Addison's disease a few weeks after delivery. She presented with hypoglycaemia and hyponatraemia and was well managed. She had been advised about increasing her insulin dose if she increased glucocorticoids in the context of intercurrent infections. She developed diabetic ketoacidosis some months after delivery. Her care appeared to be excellent and this death emphasises how rapidly women with ketoacidosis can deteriorate. The recent diagnosis of Addison's disease and the need for glucocorticoid treatment may have increased her susceptibility to hyperglycaemia and associated ketosis.

Women with long-standing diabetes mellitus are at increased risk of severe hypoglycaemia and diabetic ketoacidosis.

8.5. Connective Tissue Disorders

There were two deaths from systemic lupus erythematosus (SLE) plus another probable SLE death, one from anti-phospholipid syndrome (APS), and two from probable Ehlers Danlos syndrome type IV. In addition there were two late deaths from SLE and probable scleroderma. There was a theme of postpartum deterioration and this often coincided with lack of clarity about which healthcare professionals (GPs, obstetricians, physicians) took responsibility for care. In some deaths there was evidence of either no or late physician involvement.

A multiparous woman with a previous uncomplicated pregnancy died postnatally from SLE. The diagnosis of lupus nephritis was missed despite clear pointers during her antenatal care. Heavy proteinuria was repeatedly and wrongly attributed to urinary tract infection, despite coincident severe anaemia not responding to oral iron and profound hypoalbuminaemia. Once the diagnosis of SLE was made postpartum, treatment was appropriate, but despite this she deteriorated rapidly and died.

Note the recent Patient Safety Alert released by NHS England, highlighting possible misinterpretation of tests for proteinuria (NHS England 2014b); results from a spot Protein Creatinine Ratio (PCR) were misinterpreted as being the result for a 24 hour urine collection. Whilst there is no indication that this occurred in this death, it is important that care is exercised when interpreting different urine protein tests.

Persistent heavy proteinuria in early pregnancy requires investigation for underlying renal disease with quantification (using protein creatinine ratio) and serum creatinine as a minimum. Assuming a diagnosis of urinary tract infection (even when this is not confirmed with urine culture results) risks missing underlying renal disease, which has serious implications for the pregnancy and long term health of the mother.

All women with proteinuria should have this quantified and further investigated if found to be significant.

A woman with thrombotic anti-phospholipid syndrome in association with connective tissue disease died following a short postnatal illness after a pregnancy complicated by early onset pre-eclampsia. She was not referred back to a physician for assessment of new onset upper abdominal and chest pain. The postmortem was inadequate but the clinical features suggested a postnatal flare of connective tissue disease.

A woman with anti-phospholipid syndrome died of severe SLE affecting her heart and kidneys soon after a first trimester miscarriage. Her clinical course and deterioration was very dramatic illustrating again the tendency for connective tissue disorders to worsen after delivery / following miscarriage. A primiparous woman presented with severe multiorgan involvement of SLE in mid-pregnancy having discontinued her maintenance immunosuppression prior to conception. Her clinical course was complicated by spontaneous preterm delivery and sepsis which was the final cause of death as is common in SLE (Yang, Ye et al. 2012).

There were two deaths from probable Ehlers-Danlos syndrome type IV. A multiparous woman with an uncomplicated previous pregnancy died of intra-abdominal haemorrhage from visceral rupture despite valiant efforts by specialist surgeons following appropriate transfer to another hospital. An astute and thorough pathologist noted that the extent of the intra-abdominal trauma was out of proportion to the injury sustained, correlated other clinical features, an unusual past medical history, suspected an underlying connective tissue disorder and sent fibroblasts from a skin biopsy which allowed a definitive diagnosis and appropriate screening of surviving relatives. The other woman collapsed in late pregnancy from a ruptured splenic artery. The autopsy showed irregular medial degeneration with loss of elastic tissue and an increase in acid mucopolysaccharides and focal intimal thickening. These changes were present in the aorta, iliac arteries and splenic artery which also showed aneurysmal dilatation, indicating medial degeneration possibly due to unrecognised Ehlers-Danlos syndrome type IV. This rare subtype is well recognized to be associated with increased risks of visceral and large vessel rupture in pregnancy (Hammond and Oligbo 2012).

