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

## Surveillance of maternal deaths in the UK 2012–14 and lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2009–14

December 2016

UNIVERSITY OF OXFORD
HQIP Healthcare Quality Improvement Partnership
UNIVERSITY OF LEICESTER
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UNIVERSITY OF BIRMINGHAM
Sands Stillbirth & neonatal death charity
NHS Bradford Teaching Hospitals NHS Foundation Trust
npeu National Perinatal Epidemiology Unit

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# Foreword

We are very pleased to endorse the key lessons to be learned from the latest report from the UK and Ireland Confidential Enquiry into Maternal Deaths and Morbidity. Cardiovascular disease is the largest single cause of maternal death in the UK and a major focus of this report. The Confidential Enquiry into Maternal Morbidity in women with prosthetic heart valves highlights the additional burden of severe complications during pregnancy and childbirth in women with cardiac disease. While this report focuses on the UK and Ireland, we recognise this as a global challenge which we must address.

The very clear message that emerges from this work is the importance of multi-disciplinary care for these women across many medical specialties in addition to obstetrics, midwifery, anaesthetics and critical care. All physicians should undergo basic training in the care of pregnant women with medical co-morbidities early in their postgraduate education. However, no individual health professional can have all the expertise to provide the complex care needed by these women, particularly in an era in which subspecialisation starts at an early point in postgraduate training. The need to consult an expert in a different medical area, should not be seen as a failing but as the most appropriate action to ensure that women with complex health problems receive the highest quality care. As our maternity population becomes more clinically complex, there is a real need to build a "network of experts" on a regional or national basis to care for pregnant and postpartum women with medical and mental health comorbidities.

Allied to this need, we are pleased to support the "3Ps in a Pod" initiative, which highlights the key messages for care to prevent both cardiovascular and other indirect maternal deaths. The initiative emphasises recognition of the significance of persistent breathlessness and orthopnoea, new or increasing frequency of fits in pregnancy, the symptoms and signs of sepsis, and a mother's estrangement from her baby as a "red flag" for concern over mental health problems. We encourage all health professionals who may encounter pregnant or post-partum women in any aspect of their work to view the five minute video available on the Royal College of Physicians and Surgeons of Glasgow website. A simple poster highlighting the key messages is also available.

The successes evident in this report should also be recognised. The number of women dying from sepsis has decreased due to a dramatic reduction in influenza deaths. Immunisation against influenza remains a vital public health initiative to prevent both mothers and babies from dying. Six new toolkits issued recently by the UK Sepsis Trust have been designed to provide practical guidance for the prompt diagnosis and management of sepsis in pregnancy for all professionals involved in delivering care to pregnant and recently pregnant women. Perhaps the most striking success, however, is in the area of hypertensive disorders of pregnancy. In the UK today, one woman dies every 18 months from hypertensive disorders of pregnancy. Sixty years ago, when the Confidential Enquiries started, the figure was over 150. This is a testament to the translation of research into practice and the high quality care provided to these women as a consequence. On a worldwide basis, however, hypertensive disorders remain one of the most frequent causes of maternal death – over the same period that one woman dies in the UK, 20,000 die worldwide. The UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity are the international gold standard for maternity audit and quality improvement programmes. We must not forget their importance in highlighting messages to improve care on a global basis.

We urge all readers to translate the key messages from this report into their practice, wherever they are based, and to whichever professional specialty group they belong.

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President, Royal College of Physicians of Edinburgh

Professor David Galloway
President, Royal College of Physicians and Surgeons of Glasgow

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Chair, Institute of Obstetricians,
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# Key messages
## from the report 2016

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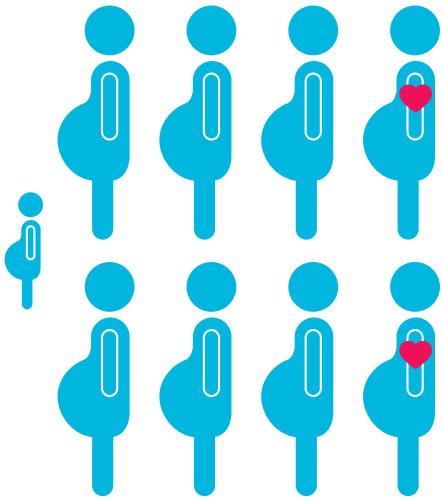


**8.5** **women** per 100,000 died during pregnancy or up to six weeks after giving birth or the end of pregnancy in 2012 - 14

**2** **women** per 100,000 died from **heart** ♥ **disease**

**Heart disease can happen**

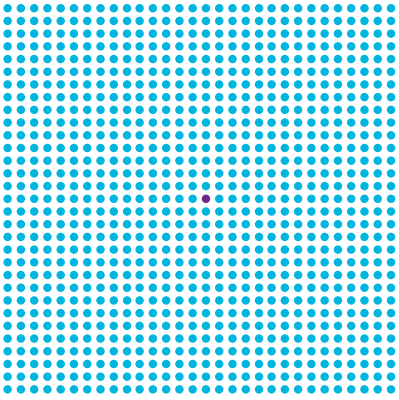
Women known to have **heart disease** are **high risk** and need specialist care

**Persistent breathlessness** when lying flat is **not normal** in pregnancy and may mean heart problems

Be aware severe **chest pain** spreading to the left arm or back may be **cardiac**

## Good care makes a difference

Less than **1 woman in every million** who gives birth now dies from **pre-eclampsia**, but to detect it blood pressure and urine must be checked at every antenatal visit



# Executive Summary

## Introduction

The UK Confidential Enquiry into Maternal Deaths (CEMD) has represented a gold standard internationally for detailed investigation and improvement in maternity care for over 60 years. It recognises the importance of learning from every woman's death, during or after pregnancy, not only for the staff and services involved in caring for her, but for the family and friends she leaves behind. This, the third of the Confidential Enquiry into Maternal Deaths annual reports produced by the MBRRACE-UK collaboration, includes data on surveillance of maternal deaths between 2012 and 2014. It also includes Confidential Enquiries for women who died between 2009 and 2014 focusing on lessons about cardiovascular disease, caring for women with hypertensive disorders of pregnancy, and messages for early pregnancy and critical care. In collaboration with MDE Ireland, the report includes Confidential Enquiries into the deaths of women from these causes in Ireland. In addition, the report includes the Confidential Enquiry into Maternal Morbidity amongst women with artificial heart valves in pregnancy. Each topic-specific Confidential Enquiry chapter now appears in an annual report once every three years on a cyclical basis, in contrast to the past when a single report was produced every three years.

Surveillance information is included for 564 women who died during or up to one year after the end of pregnancy between 2012 and 2014. The care of 183 women was reviewed in depth for the Confidential Enquiry chapters.

## Methods

Maternal deaths are reported to MBRRACE-UK or to MDE Ireland by the staff caring for the women concerned, or through other sources including coroners, procurators fiscal and media reports. In addition, identification of deaths is cross-checked with records from the Office for National Statistics and National Records of Scotland. Full medical records are obtained for all women who die as well as those identified for the Confidential Enquiry into Maternal Morbidity, and anonymised prior to undergoing confidential review. The anonymous records are reviewed by a pathologist, together with an obstetrician or physician as required to establish a woman's cause of death. The care of each woman is then assessed by one or two obstetricians, midwives, pathologists, anaesthetists and other specialist assessors as required, including 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. Subsequently the expert reviews of each woman's care are examined by a multidisciplinary writing group to enable the main themes for learning to be drawn out for the MBRRACE-UK report. These recommendations for future care are presented here, alongside a surveillance chapter reporting three years of UK statistical data.

## Key areas for action

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

Pre-pregnancy counselling should be available both within the paediatric cardiology transition service and to women of childbearing age with known cardiac disease. This should include provision of appropriate contraceptive advice.

All consultant led maternity units should have ready access to an ECG machine and someone who can interpret ECGs. Similarly, echocardiography, performed by a competent practitioner, should be available seven days a week.

Women with prosthetic valves in pregnancy are at extremely high risk, and should be referred to specialist centres early. They need expert obstetric, haematology, cardiology and anaesthetic input.

Providers and commissioners of care must ensure that there are safe pathways to transfer women from non-NHS facilities offering termination of pregnancy to local NHS services when complications arise.

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

Lack of co-location of obstetric and cardiac services jeopardises interdisciplinary working and communication. Measures such as joint obstetric cardiac clinics, multidisciplinary care plans, copying letters to the woman and all clinicians involved in her care, as well as staff from all specialties writing in the woman's hand held notes may mitigate against the inherent risk of inadequate communication between specialists.

The full range of clinical and investigatory services required to assess women with early pregnancy emergencies should be available throughout the whole week.

Critical care support can be initiated in a variety of settings. Critical care outreach nurses can work in partnership with midwives to provide care before transfer to the critical care unit. Delay caused by bed pressures in a critical care unit is not a reason to postpone therapy.

Inter-hospital referral of a sick mother should be directed by the principle 'one transfer to definitive care'. It is unlikely to be appropriate to move a sick antenatal patient to a facility without on-site obstetric cover.

## For Doctors, Midwives and Allied Health Professionals

Early involvement of senior clinicians from the obstetric and cardiology multidisciplinary team is important, wherever a pregnant or postpartum woman presents with suspected cardiac disease, but particularly if she presents to the Emergency Department.

A raised respiratory rate, chest pain, persistent tachycardia and orthopnoea are important signs and symptoms which should always be fully investigated. Key investigations must not be delayed because of pregnancy. The emphasis should be on making a diagnosis, not simply excluding a diagnosis.

A normal ECG and/or a negative Troponin does not exclude the diagnosis of an acute coronary syndrome.

There is an immediate need to determine the cardiac rhythm at cardiac arrest. Attempt defibrillation as soon as possible for women in cardiac arrest with a shockable rhythm.

Monitor blood pressure and urinalysis at each antenatal attendance in both primary and secondary care and make sure results from tests are followed-up. Keep blood pressure in all women to below 150/100, with urgent treatment to achieve this in women with severe hypertension.

Women of reproductive age presenting to the Emergency Department collapsed, in whom a pulmonary embolism is part of the differential diagnosis, should have a Focused Assessment with Sonography in Trauma (FAST) scan to exclude intra-abdominal bleeding from a ruptured ectopic pregnancy before thrombolysis is given. This should be done especially in the presence of anaemia.

Reduced or altered conscious level is not an early warning sign; it is a red flag to indicate established illness.

# Causes and trends

Overall there was no statistically significant decrease in the maternal death rate in the UK between 2009-11 and 2012-14. Considering the gradual rate of decline, achieving the Government aspiration of reducing maternal deaths by 50% by 2030 will be a challenge for UK health services, requiring coordinated action across multiple specialties.

Maternal deaths from direct causes remain unchanged with no significant change in the rates between 2009-11 and 2012-14. The rate of indirect deaths remains high with no significant change since 2003, except a decrease in deaths due to influenza. This is primarily due to a low level of influenza activity in 2012-14 compared with 2009 and 2010. Increasing immunisation rates in pregnancy against seasonal influenza must therefore remain a public health priority.

Thrombosis and thromboembolism remain the leading cause of direct maternal death and cardiovascular disease the leading cause of indirect maternal death during or up to six weeks after the end of pregnancy.

Maternal deaths from hypertensive disorders are at the lowest ever rate, with fewer than one death for every million women giving birth. This represents a major success for research, audit and evidence-based guidelines leading to improvements in care.

Maternal suicides have now been reclassified by the World Health Organisation as a direct cause of maternal death. The rate of maternal death by suicide remains unchanged since 2003 and maternal suicides are now the leading cause of direct maternal deaths occurring within a year after the end of pregnancy.

# Key topic-specific messages for care

## Lessons on cardiovascular disease

Lack of co-location of obstetric and cardiac services jeopardises interdisciplinary working and communication. Measures such as joint obstetric cardiac clinics, multidisciplinary care plans, copying letters to the woman and all clinicians involved in her care, as well as staff from all specialties writing in the woman's hand held notes may mitigate against the inherent risk of inadequate communication between specialists.

Early involvement of senior clinicians from the obstetric and cardiology multidisciplinary team is important, wherever a pregnant or postpartum woman presents with suspected cardiac disease, but particularly if she presents to the Emergency Department.

A raised respiratory rate, chest pain, persistent tachycardia and orthopnoea are important signs and symptoms which should always be fully investigated. The emphasis should be on making a diagnosis, not simply excluding a diagnosis.

A normal ECG and/or a negative Troponin does not exclude the diagnosis of an acute coronary syndrome.

New onset of cardiorespiratory symptoms and/or absence of valve clicks in women with prosthetic heart valves should prompt careful echocardiography and early review by a senior cardiologist to exclude the possibility of valve thrombosis.

Pathologists undertaking maternal autopsies where the clinical pathology points to cardiac disease should follow the protocols in the Royal College of Pathologists' autopsy guidelines.

All women who die from sudden cardiac arrest and who have a morphologically normal heart should have molecular studies at postmortem with the potential for family screening. Similarly when aortic dissection occurs in a young person, the underlying diagnosis should be assumed to be an inherited aortopathy, with a need for family screening until proven otherwise. Future sudden deaths amongst relatives may then be prevented.

## Caring for women with hypertensive disorders of pregnancy

Women with risk factors for pre-eclampsia and those who develop hypertension or proteinuria in pregnancy should have a plan for an appropriate schedule of checks (with more visits than those for low risk pregnant women). New onset hypertension or proteinuria needs prompt referral with clear communication between health professionals.

Monitor blood pressure and urinalysis at each antenatal attendance in both primary and secondary care and make sure results from tests are followed-up. Keep blood pressure in all women to below 150/100, with urgent treatment to achieve this in women with severe hypertension.

If women have a blood pressure over 140mmHg systolic or 90mmHg diastolic on two occasions in labour or immediately after birth they should be considered for transfer to a consultant unit.

Staff should be aware that agitation and restlessness may be a sign of an underlying problem in women with hypertension.

Neuroimaging should be performed urgently in any woman with hypertension or pre-eclampsia who has focal neurology or who has not recovered from a seizure.

## Lessons for early pregnancy care

Women of reproductive age presenting to the Emergency Department collapsed, in whom a pulmonary embolism is part of the differential diagnosis, should have a Focused Assessment with Sonography in Trauma (FAST) scan to exclude intra-abdominal bleeding from a ruptured ectopic pregnancy before thrombolysis is given. This should be done especially in the presence of anaemia.

Women of reproductive age presenting in a state of shock and collapse in the community, with no obvious cause, should be transferred to a hospital Emergency Department without delay for urgent assessment and treatment.

A diagnosis of ectopic pregnancy should be considered in any woman of reproductive age presenting to the emergency department with collapse, acute abdominal/pelvic pain or gastrointestinal symptoms, including diarrhoea, vomiting and dizziness, regardless of whether or not she is known to be pregnant. A bedside pregnancy test should be performed in these women.

A woman with a suspected ectopic pregnancy and deteriorating symptoms, should be seen by a senior gynaecologist as a matter of urgency.

### Messages for critical care

Early recognition of critical illness, prompt involvement of senior clinical staff and authentic multi-disciplinary team working remain the key factors in providing high quality care to sick mothers.

Reduced or altered conscious level is not an early warning sign; it is a red flag to indicate established illness.

Key investigations must not be delayed because of pregnancy.

Severe respiratory failure in pregnant women and new mothers should trigger early referral to an ECMO centre.

Obstetricians and obstetric anaesthetists must remain closely involved in the clinical management of women with obstetric specific conditions such as pre-eclampsia. These conditions are rarely seen on the general critical care unit but are common problems on the labour ward.

Pregnancy can make the differential diagnoses of critical illness more complex. There must be a balance between appropriate clinical suspicion and a conclusive diagnosis; not all hypertension is pre-eclampsia and shortness of breath is not always a pulmonary embolism.

When critical care staff have any involvement in a maternal death, it is imperative that they are included in case reviews, root cause analysis and serious incident investigations.

## Conclusions

Over a quarter of women who died during pregnancy or up to six weeks after pregnancy died from a cardiovascular cause. This represents the leading cause of maternal death in the UK; preventing these women from dying is essential in order to continue to reduce the maternal mortality rate. This report highlighted many instances when pregnant and postpartum women had clear symptoms and signs of cardiac disease, which were not recognised, often because the diagnosis was simply not considered in a young pregnant woman. There was evidence of a focus on excluding, rather than making, a diagnosis in women who presented repeatedly for care. Repeated presentation should be considered a ‘red flag’ by staff caring for pregnant and postpartum women in any setting. Once again, a number of women received fragmented care, and important messages concerning planned care were not passed between teams, highlighting the urgent need for joint, multidisciplinary, maternity and cardiac care. Nonetheless, whilst it is clear that care in many areas can still be improved, the success of evidence-based quality care for women with hypertensive disorders should be recognised. Now, in the UK and Ireland, less than one woman in every million giving birth dies from a hypertensive disorder of pregnancy; a condition from which more than 100 women still die every day globally. Taking forward the lessons for improving care identified by these Confidential Enquiries will continue this achievement across other causes of maternal death.

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Olivia Protti, Consultant Perinatal Psychiatrist, East London NHS Foundation Trust
Anthony McCarthy, Consultant Psychiatrist, National Maternity Hospital, Dublin
Fiona Blake, Consultant Psychiatrist, Cambridgeshire and Peterborough NHSFT
Janine Lynch, Consultant Psychiatrist, Belfast Health and Social Care Trust

Joanne Fenton, Consultant Psychiatrist, Coombe Women and Infants University Hospital, Dublin
Diana Hulbert, Consultant in Emergency Medicine, University Hospital Southampton NHSFT
Jim Wardrope, Emeritus Consultant in Emergency Medicine, Sheffield

## Office for National Statistics

Sue Dewane, Chris Coutes, Joanne Evans, Karen Williams, Alex Lloyd

## National Records of Scotland

Julie Ramsay, Mary McDonald, Maria Kay, Eileen Crichton

## Information Services Division Scotland, NHS National Services Scotland

Rachael Wood, Kirsten Monteath, Carole Morris, Susan Frame, Jim Chalmers

## Health Improvement Scotland

Leslie Marr, Chris Lennox, Jan Warner

## Northern Ireland Maternal and Child Health, NSC Public Health Agency

Heather Reid, Joanne Gluck, Malcolm Buchanan, Sinead Magill

## UK Obstetric Surveillance System

Melanie Workman, Anne Smith, Patsy Spark, Beth Lawson, Jonathan Livingstone-Banks

## The Maternal, Newborn and Infant Clinical Outcome Review Independent Advisory Group:

Alan Fenton, Consultant in Neonatal Medicine, Newcastle upon Tyne (member from March 2014, chair from September 2015)
Janice Allister, General Practitioner, Peterborough
Zoe Boreland, Midwifery and Children's advisor, Northern Ireland Department of Health, Social Services and Public Safety (member from September 2014)
Cath Broderick, Lay Representative (member from October 2013 until March 2016)
Jacqueline Cornish, National Clinical Director Children, Young People and Transition to Adulthood, NHS England (member from March 2014)
Phillip Cox, Consultant Perinatal Pathologist, Birmingham Women's Hospital
Caroline Davey, Chief Executive, Bliss (member from March 2015)
Helen Dolk, Professor of Perinatal Epidemiology, Director of the Centre for Maternal, Fetal and Infant Research, Institute for Nursing Research, University of Ulster
Jaqueline Dunkley-Bent, Head of Maternity, NHS England (member from March 2016)
Roshan Fernando, Consultant Anaesthetist and Honorary Senior Lecturer, University College London Hospitals NHS Foundation Trust (member from September 2014)
Melissa Green, Interim Chief Executive, Bliss (member from September 2014)
Mervi Jokinen, Practice and Standards Development Adviser, Royal College of Midwives
Matthew Jolly, National Clinical Director: maternity review and women's health (member from March 2016)
Corrine Love, Medical Advisor for Women and Children's Health for the Scottish Government (member from March 2016)
Kate McKay, Senior Medical Officer, Scottish Government
Liz McDonald, Consultant Perinatal Psychiatrist and Clinical Lead for Perinatal Psychiatry, East London Foundation Trust (member from October 2013)
Priscilla Maguire, Lay member, RCOG Women's Network (member from March 2016)
Edward Morris, Consultant in Obstetrics and Gynaecology, Norfolk & Norwich University Hospital and Honorary Senior Lecturer, University of East Anglia
Heather Payne, Senior Medical Officer for Maternal and Child Health, Welsh Government
Nim Subhedar, Consultant Neonatologist, Liverpool Women's Hospital NHS Trust (member from October 2013)
Karen Todd policy lead for maternity and neonatal care, Department of Health (member from March 2016)
Michele Upton, Patient Safety Domain, NHS England (member from September 2014)
Verena Wallace, Local Supervising Authority Midwifery Officer for Northern Ireland (member from March 2016)
Jason Waugh, Consultant and Lead for Obstetric Medicine, Newcastle Upon Tyne
David Williams, Consultant Obstetric Physician, The Institute for Women's Health, University College London Hospital

## Healthcare Quality Improvement Partnership:

Jenny Mooney, Business Manager, Clinical Outcome Review Programmes (to May 2014), Director of Operations, National Clinical Audit and Patient Outcome Programmes (to March 2016)
Tina Strack, Associate Director, Clinical Outcome Review Programmes
Lorna Pridmore, Clinical Outcome Review Programmes Facilitator
Vivien Seagrove, Programme Support Officer

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

Jane Abbott, BLISS
Francine Bates, Lullaby Trust (formerly FSID)
Beverley Beech, AIMS
Jenny Chambers, OC Support
Debbie Chippington Derrick, Caesarean.org.uk
Caroline Davey, Bliss
Jane Denton, Multiple Birth Foundation
Jane Fisher, ARC
Pauline Hull, electivecesarean.com
Penny Kerry, Miscarriage Association
Helen Kiranne, Bliss
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
Keith Reed, TAMBA
Jean Simons, Lullaby Trust (formerly FSID)
Lis Thomas, AVMA
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
Pamela Boyd, Neonatal Nurses Association
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
Flora Jessop, British and Irish Paediatric Pathology Association
Sarah Johnson, Royal College of Obstetricians and Gynaecologists
Hannah Knight, Royal College of Obstetricians and Gynaecologists
Lucy Mackillop, Royal College of Physicians
Lisa Nandi, British Association of Perinatal Medicine
Catherine Nelson-Piercy, Royal College of Physicians
Tim Overton, British Maternal Fetal Medicine Society
Lesley Page, Royal College of Midwives
Marcia Philbin, Royal College of Paediatrics and Child Health
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