A woman with no previous history of hypertension developed malignant hypertension post partum. She was appropriately investigated by nephrologists, but died of cardiac tamponade secondary to severe probably autoimmune arteriopathy most likely due to scleroderma. The postnatal review did not take place until nine weeks after delivery and only then because she had developed symptoms of severe hypertension. Earlier review may have led to earlier referral but is unlikely to have changed the outcome as the disease course was aggressive despite appropriate management with immunosuppression.

Connective tissue disorders (CTD) can flare or present postpartum and this should be remembered when women present with unusual symptoms in or after the postnatal period.

Physicians should stress the importance of continuing immunosuppression before and during pregnancy in CTD since active disease at conception increases adverse outcomes. Flares should be promptly and aggressively treated with drugs appropriate to the severity of the flare. (Ateka-Barrutia and Nelson-Piercy 2013)

8.6. Haematological Disorders

There were four deaths from haematological disorders (two from sickle cell disease; one from immune thrombocytopenic purpura (ITP) and one from thrombotic thrombocytopenic purpura (TTP)). In addition there were two other deaths in women with sickle cell disease included in other chapters. One woman who died from an intracerebral haemorrhage is included in the neurology chapter, and one who died from genital tract sepsis is included in the sepsis chapter.

Two other deaths occurred from sickle cell disease amongst an estimated 440 women with sickle cell disease who gave birth between 2009 and 2012 (Knight, McClymont et al. 2012). In both the deaths from sickle cell disease, which occurred in the context of admission with sickle cell crisis in early pregnancy, the assessors identified a lack of joined up multidisciplinary care, delays in recognising the severity of the clinical condition and subsequent deterioration as potential contributors to the deaths. There were also delays before the women received blood transfusions or exchange transfusion and transfer to intensive care. One woman had acute chest syndrome which is an indication for exchange transfusion. Both women had previous poor obstetric histories that should have prompted review of the notes from these previous pregnancies, post pregnancy and pre–pregnancy counselling regarding potential problems in pregnancy and a plan for care in a unit with obstetric and haematology teams with expertise in the management of sickle cell disease in pregnancy. In one woman care for her sickle cell disease was in another hospital.

Women admitted with sickle cell crisis should be looked after by the multidisciplinary team, involving obstetricians, midwives, haematologists and anaesthetists.

RCOG Green-top guideline 61

(Royal College of Obstetricians and Gynaecologists 2011d)

In the woman with TTP, who died mid pregnancy, there were many contacts with healthcare professionals with unusual, including neurological, symptoms, which did not prompt further investigations leading to a delay in making the correct diagnosis. TTP is rare and often fatal, but it is more common in pregnancy, easily diagnosed with a blood film and requires urgent treatment with plasmapheresis.

A woman diagnosed with ITP in late pregnancy was appropriately treated but died postpartum with severe anaemia as well as thrombocytopenia and may actually have had Evan's syndrome (autoimmune haemolytic anaemia in conjunction with immune-mediated thrombocytopenia).

8.7. Gastroenterological disorders

One woman died solely from the complications of her super morbid obesity. Her antenatal and intrapartum care and planning was excellent despite many complex comorbidities and involvement of many different specialists. However after delivery she required on-going care from medical and surgical teams; no one professional had ultimate responsibility for her care and there were many transfers to different wards, poor communication, delays in surgery and she died following multiple operations for complications after caesarean wound dehiscence.

A woman who had a 3rd degree tear, was readmitted with abdominal pain and distension. CT scan showed no evidence of perforation. She was treated with laxatives but subsequently developed signs of frank peritonitis and was found to have a large perforation in her caecum. There was persisting false reassurance based on the original CT scan and therefore a delay in the diagnosis and management of perforation which may be related to a lack of senior obstetric and general surgical input.

8.8. Aneurysm (non-aortic) rupture

There were three women who died from major intra-abdominal haemorrhage due to ruptured splenic artery aneurysm and three from other aneurysmal rupture. Two with splenic artery aneurysms had significant liver disease (see above) due to primary biliary atresia and chronic hepatitis C and one probably had underlying Ehlers Danlos syndrome type IV. In two deaths in mid pregnancy perimortem caesarean was not considered, although this is unlikely to have improved the outcome, and in the other it was inappropriately delayed until confirmation of a fetal heart rate was obtained.

One woman died a few weeks after vaginal delivery from a ruptured aneurysm of the common iliac artery. She had pre-existing hypertension and remained under obstetric follow up when she was admitted with wide-ranging symptoms including unilateral iliac fossa pain. With hindsight she had had lower abdominal pain from the third trimester but it is not clear whether earlier intervention would have been possible.

Two women collapsed in late pregnancy but died despite resuscitation, perimortem caesarean section and laparotomy. Both had retroperitoneal haemorrhage from ruptured gastric/coeliac artery aneurysms. The assessors felt that care in both women had been good and no improvements were noted.

In the last three triennia (2000–02 (Lewis 2004), 2003–05 (Lewis 2007) & 2006–08 (Lewis, Cantwell et al. 2011)) respectively there were three, two and no iliac artery aneurysm ruptures and one, two and one splenic artery aneurysm ruptures reported. Half of all arterial aneurysm ruptures in women of child-bearing age are associated with pregnancy (Selo-Ojeme and Welch 2003). Splenic artery aneurysm is the commonest visceral artery aneurysm, with up to 95% presenting during pregnancy, associated with high maternal and fetal mortality (Ha, Phillips et al. 2009). Previous maternal death reports have featured small numbers of women with arterial aneurysm rupture and a possible relationship to undiagnosed connective tissue disease has been highlighted before (Lewis 2004). These events seem largely unpredictable and unavoidable, though with prompt and rigorous action survival is occasionally possible (Holdsworth and Gunn 1992).

8.9. Unascertained

There were two deaths in which the cause of death could not be definitively ascertained. One unbooked woman was found dead after a recent delivery and the other collapsed at home in the first trimester. In both women the post-mortem evidence of sepsis was unconvincing and whilst it is possible these were sudden cardiac deaths, the assessors were not able to classify them definitively in the absence of any other clinical evidence.

CONCLUSIONS

It is clear from the deaths reported here that women with pre-existing medical conditions who become pregnant require a high standard of joined-up multidisciplinary care. Pregnant women who develop serious medical conditions in pregnancy will require urgent involvement of relevant specialists alongside the obstetric team. This should be at a senior level. A single identified professional should be responsible for co-ordinating care. High level actions are needed to ensure that physicians are appropriately trained in, and engaged with, the care of pregnant women, and that services are designed for women with medical conditions which provide appropriate and evidence-based care across the entire pathway, including pre-pregnancy, during pregnancy and delivery, and postpartum.

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Appendix

A1: The postmortem in sepsis-related maternal death

Sebastian Lucas

There are several pathogens involved in maternal sepsis deaths, and the post-mortem examination is critical in determining what actually happened (Lucas 2012). In a development of the WHO schema (1995) for puerperal infections, the taxonomy of maternal sepsis was re-organised as follows for the review of maternal deaths occurring in 2006–08 (Lewis, Cantwell et al. 2011):

Categories:

1. Sepsis following unsafe ('criminal') abortion;
2. Premature rupture of membranes and ascending genital tract infection;
3. Ascending genital tract infection following delivery of any type (miscarriage/abortion, termination, caesarean section, vaginal delivery);
4. Septic shock in a pregnant woman with intact membranes and before the onset of labour;
5. Pregnancy/delivery-related sepsis, but not involving the genital tract, such as caesarean section wound infection, infected regional anaesthesia catheter, aspiration pneumonia after general anaesthesia;
6. Other local or systemic infections that are coincidental to the pregnancy & delivery (such as HIV, tuberculosis) or aggravated by pregnancy (such as pneumococcal meningitis, influenza).

The infectious agents are numerous, but Group A Streptococcus is common in categories 3 & 4; gram-negative perineal bacilli are common in category 2.

To cause death, rather than just a local infection, in many of these categories there is the development of a severe systemic inflammatory response syndrome (SIRS) that may precipitate multi-organ failure. Undoubtedly the host's genetic response to infection is critical to the outcome. The histopathology of SIRS (see below) is a useful yardstick for determining whether or not a possible infection scenario was truly the cause of death.

The postmortem process in maternal sepsis

Thorough examination and histological sampling of all organs (including bone marrow) is important. If the placenta is available, that must be examined also. Information on the status of the fetus may be informative.