# Glossary of terms

| | |
|---|---|
| **AAGBI** | Association of Anaesthetists of Great Britain and Ireland |
| **ACE** | Angiotensin Converting Enzyme |
| **AFE** | Amniotic Fluid Embolism |
| **AFLP** | Acute Fatty Liver of Pregnancy |
| **ALS** | Advanced Life Support |
| **ART** | Assisted Reproductive Technology |
| **ARVCM** | Arrhythmogenic Right Ventricular Cardiomyopathy |
| **BMI** | Body Mass Index |
| **BP** | Blood Pressure |
| **CEMD** | Confidential Enquiries into Maternal Deaths |
| **CEMM** | Confidential Enquiries into Maternal Morbidity |
| **CI** | Confidence Interval |
| **CMACE** | Centre for Maternal and Child Enquiries |
| **CPD** | Continuing Professional Development |
| **CPR** | Cardiopulmonary resuscitation |
| **CT** | Computerised Tomography |
| **CTG** | Cardiotocography |
| **CTPA** | Computed Tomography Pulmonary Angiography |
| **CVA** | Cerebrovascular accident |
| **DNA** | Deoxyribonucleic acid |
| **ECG** | Electrocardiogram |
| **ECMO** | Extra-Corporeal Membrane Oxygenation |
| **ELLP** | Elevated Liver Enzymes Low Platelet syndrome |
| **EPAS** | Early Pregnancy Assessment Services |
| **FAST** | Focused Assessment with Sonography in Trauma |
| **GCS** | Glasgow Coma Scale |
| **GMC** | General Medical Council |
| **GP** | General Practitioner |
| **hCG** | Human Chorionic Gonadotropin |
| **HDU** | High Dependency Unit |
| **HELLP** | Haemolysis, Elevated Liver enzymes, Low Platelet count |
| **HES** | Hospital Episode Statistics |
| **HOCM** | Hypertrophic Cardiomyopathy |
| **HQIP** | Healthcare Quality Improvement Partnership |
| **ICD** | International Classification of Diseases |
| **ICD-MM** | International Classification of Diseases-Maternal Mortality |
| **ICNARC** | Intensive Care National Audit and Research centre |
| **ICP** | Intracranial pressure |
| **IMD** | Index of Multiple Deprivation |
| **INR** | International Normalised Ratio |
| **ITU** | Intensive Therapy Unit |
| **IUD** | Intrauterine death |
| **IVF** | In Vitro Fertilisation |
| **LDL** | Low Density Lipoprotein |
| **LMWH** | Low Molecular Weight Heparin |
| **LVAD** | Left Ventricular Assist Device |
| **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 |
| **MRI** | Magnetic Resonance Imaging |
| **NHS** | National Health Service |
| **NICE** | National Institute for Health and Care Excellence |
| **NIMACH** | Northern Ireland Maternal and Child Health |
| **NRS** | National Records Scotland |
| **ONS** | Office for National Statistics |
| **PE** | Pulmonary Embolism |
| **PEA** | Pulseless Electrical Activity |
| **PEFR** | Peak Expiratory Flow Rate |
| **PPCM** | Peripartum Cardiomyopathy |
| **RCOG** | Royal College of Obstetricians and Gynaecologists |
| **RR** | Risk Ratio |
| **RRR** | Ratio of Relative Risks |
| **SADS** | Sudden Adult Death Syndrome |
| **SADS/MNH** | Sudden Adult Death Syndrome with a Morphologically Normal Heart |
| **SICSAG** | Scottish Intensive Care Society Audit Group |
| **SIGN** | Intercollegiate Guidelines Network |
| **SUI** | Serious Untoward Incident |
| **UKOSS** | UK Obstetric Surveillance System |
| **VF** | Ventricular Fibrillation |
| **VT** | Ventricular Tachycardia |
| **WHO** | World Health Organisation |

# Contents

# 1. Introduction and methodology

Marian Knight

## 1.1 The 2016 Saving Lives, Improving Mothers' Care report

This report of the MBRRACE-UK Confidential Enquiry into Maternal Deaths and Morbidity is the third in the new annual series, thus completing for the first time the full three-year cycle of topic-based confidential enquiry chapters, which replaced the single previous triennial report. Detailed enquiry chapters for all causes of maternal death, with associated messages for care, have now been produced in this new format. The major focus of this 2016 report is maternal cardiovascular disease, which remains the largest single cause of maternal death during pregnancy and up to six weeks after pregnancy, as well as being associated with a substantial proportion of later maternal deaths. With cardiac disease, as with other causes of indirect maternal deaths, the clear message remains the importance of coordinated multi-professional care covering the entire pathway before, during and after pregnancy.

The findings clearly illustrate once again that maternal deaths represent only the tip of the iceberg of disease. Included in this report are confidential enquiries into the care of women with artificial heart valves in pregnancy, who survived, but many of whom experienced severe associated morbidities including intracerebral bleeding and valve thrombosis. There are many opportunities identified for improving care of these women, from very early in their care pathway when considering the type of replacement valve they should be offered, to awareness of the symptoms and signs of common complications such as valve thrombosis, to careful re-introduction of anti-coagulation regimens postnatally.

Alongside clear messages for improving the care of women with cardiovascular disease, review of the care of women with hypertensive disorders shows the huge impact that research, evidence-based guidelines and subsequent high quality antenatal and postnatal care has had in the UK. Today fewer than one in every million women giving birth in the UK will die from a hypertensive disorder in pregnancy – a condition which is still one of the commonest global causes of maternal death and which is estimated to kill 42,000 women worldwide annually (Say, Chou et al. 2014, World Health Organisation 2015). This is a clear success story, and one that needs to be repeated now across other medical and mental health causes of maternal death.

The major focus of the 2015 report was maternal mental health, and it is encouraging that there is an ongoing focus on improving maternal mental health care following the release of the report. In recognition of the importance of maternal suicide and its direct link with pregnancy, the WHO recommended in their latest guidance on classification of maternal mortality, ICD-MM, that maternal suicides are classified as direct, rather than indirect, maternal deaths (World Health Organisation 2012). We have adopted this changed classification for this report, and for comparability have included figures using both classification systems.

Since the introduction of the guidance in 2012, there have been widespread concerns about the impact of this reclassification on calculated mortality rates, and therefore countries' apparent progress towards meeting both current and former targets to reduce maternal mortality (United Nations 2000, United Nations 2015). We conducted an analysis using MBRRACE-UK data on maternal deaths between 2009 and 2013 to examine the impact of this reclassification of maternal suicides on the observed UK rates and trends in maternal mortality (Knight, Nair et al. 2016). The UK rates and trends in direct and indirect causes of maternal death between 2003–5 and 2011–13 calculated using the historical classification were not materially different from the rates and trend calculated following reclassification of maternal suicides using ICD-MM (Table 2.3, Chapter 2). The messages remain the same; there is little change in rates of maternal death from medical and mental health conditions, with the notable exception of influenza. Tackling these causes of death has to be our priority if we are to meet the aspiration of the UK Government's 'halve it' campaign, to reduce by 50% maternal deaths by 2030 (Department of Health 2015).

## 1.2 Actions following the release of the 2014 and 2015 reports

A number of important initiatives to improve the care of women in pregnancy and postpartum have followed on from the previous two annual reports and we are very grateful to the wide groups of individuals who have taken these actions forward. Some key national initiatives are summarised here; we are aware of many more regional and local actions.

### Three Ps in a Pod

**High level actions are needed to ensure that physicians are appropriately trained in, and engaged with, the care of pregnant women.**

**Saving Lives, Improving Mother's Care 2014 (Knight, Kenyon et al. 2014)**

Recognising the importance of awareness of the key causes of maternal death in setting such as Acute Medicine Units and Emergency Departments, a collaboration between the Royal College of Physicians and Surgeons of Glasgow, the Royal College of Obstetricians and Gynaecologists, the Royal College of Physicians of Edinburgh, The Royal College of Physicians, MBRRACE-UK and the Royal College of Emergency Medicine, and led by Dr Rebecca Northridge, a Scottish Clinical Leadership Fellow, has produced a series of educational resources focussed on the theme of 'Three Ps in a Pod'. The three Ps represent pregnancy, postnatal and 'pick up the problem', and are illustrated in the poster shown in Figure 1.1. This poster has been distributed to all Acute Medical Units and Emergency Departments in the UK; it and a more detailed version is available to download from *https://rcpsg.ac.uk/college/influencing-healthcare/policy/maternal-health*. Additionally, a five-minute video was produced to highlight the key messages in relation to indirect maternal deaths in the UK, this is also available to view at the same link.

### NHS Education Scotland Maternal Sepsis e-Learning Package

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

**Saving Lives, Improving Mother's Care 2014 (Knight, Kenyon et al. 2014)**

NHS Education Scotland have produced a 60 minute e-learning package, featuring scenarios based on the vignettes included in the MBRRACE-UK 2014 report, to help improve identification and early management of maternal sepsis. The package is available at: *http://www.knowledge.scot.nhs.uk/scormplayer.aspx?pkgurl=%2fecomscormplayer%2fsepsis%2f*.

### UK Sepsis Trust Clinical Toolkits

**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**

**Saving Lives, Improving Mother's Care 2014 (Knight, Kenyon et al. 2014)**

Linking directly with new NICE guidance on recognition, diagnosis and early management of sepsis (National Institute for Health and Care Excellence 2016b), the UK Sepsis Trust has released six new clinical toolkits specifically for women in pregnancy. Tools are available for out of hours/telephone triage, community midwives, pre-hospital/ambulance services, general practice, emergency departments and acute medical units, as well as acute hospital inpatients. All are available from *http://sepsistrust.org/clinical-toolkit/* as pdfs which may be edited to suit local need. The tool for community midwives is shown in Figure 1.2.

## Royal College of Obstetricians and Gynaecologists Epilepsy in Pregnancy Guideline

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

**Saving Lives, Improving Mother's Care 2014 (Knight, Kenyon et al. 2014)**

RCOG Green-top guideline number 68, Epilepsy in Pregnancy (available from *https://www.rcog.org.uk/en/guidelines-research-services/guidelines/gtg68/*) was released in 2016 and has been endorsed by the Association of British Neurologists, Epilepsy Action, the Royal College of General Practitioners, the Royal College of Midwives and the Royal College of Physicians. It covers the care of women with epilepsy pre-pregnancy, during pregnancy and delivery and postnatally.

# 1.3 Topics covered in MBRRACE-UK maternal reports 2014–16

The Maternal, Newborn and Infant Clinical Outcome Review Programme now 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 now appears in an annual report once every three years on a cyclical basis, alongside a surveillance chapter reporting three years of statistical data. All causes of maternal death have now been covered once in this three-year cycle; readers will find topic specific chapters in the following reports published between 2014 and 2016:

- **2014:** Surveillance data on maternal deaths from 2009–12. Confidential Enquiry reports on deaths and severe morbidity from sepsis, 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 from psychiatric causes, deaths due to thrombosis and thromboembolism, malignancy, homicides and late deaths
- **2016 (this report):** Surveillance data on maternal deaths from 2012–14. Confidential Enquiry reports on deaths and severe morbidity from cardiac causes, deaths from pre-eclampsia and eclampsia and related causes, deaths in early pregnancy, and messages for critical care.

# 1.4 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 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.

**Figure 1.1: Three Ps in a Pod Poster**

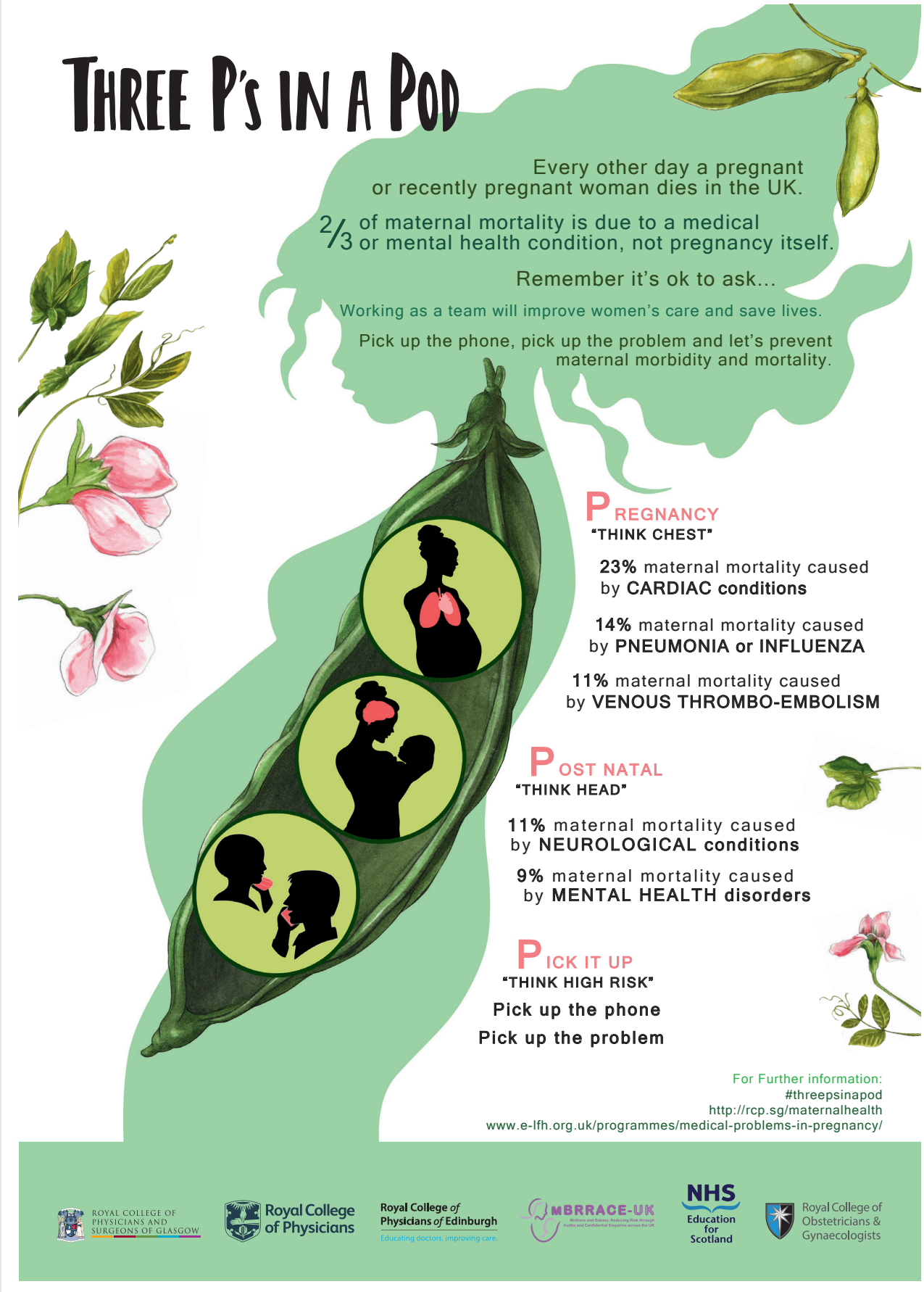


**Figure 1.2: UK Sepsis Trust Community Midwifery Sepsis Screening and Action Tool**

# Community Midwifery Sepsis Screening and Action Tool

THE UK SEPSIS TRUST

To be applied to all women who are pregnant (or have been pregnant in the last 6 weeks irrespective of outcome) with fever (or recent fever) symptoms or who have unexplained illness

**1.** In the context of presumed infection, are any of the following true:

(common sources: pneumonia, UTI, breast abscess/ mastitis, endometritis, chorioamnionitis, infected caesarean or perineal wound, influenza, intra-abdominal infection)

| | Tick |
|---|---|
| Patient looks, or says they are, very unwell | ☐ |
| Family or carer is very concerned | ☐ |
| There is ongoing deterioration | ☐ |

N → Low risk of sepsis. Consider other diagnoses. Use clinical judgement and/or standard protocols.

Give safety netting advice to patient & family:
call 999 if deteriorates rapidly, call 111/ arrange to see GP if condition fails to improve or gradually worsens.
Signpost to available resources as appropriate.
Consider obstetric assessment

Y

Perform a full set of observations:
NEWS is valid after delivery

**2.** Is **ONE** maternal Red Flag present?

| | Tick |
|---|---|
| Responds only to voice or pain/ unresponsive | ☐ |
| Acute confusion | ☐ |
| Systolic B.P ≤ 90 mmHg | ☐ |
| Heart rate ≥ 130 per minute | ☐ |
| Respiratory rate ≥ 25 per minute | ☐ |
| Needs oxygen to keep $SpO_2$ ≥92% | ☐ |
| Non-blanching rash, mottled/ ashen/ cyanotic | ☐ |
| Not passed urine in last 18 hours | ☐ |

N

**3.** Is any Maternal Amber Flag present?

| | Tick |
|---|---|
| Relatives worried about mental state/ behaviour | ☐ |
| Acute deterioration in functional ability | ☐ |
| Respiratory rate 21-24 OR very breathless | ☐ |
| Heart rate 91-129 OR new dysrhythmia | ☐ |
| Systolic BP 91-100 mmHg | ☐ |
| Not passed urine in last 12-18 hours | ☐ |
| Temperature < 36ºC | ☐ |
| Immunosuppressed/ diabetes/ gestational diabetes | ☐ |
| Has had invasive procedure in last 6 weeks (e.g. CS, forceps delivery, ERPC, cerclage, CVs, miscarriage, termination) | ☐ |
| Prolonged rupture of membranes | ☐ |
| Close contact with GAS | ☐ |
| Bleeding/ offensive wound/ vaginal discharge | ☐ |

*If immunity also impaired treat as Red Flag Sepsis*

Y

## At risk of sepsis

1. Same day assessment by GP/ Team Leader
2. Is urgent hospital referral required?
3. Agree and document ongoing management plan (including observations frequency, planned second review as agreed with GP / Team Leader)
4. Monitor urine output

Consider life threatening sepsis mimics e.g. P.E.

Y

## Red Flag Sepsis! This is a time critical condition, immediate action is required.

1. Dial 999, arrange blue light transfer
2. If available give $O_2$ to keep saturations >94%
3. Cannulate if skills & competencies allow
4. Consider IV fluids
5. Inform family
6. Ensure crew pre-alert as 'Red Flag Sepsis'

## 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 1.3). 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 MBRRACE-UK hospital contact is asked to return the surveillance form together with the details of the local clinicians within one month of the death occurring. The MBRRACE-UK hospital 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 as well as 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 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

Deaths from the UK and Ireland are 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 are 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 (O'Hare, Manning et al. 2016); 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 deaths occurring in 2009–11 and selected late maternal deaths.

## Expert Review

MBRRACE-UK has over 100 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 are appointed in a selection process organised by the relevant Royal Colleges or professional organisations, which require 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 anonymised records are reviewed by a pathologist, together with an obstetrician or physician as required. This establishes the most likely cause of the woman's death and allows her records to be allocated to the appropriate speciality assessors. The care of each woman is then assessed by one or two obstetricians, midwives, anaesthetists and other specialist assessors as required, including psychiatrists, general practitioners, physicians, emergency medicine specialists and intensive care specialists. 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 when specific issues are identified. 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 country. 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

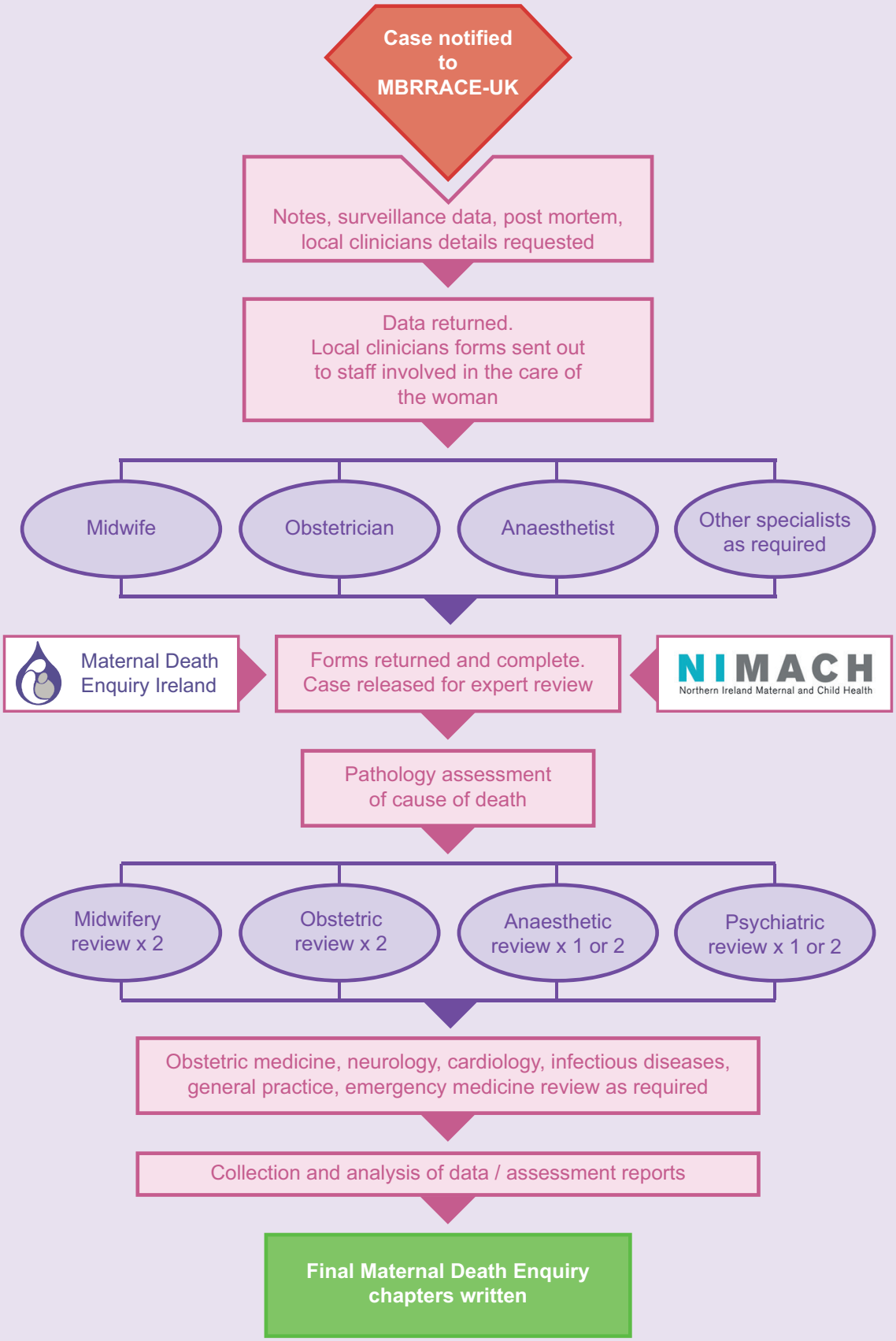
*Improvements in care are interpreted to include adherence to guidelines, where these exist and have not been followed, as well as other improvements which would normally be considered part of good care, where no formal guidelines exist.

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

**Figure 1.3: MBRRACE-UK Data Collection and Assessment Processes**



## 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-UK report. Lead members of each chapter-writing group will then draft the initial chapter, which is then edited by one of the MBRRACE-UK collaborators and reviewed by all the other group members and editors as well as external peer reviewers if required, prior to reaching a final agreed version. Where possible, recommendations are linked to national guidance from organisations such as NICE and SIGN.

## 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 2013 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).

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 (Nair, Kurinczuk et al. 2015) if there are no other possible sources of comparative data.

A non-parametric test for trend across ordered groups was used to investigate the change in three-yearly rolling maternal mortality rates over time, and linear regression was used to analyse the change in non-overlapping triennial rates. 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).

## 1.5 The Confidential Enquiry into Maternal Morbidity

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), have 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 2016 report is pregnancy in women with artificial heart valves.