The autopsy is also helpful in delineating co-morbidities that render the woman more susceptible to severe infection. These include sickle cell disease, congenital immunodeficiency syndromes, hyposplenism, chronic organ diseases (lung, musculo-skeletal, cardiac, liver, renal), immunosuppressive therapies, connective tissue and malignant diseases. Such conditions are increasingly common in pregnant women in high-income countries.

Microbiological samples to be taken where possible:

- Blood cultures as soon as possible after death; these must be taken from the heart or neck veins, not from below the umbilicus, and before the body is opened; if this is not possible, a clean sample of spleen parenchyma may be cultured;
- CSF if meningitis is suspected;
- Decidua;
- Any focal sepsis in any other organ;
- For suspected influenza, posterior nasal swabs can be taken at autopsy for PCR testing as described below;
- In suspected viral myocarditis, a sample of heart muscle for PCR testing;
- If HIV is suspected, but not known pre-mortem, postmortem blood is suitable for testing.
- The pre-mortem laboratory data if available are often invaluable. This includes haematology and blood clotting studies, biochemistry, as well as any microbiology cultures and urine antigen tests, and virology data.

Influenza deaths

As discussed in Chapter 3, influenza-related deaths were numerous in the 2009–12 period, coinciding with the pandemic of H1N1. Few of the women diagnosed with H1N1 in life were autopsied; this is not surprising given the known diagnosis and the fact that many spent weeks in intensive care before dying. A postmortem would have provided no new information apart from demonstrating organising pneumonia and pathologies induced by multi-organ support (Lucas 2010).

If there is a suspicion of, but no confirmed influenza infection by the time of autopsy, then sampling for the virus is straightforward (Lucas 2009). Whilst fresh samples of lower airways and lung tissue may be sent to virology departments, it is easier and equally sensitive to take nasophangeal swabs:

- Before the dissection commences, have ready two bottles of virology transport medium with intrinsic swabs;

- Insert one deep into one nasal sinus of the woman, remove and place in the bottle after snapping short the swab stalk;
- Repeat for the other sinus with the second bottle;
- The virology lab will analyse the swabs by PCR.

The pathology of SIRS

The gross features are not specific unless there is visible purulent infection in an organ, although in toxic shock syndrome most of the organs are certainly red, flabby and soft. The so-called 'septic spleen' has no predictive value whatsoever in identifying fatal systemic infection. The following histopathological features are useful positive markers for SIRS:

- Haemophagocytosis in bone marrow, liver and spleen (CD68 immunohistochemistry is helpful to demonstrate this);
- Disseminated intravascular coagulation thrombi (DIC) in the kidney glomeruli;
- Adrenal interstitial haemorrhage;
- Acute lung injury;
- Up-regulation of intercellular adhesion molecule-1 (ICAM-1) expression in lung endothelial cells (using CD54 immunohistochemistry);
- Interstitial oedema and inflammation in the heart muscle ('SIRS heart');
- Lymphoid atrophy in nodes and spleen.

Interpretation of postmortem-identified infections

Genital tract infection is usually evident grossly and histopathologically; if the placenta is available, acute inflammation will also be seen there in many instances.

Women who are taken to intensive care and survive for a week or longer before dying can be difficult to evaluate at autopsy, because the original septic loci may be resolving, and the effects of long-stay in intensive care emerge. These include severe opportunistic infections such as disseminated aspergillosis and herpes simplex, particularly if the woman has been sustained on ECMO before death. Identifying such infections should not mislead the pathologist into thinking that the underlying cause of death has been determined.

Conclusion

Expert assessment of the cases included in this report reclassified the cause of several deaths. This followed from incorrect appreciation of the significance of any identified infectious agents in the context of the death (e.g. contaminant versus true pathogen), incorrect appreciation of SIRS, and incorrect appreciation of other pathologies present that indicate a different cause of death.

Consultation with microbiologists experienced in the diagnosis and management of severe sepsis due to bacterial infection is invaluable in correctly categorising possible maternal sepsis deaths, as is good clinico-pathological correlation which can only occur following thorough review of the case notes and discussion with the clinicians involved in the death.

A2: The pathology of AFE

Adrian Yoong

Pathological Diagnosis of Amniotic Fluid Embolism

Of the current 11 deaths, nine underwent postmortem; in the other two deaths the local Coroner/Procurator Fiscal accepted the clinicians' views that the deaths were most likely due to amniotic fluid embolism (AFE), without the need for post-mortem examination. However, post mortem examination is important not only to confirm a positive diagnosis of AFE but also to rule out other possible causes especially when the presentation is atypical.

The diagnosis of AFE is based on the clinical features combined with pathological confirmation, if possible, of the occurrence of AFE, by virtue of finding amniotic fluid material (AFM) in the maternal circulation, together with the exclusion of other disorders that may present in a similar fashion. The role of the post-mortem examination is essentially two-fold, namely, confirmation of the presence of pathological features that are consistent with AFE and consideration and exclusion of other disease that could mimic AFE and represent an alternative cause of the death. Recommendation 10 of the last Confidential Enquiry Report suggested that the maternal postmortem should be performed by a specialist pathologist who is best placed to carry out this examination (Lewis, Cantwell et al. 2011).

Maternal postmortem should be performed by a specialist pathologist who is best placed to carry out this examination

(Lewis, Cantwell et al. 2011)

The initial examination should carefully document the presence of any injury to the genital tract, which could provide a portal of entry of amniotic fluid, including the caesarean section surgical wound, if present, cervix and the vagina, with appropriate

sampling for histology. Similarly, the placenta, if available, and the uterus, often already removed as a hysterectomy specimen for the severe bleeding that is characteristic of AFE, should always undergo pathological examination with review by a specialist pathologist, as needed in individual circumstances.

Fetal squames

The pathological diagnosis of AFE rests principally on the finding of the contents of amniotic fluid (AFM) in the maternal circulation. This is usually taken to mean the finding of squamous epithelial cells, which are presumed to have previously exfoliated from the skin of the fetus into the amniotic fluid, in the (mother's) pulmonary vasculature, however there are other constituents of amniotic fluid, which may be detected, including mucin, vellus hair, vernix fat and meconium. AFM may also be observed, although less frequently, in blood vessels elsewhere in the body, particularly the uterine cervix and lower segment. The detection of fetal squames may be done most simply by light microscopy of routine well-stained H&E sections. It is advised that if found, their presence should be confirmed by means of immunohistochemistry for either a pancytokeratin marker, such as AE1/AE3, or a high-molecular-weight cytokeratin (34 beta E12 has been advocated, although the author prefers CK5/6), as what may be thought to be squames, by virtue of an elongated spindly shape, more often are endothelial cells which have become detached. Conversely, if fetal squames are not found by routine light microscopy, then consideration should be given to the use of immunohistochemistry for a cytokeratin, which in practice needs only to be applied to the lung blocks.

Of the current series of nine postmortems, fetal squames were found in six; in all six post-mortem reports there was some description, of variable quality, of the extent of the presence of the squames. Of the three deaths where no fetal squames were reported, only one indicated the use of immunohistochemistry to try to find fetal squames. Although the recognition of fetal squames in the pulmonary vasculature is regarded as the defining pathological feature of AFE, various studies have noted that fetal squames and other AFM may not be found in women thought clinically to have died from AFE (Clark et al 1995). It is usually considered that the chance of detecting fetal squames in the pulmonary vasculature at postmortem diminishes with time after death, prompting the need to perform the post-mortem as soon as is practicable. However, it may be noted in the current series of deaths, that there was essentially no difference between deaths where evidence of AFM was or was not found with respect to both the intervals between collapse and death and between death and postmortem; this is consistent with the findings of Sinicina et al. (Sinicina, Pankratz et al. 2010). In the current series, the longest overall time, from collapse to post-mortem examination, for the detection of fetal squames was over 7 days.

Mucin

Apart from fetal squames, mucin is the easiest component of AFM to look for. Use of Alcian blue staining for acidic mucin from amniotic fluid, likely from the fetal gut, but also possibly from the respiratory tract, is easy to perform and easy to assess by microscopy. The author suggests that it should always be employed in this context. Mucin stains were undertaken in two deaths.

Other amniotic fluid material

This section will not discuss the methods of identification of the other constituents of amniotic fluid which may be found in the pulmonary vasculature in AFE, as these are the same as in other settings, save to note that in only one death was there mention of the finding of amniotic fluid material other than squames or mucin, which was a hair fragment and in no report was it stated that AFM was found in blood vessels other than the lungs.