Women are identified for the CEMM in different ways according to the topic. The women with artificial heart valves were identified from an existing UKOSS study which identified women with artificial heart valves fulfilling the criteria in Box 1.4 between February 2013 and January 2015 (Vause, Clarke et al. 2016).

**Box 1.4: Case definition used in the UKOSS pregnancy in women with artificial heart valves study 2013–15**

Any woman with an artificial mechanical prosthetic heart valve who became pregnant during the study period, irrespective of the outcome of the pregnancy.

This included any woman in whom one or more heart valves had been replaced with an artificial mechanical prosthetic heart valve eg Starr-Edwards ball in cage, Bjork-Shiley tilting disc or St Jude's bi-leaflet valve.

EXCLUDED

Women with a bioprosthetic valve eg Carpentier-Edwards, Medtronic Intact or Hancock, women with a homograft or women who had had a valvotomy or valvoplasty (unless they also had an artificial mechanical prosthetic heart valve).

All 53 surviving women notified nationally were used as the sampling frame. A geographically representative sample of 32 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.

# 2. Maternal Mortality in the UK 2012–14: Surveillance and Epidemiology

Manisha Nair and Marian Knight

## 2.1 Key points

Overall there was no statistically significant decrease in the maternal death rate in the UK between 2009–11 and 2012–14. Considering the gradual rate of decline, achieving the Government aspiration of reducing maternal deaths by 50% by 2030 will be a major challenge for UK health services, requiring coordinated action across multiple specialties.

Maternal deaths from direct causes remain unchanged with no significant change in the rates between 2009–11 and 2012–14.

The rate of indirect deaths remains high with no significant change since 2003, except a decrease in deaths due to influenza. This is primarily due to a low level of influenza activity in 2012–14 (compared with 2009 and 2010). Increasing immunisation rates in pregnancy against seasonal influenza must remain a public health priority.

Thrombosis and thromboembolism remains the leading cause of direct maternal death and cardiac disease the leading cause of indirect maternal death during or up to six weeks after the end of pregnancy.

Maternal deaths from hypertensive disorders are at the lowest ever rate, with fewer than one death for every million women giving birth. This represents a major success for research, audit and evidence-based guidelines leading to improvements in care.

Maternal suicides have now been reclassified by the World Health Organisation as a direct cause of maternal death. The rate of maternal death by suicide remains unchanged since 2003 and maternal suicides are now the leading cause of direct maternal deaths occurring within a year after the end of pregnancy.

## 2.2 Causes and trends

Overall, 241 women died in 2012–14 during or within 42 days of the end of pregnancy in the UK. The deaths of 41 women were classified as coincidental. Thus in this triennium 200 women died from direct and indirect causes among 2,341,745 maternities, a maternal death rate of 8.54 per 100,000 maternities (95% CI 7.40–9.81). This compares to a rate of 9.02 per 100,000 maternities (95% CI 7.85–10.31) in 2011–13. As in the previous reports, 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. However, as discussed in Chapter 1 direct and indirect maternal deaths are now classified using ICD-MM (World Health Organisation 2012) which reclassifies maternal suicide as direct death.

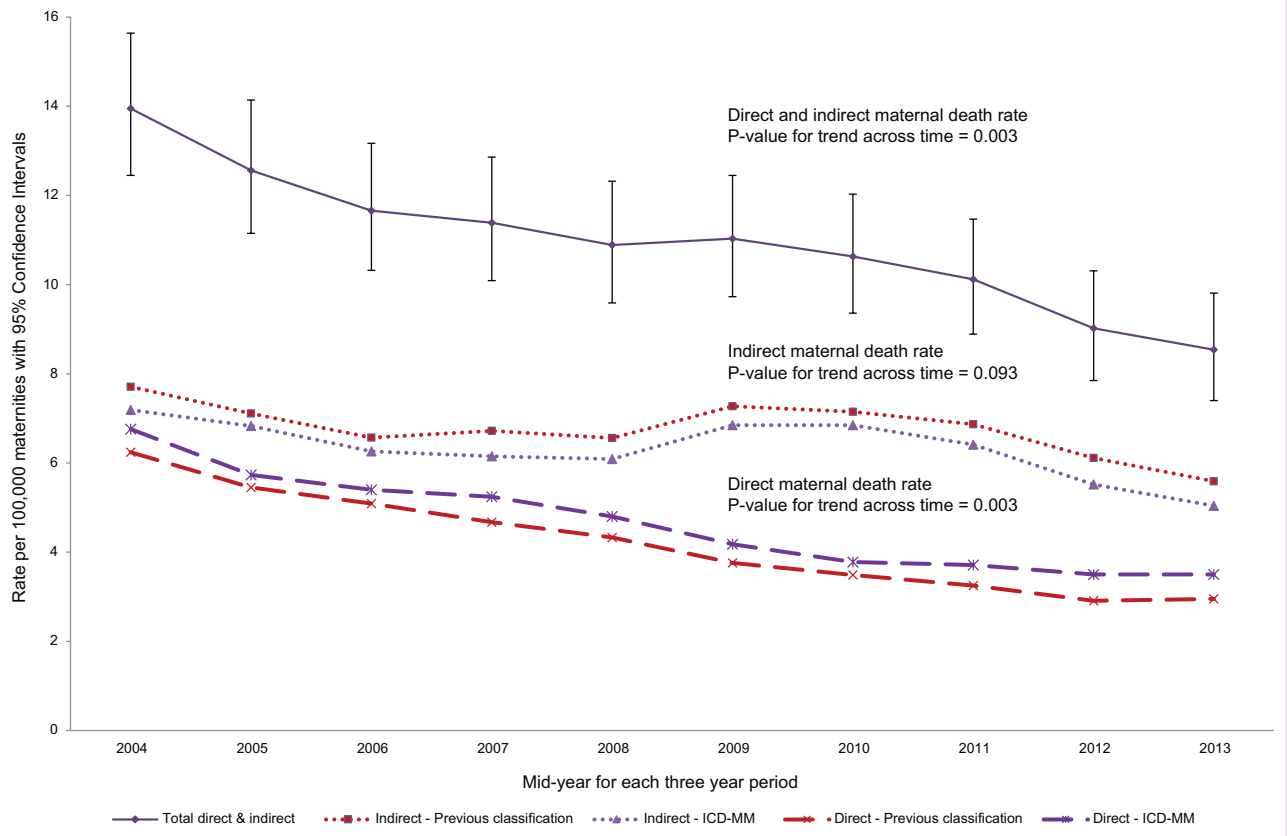
Table 2.1 and figure 2.1 show rolling three-yearly maternal death rates since 2003 using ICD-MM. There was an overall 39% decrease (95% CI 27% to 49%) in maternal death rates between 2003–05 and 2012–14 (rate ratio (RR) 0.61; 95% CI 0.51–0.73 comparing 2003–05 with 2012–14; p=0.003 for trend in rolling rates over time). The direct maternal death rate has decreased by 49% since 2003–05 with a RR of 0.51 (95% CI 0.38–0.68) when comparing 2012–14 with 2003–05, p=0.003 for trend in rolling rates over time. There was a 30% decrease in the rate of indirect maternal deaths when comparing 2012–14 with 2003–05 (RR 0.71, 95% CI 0.55 to 0.90), but the trend over time was not statistically significant p=0.093.

**Table 2.1: Rolling three-year average Direct and Indirect maternal mortality rates per 100,000 maternities, deaths classified using ICD-MM; UK 2003–14**

| 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 | 143 | 6.76 | 5.70–7.97 | 152 | 7.19 | 6.09–8.43 | 295 | 13.95 | 12.45–15.64 |
| 2004–06 | 2 165 909 | 124 | 5.73 | 4.76–6.83 | 148 | 6.83 | 5.78–8.03 | 272 | 12.56 | 11.15–14.14 |
| 2005–07 | 2 220 979 | 120 | 5.40 | 4.48–6.46 | 139 | 6.26 | 5.26–7.39 | 259 | 11.66 | 10.32–13.17 |
| 2006–08 | 2 291 493 | 120 | 5.24 | 4.34–6.26 | 141 | 6.15 | 5.18–7.26 | 261 | 11.39 | 10.09–12.86 |
| 2007–09 | 2 331 835 | 112 | 4.80 | 3.95–5.78 | 142 | 6.09 | 5.13–7.18 | 254 | 10.89 | 9.59–12.32 |
| 2008–10 | 2 366 082 | 99 | 4.18 | 3.40–5.09 | 162 | 6.85 | 5.83–7.99 | 261 | 11.03 | 9.73–12.45 |
| 2009–11 | 2 379 014 | 90 | 3.78 | 3.04–4.65 | 163 | 6.85 | 5.84–7.99 | 253 | 10.63 | 9.36–12.03 |
| 2010–12 | 2 401 624 | 89 | 3.71 | 2.98–4.56 | 154 | 6.41 | 5.44–7.51 | 243 | 10.12 | 8.89–11.47 |
| 2011–13 | 2 373 213 | 83 | 3.50 | 2.79–4.34 | 131 | 5.52 | 4.62–6.55 | 214 | 9.02 | 7.85–10.31 |
| 2012–14 | 2 341 745 | 81 | 3.46 | 2.75–4.30 | 119 | 5.08 | 4.21–6.08 | 200 | 8.54 | 7.40–9.81 |

Sources: 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 using ICD-MM and Previous UK classification systems; rolling three year average rates 2003–2014**




Sources: CMACE, MBRRACE-UK

The impact of reclassifying direct and indirect maternal deaths according to ICD-MM had minimal impact on the observed rates (Knight, Nair et al. 2016). Rolling three-year rates of direct and indirect maternal deaths using the previous classification system are shown for comparison in Table 2.2 and Figure 2.1. Reclassifying maternal suicides increases the rate of direct deaths and decreases the rate of indirect maternal deaths, but the changed classification did not result in statistically significantly different rates (Table 2.3), noting that small numbers limit the statistical power of this comparison.

**Table 2.2: Rolling three-year average Direct and Indirect maternal mortality rates per 100,000 maternities using the previous UK classification; 2003–14**

| 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 |
| 2011–13 | 2 373 213 | 69 | 2.91 | 2.26–3.68 | 145 | 6.11 | 5.16–7.19 | 214 | 9.02 | 7.85–10.31 |
| 2012–14 | 2 341 745 | 67 | 2.86 | 2.22–3.63 | 133 | 5.68 | 4.76–6.73 | 200 | 8.54 | 7.40–9.81 |

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

**Table 2.3: Change in maternal mortality rates per 100,000 maternities according to the ICD-MM classification compared with the previous classification system used in the UK**

| 3-year period | Direct deaths | | | | | | | Indirect deaths | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Previous classification | | ICD-MM classification | | Change in rate compared to previous classification | | | Previous classification | | ICD-MM classification | | Change in rate compared to previous classification | | |
| | Rate | 95% CI | Rate | 95% CI | Rate ratio | 95% CI | p-value | Rate | 95% CI | Rate | 95% CI | Rate ratio | 95% CI | p-value |
| 2003–05 | 6.24 | 5.26–7.41 | 6.76 | 5.70 - 7.97 | 1.08 | 0.85 to 1.38 | 0.508 | 7.71 | 6.61–8.99 | 7.19 | 6.09 - 8.43 | 0.93 | 0.74 to 1.17 | 0.536 |
| 2004–06 | 5.45 | 4.55–6.53 | 5.73 | 4.76 - 6.83 | 1.05 | 0.81 to 1.36 | 0.700 | 7.11 | 6.07–8.33 | 6.83 | 5.78 - 8.03 | 0.96 | 0.76 to 1.21 | 0.730 |
| 2005–07 | 5.09 | 4.23–6.12 | 5.40 | 4.48 - 6.46 | 1.06 | 0.81 to 1.39 | 0.647 | 6.57 | 5.59–7.73 | 6.26 | 5.26 - 7.39 | 0.95 | 0.75 to 1.21 | 0.679 |
| 2006–08 | 4.67 | 3.86–5.64 | 5.24 | 4.34 - 6.26 | 1.12 | 0.86 to 1.47 | 0.389 | 6.72 | 5.74–7.87 | 6.15 | 5.18 - 7.26 | 0.92 | 0.72 to 1.16 | 0.449 |
| 2007-09 | 4.33 | 3.53-5.26 | 4.80 | 3.95 - 5.78 | 1.11 | 0.84 to 1.47 | 0.452 | 6.56 | 5.56-7.69 | 6.09 | 5.13 - 7.18 | 0.93 | 0.73 to 1.17 | 0.523 |
| 2008-10 | 3.76 | 3.02-4.63 | 4.18 | 3.40 - 5.09 | 1.11 | 0.83 to 1.50 | 0.467 | 7.27 | 6.22-8.44 | 6.85 | 5.83 - 7.99 | 0.94 | 0.76 to 1.17 | 0.585 |
| 2009-11 | 3.49 | 2.78-4.32 | 3.78 | 3.04 - 4.65 | 1.08 | 0.80 to 1.48 | 0.596 | 7.15 | 6.11-8.30 | 6.85 | 5.84 - 7.99 | 0.96 | 0.77 to 1.20 | 0.702 |
| 2010-12 | 3.25 | 2.57-4.05 | 3.71 | 2.98 - 4.56 | 1.14 | 0.83 to 1.57 | 0.396 | 6.87 | 5.86-8.00 | 6.41 | 5.44 - 7.51 | 0.93 | 0.74 to 1.17 | 0.539 |
| 2011-13 | 2.91 | 2.26 – 3.68 | 3.50 | 2.79 - 4.34 | 1.20 | 0.86 to 1.68 | 0.258 | 6.11 | 5.16–7.19 | 5.52 | 4.62 - 6.55 | 0.90 | 0.71 to 1.15 | 0.436 |
| 2012-14 | 2.86 | 2.22–3.63 | 3.46 | 2.75 – 4.30 | 1.21 | 0.87 to 1.69 | 0.261 | 5.68 | 4.76 – 6.73 | 5.08 | 4.21 – 6.08 | 0.89 | 0.69 to 1.15 | 0.386 |

Sources: CMACE, MBRRACE-UK. This table is adapted from (Knight, Nair et al. 2016)

Detailed data on the classification of the causes of death were only available from CMACE after 2003, therefore the triennial rates of direct and indirect deaths using the ICD-MM classification can only be generated from 2003–05 onwards, shown in Table 2.4 and Figure 2.2. There was a statistically significant decreasing trend in the triennial rates of overall maternal deaths between 2003–05 and 2012–14, p=0.018. While the triennial rates of direct deaths showed a significant downward trend between 2003–05 and 2012–14, p=0.031, there was no statistically significant change in the rate of direct deaths in 2012–14 compared with 2009–11 (RR 0.91, 95% CI 0.67 to 1.25; p=0.559). Conversely, there was no significant trend in the triennial rates of indirect death between 2003–05 and 2012–14, p=0.220, but the indirect death rate decreased significantly by 26% in 2012–14 compared with 2009–11 (RR 0.74, 95% CI 0.58 to 0.94; p=0.012).

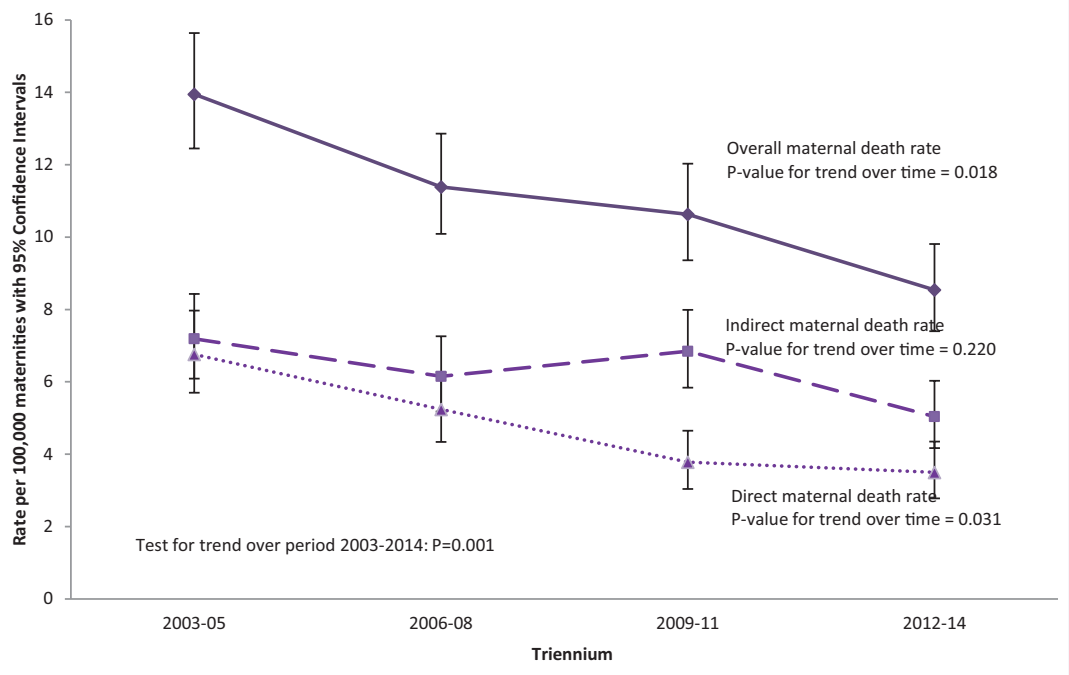
Detailed analysis showed that the decrease in indirect maternal deaths was primarily due to a decrease in deaths due to influenza (RR 0.11, 95% CI 0.003–0.81 when comparing 2012–14 with 2009–11; p<0.001 for trend over time). There was one death from influenza in 2014 and no deaths in 2012 and 2013, which also contributed to the decrease in the overall rate of maternal death in this triennium. As noted in the 2015 report, this was mainly due to a low level of influenza activity in 2012–14 (compared to 2009 and 2010) rather than an increase in the uptake of vaccination among pregnant women in the UK (Public Health England 2015). Increasing immunisation rates in pregnancy against seasonal influenza must remain a public health priority (Knight, Tuffnell et al. 2015). Considering the gradual plateauing of the triennial rates of direct and indirect maternal deaths, achieving the UK Government aspiration of reducing maternal deaths by 50% by 2030 (Department of Health 2015) will be a major challenge for UK health services, requiring coordinated action across multiple specialties.

**Table 2.4: *Direct* and *Indirect* maternal deaths and mortality rates per 100,000 maternities by triennium, UK using ICD-MM; UK 2003–14**

| 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 |
| 2003–05 | 143 | 6.76 | 5.70–7.97 | 152 | 7.19 | 6.09–8.43 | 295 | 13.95 | 12.45–15.64 |
| 2006–08 | 120 | 5.24 | 4.34–6.26 | 141 | 6.15 | 5.18–7.26 | 261 | 11.39 | 10.09–12.86 |
| 2009–11 | 90 | 3.78 | 3.04–4.65 | 163 | 6.85 | 5.84–7.99 | 253 | 10.63 | 9.36–12.03 |
| 2012–14 | 81 | 3.46 | 2.75–4.30 | 119 | 5.08 | 4.21–6.08 | 200 | 8.54 | 7.40–9.81 |

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

**Figure 2.2: *Direct* and *Indirect* maternal mortality rates per 100,000 maternities; UK: 2003-2014 (using ICD-MM)**




Sources: CMACE, MBRRACE-UK

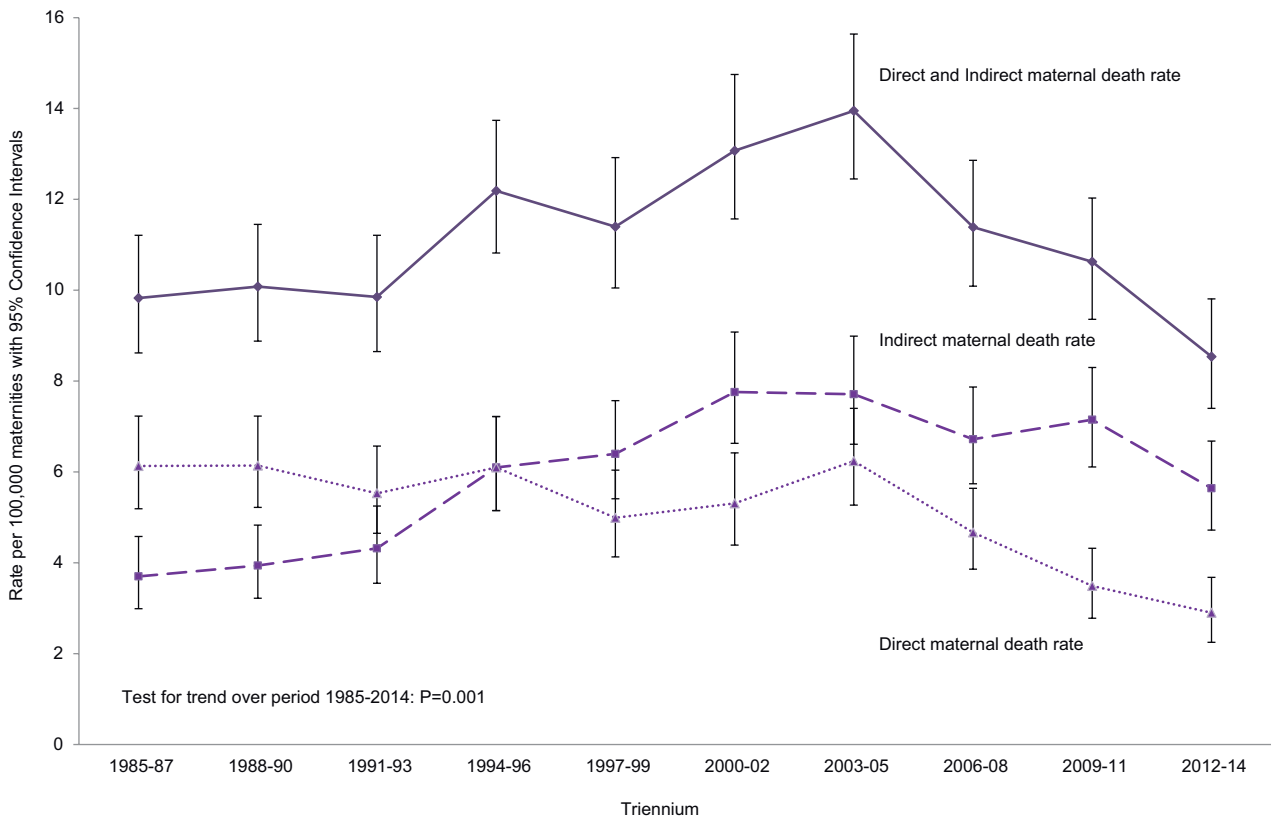
The trends in triennial rates since 1985–87 using the previous classification are shown in Table 2.5 and Figure 2.3. While direct and indirect maternal deaths have decreased in the UK since 1985, the rate of direct deaths did not decrease significantly in 2012–14 compared with 2009–11 (RR 0.82, 95% CI 0.59 to 1.15; p=0.227). The indirect death rate decreased by 21% in 2012–14 compared with the previous triennium (RR 0.79, 95% CI 0.63 to 1.00; p=0.046); this was primarily driven by a decrease in influenza deaths as noted above.