Of note, it should be remembered that is possible to find amniotic fluid material in peripartum women without clinical evidence of AFE (Kuhlman, Hidvegi et al. 1985). Hence, vigilance is required not to make a diagnosis of AFE, based solely on the finding of AFM, but to carefully correlate this and the other pathological findings with the clinical history to come to a correct conclusion with respect to the cause of death.

Complementary laboratory tests for AFE

There are other laboratory tests for the possible occurrence of AFE, although some are of doubtful utility (serum tryptase and complement levels), while others appear promising (Kobayashi, Ooi et al. 1997, Oi, Kobayashi et al. 1998, Legrand, Rossignol et al. 2012), but appear to be of limited availability (sialyl (or sialosyl)-Tn and insulin-like growth factor binding protein-1). These were used in only one of the deaths described here.

The resemblance of the clinical presentation of AFE to anaphylaxis has suggested in the past that anaphylaxis may be an underlying factor in the pathogenesis of AFE; consequently, it was thought that measurement of the serum tryptase level may be useful in the diagnosis of AFE. However, in most women with AFE, it has been found that there is no rise in the serum tryptase level (Benson, Kobayashi et al. 2001). The same article (Benson, Kobayashi

et al. 2001) considered complement levels, but it has been concluded that "complement levels in AFE remain an investigational tool and should not be used to either confirm or refute a clinical diagnosis" (Benson 2012).

Clinical correlation

Careful attention should be paid to the clinical findings. In view of the usual presentation of AFE, there is a fairly wide clinical differential diagnosis, including, but not limited to, pulmonary thrombo-embolism, air embolism, cardiac disease (for example, arrhythmia, infarction, aortic dissection, peripartum cardiomyopathy (although unlikely in view of its case definition), anaesthetic complications (total spinal, high epidural block and reaction to local anaesthetic drugs), anaphylaxis or an anaphylactoid reaction, sepsis and postpartum haemorrhage (placental abruption and other causes). Disseminated intravascular coagulation (DIC) is a very common finding in AFE, but may also be a complication of a number of other obstetric and non-obstetric disorders in pregnancy, which should be part of the differential diagnosis of AFE. Some women with AFE present with what appears to have been a seizure, which should raise a suspicion of eclampsia and vice-versa. Sometimes, AFE may present in an atypical way with a predominant clinical picture of haemorrhage, but the pathologist, in such circumstances, should be vigilant to consider and attempt to confirm or exclude the possibility of an underlying AFE. This uncommon situation is exemplified in one of the deaths in the current series:

In one woman, AFE was not stated as a possible cause of death in the only documentation provided to the pathologist. However, the clinical history showed that the woman's haemorrhage was not excessive at the outset and there was a suggestion of an early cardiovascular collapse with rapidity of onset of the symptoms, accompanied by a coagulopathy, a history considered by the reviewers to be suggestive of AFE. Insufficient attention was paid to this clinical history as AFE was not apparently considered by the pathologist, and therefore the lung histology carried out was inadequate to diagnose or exclude the condition.

A3: The postmortem in suspected anaesthesia-related maternal deaths

Sebastian Lucas

Anaesthesia in obstetrics involves general and regional (epidural or spinal) anaesthesia. Frequently, both pertain at the time of delivery. The majority (>80%) of deaths under general anaesthesia occur around the time of caesarean section (Hawkins, Chang et al. 2011).

General anaesthesia problems that can lead to morbidity and death include:

- Tracheal intubation failure or tube malposition
- Respiratory problems e.g. aspiration of gastric contents, hypoventilation/airway obstruction, bronchospasm
- Cardiovascular abnormalities e.g. blood pressure, arrhythmias
- Fluid balance and blood loss
- Blood electrolyte abnormalities e.g. potassium
- Drug reactions e.g. neuromuscular blocking drugs, antibiotics
- Accidental intravascular injection of local anaesthetic agent
- Air embolus
- Malignant hyperthermia

Regional anaesthesia problems that can lead to morbidity and death include:

- Infection – meningitis and epidural abscess
- Haematoma
- Dural puncture and later subdural haemorrhage
- Neurological injury
- High block, with cardiorespiratory effects
- Accidental intravascular injection of anaesthetic agent