**Table 2.5: Direct and indirect maternal deaths and mortality rates per 100,000 maternities by triennium using the previous UK classification, 1985–2014**

| 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 |
| 2012–14 | 67 | 2.86 | 2.22–3.63 | 133 | 5.68 | 4.76–6.73 | 200 | 8.54 | 7.40–9.81 |

Sources: CMACE, MBRRACE-UK

**Figure 2.3: *Direct* and *Indirect* maternal mortality rates per 100,000 maternities; UK: 1985–2014 (previous classification system)**

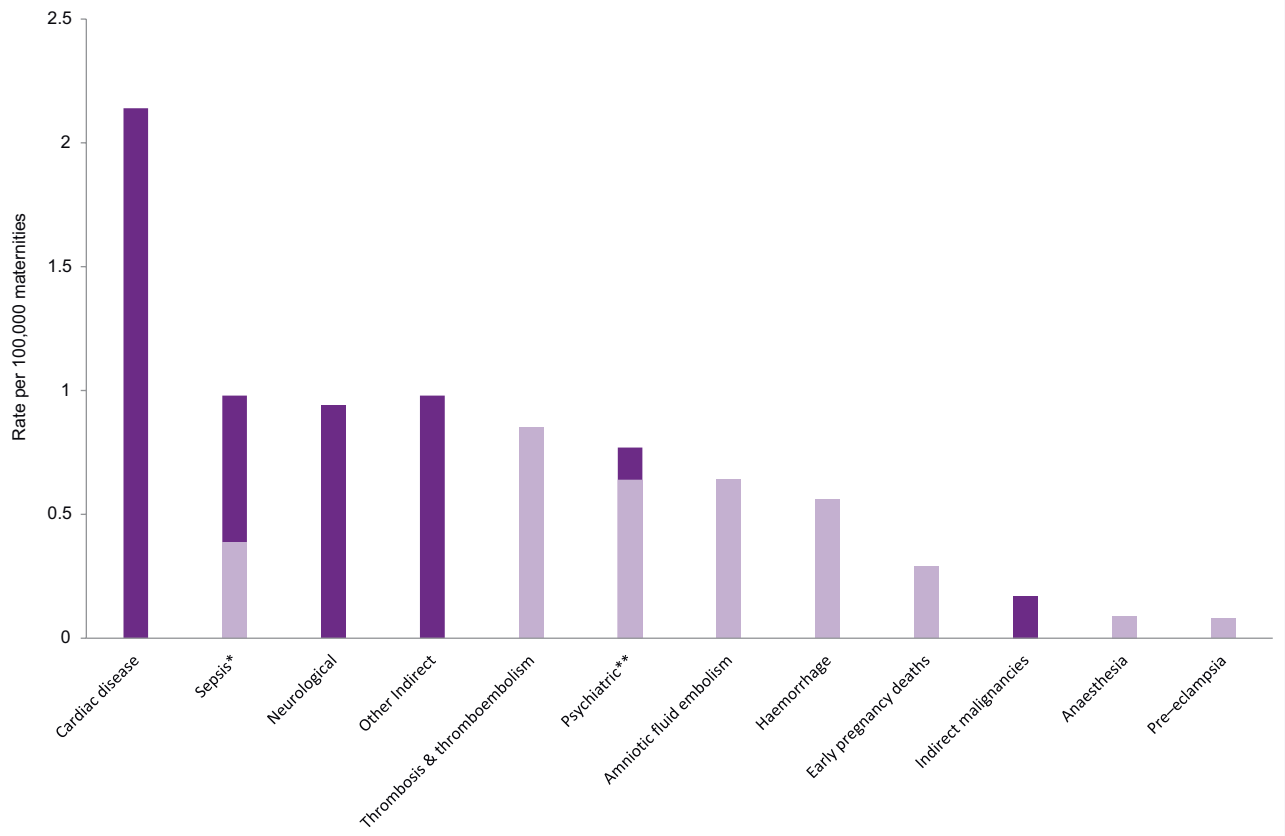



Sources: CMACE, MBRRACE-UK

## Deaths due to individual causes

Maternal deaths by cause are shown in Tables 2.6 and 2.7, and Figure 2.4. Rolling three year rates for individual causes are presented for four overlapping triennial reporting periods (2009–11, 2010–12, 2011–13 and 2012–14) (Table 2.6 and Figure 2.4) and for non-overlapping triennial periods between 1985–7 and 2012–14 (Table 2.7). Note that in table 2.7 maternal deaths by suicide have been included amongst indirect deaths to allow for comparability to earlier years. The causes of death have also been classified using ICD-MM sub-groups and three-year rolling rates are presented in Table 2.8.

**Figure 2.4: Maternal mortality by cause 2012–14**




Dark bars indicate indirect causes of death, pale bars show direct causes of death;

*Rate for direct sepsis (genital tract sepsis and other pregnancy related infections) is shown in pale and rate for indirect sepsis (influenza, pneumonia, others) in dark bar

**Rate for suicides is shown in pale and rate for indirect psychiatric causes (drugs/alcohol) in dark bar

Source: MBRRACE-UK

**Table 2.6: Maternal mortality rates by cause, per 100,000 maternities, 2009 to 2014**

| Cause of death | 2009-11 | | | 2010-12 | | | 2011-13 | | | 2012-14 | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | Rate | 95% CI | n | Rate | 95% CI | n | Rate | 95% CI | n | Rate | 95% CI |
| **All Direct and Indirect deaths** | 253 | 10.63 | 9.36 – 12.03 | 243 | 10.12 | 8.89 – 11.47 | 214 | 9.02 | 7.85 – 10.31 | 200 | 8.54 | 7.40 – 9.81 |
| **Direct deaths** | | | | | | | | | | | | |
| Pregnancy related infections - Sepsis* | 16 | 0.67 | 0.38 - 1.09 | 13 | 0.54 | 0.29 - 0.93 | 8 | 0.34 | 0.15 – 0.66 | 7 | 0.29 | 0.12 – 0.61 |
| Pre-eclampsia and eclampsia | 10 | 0.42 | 0.20 - 0.77 | 9 | 0.38 | 0.18 - 0.71 | 6 | 0.25 | 0.09 – 0.55 | 2 | 0.08 | 0.01 – 0.31 |
| Thrombosis and thromboembolism | 30 | 1.26 | 0.85 - 1.80 | 26 | 1.08 | 0.71 - 1.59 | 24 | 1.01 | 0.65 – 1.50 | 20 | 0.85 | 0.52 - 1.32 |
| Amniotic fluid embolism | 7 | 0.29 | 0.12 - 0.61 | 8 | 0.33 | 0.14 - 0.66 | 10 | 0.42 | 0.20 – 0.78 | 16 | 0.68 | 0.39 – 1.11 |
| Early pregnancy deaths | 4 | 0.17 | 0.05 - 0.43 | 8 | 0.33 | 0.14 - 0.66 | 6 | 0.25 | 0.09 – 0.55 | 7 | 0.29 | 0.12 – 0.61 |
| Haemorrhage | 14 | 0.59 | 0.32 - 0.99 | 11 | 0.46 | 0.23 - 0.82 | 13 | 0.55 | 0.29 – 0.94 | 13 | 0.56 | 0.29 – 0.95 |
| Anaesthesia | 3 | 0.12 | 0.03 - 0.37 | 4 | 0.17 | 0.05 - 0.43 | 3 | 0.13 | 0.03 – 0.37 | 2 | 0.09 | 0.01 – 0.31 |
| Psychiatric - Suicides | 6 | 0.25 | 0.09 – 0.55 | 10 | 0.42 | 0.20 - 0.77 | 13 | 0.55 | 0.29 – 0.94 | 14 | 0.60 | 0.33 – 1.00 |
| All Direct | 90 | 3.78 | 3.04 - 4.65 | 89 | 3.71 | 2.98 - 4.56 | 83 | 3.50 | 2.79 - 4.34 | 81 | 3.46 | 2.75 – 4.30 |
| **Indirect** | | | | | | | | | | | | |
| Cardiac disease | 51 | 2.14 | 1.60 - 2.82 | 54 | 2.25 | 1.69 - 2.93 | 49 | 2.06 | 1.53 – 2.73 | 51 | 2.18 | 1.62 – 2.86 |
| Indirect Sepsis - Influenza | 27 | 1.13 | 0.75 - 1.65 | 13 | 0.54 | 0.29 - 0.93 | 9 | 0.38 | 0.17 – 0.72 | 1 | 0.04 | 0.001 – 0.24 |
| Indirect Sepsis – Pneumonia/ others | 15 | 0.63 | 0.35 - 1.04 | 21 | 0.87 | 0.54 - 1.34 | 20 | 0.84 | 0.52 – 1.30 | 14 | 0.60 | 0.33 – 1.00 |
| Other Indirect causes | 29 | 1.22 | 0.82 - 1.75 | 26 | 1.08 | 0.71 - 1.59 | 22 | 0.93 | 0.58 – 1.40 | 23 | 0.98 | 0.62 – 1.47 |
| Indirect neurological conditions | 30 | 1.26 | 0.85 - 1.80 | 31 | 1.29 | 0.88 - 1.83 | 24 | 1.01 | 0.65 – 1.5 | 22 | 0.94 | 0.59 – 1.42 |
| Psychiatric – Drugs/alcohol/others | 7 | 0.29 | 0.12 - 0.61 | 6 | 0.25 | 0.09 - 0.54 | 6 | 0.25 | 0.09 – 0.55 | 4 | 0.17 | 0.05 – 0.44 |
| Indirect malignancies | 4 | 0.17 | 0.05 - 0.45 | 3 | 0.13 | 0.03 - 0.37 | 1 | 0.04 | 0.001 – 0.24 | 4 | 0.17 | 0.05 – 0.44 |
| All Indirect | 163 | 6.85 | 5.84 - 7.99 | 154 | 6.41 | 5.44 - 7.51 | 131 | 5.52 | 4.62 - 6.55 | 119 | 5.08 | 4.21 – 6.08 |
| **Coincidental** | | | | | | | | | | | | |
| Homicide | 7 | 0.29 | 0.12 - 0.61 | 10 | 0.42 | 0.20 - 0.77 | 8 | 0.34 | 0.15 – 0.66 | 9 | 0.38 | 0.18 – 0.73 |
| Other coincidental | 16 | 0.67 | 0.38 - 1.09 | 16 | 0.67 | 0.38 - 1.08 | 18 | 0.76 | 0.45 - 1.20 | 32 | 1.37 | 0.94 - 1.93 |
| All coincidental | 23 | 0.98 | 0.61 - 1.45 | 26 | 1.08 | 0.71 - 1.59 | 26 | 1.10 | 0.72 – 1.61 | 41 | 1.75 | 1.26 – 2.38 |
| **Late deaths** | 325 | 13.66 | 12.22 - 15.33 | 313 | 13.03 | 11.63-14.56 | 335 | 14.12 | 12.64 – 15.71 | 323 | 13.79 | 12.33 – 15.38 |

*Genital/ urinary tract sepsis deaths, including early pregnancy deaths as a result of genital/ urinary tract sepsis. Other deaths from infectious causes are classified under indirect causes.

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

## Table 2.7: UK Maternal deaths and mortality rates per 100,000 maternities by cause 1985–2014 (Maternal deaths by suicide classified as indirect for comparability)

| 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 | 2012-14 | 1985-87 | 1988-90 | 1991-93 | 1994-96 | 1997-99 | 2000-02 | 2003-05 | 2006-08 | 2009-11 | 2012-14 |
| **All Direct and Indirect deaths** | 223 | 238 | 228 | 268 | 242 | 261 | 295 | 261 | 253 | 200 | 9.83 | 10.08 | 9.85 | 12.19 | 11.4 | 13.07 | 13.95 | 11.39 | 10.63 | 8.54 |
| **Direct deaths** | | | | | | | | | | | | | | | | | | | | |
| **Sepsis*** | 9 | 17 | 15 | 16 | 18 | 13 | 18 | 26 | 16 | 7 | 0.40 | 0.72 | 0.65 | 0.73 | 0.85 | 0.65 | 0.85 | 1.13 | 0.63 | 0.29 |
| **Pre-eclampsia and eclampsia** | 27 | 27 | 20 | 20 | 16 | 14 | 18 | 19 | 10 | 2 | 1.19 | 1.14 | 0.86 | 0.91 | 0.75 | 0.70 | 0.85 | 0.83 | 0.42 | 0.08 |
| **Thrombosis and thromboembolism** | 32 | 33 | 35 | 48 | 35 | 30 | 41 | 18 | 30 | 20 | 1.41 | 1.40 | 1.51 | 2.18 | 1.65 | 1.50 | 1.94 | 0.79 | 1.26 | 0.85 |
| **Amniotic fluid embolism** | 9 | 11 | 10 | 17 | 8 | 5 | 17 | 13 | 7 | 16 | 0.40 | 0.47 | 0.43 | 0.77 | 0.38 | 0.25 | 0.80 | 0.57 | 0.29 | 0.68 |
| **Early pregnancy deaths** | 16 | 24 | 17 | 15 | 17 | 15 | 14 | 11 | 4 | 7 | 0.71 | 1.02 | 0.73 | 0.68 | 0.80 | 0.75 | 0.66 | 0.48 | 0.17 | 0.29 |
| **Haemorrhage** | 10 | 22 | 15 | 12 | 7 | 17 | 14 | 9 | 14 | 13 | 0.44 | 0.93 | 0.65 | 0.55 | 0.33 | 0.85 | 0.66 | 0.39 | 0.59 | 0.56 |
| **Anaesthesia** | 6 | 4 | 8 | 1 | 3 | 6 | 6 | 7 | 3 | 2 | 0.26 | 0.17 | 0.35 | 0.05 | 0.14 | 0.30 | 0.28 | 0.31 | 0.12 | 0.09 |
| **Other Direct‡** | 27 | 17 | 14 | 7 | 7 | 8 | 4 | 4 | 0 | 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 | 67 | 6.13 | 6.14 | 5.53 | 6.10 | 4.99 | 5.31 | 6.24 | 4.67 | 3.49 | 2.86 |
| **Indirect deaths** | | | | | | | | | | | | | | | | | | | | |
| **Cardiac disease** | 23 | 18 | 37 | 39 | 35 | 44 | 48 | 53 | 51 | 51 | 1.01 | 0.76 | 1.60 | 1.77 | 1.65 | 2.20 | 2.27 | 2.31 | 2.14 | 2.18 |
| **Other Indirect causes** | 43 | 45 | 38 | 39 | 41 | 50 | 50 | 49 | 72 | 38 | 1.90 | 1.91 | 1.64 | 1.77 | 1.93 | 2.50 | 2.37 | 2.14 | 3.03 | 1.62 |
| **Indirect neurological conditions** | 19 | 30 | 25 | 47 | 34 | 40 | 37 | 36 | 30 | 22 | 0.84 | 1.27 | 1.08 | 2.14 | 1.60 | 2.00 | 1.75 | 1.57 | 1.26 | 0.94 |
| **Psychiatric causes** | † | † | † | 9 | 15 | 16 | 18 | 13 | 13 | 18 | † | † | † | 0.41 | 0.71 | 0.80 | 0.85 | 0.57 | 0.55 | 0.77 |
| **Indirect malignancies** | † | † | † | † | 11 | 5 | 10 | 3 | 4 | 4 | † | † | † | † | 0.52 | 0.25 | 0.47 | 0.13 | 0.17 | 0.17 |
| **All Indirect** | 84 | 93 | 100 | 134 | 136 | 155 | 163 | 154 | 170 | 133 | 3.70 | 3.94 | 4.32 | 6.10 | 6.40 | 7.76 | 7.71 | 6.59 | 7.15 | 5.68 |
| **Coincidental** | 26 | 39 | 46 | 36 | 29 | 36 | 55 | 50 | 22 | 41 | 1.15 | 1.65 | 1.99 | 1.64 | 1.37 | 1.80 | 2.60 | 2.18 | 0.98 | 1.75 |

*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

Sources: CMACE, MBRRACE-UK

**Table 2.8: Maternal mortality rates by cause using ICD-MM classification, per 100,000 maternities, 2009 to 2014**

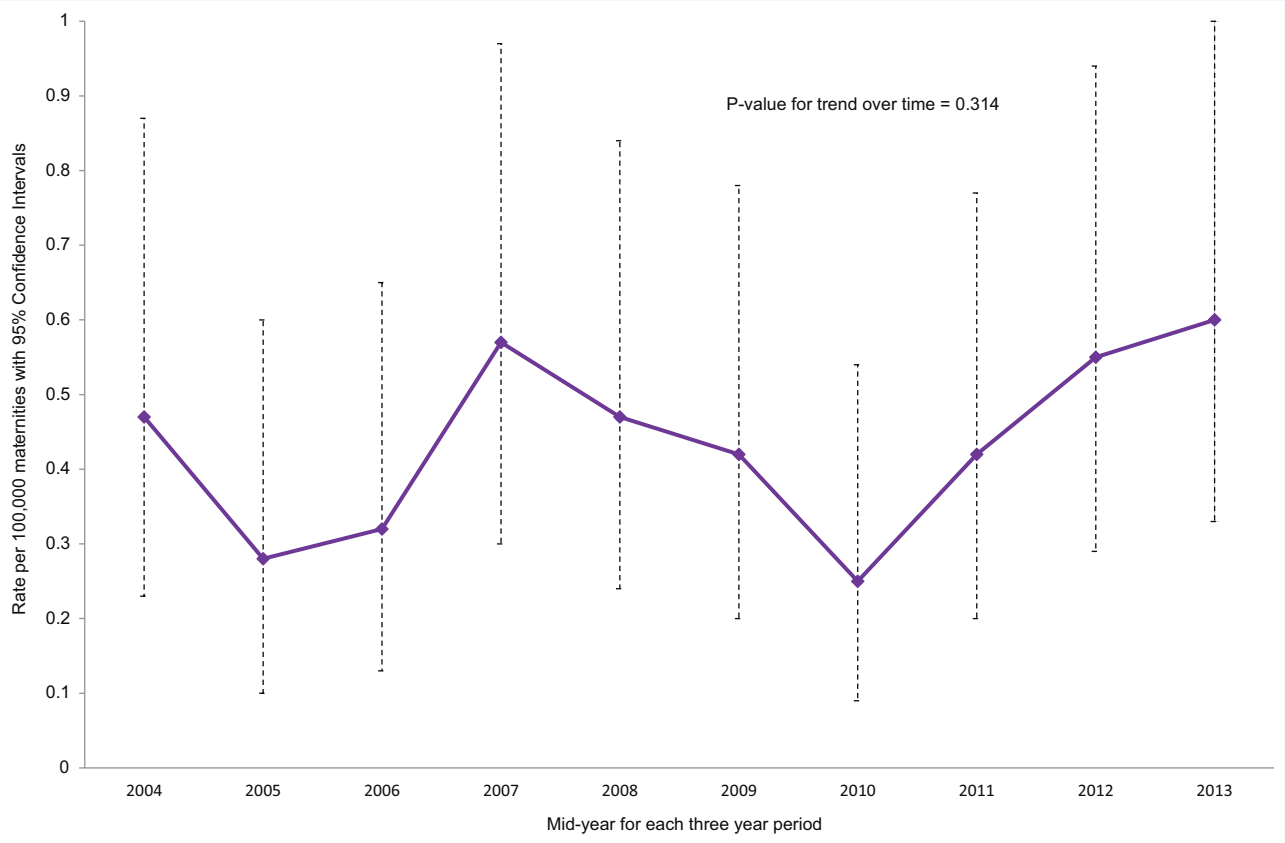
| Cause of death | 2009-11 | | | 2010-12 | | | 2011-13 | | | 2012-14 | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | Rate | 95% CI | n | Rate | 95% CI | n | Rate | 95% CI | n | Rate | 95% CI |
| **Direct causes** | | | | | | | | | | | | |
| Group 1: Pregnancy with abortive outcome | 4 | 0.17 | 0.05 - 0.43 | 8 | 0.33 | 0.14-0.66 | 6 | 0.25 | 0.09 – 0.55 | 7 | 0.29 | 0.12 – 0.62 |
| Group 2: Hypertensive disorders | 10 | 0.42 | 0.20 - 0.77 | 9 | 0.38 | 0.18-0.71 | 6 | 0.25 | 0.09 – 0.55 | 2 | 0.08 | 0.01 – 0.31 |
| Group 3: Obstetric Haemorrhage | 14 | 0.59 | 0.32 - 0.99 | 11 | 0.46 | 0.23-0.82 | 13 | 0.55 | 0.29 – 0.94 | 13 | 0.56 | 0.29 – 0.95 |
| Group 4: Pregnancy-related infection | 16 | 0.67 | 0.38 - 1.09 | 13 | 0.54 | 0.29-0.93 | 8 | 0.34 | 0.15 – 0.66 | 7 | 0.29 | 0.12 – 0.61 |
| Group 5: Other obstetric complications | 43 | 1.81 | 1.31 - 2.43 | 44 | 1.83 | 1.33-2.46 | 47 | 1.98 | 1.46 – 2.63 | 50 | 2.14 | 1.58 – 2.81 |
| Group 6: Unanticipated complications of management | 3 | 0.12 | 0.03 - 0.37 | 4 | 0.17 | 0.05-0.43 | 3 | 0.13 | 0.03 – 0.37 | 2 | 0.09 | 0.01 – 0.31 |
| **Indirect causes** | | | | | | | | | | | | |
| Group 7: Non-obstetric complications | 163 | 6.85 | 5.84 - 7.99 | 154 | 6.41 | 5.44 - 7.51 | 131 | 5.52 | 4.62 - 6.55 | 119 | 5.08 | 4.21 – 6.08 |
| Group 8: Unknown/undetermined | 0 | 0 | - | 0 | 0 | - | 0 | 0 | - | 0 | 0 | - |
| **Coincidental causes** | | | | | | | | | | | | |
| Group 9: Coincidental causes | 23 | 0.98 | 0.61 - 1.45 | 26 | 1.08 | 0.71-1.59 | 26 | 1.10 | 0.72 – 1.61 | 41 | 1.75 | 1.26 – 2.38 |

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

# Maternal deaths by suicide

Between 2009 and 2014, 111 women died by suicide in the UK during or up to a year after the end of pregnancy (20 of whom died during or within 42 days of the end of pregnancy) making this the leading cause of direct maternal deaths occurring up to one year after the end of pregnancy. Rolling three year rates for maternal suicides in the UK during or within 42 days of end of pregnancy are shown in Figure 2.5. It is important to note that there has been no significant change in the rate of maternal suicides since 2003, p = 0.314 for trend over time.

**Figure 2.5: Rolling three year average rates for maternal suicide deaths in the UK within 42 days of the end of pregnancy; 2003–14**




Sources: CMACE, MBRRACE-UK

The 2015 report presented a detailed assessment of care received by women who died by suicide and highlighted the need for specialist multidisciplinary care for women with pre-existing mental health problems (Cantwell, Knight et al. 2015). Key messages from the report are reiterated below.

## Key messages for care for preventing maternal deaths by suicide

**The following are 'red flag' signs for severe maternal illness and require urgent senior psychiatric assessment:**

- **Recent significant change in mental state or emergence of new symptoms,**
- **New thoughts or acts of violent self-harm,**
- **New and persistent expressions of incompetency as a mother or estrangement from the infant.**

**Admission to a mother and baby unit should always be considered where a woman has any of the following:**

- **rapidly changing mental state,**
- **suicidal ideation (particularly of a violent nature),**
- **pervasive guilt or hopelessness,**
- **significant estrangement from the infant,**
- **new or persistent beliefs of inadequacy as a mother,**
- **evidence of psychosis.**

**Mental health assessments should always include a review of previous history and take into account the findings of recent presentations and escalating patterns of abnormal behaviour.**

**Investigations into deaths from psychiatric causes at any stage during pregnancy and the first postnatal year should be carried out and should be multi-agency and include all the services involved in caring for the woman.**

**Saving lives, Improving Mothers' Care 2015 (Cantwell, Knight et al. 2015)**

## Other direct deaths

Thrombosis and thromboembolism continue to be the leading cause of direct deaths occurring within 42 days of the end of pregnancy, followed by deaths due to amniotic fluid embolism and deaths by suicide (Figure 2.4). The maternal death rate from pre-eclampsia and eclampsia was again the lowest ever reported; only two women died from hypertensive disorders in this triennium. An in-depth review of the care of the women who died from hypertensive disorders over the past six years is presented in chapter 4. There was no statistically significant change in the rate of direct maternal deaths from any cause between 2009 and 2014.

## Indirect deaths

Consistent with the previous reports, there was no statistically significant decrease in the rates of indirect maternal death over the years from 2003–05 to 2012–14 and deaths due to indirect causes still remain the major proportion (59%) of maternal deaths in the UK (Figure 2.4). As in the previous reports, cardiac disease remains the largest single cause of indirect maternal deaths in 2012–14. There was no significant change in the maternal mortality rate from cardiac disease between 2009 and 2014 ($p=0.129$). A detailed assessment of the specific conditions and care of the women who died from cardiac disease is included in chapter 3.

Deaths from neurological causes were the second most frequent cause of indirect maternal death. There was a 25% decrease in the rate of deaths due to neurological causes in 2012–14 compared with 2009–11, but this decrease is not statistically significant ($p=0.297$). Indirect sepsis deaths due to causes other than influenza have not significantly changed between 2009 and 2014. Thus, other than the decrease in deaths due to influenza (noted above), there have been no statistically significant changes in the rates of maternal death due to specific indirect causes.

## International comparison

The international comparison of the UK MMR calculated using routine data collected through death certificates and live births as denominators for 2012–14 is presented in Table 2.9. As highlighted in the previous reports, the maternal mortality rates for the UK using routinely reported data are much lower than the actual rates as identified through the UK CEMD, which uses multiple sources of death identification.

**Table 2.9: Maternal mortality ratios* per 100,000 live births, UK: 1985–2014**

| Triennium | No. of deaths identified through death certificates | Maternal mortality ratio | 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 |
| 2012–14 | 110 | 4.65 | 3.82–5.60 | 2,368,125 |

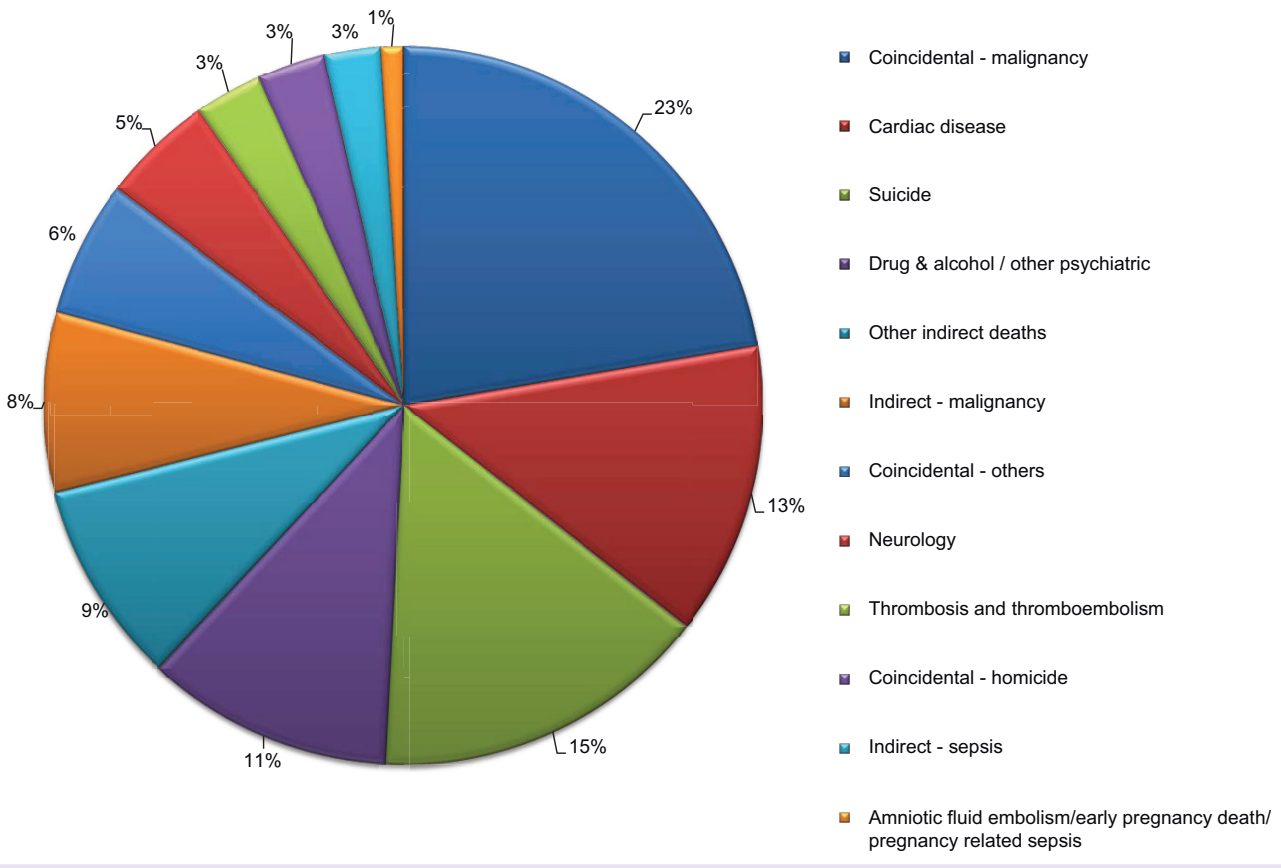
Source: Office for National Statistics, National Records Scotland, Northern Ireland Statistics and Research Agency

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

## Women who died between six weeks and one year after the end of pregnancy

Between 2012 and 2014, 323 women died between six weeks and one year after the end of pregnancy, representing a maternal mortality rate of 13.79 per 100,000 maternities (95% CI 12.33–15.38). Their causes of death are shown in Figure 2.6.

**Figure 2.6: Causes of death amongst women who died between six weeks and one year after the end of pregnancy, UK 2012–14**



# 2.3 The characteristics of women who died 2012-14

## The women and babies

A quarter (49 women) of the 200 women who died in 2012–14 were still pregnant at the time of their death and about two-thirds of these women were ≤20 weeks' gestation when they died (Table 2.10). Sixteen (8%) women had a pregnancy loss at ≤20 weeks' gestation and the remaining 135 women gave birth to a total of 141 infants, 105 (74%) survived, 36 died (24 stillborn and 12 neonatal deaths). The women who died left behind a further 253 children, thus together a total of 358 motherless children remain. The majority of women who gave birth did so in hospital (79%); 16% of women gave birth in an accident and emergency department or an ambulance, and 4% at home (Table 2.11). Eighty-six of the women who died were delivered by caesarean section in 2012–14, 37% of these were perimortem caesarean sections. Nineteen babies were born by perimortem caesarean section after 32 weeks' gestation of whom nine survived (six were stillborn and four died in the neonatal period) and 13 babies were born by perimortem caesarean at 32 weeks or less of whom 10 died (four were stillborn and six died in the neonatal period). Thus, 38% of the total 32 babies delivered by perimortem caesarean section survived (31% were stillborn and 31% died in the neonatal period).

**Table 2.10: Timing of maternal deaths in relation to pregnancy 2012–14**

| Time period of deaths in the pregnancy care pathway | Direct (n=81) Frequency (%) | Indirect (n=119) Frequency (%) | Total (n=200) Frequency (%) |
|---|---|---|---|
| **Antenatal period** | | | |
| *≤20 weeks* | 14 (17) | 15 (13) | 30 (15) |
| *>20 weeks* | 7 (9) | 13 (11) | 19 (10) |
| **Postnatal on day of delivery** | 22 (27) | 26 (22) | 48 (24) |
| **Postnatal 1–41 days after delivery** | 38 (47) | 65 (54) | 103 (51) |

**Table 2.11: Place of delivery amongst women >20 weeks' gestation who died after delivery 2012–14**

| Place of delivery (for women who had a childbirth) | Direct (n=50) Frequency (%) | Indirect (n=85) Frequency (%) | Total (n=135) Frequency (%) |
|---|---|---|---|
| **Home** | 3 (6) | 3 (4) | 6 (4) |
| **Hospital (except A&E)** | 41 (82) | 65 (76) | 106 (79) |
| **Emergency Department or ambulance** | 6 (12) | 16 (19) | 22 (16) |
| **Not known** | 0 (0) | 1 (1) | 1 (1) |

## Socio-demographic characteristics

The socio-demographic characteristics of women who died in 2012–14 are shown in Table 2.12. Information on whether women were subject to domestic abuse before or during pregnancy was missing for 40% of women who died. This is unchanged from the figure of 42% missing in the 2015 report (Knight, Tuffnell et al. 2015). NICE guidance states that all women should be asked whether they have experienced domestic violence or abuse, even where there are no indicators of such violence and abuse (National Institute for Health and Care Excellence 2014b). This is an important action in both primary and secondary care.

The rates of maternal mortality varied by age, socioeconomic status and ethnic background of the women, being higher amongst older women, those living in the most deprived areas and amongst women from some ethnic minority groups (Table 2.13). These characteristics have been shown to be independently associated with increased odds of direct and indirect maternal death in the UK after controlling for other known risk factors (Nair, Kurinczuk et al. 2015, Nair, Knight et al. 2016). The risk of death from direct and indirect causes is significantly higher among women 35 years and older. A study using the MBRRACE-UK surveillance data to investigate the reasons for this increased risk showed that the known risk factors for maternal death including medical comorbidities, BMI, pregnancy-related and socioeconomic factors could not completely explain the association between increasing age and maternal mortality (McCall, Nair et al. 2016).

As was noted in the 2015 report, there was no statistically significant difference between women living in the most deprived areas and those living in the least deprived areas in this triennium, however, the absolute estimates of the risk difference remain unchanged between the two triennia. In the previous reports incidence rates were presented for specific ethnic minority groups in England, however this year we were unable to obtain denominator figures for the specific groups due to restrictions, requirements and charges placed on us by the Health and Social Care Information Centre. Since the basic aggregate denominator data were not available for the standard census ethnicity groupings, aggregate rates using larger ethnicity groupings are presented in Tables 2.13 and 2.14. Similar to the previous triennium (2009–11), the risk of maternal death in 2012–14 was found to be significantly higher among women from Black ethnic minority backgrounds compared with White (RR 4.19; 95% CI 2.69 to 6.35). Estimated ratios of relative risk (RRR) (Altman and Bland 2003) of maternal death in the different age, socioeconomic and ethnic groups did not show any statistically significant difference between 2009–11 and 2012–14 (Table 2.14), suggesting that there was no significant change in the inequality gaps across these time-periods.

A quarter of women who died in 2012–14 were born outside the UK; 46% of these women were not UK citizens. Overall 13% of the women who died were not UK citizens. Women who died who were born abroad had arrived in the UK a median of 4 years before they died (range 1 month to 22 years), and 65% were from Asia (mainly Pakistan, Sri Lanka and Bangladesh) and Africa (mainly Nigeria, Somalia and Democratic Republic of Congo), about 14% from Eastern Europe (mostly from Poland) and the remainder from other parts of Europe, North America and the Caribbean. Table 2.15 shows the rates of death amongst women born in selected countries with the highest number of deaths. Overall, there was no statistically significant difference in maternal death rate between women born in the UK and those born outside the UK in 2012–14, a finding similar to 2011–13. The RR of death among women born outside the UK in 2012–14 was not statistically significantly different from the RR in 2011–13 (RRR = 0.84; 95% CI = 0.54 to 1.32; p=0.45). However, women born in certain specific countries had a significantly higher risk of death compared to women born in the UK (Table 2.15). In this triennium the non-UK country from which the highest number of women died was Pakistan (n=10); these women died from a variety of both direct (n=5) and indirect (n=5) causes. Of the 26 women who were not UK citizens and born outside the UK, 3 were refugees (12%) and 4 were visitors (15%), 17 (65%) had another status, including wife of UK resident. The status of 2 women (8%) was unknown.

## Table 2.12: The socio-demographic characteristics of women who died 2012–14

| Characteristics | Direct (n=81) Frequency (%) | Indirect (n=119) Frequency (%) | Total (n=200) Frequency (%) |
|---|---|---|---|
| **Socio-demographic** | | | |
| **Age** | | | |
| *<20* | *0 (0)* | *5 (4)* | *5 (3)* |
| *20–24* | *7 (9)* | *17 (14)* | *24 (12)* |
| *25–29* | *17 (21)* | *30 (25)* | *47 (24)* |
| *30–34* | *27 (33)* | *29 (24)* | *56 (28)* |
| *35–39* | *20 (25)* | *31 (26)* | *51 (25)* |
| *≥ 40* | *10 (12)* | *7 (6)* | *17 (8)* |
| **Parity** | | | |
| *0* | *22 (27)* | *41 (34)* | *63 (32)* |
| *1 to 2* | *42 (52)* | *59 (50)* | *101 (50)* |
| *≥3* | *11 (13)* | *18 (15)* | *29 (15)* |
| *Missing* | *6 (7)* | *1 (1)* | *7 (3)* |
| **UK citizen** | | | |
| *Yes* | *64 (79)* | *102 (86)* | *166 (83)* |
| *No* | *14 (17)* | *12 (10)* | *26 (13)* |
| *Missing* | *3 (4)* | *5 (4)* | *8 (4)* |
| **Ethnicity** | | | |
| *White European* | *50 (62)* | *92 (77)* | *142 (71)* |
| *Indian* | *1 (1)* | *1 (1)* | *2 (1)* |
| *Pakistani* | *6 (7)* | *6 (5)* | *12 (6)* |
| *Bangladeshi* | *1 (1)* | *2 (2)* | *3 (1)* |
| *Other Asian* | *3 (4)* | *1 (1)* | *4 (2)* |
| *Black Caribbean* | *5 (6)* | *3 (2)* | *8 (4)* |
| *Black African* | *11 (13)* | *8 (7)* | *19 (10)* |
| *Others/ Mixed* | *3 (4)* | *5 (4)* | *8 (4)* |
| *Missing* | *1 (1)* | *1 (1)* | *2 (1)* |
| **Woman's region of birth** | | | |
| *United Kingdom* | *52 (64)* | *88 (74)* | *140 (70)* |
| *Eastern Europe* | *3 (4)* | *4 (3)* | *7 (4)* |
| *Western Europe* | *0 (0)* | *2 (2)* | *2 (1)* |
| *Asia* | *10 (12)* | *11 (9)* | *21 (10)* |
| *Africa* | *9 (11)* | *9 (8)* | *18 (9)* |
| *Australia and North America* | *2 (2)* | *0 (0)* | *2 (1)* |
| *Missing* | *5 (6)* | *5 (4)* | *10 (5)* |
| **Socioeconomic status (Index of Multiple Deprivation (IMD) of postcode of residence)** | | | |
| *First quintile (Least deprived)* | *8 (10)* | *14 (12)* | *22 (11)* |
| *Second quintile* | *13 (16)* | *9 (8)* | *22 (11)* |
| *Third quintile* | *13 (16)* | *16 (13)* | *29 (15)* |
| *Fourth quintile* | *16 (20)* | *26 (22)* | *42 (21)* |
| *Fifth quintile (Most deprived)* | *19 (23)* | *36 (30)* | *55 (27)* |
| *Missing* | *12 (15)* | *18 (15)* | *30 (15)* |
| **Socioeconomic status (Occupational classification)** | | | |
| *Employed (Either woman or partner)* | *49 (60)* | *72 (61)* | *121 (61)* |
| *Unemployed (Both)* | *4 (5)* | *7 (6)* | *11 (5)* |
| *Missing* | *28 (35)* | *40 (33)* | *68 (34)* |
| **Able to speak/understand English** | | | |
| *Yes* | *72 (89)* | *113 (95)* | *185 (93)* |
| *No* | *7 (9)* | *5 (4)* | *12 (6)* |
| *Missing* | *2 (2)* | *1 (1)* | *3 (1)* |
| **Living arrangements** | | | |
| *With partner* | *52 (64)* | *91 (76)* | *143 (72)* |
| *Living alone* | *12 (15)* | *9 (8)* | *21 (10)* |
| *With parents/extended family* | *8 (10)* | *9 (8)* | *17 (9)* |
| *Others* | *1 (1)* | *3 (2)* | *4 (2)* |
| *Missing* | *8 (10)* | *7 (6)* | *15 (7)* |
| **Domestic abuse (prior to pregnancy/ during pregnancy)** | | | |
| *Yes* | *7 (9)* | *6 (5)* | *13 (6)* |
| *No* | *40 (49)* | *67 (56)* | *107 (54)* |
| *Missing* | *34 (42)* | *46 (39)* | *80 (40)* |
| **Known to social services** | | | |
| *Yes* | *9 (11)* | *15 (13)* | *24 (12)* |
| *No* | *69 (85)* | *100 (84)* | *169 (85)* |
| *Missing* | *3 (4)* | *4 (3)* | *7 (3)* |

## Table 2.13: Maternal mortality rates amongst different population groups 2012–14

| | Total maternities 2012–14 | Total deaths | Rate per 100,000 maternities | 95% CI | Relative risk (RR) | 95% CI |
|---|---|---|---|---|---|---|
| **Age** | | | | | | |
| *<20* | *100014* | *5* | *5.0* | *1.62 to 11.67* | *0.84* | *0.25 to 2.25* |
| *20–24* | *403278* | *24* | *5.95* | *3.81 to 8.85* | *1 (Ref)* | *-* |
| *25–29* | *657886* | *47* | *7.14* | *5.25 to 9.5* | *1.20* | *0.72 to 2.05* |
| *30–34* | *710835* | *56* | *7.88* | *5.95 to 10.23* | *1.32* | *0.81 to 2.23* |
| *35–39* | *374528* | *51* | *13.62* | *10.14 to 17.9* | *2.29* | *1.38 to 3.89* |
| *≥ 40* | *95083* | *17* | *17.88* | *10.42 to 28.6* | *3.00* | *1.51 to 5.83* |
| **IMD Quintiles (England only)** | | | | | | |
| *I (Least deprived/ highest 20%)* | *286878* | *17* | *5.93* | *3.45 to 9.49* | *1 (Ref)* | *-* |
| *II* | *305930* | *18* | *5.88* | *3.49 to 9.3* | *0.99* | *0.48 to 2.05* |
| *III* | *355782* | *21* | *5.9* | *3.65 to 9.02* | *1.00* | *0.50 to 2.01* |
| *IV* | *433834* | *40* | *9.22* | *6.59 to 12.55* | *1.56* | *0.86 to 2.93* |
| *V (Most deprived/ lowest 20%)* | *531779* | *51* | *9.59* | *7.14 to 12.61* | *1.62* | *0.92 to 2.99* |
| **Ethnic group (England only)** | | | | | | |
| *White (inc. not known)* | *1550562* | *115* | *7.42* | *6.12 to 8.9* | *1 (Ref)* | *-* |
| *Asian* | *207975* | *21* | *10.1* | *6.25 to 15.43* | *1.36* | *0.81 to 2.18* |
| *Black* | *93151* | *29* | *31.13* | *20.8 to 44.7* | *4.19* | *2.69 to 6.35* |
| *Chinese/ others* | *72976* | *3* | *4.11* | *0.84 to 12.01* | *0.55* | *0.11 to 1.66* |
| *Mixed* | *30138* | *1* | *3.32* | *0.08 to 18.49* | *0.44* | *0.01 to 2.54* |

## Table 2.14: Comparing the relative risk of maternal death among different population groups between 2010–11 and 2012–14

| | 2009–11 | | 2012–14 | | Ratio of the relative risks (RRR) (comparing 2012–14 with 2009–11) | 95% CI | P-value |
|---|---|---|---|---|---|---|---|
| | Relative risk (RR) | 95% CI | Relative risk (RR) | 95% CI | | | |
| **Age** | | | | | | | |
| *<20* | *1.30* | *0.65 to 2.47* | *0.84* | *0.25 to 2.25* | *0.65* | *0.18 to 2.34* | *0.506* |
| *20–24* | *1 (Ref)* | *-* | *1 (Ref)* | *-* | *-* | *-* | *-* |
| *25–29* | *1.01* | *0.65 to 1.59* | *1.20* | *0.72 to 2.05* | *1.19* | *0.60 to 2.36* | *0.624* |
| *30–34* | *1.26* | *0.83 to 1.95* | *1.32* | *0.81 to 2.23* | *1.05* | *0.54 to 2.03* | *0.891* |
| *35–39* | *1.95* | *1.26 to 3.03* | *2.29* | *1.38 to 3.89* | *1.17* | *0.60 to 2.32* | *0.643* |
| *≥ 40* | *3.16* | *1.79 to 5.48* | *3.00* | *1.51 to 5.83* | *0.95* | *0.39 to 2.28* | *0.908* |
| **IMD Quintiles (England only)** | | | | | | | |
| *I (Least deprived/ highest 20%)* | *1 (Ref)* | *-* | *1 (Ref)* | *-* | *-* | *-* | *-* |
| *II* | *1.24* | *0.69 to 2.26* | *0.99* | *0.48 to 2.05* | *0.80* | *0.31 to 2.04* | *0.638* |
| *III* | *1.25* | *0.71 to 2.24* | *1.00* | *0.50 to 2.01* | *0.80* | *0.32 to 1.97* | *0.628* |
| *IV* | *1.65* | *0.99 to 2.84* | *1.56* | *0.86 to 2.93* | *0.95* | *0.42 to 2.12* | *0.892* |
| *V (Most deprived/ lowest 20%)* | *1.69* | *1.03 to 2.87* | *1.62* | *0.92 to 2.99* | *0.96* | *0.44 to 2.09* | *0.916* |
| **Ethnic group (England only)** | | | | | | | |
| *White (inc. not known)* | *1 (Ref)* | *-* | *1 (Ref)* | *-* | *-* | *-* | *-* |
| *Asian* | *1.82* | *1.21 to 2.66* | *1.36* | *0.81 to 2.18* | *0.74* | *0.39 to 1.40* | *0.367* |
| *Black* | *2.68* | *1.68 to 4.13* | *4.19* | *2.69 to 6.35* | *1.56* | *0.83 to 2.91* | *0.158* |
| *Chinese/ others* | *1.50* | *0.67 to 2.94* | *0.55* | *0.11 to 1.66* | *0.36* | *0.07 to 1.71* | *0.203* |
| *Mixed* | *0.72* | *0.08 to 2.66* | *0.44* | *0.01 to 2.54* | *0.61* | *0.02 to 16.18* | *0.768* |

**Table 2.15: Maternal mortality rates according to mother's country of birth (selected countries)**

| Woman's country of birth | Maternities 2012–14 | Total Deaths | Rate per 100,000 maternities | 95% CI | Relative risk (RR) | 95% CI |
|---|---|---|---|---|---|---|
| **UK** | 1,765,665 | 139 | 7.87 | 6.62 to 9.30 | 1 (Ref) | - |
| **Outside UK** | 576,080 | 51 | 8.85 | 6.59 to 11.64 | 1.12 | 0.80 to 1.56 |
| **Specific countries** | | | | | | |
| *Bangladesh* | *24029* | *3* | *12.5* | *2.57 to 36.5* | *1.58* | *0.32 to 4.73* |
| *Pakistan* | *56799* | *10* | *17.6* | *8.44 to 32.4* | *2.24* | *1.05 to 4.24* |
| *Jamaica* | *5995* | *3* | *50.0* | *10.3 to 146.2* | *6.36* | *1.29 to 18.9* |
| *Nigeria* | *22564* | *4* | *17.7* | *4.83 to 45.4* | *2.25* | *0.60 to 5.89* |
| *Poland* | *69247* | *4* | *5.78* | *1.57 to 14.8* | *0.73* | *0.20 to 1.92* |

## Medical and pregnancy-related characteristics

Studies using surveillance data from the MBRRACE-UK for women who died between 2009 and 2014 showed that medical comorbidities were significantly associated with maternal death from both direct and indirect causes (Nair, Kurinczuk et al. 2015, Nair, Knight et al. 2016). At the population level, 66% of the increased risk of maternal death in the UK could be attributed to medical comorbidities (Nair, Knight et al. 2016). More than two-thirds (69%) of the women who died in 2012–14 were known to have pre-existing medical problems (Table 2.16), 17% were known to have pre-existing mental health problems. A third (33%) of the women who died in 2012–14 were obese and 18% were overweight (Table 2.16). Obesity has been shown to be associated with higher odds of maternal death in the UK with its effect primarily manifested through medical comorbidities (Nair, Kurinczuk et al. 2015, Nair, Knight et al. 2016).