The scenarios that the pathologist may encounter performing a maternal death postmortem where anaesthesia processes could be an issue include:

- Sudden cardiorespiratory collapse around the time of delivery
- Airway obstruction/hypoventilation during anaesthesia (including on induction)
- Respiratory problems during recovery from general anaesthesia
- Meningitis and generalised sepsis

Sudden cardio-respiratory collapse

The differential diagnosis includes:

- Cardiac arrest or arrhythmia
- Pulmonary thromboembolism
- Severe haemorrhage – vaginal or internal
- Amniotic fluid embolism

- Air embolism
- Acute anaphylaxis
- Hyperkalaemia
- Severe bronchospasm
- Severe sepsis (unlikely without any premonitory features)
- Accidental intravenous local anaesthetic injection
- High regional block (spinal anaesthesia)

The causes of cardiac arrest include:

- Coronary artery diseases and myocardial ischaemia – acute and chronic
- Cardiomyopathy
- Valve diseases
- Hypertension
- Myocarditis
- Drug toxicity – cocaine and other stimulatory drugs, local anaesthetic
- Electrolyte abnormality – typically potassium
- Sudden cardiac death with a morphologically normal heart (SADS/MNH)
- Hypovolaemia usually secondary to major haemorrhage

Pathogeneses of Sudden Adult Death Syndrome with a Morphologically Normal Heart include:

- Channelopathy, eg long QT syndrome, Brugada syndrome
- Diabetic dead-in-bed syndrome
- Sudden unexpected death in epilepsy (SUDEP)
- Sudden unexpected death related to alcohol misuse
- Pre-eclampsia (controversial as a cause of SADS)
- Obesity cardiomyopathy

The postmortem process

Critical samples to take at postmortem – the comprehensive list, in addition to standard histology:

- Blood cultures for sepsis
- Femoral blood sample for mast cell tryptase and relevant drug levels
- Cerebrospinal fluid (CSF) for culture and/or drug levels
- Five lobes of lung tissue for identification of amniotic fluid embolism
- Spleen sample in freezer for investigation of SADS/MNH

Actual blood & CSF levels of the agents used for anaesthesia are a) difficult to measure and not routinely available in toxicology laboratories, and b) almost impossible to interpret. Unless the issue is simply whether or not a particular agent was used/injected or not, such sampling is not advised.

Pathological aspects of the deaths and conclusion

Many of the possible pathologies outlined above are solved at postmortem with appropriate histology and other investigations. However, a minority will require a multi-disciplinary investigation that includes the postmortem findings in conjunction with all the clinical features, physiological data around time of collapse, anaesthetic records, and pre-mortem laboratory investigation data. In chapter 6, all the cited deaths required such collaboration to identify the likely sequence of events that led to death. Pathologically, for example, detecting the fatal subdural haemorrhage was not problematic, but the link to the earlier dural puncture came from the clinical history, for the dura was not examined specifically for this at postmortem.

In the death associated with prolonged hypoventilation, an exhaustive process of exclusion of all the possible pathogeneses listed above under general anaesthesia problems and causes of cardiac arrest was necessary to arrive at what happened: extubation complications and respiratory arrest, which leave no specific pathology.

The collapse and death temporally associated with anaesthesia might have been attributed to epidural top-up neurotoxicity, were it not for the emphatic presence of AFE on postmortem histopathology. In contrast, one of the other deaths reviewed was attributed to AFE by a pathologist inexperienced in maternal mortality. However, review of the lung slides found no evidence of such embolism. The true pathogenesis is unclear, but anaesthetic factors and sudden cardiac death (SADS/MNH) are the main considerations.

The identification of the cause and effects of the fatal hyperkaelaemia required not only an exhaustive postmortem analysis but advice from an obstetric physician on drug toxicity.

One obvious function of the postmortem is to depict co-morbidities that made anaesthetic processes more liable to complications, such as reduced chest capacity, overt cardiac disease, and obesity.

In complex deaths, the pathologist is advised not to close discussion by, perhaps erroneously, focussing on one particular pathogenesis in his/her report, but delineate all the possible scenarios. These reviews may take place before or during inquests (most such deaths have inquests) and often have medical negligence claims as a result. Thus it is important that all possible postmortem investigations have been done that could assist in resolving uncertainties over the causes of death.

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