The pregnancy-related characteristics of the women who died in 2012–14 are shown in Table 2.17.

**Table 2.16: Selected medical conditions and characteristics identified amongst women who died 2012–14**

| Medical condition/characteristic | Direct (n=81) Frequency (%) | Indirect (n=119) Frequency (%) | Total (n=200) Frequency (%) |
|---|---|---|---|
| **Body mass index (BMI)** | | | |
| *<18* | *1 (1)* | *4 (3)* | *5 (3)* |
| *18–24* | *27 (33)* | *50 (42)* | *77 (38)* |
| *25–29* | *17 (21)* | *20 (17)* | *37 (18)* |
| *≥ 30* | *27 (33)* | *38 (32)* | *65 (33)* |
| *Missing* | *9 (11)* | *7 (6)* | *16 (8)* |
| **Mental health problems or psychiatric disorders** | | | |
| *Yes* | *15 (18)* | *18 (15)* | *33 (17)* |
| *No* | *62 (77)* | *99 (83)* | *161 (80)* |
| *Missing* | *4 (5)* | *2 (2)* | *6 (3)* |
| **Any pre-existing medical problem (excluding obesity)** | | | |
| *Yes* | *50 (62)* | *87 (73)* | *137 (69)* |
| *No* | *27 (33)* | *30 (25)* | *57 (28)* |
| *Missing* | *4 (5)* | *2 (2)* | *6 (3)* |

**Table 2.17: Pregnancy-related characteristics of the women who died 2012–14**

| Characteristics | Direct (n=81) Frequency (%) | Indirect (n=119) Frequency (%) | Total (n=200) Frequency (%) |
|---|---|---|---|
| **Pregnancy known to be as a result of assisted reproductive techniques** | | | |
| *Yes* | *2 (2)* | *2 (2)* | *4 (2)* |
| *No* | *73 (90)* | *112 (94)* | *185 (93)* |
| *Missing* | *6 (7)* | *5 (4)* | *11 (5)* |
| **Multiple pregnancy** | | | |
| *Yes* | *2 (2)* | *4 (3)* | *6 (3)* |
| *No* | *75 (93)* | *112 (94)* | *187 (94)* |
| *Missing* | *4 (5)* | *3 (3)* | *7 (3)* |
| **Previous caesarean section** | | | |
| *Yes* | *22 (27)* | *25 (21)* | *47 (24)* |
| *No* | *53 (65)* | *92 (77)* | *145 (72)* |
| *Missing* | *6 (7)* | *2 (2)* | *8 (4)* |
| **Previous caesarean numbers (among women who had a previous caesarean section)** | | | |
| *1* | *16 (73)* | *18 (72)* | *34 (72)* |
| ≥2 | *6 (27)* | *7 (28)* | *13 (28)* |

## Other characteristics of women who died

Inadequate utilisation of antenatal care services and substance misuse have been shown to be associated with increased odds of direct and indirect causes of maternal death in the UK (Nair, Kurinczuk et al. 2015, Nair, Knight et al. 2016). The prevalence of these risk factors among women who died in 2012–14 did not differ from that noted in the previous reports (Table 2.18) and use of antenatal care still remains an issue. Whether due to lack of access or other factors, just over a quarter of women who received 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).

**Table 2.18: Other characteristics of women who died 2012–14**

| Characteristics | Direct (n=81) Frequency (%) | Indirect (n=119) Frequency (%) | Total (n=200) Frequency (%) |
|---|---|---|---|
| **Smoking** | | | |
| *Smoker* | *13 (16)* | *27 (22)* | *40 (20)* |
| *Non-smoker* | *55 (68)* | *78 (66)* | *133 (67)* |
| *Missing* | *13 (16)* | *14 (12)* | *27 (13)* |
| **Substance user** | | | |
| *Yes* | *3 (4)* | *8 (7)* | *11 (6)* |
| *No* | *75 (92)* | *109 (91)* | *184 (92)* |
| *Missing* | *3 (4)* | *2 (2)* | *5 (2)* |
| **Received any antenatal care*** | | | |
| *Yes* | *68 (84)* | *113 (95)* | *181 (90)* |
| *No* | *13 (16)* | *6 (5)* | *19 (10)* |
| *Missing* | *0 (0)* | *0 (0)* | *0 (0)* |
| **Gestational age at booking (among women who received any antenatal care)** | | | |
| *≤10* | *26 (38)* | *41 (36)* | *67 (37)* |
| *11–12* | *30 (44)* | *41 (36)* | *71 (39)* |
| *>12* | *9 (13)* | *23 (20)* | *32 (18)* |
| *Missing* | *3 (4)* | *8 (7)* | *11 (6)* |
| **Received recommended antenatal care† (among women who received any antenatal care)** | | | |
| *Yes* | *16 (24)* | *35 (31)* | *51 (28)* |
| *No* | *47 (69)* | *70 (62)* | *117 (65)* |
| *Missing* | *5 (7)* | *8 (7)* | *13 (7)* |
| **Received a minimum level of antenatal care† (among women who received any antenatal care)** | | | |
| *Yes* | *52 (76)* | *77 (68)* | *129 (71)* |
| *No* | *11 (16)* | *24 (21)* | *35 (19)* |
| *Missing* | *5 (7)* | *12 (11)* | *17 (9)* |

*Includes 7 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.

## Classification of quality of care

This section includes information on women who died between 2009 and 2014 and are included in the confidential enquiry chapters of this report (including 50 women who died between six weeks and a year after the end of pregnancy and women from the Republic of Ireland). Table 2.19 shows the classification of care as agreed by the assessors for 183 women whose case notes were available with sufficient information for an in-depth review. Among women who died 46% were assessed to have received good care, but detailed assessment showed that for another 42% improvements in care could have made a difference to their outcome.

**Table 2.19: Classification of care received by women who died and for whom case notes were available for an in-depth review and are included in the confidential enquiry chapters, UK and Ireland (2009–14)**

| | (n=183)* Number (%) |
|---|---|
| **Classification of care received** | |
| *Good care* | *85 (46)* |
| *Improvements to care which would have made no difference to outcome* | *22 (12)* |
| *Improvements to care which may have made a difference to outcome* | *76 (42)* |

*includes women whose case notes were available with sufficient information for an in-depth review

## Local clinicians reports

The increase in proportion of reports received from local clinicians of those requested for the confidential enquiry is encouraging. The figures have increased from 18% in 2012 to 60% in 2013 and further to 65% in 2014. However, as mentioned previously, only with 100% can MBRRACE-UK assessors fully take account of any local factors impacting on care. Figures for different specialty groups are listed in table 2.20.

**Table 2.20: Percentages of local clinicians' reports received for women who died in 2014**

| Specialty group | Percentage of reports requested that were received |
|---|---|
| **Obstetricians** | 63 |
| **Anaesthetists** | 69 |
| **Midwives** | 67 |
| **Critical Care Clinicians** | 68 |
| **Emergency Medicine Specialists** | 49 |
| **GPs** | 79 |
| **Physicians** | 52 |
| **Psychiatrists** | 36 |
| **Total** | **66** |

## 2.4 The women who survived: women with artificial heart valves in pregnancy

A national cohort study was undertaken through the UK Obstetric Surveillance System between February 2013 and January 2015, identifying all pregnant women with a prosthetic heart valve (Vause, Clarke et al. 2016). The study identified 58 women giving an estimated 3.7 cases per 100,000 maternities (95% CI 2.7 to 4.7). Five of the 58 women died. The characteristics of the women who survived are shown in Table 2.21. As noted in section 1.5, a stratified random sample of 32 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 2.21: Characteristics of women with a prosthetic heart valve who survived**

| Characteristics | Total (n=32) Frequency (%) |
|---|---|
| **Age** | |
| *<25* | *4 (12)* |
| *25–34* | *21 (66)* |
| *≥ 35* | *7 (22)* |
| **Parity** | |
| *0* | *13 (41)* |
| *≥1* | *18 (56)* |
| *Missing* | *1 (3)* |
| **Ethnicity** | |
| *White European* | *24 (75)* |
| *Other* | *8 (25)* |
| **Socioeconomic status (Occupational classification)** | |
| *Employed (Either woman or partner)* | *17 (53)* |
| *Unemployed (Both)* | *10 (31)* |
| *Missing* | *5 (16)* |
| **Smoking** | |
| *Smoker* | *8 (25)* |
| *Non-smoker* | *24 (75)* |
| **Substance misuse** | |
| *Yes* | *3 (9)* |
| *No* | *28 (88)* |
| *Missing* | *1 (3)* |
| **Body mass index (BMI)** | |
| *<18* | *2 (6)* |
| *18–24* | *15 (47)* |
| *25–29* | *10 (31)* |
| *≥ 30* | *5 (16)* |
| **Any pre-existing medical problem in addition to cardiac disease (excluding obesity)** | |
| *Yes* | *13 (41)* |
| *No* | *18 (56)* |
| *Missing* | *1 (3)* |

# 3. Lessons on cardiovascular disease

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## 3.1 Key messages

Pre-pregnancy counselling should be available both within the paediatric cardiology transition service and to women of child-bearing age with known cardiac disease. This should include provision of appropriate contraceptive advice.

Lack of co-location of obstetric and cardiac services jeopardises interdisciplinary working and communication. Measures such as joint obstetric cardiac clinics, multidisciplinary care plans, copying letters to the woman and all clinicians involved in her care, as well as staff from all specialties writing in the woman's hand held notes may mitigate against the inherent risk of inadequate communication between specialists.

Early involvement of senior clinicians from the obstetric and cardiology multidisciplinary team is important, wherever a pregnant or postpartum woman presents with suspected cardiac disease, but particularly if she presents to the Emergency Department.

A raised respiratory rate, chest pain, persistent tachycardia and orthopnoea are important signs and symptoms which should always be fully investigated. The emphasis should be on making a diagnosis, not simply excluding a diagnosis.

All consultant led maternity units should have ready access to an ECG machine and someone who can interpret ECGs. Similarly, echocardiography, performed by a competent practitioner, should be available seven days a week.

A normal ECG and/or a negative Troponin does not exclude the diagnosis of an acute coronary syndrome.

Women with prosthetic valves in pregnancy are at extremely high risk, and should be referred to specialist centres at the earliest opportunity. They need expert obstetric, haematology, cardiology and anaesthetic input.

New onset of cardiorespiratory symptoms and/or absence of valve clicks in women with prosthetic heart valves should prompt careful echocardiography and early review by a senior cardiologist to exclude the possibility of valve thrombosis.

There is an immediate need to determine the cardiac rhythm at cardiac arrest. Attempt defibrillation as soon as possible for women in cardiac arrest with a shockable rhythm.

All women who die from sudden cardiac arrest and who have a morphologically normal heart should have molecular studies at postmortem with the potential for family screening. Similarly when aortic dissection occurs in a young person, the underlying diagnosis should be assumed to be an inherited aortopathy, with a need for family screening until proven otherwise. Future sudden deaths amongst relatives may then be prevented.

## 3.2 Background

Maternal deaths from cardiac disease are classified as indirect maternal deaths. Cardiac disease has been the leading cause of indirect maternal mortality, and the leading overall cause of maternal mortality in the UK since the 2000–02 triennium. Deaths from cardiac disease have increased (Table 2.7) and this has been attributed to increasing maternal age, increasing levels of obesity, and more precise recognition of cardiac pathology by pathologists at autopsy.

Previous maternal mortality reports have repeatedly stressed that clinicians should have a low threshold for investigating women with risk factors for cardiac disease, or symptoms which could possibly be cardiac or respiratory in origin, including agitation. The need for performing ECGs, echocardiography, chest X-rays, cardiac enzymes (Troponin) and computed tomographic pulmonary angiography and that investigations should be not be denied to women who need them on the basis that they are pregnant has been reiterated. The importance of close multidisciplinary working, with direct communication between clinicians, has also been emphasised. This report highlights these messages once again.

## 3.3 Summary of key findings

### The women who died

Between 2009–2014 the deaths of 189 women who died from heart disease associated with, or aggravated by, pregnancy were reported to the Enquiry. Of these, 108 occurred during pregnancy or within 42 days of delivery. This represents a maternal mortality rate from cardiac disease in the UK for 2009–11 of 2.14 per 100,000 maternities and for 2012–14 of 2.18 per 100,000 maternities. Cardiac disease therefore remains the commonest cause of indirect maternal death and the commonest cause of maternal death overall.

Among the 108 women who died from cardiac disease during or up to six weeks after pregnancy in the UK and Ireland, 24 died antenatally, and 84 postnatally. There were 81 late deaths (more than six weeks and up to 1 year after delivery) (Table 3.1).

**Table 3.1: Timing of maternal deaths due to cardiac causes in relation to pregnancy, UK and Ireland, 2009–14**

| Time period of deaths in the pregnancy care pathway | Total (n=153)* Frequency (%) |
|---|---|
| Antenatal period/ still pregnant | 24 (15) |
| Postnatal on day of delivery | 32 (21) |
| Postnatal 1 to 42 days after delivery | 52 (34) |
| Postnatal 43–91days | 18 (12) |
| Postnatal 92–182 days | 12 (8) |
| Postnatal 183–273 days | 9 (6) |
| Postnatal 274–364 days | 6 (4) |

*Excludes 36 late cardiac deaths identified from the records of the ONS and NRS

### Diagnostic groupings

For the purposes of this Enquiry, the deaths of 153 women from cardiac disease were reviewed in detail. The cardiac diagnoses of the women who died were as shown in Table 3.2. Sudden arrhythmic cardiac death with a normal heart (SADS) was the most common cause of death (n=53 women, 35% of women who died from cardiac causes), with ischaemia the next most common cause (n=34, 22% of women who died from cardiac causes).

**Table 3.2: Sub-classification of cardiac deaths for whom information was available for an in-depth review, UK and Ireland, 2009–14**

| Sub-classification | Number of deaths | Percentage of total (n=153)* |
|---|---|---|
| **Ischaemic deaths** | **34** | **22** |
| *Atherosclerosis* | *16* | |
| *Coronary artery dissection* | *11* | |
| *Other* | *7* | |
| **Valvular heart disease** | **11** | **7** |
| *Valve disease* | *9* | |
| *Endocarditis* | *2* | |
| **Essential hypertension** | **6** | **4** |
| **Myocardial disease/ cardiomyopathy** | **27** | **18** |
| *Dilated cardiomyopathy* | *4* | |
| *Left ventricular hypertrophy (LVH) with or without fibrosis* | *5* | |
| *Obesity cardiomyopathy* | *2* | |
| *Myocarditis* | *3* | |
| *Peripartum cardiomyopathy* | *9* | |
| *Defined cardiomyopathy* | | |
| *Hypertrophic obstructive cardiomyopathy* | *1* | |
| *Arrhythmogenic right ventricular cardiomyopathy* | *2* | |
| *Ventricular disease (not otherwise specified)* | *1* | |
| **Sudden arrhythmic cardiac deaths with a morphologically normal heart (SADS/MNH)** | **47** | **31** |
| **Aortic dissection** | **21** | **14** |
| **Others** | **7** | **5** |
| *Pulmonary arterial hypertension* | *6* | |
| *Undetermined cardiovascular disease* | *1* | |
| **TOTAL** | **153** | |
| | | |
| **Women with Congenital Heart Disease (CHD) (included in figures above)** | *11* | *7* |
| *Deaths from aortic dissection* | *5* | |
| *Deaths from valvular heart disease* | *4* | |
| *Deaths from pulmonary arterial hypertension* | *2* | |

*Excludes 36 late cardiac deaths identified from the records of the Office for National Statistics (ONS) and National Records of Scotland (NRS) for which no information was available.

Only seventeen percent of women who died were known to have pre-existing cardiac problems (Table 3.3). Importantly, 77% were not known to have pre-existing cardiac problems and therefore there is a need for all clinicians to be alert to the possibility of undiagnosed cardiac disease in pregnant or recently delivered women.

Almost three-quarters of women who died had additional pre-existing medical problems and half were overweight or obese (Table 3.3). The age distribution of the women who died is shown in Table 3.4; 36% were aged 35 years or over. The risk of cardiac death increased with increase in age and was twice as high in women aged 35–39 years and nearly four times higher in women 40 years or older (Table 3.5).

Almost one third of the women who died lived in areas within the most deprived quintile. The pregnancies of 5 women (3%) were known to be as a result of assisted reproductive technologies (Table 3.6). Twenty-six percent of women who died smoked (Table 3.7), compared with a reported 11% of women who gave birth in England in 2014–15 (Health and Social Care Information Centre 2015).

**Table 3.3: Selected medical conditions and characteristics identified amongst women who died from a cardiac cause for whom information was available, UK and Ireland, 2009–14**

| Medical condition/characteristic | Total (n=153)* Frequency (%) |
|---|---|
| **Body mass index (kg/m2)** | Median=25.2, min to max=16.8 to 57.4 |
| *<18.5* | 4 (3) |
| *18.5–24* | 64 (42) |
| *25–29* | 28 (18) |
| *≥ 30* | 47 (31) |
| *Missing* | 10 (6) |
| **Known pre-existing cardiac problems (including congenital)** | |
| *Yes* | 26 (17) |
| *No* | 118 (77) |
| *Missing* | 9 (6) |
| **Any pre-existing medical problem (excluding obesity)** | |
| *Yes* | 115 (75) |
| *No* | 34 (22) |
| *Missing* | 4 (3) |

*Excludes 36 late cardiac deaths identified from the records of the ONS and NRS for which no information was available

**Table 3.4: The socio-demographic characteristics of women who died from a cardiac cause for whom information was available, UK and Ireland, 2009–14**

| Characteristics | Total (n=153)* Frequency (%) |
|---|---|
| **Socio-demographic** | |
| **Age (n=189)** | |
| *<20* | *7 (4)* |
| *20–24* | *24 (13)* |
| *25–29* | *38 (20)* |
| *30–34* | *52 (27)* |
| *35–39* | *48 (25)* |
| *≥ 40* | *20 (11)* |
| **Parity** | |
| *0* | *53 (35)* |
| *1 to 2* | *62 (40)* |
| *≥3* | *34 (22)* |
| *Missing* | *4 (3)* |
| **UK/Irish citizen** | |
| *Yes* | *133 (87)* |
| *No* | *13 (9)* |
| *Missing* | *7 (4)* |
| **Ethnicity** | |
| *White European* | *126 (82)* |
| *Asian* | *9 (6)* |
| *African/Caribbean* | *13 (9)* |
| *Others* | *3 (2)* |
| *Missing* | *2 (1)* |
| **Woman's region of birth** | |
| *United Kingdom/ Ireland* | *101 (66)* |
| *Outside UK* | *37 (24)* |
| *Missing* | *15 (10)* |
| **Socioeconomic status (Index of Multiple Deprivation)** | |
| *First quintile (Least deprived)* | *18 (12)* |
| *Second quintile* | *20 (13)* |
| *Third quintile* | *20 (13)* |
| *Fourth quintile* | *30 (20)* |
| *Fifth quintile (Most deprived)* | *43 (28)* |
| *Missing* | *22 (14)* |
| **Socioeconomic status (Occupational classification)** | |
| *Employed (Either woman or partner)* | *99 (65)* |
| *Unemployed (Both)* | *10 (6)* |
| *Missing* | *44 (29)* |
| **Able to speak/understand English** | |
| *Yes* | *143 (93)* |
| *No* | *7 (5)* |
| *Missing* | *3 (2)* |
| **Living arrangements** | |
| *With partner* | *126 (82)* |
| *Living alone* | *8 (5)* |
| *With parents/extended family* | *9 (6)* |
| *Homeless/in social care/Others* | *2 (1)* |
| *Missing* | *8 (5)* |

*Excludes 36 late cardiac deaths identified from the records of the ONS and NRS for which no information was available

**Table 3.5: Maternal mortality rates by age from cardiovascular causes, UK 2009–14**

| Age (years) | Number of maternities (%)* | Number of women who died from a cardiovascular cause (%) | Mortality rate per 100,000 maternities (95% CI) | Relative risk (95% CI) |
|---|---|---|---|---|
| <20 | 235,145 (5) | 7 (4) | 2.9 (1.2 to 6.1) | 1.06 (0.39 to 2.53) |
| 20–24 | 854,236 (18) | 24 (14) | 2.8 (1.8 to 4.2) | 1 (Ref) |
| 25–29 | 1,315,875 (28) | 36 (20) | 2.7 (1.9 to 3.8) | 0.97 (0.57 to 1.71) |
| 30–34 | 1,374,596 (29) | 48 (27) | 3.5 (2.6 to 4.6) | 1.24 (0.75 to 2.12) |
| 35–39 | 754,368 (16) | 42 (24) | 5.6 (4.0 to 7.5) | 1.98 (1.17 to 3.42) |
| ≥ 40 | 186,333 (4) | 20 (11) | 10.7 (6.6 to 16.6) | 3.82 (2.00 to 7.22) |

*Age not known for 206 women (0.004%)

Sources of maternity data: Office for National Statistics, General Register Office for Scotland, Northern Ireland Statistics and Research Agency

**Table 3.6: Pregnancy-related characteristics of the women who died from a cardiac cause for whom information was available, UK and Ireland, 2009–14**

| Characteristics | Total (n=153)* Frequency (%) |
|---|---|
| **Pregnancy known to be as a result of assisted reproductive technologies** | |
| *Yes* | *5 (3)* |
| *No* | *141 (92)* |
| *Missing* | *7 (5)* |
| **Multiple pregnancy** | |
| *Yes* | *5 (3)* |
| *No* | *146 (95)* |
| *Missing* | *2 (1)* |
| **Previous caesarean section** | |
| *Yes* | *35 (23)* |
| *No* | *114 (74)* |
| *Missing* | *4 (3)* |
| **Previous caesarean numbers (among women who had a previous caesarean section)** | |
| *1* | *24 (69)* |
| ≥2 | *11 (31)* |

*Excludes 36 late cardiac deaths identified from the records of the ONS and NRS for which no information was available

**Table 3.7: Other characteristics of women who died from a cardiac cause for whom information was available, UK and Ireland, 2009–14**

| Characteristics | Total (n=153)* Frequency (%) |
|---|---|
| **Smoking** | |
| *Smoker* | *40 (26)* |
| *Non-smoker* | *98 (64)* |
| *Missing* | *15 (10)* |
| **Substance user** | |
| *Yes* | *10 (6)* |
| *No* | *140 (92)* |
| *Missing* | *3 (2)* |
| **Received any antenatal care**** | |
| *Yes* | *142 (93)* |
| *No* | *9 (6)* |
| *Missing* | *2 (1)* |
| **Gestational age at booking (among women who received any antenatal care)** | |
| *≤10* | *53 (37)* |
| *11–12* | *43 (30)* |
| *>12* | *33 (23)* |
| *Missing* | *13 (9)* |
| **Received recommended antenatal care† (among women who received any antenatal care)** | |
| *Yes* | *44 (31)* |
| *No* | *85 (60)* |
| *Missing* | *13 (9)* |
| **Received a minimum level of antenatal care† (among women who received any antenatal care)** | |
| *Yes* | *85 (60)* |
| *No* | *37 (26)* |
| *Missing* | *20 (14)* |

*Excludes 36 late cardiac deaths identified from the records of the ONS and NRS for which no information was available; **Includes 3 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.

Almost one in five women died in an ambulance or Emergency Department (Table 3.8). Paramedics and all Emergency Department staff need to be aware of the appropriate modifications to resuscitation which are needed in a pregnant woman, including uterine displacement by lateral tilt, early intubation with a cuffed tracheal tube and early recourse to perimortem caesarean section. Emergency Departments should have the appropriate equipment available on the resuscitation trolley for this to be performed i.e. a scalpel and umbilical cord clamp (or artery forceps). In several instances, extensive and prolonged attempts were made to resuscitate the woman prior to transferring her to hospital. A perimortem caesarean section is an integral part of maternal resuscitation and therefore prompt transfer is needed to enable this to take place.

**Table 3.8: Place of delivery amongst women who died from a cardiac cause for whom information was available, UK and Ireland, 2009–14**

| Place of delivery (for women who delivered and for whom information was available) | Total (n=129)* Frequency (%) |
|---|---|
| Home | 0 |
| Hospital (except A&E) | 102 (79) |
| Emergency Department or ambulance | 22 (17) |
| Not known | 5 (4) |

*Excludes 36 late cardiac deaths identified from ONS and NRS for which no further clinical information was available and 24 women who died antenatally.

## 3.4 Overall messages for future care

### Pre-pregnancy counselling

A teenager with a repaired VSD (ventricular septal defect) and persistent pulmonary arterial hypertension died 3 days after delivery. It is unclear whether she received pregnancy or contraception counselling from the paediatric cardiology services. She was referred to the specialist adult congenital heart disease unit for the first time when she found herself pregnant. She elected to continue her pregnancy and was delivered at 34/40 after she became increasingly symptomatic. She was closely monitored post-delivery on ITU, but she collapsed suddenly and died the following day.

In the context of cardiac disease, it is important that discussions about the risks of pregnancy and appropriate contraception are initiated opportunistically, and start prior to girls becoming sexually active. In the UK a quarter of women have their first sexual experience before the age of 16, and there is no reason to believe that this would be any different in young women with heart disease.

**Pre-pregnancy counselling should be available both within the paediatric cardiology transition service and to women of child bearing age with known cardiac disease. This should include provision of appropriate contraceptive advice.**

### Risk factors for cardiac disease

An older woman with a high BMI who had a history of hypertension and poorly controlled type 2 diabetes conceived using clomiphene, following which she miscarried. Four weeks after medical management of her miscarriage she presented with breathlessness and ankle swelling which she said predated the pregnancy. Investigations revealed a severe dilated cardiomyopathy and despite treatment she died at home a few weeks later.

Although this woman had several risk factors for cardiac disease, and may have had symptoms prior to pregnancy, referral for evaluation of her cardiac function was not considered before she was prescribed clomiphene. Previous Confidential Enquiry reports have highlighted that *'women at higher risk of developing cardiac disease in pregnancy, i.e. the obese, those who smoke or who have existing hypertension and/or diabetes, a family history of heart disease and those over the age of 35, should be appropriately counselled of these risks pre-conception and particularly prior to receiving assisted reproductive technology (ART) or other infertility treatment' (Lewis 2004)*. This message remains the same and should be included in national guidance. This is a responsibility of both primary care practitioners prescribing or referring for infertility treatment as well as secondary care practitioners undertaking the treatment.

**Women with cardiac risk factors, for example older maternal age or obesity should have a cardiac assessment prior to receiving assisted reproductive technology or other infertility treatment.**

**Women should have the opportunity to make informed decisions regarding their care and treatment [for fertility problems] via access to evidence-based information. These choices should be recognised as an integral part of the decision-making process. Verbal information should be supplemented with written information or audio-visual media.**

**NICE CG156 Fertility problems: assessment and treatment (National Institute for Health and Care Excellence 2013)**

## Multi-disciplinary working

A woman with a history of cardiomyopathy but with normalised ventricular function, conceived having stopped cardiac medication in consultation with her cardiologist. During her pregnancy she had regular obstetric and midwifery review, with regular but separate cardiology review. When ventricular function deteriorated in the early third trimester this was not communicated to the obstetric team; the information was contained in a letter which was not generated until two weeks after the cardiology appointment, rather than written in the hand held notes. In the late third trimester she developed pre-eclampsia and breathlessness, and a further echocardiogram showed that her ventricular function had worsened. She was delivered by caesarean section but died a few days postpartum.

The best multidisciplinary care occurs when different specialists consult together on the same day in the same room and talk with each other and the woman together. This woman's care demonstrates delay on the part of all the parties involved in her care appreciating a change in her health, accelerated by the onset of pre-eclampsia. Writing in the hand held maternity notes rather than relying on hard copy letters may help mitigate the risk of inadequate communication which is inherent in separate clinical assessments; picking up the phone and having a direct conversation may be the most appropriate action.

**Lack of co-location of obstetric and cardiac services jeopardises interdisciplinary working and communication. Measures such as joint obstetric cardiac clinics, multidisciplinary care plans, copying letters to the woman and all clinicians involved in her care, as well as staff from all specialties writing in the woman's hand held notes may mitigate against the inherent risk of inadequate communication between specialists.**

**Traditional referral mechanisms may be too slow in pregnancy. Where time dependent intervention is needed, such as for anticoagulation advice, clinicians should make direct contact with each other.**

A woman with known ischaemic heart disease presented to the Emergency Department with chest pain in the second trimester of pregnancy. There were some atypical features to her pain but it had made her anxious. Her ECGs had been reported as normal but they showed evidence of a previous infarct. Her Troponin was not raised. She was diagnosed as having dyspepsia and discharged. No referral to obstetrics or cardiology was made. Shortly after discharge she collapsed at home and was found to be in ventricular fibrillation. She could not be resuscitated.

**Early involvement of senior clinicians from the obstetric and cardiology multidisciplinary team is important, wherever a pregnant or postpartum woman presents, but particularly if she presents to the Emergency Department.**

## Delays in diagnosis

During her pregnancy a woman presented on five occasions within two weeks to different hospitals and her GP complaining of cough, dyspnoea and orthopnoea. She was noted to be tachycardic. She was prescribed multiple courses of antibiotics to which she failed to respond but no further investigations were done. Eventually a diagnosis of peripartum cardiomyopathy was made and she was delivered by Caesarean section. Despite insertion of an intra-aortic balloon pump, Extracorporeal Membrane Oxygenation (ECMO) and attempted Left Ventricular Assist Device (LVAD) insertion, she died shortly postpartum.

This woman presented repeatedly with cardiac symptoms and objective signs. Even when she failed to respond to multiple courses of antibiotics, cardiomyopathy was not considered as a diagnosis. Although earlier diagnosis may not have changed the final outcome for this woman, cardiac disease is the leading cause of maternal death and clinicians should ensure that it is considered within the differential diagnosis.

**A raised respiratory rate, persistent tachycardia and orthopnoea are important signs and symptoms which should always be fully investigated.**

**It is important to be mindful of the possibility of a cardiac diagnosis when repeated attempts are made to access medical care, particularly when extreme anxiety and breathlessness are prominent symptoms.**

A woman presented in the early third trimester with severe chest pain causing her to sit up in a chair for some of the night. The pain was consistently described as interscapular and she required repeated analgesia. Troponin and a VQ perfusion scan were normal and therefore since pulmonary embolism had been excluded she was discharged home. Approximately 36 hours after her discharge she collapsed at home with severe abdominal and chest pain. An ambulance was called and she was delivered by perimortem caesarean section in the Emergency Department. During her resuscitation which lasted over an hour she had thrombolysis, but no echocardiogram or a pericardiocentesis. Tamponade was not considered as a possible cause of her arrest. Postmortem examination showed a dissection of the ascending aorta and a haemopericardium.

For this woman and several others reported to the enquiry, the search for a definitive diagnosis ceased once pulmonary embolism had been excluded. Despite the women having pain which was so severe she sat in a chair for part of the night, she was discharged without an explanation for the pain. Even after she had arrested, an echocardiogram was not performed, which would have revealed the diagnosis of tamponade and haemopericardium, secondary to an aortic dissection. Had an echocardiogram or CT of the aorta been performed at the time of her initial presentation, it may have been possible to intervene surgically and prevent her death, but this window of opportunity was missed.

There were several instances where echocardiography would have revealed the correct diagnosis but it was either not done; not available out of hours; or done but misinterpreted. The NHS England standards on Seven Day Services stipulate that echocardiography should be available consistently across the week. On other occasions ECGs or serial ECGs were not performed, or the ECG was not interpreted correctly. An ECG machine should be available in all consultant led maternity units.

**In women with chest pain and breathlessness the emphasis should be on making a diagnosis, not simply excluding a diagnosis.**

**All consultant led maternity units should have ready access to an ECG machine and someone who can interpret ECGs. Similarly, echocardiography, performed by a competent practitioner, should be available seven days a week.**

**NHS Services Seven Days a Week Forum Summary of Initial Findings (NHS England 2013b)**

## Medication and investigation

Withholding essential medications or investigations because a woman is pregnant or breastfeeding continues to be a theme identified by reviewers for the Confidential Enquiry.

A woman referred herself to hospital on the third day postpartum with symptoms of breathlessness, palpitations and coughing up pink frothy sputum. She was extremely anxious, tachycardic, had low oxygen saturations, tachypnoea and reduced air entry in the base of her right lung. She was seen by several junior doctors and a chest infection, a panic attack or a pulmonary embolus were considered as possible diagnoses. Peripartum cardiomyopathy was only considered subsequently, when she was seen by a consultant, who suggested an echocardiogram but this was not available outside normal working hours. A consultant radiologist declined to perform a CTPA, to exclude pulmonary embolism, because of the theoretical risk of radiation induced breast cancer. The woman deteriorated and subsequently had a cardiac arrest. Resuscitation achieved return of cardiac output. Following the cardiac arrest, she was eventually reviewed by a cardiologist and an echocardiogram performed which showed extremely poor ventricular function. The woman became increasingly unstable and died the following day.

**Pink frothy sputum is very suggestive of pulmonary oedema, and should be investigated and treated accordingly.**

A woman with dilated cardiomyopathy and arrhythmias which were difficult to control, was delivered by caesarean section early in the third trimester, because of increasing breathlessness on minor exertion. Despite poor ventricular function and the need for multiple medications, ACE inhibitors were withheld because she was breastfeeding. She died suddenly approximately two months after delivery.

ACE inhibitors are a mainstay of the management of patients with heart failure and should be restarted in the early postpartum period. They are safe to use when breastfeeding (National Institute for Health and Care Excellence 2010b). In several other women whose care was examined by the enquiry, important investigations such as CT scans were inappropriately withheld because a woman was pregnant, breastfeeding or because of fears of the long term increase in risk of breast cancer.

**Women should not be denied relevant investigations or treatments for life threatening conditions, simply because they are pregnant or breastfeeding.**

### Perimortem caesarean section

A woman in her third trimester collapsed at home. The ambulance arrived in six minutes but CPR was carried out for 45 minutes before the woman was transferred to hospital. A perimortem caesarean section was performed within two minutes of arrival at hospital by a senior multidisciplinary team.

On this occasion the ambulance arrived quickly, the caesarean section was performed extremely promptly on the woman's arrival at the Emergency Department and the transfer time was unavoidable. However, whilst a prolonged attempt at CPR by paramedics in the community may have been appropriate in a non-pregnant patient, in this pregnant woman it delayed a crucial element of her resuscitation. Ambulance crews need to be aware of the need for a prompt transfer, of any woman who is 'visibly pregnant' so that perimortem caesarean section can be carried out promptly to aid resuscitation. The Joint Royal Colleges Ambulance Liaison Committee Guidelines (Joint Royal Colleges Ambulance Liaison Committee and Association of Ambulance Chief Executives 2016) state that there should be a time critical transfer as soon as ventilation is achieved and CPR commenced.

**Perimortem caesarean section is an important part of the resuscitation of a pregnant woman. Ambulance crews should not delay this by prolonged attempts at resuscitation in the community before transferring the woman to hospital.**

**Paramedic services should review protocols for the management in the community of the collapsed/shocked woman of reproductive age.**

## 3.5 Lessons for care of specific cardiac morbidities

### 3.5.1 Aortic Dissection

#### Background

Dissection of the aorta is a rare but frequently fatal event. Women with dissection are not only more likely than men to die before reaching hospital, but they also have poorer surgical outcomes, especially during pregnancy (Nienaber, Fattori et al. 2004, Howard, Banerjee et al. 2013, Yates, Soppa et al. 2015). The majority of aortic dissections in women of childbearing age occur during late pregnancy and the puerperium, time periods that are associated with a 25-fold increased risk of dissection (Nasiell and Lindqvist 2010).

The commonest mode of death is extension of a dissection of the ascending aorta into the aortic root causing haemopericardium and tamponade. Death rates rise with every hour of delay between the onset of the dissection and control of the haemorrhage in theatre. Survival is critically dependent on the early recognition of the symptoms of aortic dissection – classically severe tearing chest pain radiating to the back – with rapid diagnosis and emergency surgical repair.

#### The women who died

Twenty-one women died from aortic dissection, all except one of which involved the ascending aorta. The median age of the women who died was 34 years (range 20–41 years); two women died undelivered during the third trimester of pregnancy, five women had a perimortem CS and one died on the day of delivery, another 12 died within 20 days after delivery and one woman died 49 days after delivery.

Few women had recognised risk factors for aortopathy at the beginning of their pregnancy. Two women had repaired congenital heart disease with complex coarctation or interruption of the aorta, both had required several aortic procedures in the past and were managed as high risk because of their aortic pathology. None of the women who died were recognised as having a familial aortopathy such as Marfan syndrome, but five (26%) had a family history of aneurysm, sudden death or other anomalies associated with familial aortopathy syndromes. Several had a bicuspid aortic valve identified at autopsy. Four women who died from aortic dissection were current smokers and only three had treatment for hypertension during pregnancy. Four of the women who died were obese (21%).

Eight women (42%) had presented in the days before their deaths with symptoms suggestive of significant pathology, such as severe chest and interscapular pain, but a diagnosis of aortic dissection was not considered. Five further women (26%) presented acutely unwell with atypical chest or back pain and neurological symptoms including faecal incontinence and leg weakness due to dissection of the entire aorta; the diagnosis of dissection was delayed or missed until post mortem in these women. Eight (42%) of the women who died from aortic dissection died suddenly at home or arrested out of hospital and could not be resuscitated in the Emergency Department.

The assessors found improvements to care that might have made a difference to the outcome in 11 of the 19 women (58%), and improvements to care that would have been unlikely to change the outcome in a further 3 women (16%).

## Messages for care of women with aortic dissection

### *Assessment of severe chest pain in pregnancy and the puerperium*

Early senior cardiology review or assessment by another senior physician may help to identify the cause of severe chest pain.

> A woman who had delivered a few days earlier presented by ambulance in the middle of the night to the Emergency Department with severe sudden onset chest and neck pain. Her pregnancy had been complicated by disabling symphysis pubis dysfunction. On arrival at A&E she was anxious and described severe pain starting in the neck and radiating in waves to the chest and back. She was clear that the pain was different to the 'all over pain' of her symphysis pubis dysfunction. She was seen by junior doctors who considered pulmonary embolism or anxiety attack as possible diagnoses. They decided on the latter and sent her home without investigation or senior review. She died suddenly at home a few days later. Post mortem confirmed dissection of the entire aorta with a bicuspid aortic valve and extensive cystic medial necrosis.

The description in the vignette of sudden onset, severe localising pain with attendant anxiety is typical of aortic dissection. Pain severe enough for a mother to leave her baby at home in the night to attend the Emergency Department requires a diagnosis; co-existing anxiety and musculoskeletal pain should not be accepted as the cause.

> A woman in her third trimester was admitted to an obstetric ward with severe chest pain that required opiate analgesia. She was an inpatient for three days, during which time myocardial ischaemia and pulmonary embolism were excluded. She continued to need opiates for her severe intermittent chest pain. It was interscapular and worse lying flat, so that she had to sleep in a chair. She had no senior obstetric review and no review by a cardiologist or other physician. A diagnosis of aortic dissection was not considered although she continued to have severe pain at the time of discharge. She collapsed at home a few days later with chest and abdominal pain and could not be resuscitated. Post mortem showed extensive ascending aortic dissection with haemopericardium, but no cystic medial necrosis.

This woman's description of her pain was typical for aortic dissection. Senior and cardiology review may have helped to determine the cause of pain in both these instances.

**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.**

**Saving Lives, Improving Mothers' Care 2014 (Knight, Kenyon et al. 2014)**

**Any woman presenting with chest pain severe enough to require opiate analgesia requires a positive diagnosis, not simply the exclusion of an acute coronary syndrome or pulmonary embolism.**

### *Neurological symptoms in aortic dissection*

An obese, multiparous woman was hypertensive in late pregnancy. She was delivered at term by emergency caesarean section for fetal distress. She was hypertensive post-delivery and discharged home on labetalol. A week later she developed severe back pain associated with incontinence and leg numbness and paralysis with marked hypertension. She had cold mottled peripheries. Cauda equina syndrome was considered but excluded by MRI. No further attempt was made to make a positive diagnosis until several hours later when she collapsed with hypotension and profound metabolic acidosis. An urgent CT of the chest, abdomen and pelvis was planned, but did not take place for a further 2 hours, by which time she was in extremis. It showed dissection of the whole descending aorta. She was transferred to a regional centre but died on arrival. Post mortem confirmed extensive descending aortic dissection with cystic medial necrosis.

A woman had sudden onset of severe interscapular pain with frontal headache, visual loss and faecal incontinence two weeks postpartum. She was hypertensive on arrival in the Emergency Department but then became hypotensive with a tachycardia and a cold pulseless left arm. She was seen by a junior doctor who arranged a CT head scan. Two hours later another junior doctor considered aortic dissection, but the situation was not recognised as urgent and the diagnosis of extensive dissection of the ascending aorta and aortic arch was not established for a further six hours, by which time she was moribund. She was transferred to a cardiothoracic centre where she died.

Aortic dissection is an emergency in which the chance of survival falls rapidly for each hour of delay in diagnosis and treatment. Aortic dissection that extends into the arterial tree causes neurovascular symptoms as well as pulseless limbs and severe localising chest and back pain. The diagnosis of aortic dissection should be considered in women who present with neurological symptoms as well as chest and back pain, as the condition may be missed if only neurological causes are considered.

### *Seeking tamponade as a cause of cardiac arrest*

A woman who had a preterm delivery for pre-eclampsia had an unheralded, witnessed pulseless cardiac arrest in hospital a week postpartum. Tamponade was not considered as a cause for her arrest although resuscitation was otherwise appropriate. The diagnosis of ascending aortic dissection extending into the pericardial sac and causing haemopericardium was made post mortem.

An echocardiogram performed during the attempted resuscitation of this woman would have led to the diagnosis of tamponade, but would have been unlikely to have altered the outcome. This woman's father had had an 'aneurysm' many years earlier, so the family were referred for genetic screening. Her family was one of the few in this report who were referred for genetic review and screening for a familial aortopathy.

An older woman presented at term to the maternity unit with severe crushing chest pain. She was hypotensive, cold and clammy. The chest X-ray showed a widened mediastinum, but since the ECG had subtle T wave changes, she was thought to have an acute coronary syndrome. She continued to have episodes of severe chest pain radiating to the back and arrested three hours after admission. During attempted resuscitation an echocardiogram showed a large effusion and extensive ascending aortic dissection was confirmed at post mortem.

Once cardiac arrest has occurred as a result of aortic dissection, the chances of survival are small. However, arrest is often due to cardiac tamponade and if diagnosed, emergency transfer to cardiac theatres may be life-saving.

**The Advanced Life Support 4Hs and 4Ts algorithm (box 1) should be followed in all cases of cardiac arrest (Resuscitation Council (UK) 2010).**

**Box 3.1: Causes of maternal collapse**

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

- Hypoxia
- Hypovolaemia
- Hypo/hyperkalaemia/metabolic
- Hypothermia
- Tension pneumothorax
- Tamponade - cardiac
- Toxins
- Thrombosis (coronary or pulmonary)

### *Establishing the underlying cause of aortic dissection*

Post mortem examination revealed a possible underlying cause of aortic dissection in six women (29%). One woman died from aortic dissection secondary to previously undiagnosed aortitis, and one was also found at autopsy to have vascular-type Ehlers Danlos Syndrome. Two further women had had repair of complex coarctation or interruption. Four had bicuspid aortic valves – one in association with complex coarctation and another also had other anomalies typical of Loeys Dietz syndrome, although this was not recognised by the clinicians or pathologist.

Although some pathology reports described the typical cystic medial necrosis found in the familial aortopathies, or sought genetic assessment to exclude Marfan syndrome and saved splenic tissue for later DNA analysis, the majority made no comment on seeking the underlying cause of the dissection. No pathology report mentioned genetic assessment for familial aortopathies other than Marfan syndrome.

**When aortic dissection occurs in a young person, the underlying diagnosis should be assumed to be an inherited aortopathy until proven otherwise.**

Although pregnancy associated aortic dissection is sometimes thought to occur in women without predisposing risk factors, no such assumption should be made unless efforts are made to exclude a genetic cause. Bicuspid aortopathy, Marfan syndrome, Loeys Dietz syndrome, vascular Ehlers Danlos syndrome and familial thoracic aortic aneurysm should all be considered. Post mortem examination should include an assessment of dysmorphic features and aortic histology, and samples should be retained for later DNA analysis. First degree relatives of patients with a suspected familial aortopathy should be referred for screening and genetic counselling.

Bicuspid aortic valve is common, affecting 0.5–2% of the population (Michelena, Della Corte et al. 2015). It may be associated with an ascending aortic aortopathy, although its progression is temporal, and age-related. The risk of aortic dissection is lower than that associated with other aortopathies, but up to eight times higher than in the general population. Women with a bicuspid aortic valve and no aortic dilatation do not appear to be at increased risk of dissection in pregnancy. The risk of pregnancy related dissection in women with bicuspid aortic valve and aortic dilatation is unknown (Michelena, Della Corte et al. 2015).

Women with isolated, simple repaired coarctation of the aorta are not usually considered at particularly high risk of aortic dissection. The two women with coarctation who died in this report had complex aortas. Both the women received appropriate pre-pregnancy counselling.

A woman was found dead in bed in the third trimester. A post mortem showed dissection of the ascending aorta extending to cause a haemopericardium, and histology showed cystic medial necrosis. She had a bicuspid aortic valve and non-Marfanoid dysmorphic features: clubbed feet, cleft palate, long fingers and unusual facies. The fetus also had some of these features. Her syndrome remained undiagnosed, no tissue was saved for DNA analysis and the family was not referred for genetic screening.

This woman had classical features of Loeys-Dietz syndrome, an aggressive familial aortopathy first described in 2005 (MacCarrick, Black et al. 2014). It follows an autosomal dominant inheritance pattern and is due to TGFβR or SMAD3 gene mutations. Commonly associated with bicuspid aortic valve, skeletal and craniofacial anomalies, arteries can dissect without preceding dilatation. As a relatively newly described condition, data are still emerging. The risk of aortic dissection associated with pregnancy is estimated at between 1–5%; there also appears to be a risk of uterine rupture. The condition often remains unrecognised, since awareness of the condition is poor. Patient outcome and that of affected family members is improved with the correct diagnosis and appropriate surveillance and intervention to prevent catastrophic vascular events, and thus it is an important diagnosis to consider in women with aortic dissecction.

## Pathology in aortic dissections

There were 21 deaths due to aortic dissection (coronary artery dissection is addressed in the ischaemic deaths section). Dissections of other arteries (such as splenic artery rupture) have been addressed in previous reports (Knight, Kenyon et al. 2014).

A link between pregnancy and the development or rupture of arterial dissections has been hypothesised. There are major physiological changes in the cardiovascular system during pregnancy and hormonal effects on vessel walls, with oestrogen suppression of collagen and elastin synthesis. However, inheritable genetic disorders must be considered even in the setting of pregnancy (Braverman 2010, Yuan 2013). Genetic disorders such as Marfan syndrome may lead to arterial dissection at any point, including in the early stages of pregnancy, whereas those due to pregnancy-related physiological effects tend to be seen in the third trimester or early postpartum period (Yuan 2013).

The pathological investigations of 20 of the 21 women who died were reviewed for the purpose of this chapter; detailed pathological information was not available for one woman. Post mortem examination was performed in 18 women (90%). The standard of post-mortem reports was generally high. The most common site of the dissection was the aortic root with consequent haemopericardium (8 women). Bicuspid aortic valve was noted in four women, although for three women the morphology of the valve was not mentioned specifically. Histology was undertaken in 14 women (70%), and toxicology in three women. The opinion of a cardiac pathologist was sought for three women. Material for genetic analysis was retained from seven women (35%) (commonly spleen).

In six women (30%) the potential causes of aortic dissection were not considered. Arterial dissections may be seen in association with hypertension and with genetic abnormalities, especially connective tissue disorders such as Marfan, Ehlers Danlos syndrome and Loeys Dietz syndrome. Thoracic aortic dissections may also have a genetic basis (Spin 2011, Milewicz and Regalado 2012), some associated with Marfan or Loeys Dietz syndromes, but in the absence of a syndrome, 20% of thoracic aortic dissections may be familial (Spin 2011).

Upon encountering an arterial dissection, the pathologist should not simply accept the diagnosis without considering the possible underlying causes. Given that the above disorders are heritable, genetic material for DNA testing should be preserved at post mortem; a sample of spleen or blood should be frozen and either stored locally or sent to the genetics laboratory for retention for future analysis as needed for the benefit of family members. Guidance for family referral to genetics should be provided in the autopsy report. If specific features of one of these syndromes are identified, the common genetic abnormalities can be specifically tested for, eg. FBN1 mutations in Marfan syndrome. Not all cases of Marfan syndrome will have a known mutation and the diagnosis is therefore based on a combination of clinical, pathological and genetic findings. Amongst the women considered here, three specific abnormalities were tested for. Two were negative for the FBN1 mutation, and one vascular Ehlers Danlos syndrome was confirmed. The MBRRACE-UK assessor panel identified one likely case of Loeys Dietz syndrome but this was not considered as a possible diagnosis prior to the MBRRACE-UK review.

## Key messages for pathology

- **Consider possible causes of arterial dissections, over and above pregnancy alone**
- **Describe the morphology of the aortic valve (tricuspid or bicuspid)**
- **Take histology of the dissection and of normal aorta, and consider seeking the specialist opinion of a cardiovascular pathologist**
- **Retain material for genetic analysis**
- **Recommend family referral to Medical Genetics in confirmed or suspected cases of Marfan, Loeys Dietz, or Ehlers Danlos syndromes, bicuspid aortic valve and thoracic aortic dissection.**

## 3.5.2 Cardiac ischaemic disease

### Background

Ischaemic heart disease can present with the symptoms of inadequate myocardial perfusion, typically chest pain, or as a malignant ventricular arrhythmia and sudden cardiac death. Ischaemic heart disease accounted for over a fifth of all cardiac deaths reviewed for this Enquiry. Acute coronary syndrome, the umbrella term which covers different presentations of acute myocardial ischaemia from unstable angina to myocardial infarction, usually results from atherosclerotic coronary artery disease when plaque rupture or fissuring results in coronary artery occlusion due to acute thrombosis. Individuals with atherosclerosis typically have risk factors, and pregnant women are no exception, with lifestyle factors such as smoking, older maternal age and obesity being particularly important (Lameijer, Kampman et al. 2015). Myocardial ischaemia can also result from acute coronary artery dissection and many of these women will not have classical risk factors although a history of smoking was common in the women described here. Rarely death resulted from thrombosis in a normal coronary artery or vasculitis.

The incidence of acute coronary syndrome in pregnancy is an area of debate with older series from the USA reporting 3–6.2 per 100,000 deliveries (Ladner, Danielsen et al. 2005, James, Jamison et al. 2006) but the more recent UK Obstetric Surveillance System (UKOSS) study identified fewer cases and reported an incidence of 1.7 per 100,000 (Bush, Nelson-Piercy et al. 2013). There are methodological differences between the studies which may account for the variation. The older studies relied on hospital discharge records of myocardial infarction, they were retrospective and included a longer postpartum period. The older studies also pre-dated the use of cardiac biomarkers. The more recent UKOSS study covered pregnancy and a week postpartum and used the universal definition of myocardial infarction. However it relied on a member of the obstetric team reporting the cardiac event with the potential for underreporting, particularly of women who died suddenly at home and in whom the diagnosis was not made until autopsy. Neither study included unstable angina (ischaemic pain but no myocardial damage).

### The women who died

The care of 34 women who died from ischaemic causes was reviewed for this chapter. Of the 34 women whose care was reviewed, 16 died from atherosclerotic heart disease, 11 from coronary artery dissection and seven from other causes including coronary arteritis, Takotsubo cardiomyopathy and myocardial bridging with acute myocardial infarction. The majority of women who died from coronary ischaemia died suddenly. In a minority of these sudden deaths women had experienced chest pain prior to arresting, either immediately before collapsing or in the days before, however some had not reported their symptoms to a health professional.

All but one of the women who died from atherosclerotic coronary artery disease had at least one identifiable risk factor. A current or past history of smoking, including up until the pregnancy was confirmed in eight women. A smoking history was not recorded for five women, three women were non-smokers. Half of the women, for whom a body mass index was recorded (14 out of the 16 women who died), were overweight or obese (median BMI 27, range 21–53). The median age of women who died from atherosclerotic coronary artery disease was 36 years (range 25–46); 56% of women (n=9) were aged 35 or over. Ten women died from acute myocardial infarction. 6 women had a cardiac arrest and were found to have underlying coronary artery disease but no evidence of acute infarction.

Women dying from coronary artery dissection had a similar history of smoking; five women were non-smokers and the remainder smoked at some point prior to or during the pregnancy. The median BMI of women who died from coronary artery dissection was 24 (range 21–42). The women dying from coronary artery dissection had a median age of 34 years (range 30–41).

## Messages for care

### *Risk Factors*

**Box 3.2: Risk factors for ischaemic heart disease**

- Older age
- Smoking
- Obesity
- Diabetes
- Hypertension
- Family history of premature coronary disease
- Hypercholesterolaemia

Lifestyle issues appear to play an important part in maternal risk from ischaemic heart disease (Box 3.2). Smoking was most common risk factor identified amongst women who died, consistent with other reports of myocardial infarction in pregnancy (Elkayam, Jalnapurkar et al. 2014). Age was an important risk factor. In the UKOSS study, for every year increase in maternal age there was a 20% increase in the risk of myocardial infarction (Bush, Nelson-Piercy et al. 2013). The majority of women dying from atherosclerotic coronary disease in this Enquiry were older pregnant or postpartum women. Being overweight or obese was also an important risk factor identified; the relationship between ischaemic heart disease and obesity with a gradient of increasing risk and weight is well documented outside of pregnancy. Finally, many women had multiple risk factors for ischaemic heart disease and this clustering of risk factors is also important.

An older, grand-multiparous woman who smoked died a month after delivery. She had a long history of hypertension but had declined antihypertensive medication in the pregnancy. She died following a cardiac arrest at home. Post mortem revealed significant atheroma in all three coronary arteries.

This woman had severe three vessel disease and had multiple risk factors for atherosclerosis. Smoking is the single factor most strongly associated with ischaemic heart disease in pregnancy. She had poorly controlled hypertension and declined treatment. This highlights increasing cardiovascular risk in pregnant and postpartum women.

With increasing maternal age, smoking and obesity in young women, ischaemic heart disease is likely to remain a major cause of maternal morbidity and death. Both smoking and obesity are preventable. Population-based interventions to modify risk are valuable but women should also be educated about the specific cardiac risk of pregnancy and which symptoms to report. Pregnancy is a stress test and as older women and even postmenopausal women become pregnant with assisted reproductive technologies, this raises the question of the need for further research to evaluate screening for inducible ischaemia prior to embarking on a pregnancy.

A previously fit and well woman in her mid-thirties died following a cardiac arrest three months after a normal delivery. She did not smoke but was overweight. Her LDL cholesterol was normal. She had experienced chest pain and arm tingling one to two days before collapsing at home. Post mortem examination showed an anterior infarct with three vessel coronary disease.

This woman's death is unusual. She had no conventional risk factors for coronary artery disease and yet had widespread atherosclerosis. This highlights the need for vigilance in considering specific symptoms. The woman did not seek medical advice concerning her pain and it raises the issue of awareness and education particularly as ischaemic heart disease remains an important cause of cardiac disease related death.

An older woman undergoing a termination of pregnancy in a non-NHS setting had a cardiac arrest during her general anaesthetic from which she could not be resuscitated. She had no known risk factors for cardiac disease and no previous symptoms of ischaemic heart disease but at autopsy was found to have severe narrowing of all three coronary arteries.

This woman's death highlights the importance of ensuring adequate facilities for resuscitation are available in whatever setting pregnancy-related procedures are carried out. Ischaemic heart disease cannot necessarily be predicted and availability of resuscitation expertise in all settings is essential. Ischaemic heart disease is a common cause of maternal death and most women who die have identifiable risk factors. Women at increased risk should be informed about the symptoms of ischaemic pain and the importance of reporting symptoms.

### *Assessment of chest pain*

**Box 3.3: Chest pain which may be indicative of cardiac ischaemia**

- Discomfort developing over minutes in the anterior chest or epigastric area
- Band-like, squeezing, sensation of pressure
- Radiation to the jaw, arms, shoulders
- Radiation into the back
- Associated with breathlessness
- Associated with nausea and/or sweating
- Associated with syncope

There remains a reluctance for doctors to diagnose cardiac ischaemia in pregnant women (Box 3.3). Clinical presentation in many pregnant or postpartum women is the same as for the general population with chest discomfort which may radiate to the throat, arms, back and shoulders. The pain may be associated with nausea, sweating and breathlessness or even syncope. However, women in general tend to present with less typical symptoms than men and the diagnosis can be overlooked. Angina in women is more likely to radiate to the throat, into the back and between the shoulder blades (Canto, Goldberg et al. 2007). Women are more likely to report symptoms of feeling hot, breathless or experiencing a cold sweat. Some women have these symptoms but no chest pain (Khan, Daskalopoulou et al. 2013). Women and health professionals should be aware of cardiac symptoms and their importance.

**Consider myocardial ischaemia in any woman presenting with chest pain particularly if it is associated with breathlessness, feeling faint, sweating and/or nausea.**

**If myocardial ischaemia is suspected, the investigation of women in pregnancy or in the postpartum period should be the same as for the general population:**

- **Physical examination to determine the haemodynamic status and elicit signs of any complications**
- **Serial ECGs**
- **Troponin levels**

**Acute coronary syndrome in adults. NICE quality standards QS68 (National Institute for Health and Care Excellence 2014c)**

**Chest pain of recent onset: assessment and diagnosis. NICE clinical guideline CG95. (National Institute for Health and Care Excellence 2010a)**

An older woman had an uneventful pregnancy until 34 weeks when she developed chest pain. The pain had been off and on over three days and radiated into her back and left arm. The woman smoked, had a family history of ischaemic heart disease and a history of hypertension. She had been given entonox in the ambulance which is known to treat ischaemic pain. When she was assessed in the Emergency Department, no one asked about her risk factors for coronary disease. Despite an abnormal ECG, she had no further investigations. The obstetric team was not contacted. She was discharged home from the Emergency Department and found dead in bed the following day. Extensive coronary artery atherosclerosis and a thrombosed left anterior descending artery were found at post mortem examination.

The woman had multiple risk factors for ischaemic heart disease. The history elicited by the Emergency Department doctor was suggestive of non-cardiac pain but the history obtained by the ambulance crew before entonox was given was consistent with ischaemic pain.

**When assessing a woman with chest pain care should be given to review the presenting symptoms the woman had before she was given analgesia and abnormal ECGs should not be ignored.**

If the history is consistent with ischaemia, a normal ECG and/or negative Troponin do not exclude the diagnosis and further investigation should be undertaken. It is of paramount importance that a formal diagnosis is made in a woman presenting with chest pain rather than simply using a negative Troponin to exclude a diagnosis and then discharging the woman.

An older overweight woman died in the second trimester. She was an ex-smoker. She had known ischaemic heart disease including a myocardial infarction in a previous pregnancy and was taking aspirin and a beta-blocker. She presented to the Emergency Department with chest pain. There were some atypical features to her pain but it had made her anxious. Her ECGs had been reported as normal but they showed evidence of a previous antero-septal infarct. Her Troponin was not raised. She was diagnosed as having dyspepsia and discharged. No referral to obstetrics was made. Shortly after discharge she collapsed at home and was found to be in ventricular fibrillation. She could not be resuscitated. Post mortem examination confirmed an old antero-septal infarct and a tight stenosis in the left anterior descending artery.

The ECG abnormality and the woman's known history of ischaemic heart disease should have triggered an admission rather than relying on a negative Troponin. Although the implications of a pregnancy had been previously discussed in the cardiology clinic, the woman did not receive pre-pregnancy counselling or assessment and her pregnancy was not managed in a combined clinic setting.

**If an acute coronary syndrome is excluded, other causes for chest pain should be considered including aortic dissection or pulmonary embolism. It should be noted that ECG changes and elevated Troponin levels can be associated with both these conditions.**

**A normal ECG and/or a negative Troponin does not exclude the diagnosis of an acute coronary syndrome.**

The uterotonic ergometrine (contained within syntometrine) produces vasoconstriction and can cause coronary artery vasospasm and myocardial ischaemia. It was a factor associated with the deaths of two women from atherosclerotic coronary disease in this Enquiry. Both deaths occurred in women with risk factors for atherosclerosis. They both developed chest pain shortly after being given syntometrine and both women had a cardiac arrest. One woman was found to have severe coronary atheroma and the other had evidence of both acute and sub-acute myocardial infarction. It should be remembered that ergometrine can induce coronary artery spasm and severe postpartum haemorrhage may also result in myocardial ischaemia.

### *ECG access and interpretation*

> An older multiparous woman reported feeling unwell and breathless half an hour after a spontaneous vaginal delivery. She was not obese but smoked. She was found to be bradycardic and hypotensive and was treated with intravenous fluids, glycopyrrolate and then atropine. She developed acute breathlessness and chest pain. There was a delay in obtaining an ECG machine from another ward area. She had a cardiac arrest and died. Post mortem examination revealed acute myocardial infarction.

> A woman collapsed and died a few weeks postpartum. She had clear risk factors for ischaemic heart disease. Post mortem examination showed acute and subacute thrombotic coronary artery occlusion with clear evidence of myocardial infarction. At caesarean section she had been found to have an abnormal ECG with peaked T waves but no investigations were undertaken and the findings were attributed to potassium levels.

Serial 12-lead ECGs should be recorded as soon as possible in a pregnant or postpartum woman presenting with chest pain. ECGs need to be interpreted by a qualified individual as well as taking into account the automated report generated by the ECG machine (National Institute for Health and Care Excellence 2010a). In some instances there was a delay in obtaining a 12-lead ECG for a woman in labour. Delivery suites must have timely access to an ECG machine and abnormal ECG findings must be pursued and investigated further.

## Pathology in ischaemic heart disease deaths

The 34 women who died from ischaemic heart disease underwent detailed review by the MBRRACE-UK pathology assessors. Data were available for 15 of 16 women with atherosclerosis-related deaths; all underwent post-mortem examination. Table 3.9 illustrates the key findings following autopsy.

**Table 3.9: Key pathological findings/actions at autopsy among women who died from atherosclerosis-related ischaemic disease**

| | Present n (%) N=15 |
|---|---|
| Coronary artery thrombosis | 8 (53) |
| Coronary artery critical stenosis | 12 (80) |
| Acute myocardial infarction | 7 (47) |
| Myocardial fibrosis | 1 (7) |
| Histology performed | 11 (73) |
| Toxicology performed | 4 (27) |
| Referral to cardiac pathologist | 0 (0) |
| Material for DNA retained | 1 (7) |
| Lipid screening of family members considered/advised | 4 (27) |

The quality of autopsy reports was assessed as mostly good or excellent (67%). Ischaemic heart disease is a condition familiar to all autopsy pathologists, even in young people. The frequent use of histology sampling in this group, and consideration of any associated conditions which may have implications for surviving family members were particular features of excellence.

The utility of histology in ischaemic heart disease deaths is particularly emphasised when considering the deaths from coronary artery dissection. In the five deaths where full information was available, histology was undertaken in all. In this small group, many of the naked eye appearances were of “thrombus” within the coronary artery and only histological examination confirmed the true nature, that they were in fact arterial dissections. In the group of deaths from atheroma and related pathology, there were two instances where histology was not taken in the context of the identification of coronary artery thrombosis. In one, it is possible that this could have been a coronary artery dissection.

In only four women was there consideration of the potential for familial hypercholesterolaemia (FH) and a recommendation to refer the family for investigation.

**Healthcare professionals should consider the possibility of familial hypercholesterolaemia, especially where there is a personal or family history of premature coronary heart disease.**

**The absence of clinical signs (for example, tendon xanthomata) in adults and children/young people does not exclude a diagnosis of familial hypercholesterolaemia.**

**NICE guideline CG71: Familial hypercholesterolaemia: Identification and management (National Institute for Health and Care Excellence 2016a)**

Among the women who died from coronary artery dissection, five had autopsy data. The quality of autopsy reports was satisfactory (1), good (2) or excellent (2). The dissection involved the left anterior descending artery in four women and the circumflex artery in the remaining woman. This is in accord with a large study of coronary artery dissections in the general population which identified that in women the left coronary circulation is predominantly involved (88%) whereas in men the right coronary artery is involved (73%) (DeMaio, Kinsella et al. 1989).

Coronary artery dissection is well recognised to be associated with pregnancy, usually occurring in the postpartum period, and has no genetic or familial implications for the surviving family. Dissections can be seen in association with heritable vascular disorders such as Ehlers Danlos and Marfan syndromes, although a study of 116 non-pregnant patients from the Mayo Clinic identified a genetic abnormality in just 5% (Henkin, Negrotto et al. 2016). In the setting of pregnancy this is even less likely to be the case, and routine sampling of genetic material for testing is therefore not recommended. In early pregnancy, however, the cardiovascular haemodynamic and connective tissue changes associated with pregnancy are less likely to play a role so it may be prudent to consider connective tissue disorders in this setting.

## Recommendations for pathologists:

- **Examine the histology of the coronary vessels in women who die from ischaemic heart disease, especially when a "thrombus" is seen, to identify a coronary artery dissection.**
- **Recommend referral of family members of pregnant or postpartum women who died from ischaemic heart disease for consideration of screening for familial hypercholesterolaemia.**
- **Genetic material is not required in cases of coronary artery dissection associated with pregnancy unless the dissection occurs in early pregnancy.**

### 3.5.3 Myocardial disease/cardiomyopathy and other ventricular dysfunction syndromes

#### Background

There are many causes of ventricular dysfunction in pregnancy, including cardiomyopathy (i.e. structural heart muscle disease). Cardiomyopathies can be acquired or inherited, may be primary or secondary, and principally fall into dilated, hypertrophic or restrictive types. Peripartum cardiomyopathy is a form of dilated cardiomyopathy. Whatever the aetiology, a poorly functioning ventricle may be unable to provide the increased cardiac output required in pregnancy, resulting in pulmonary oedema and an increased risk of arrhythmia.

Women with hypertrophic cardiomyopathy may be unable to tolerate hypotension or tachycardia. The thick, hypertrophic ventricular walls may obliterate the ventricular cavity and ventricular outflow tracts, resulting in a reduction, rather than an increase in cardiac output if the woman becomes tachycardic. There is an increased risk of arrhythmias and sudden death.

#### The women who died

Twenty-seven women died due to myocardial disease/cardiomyopathy (Table 3.2), nine of whom had peripartum cardiomyopathy. A further five women died from ventricular dysfunction associated with essential hypertension and one died from other complications of her essential hypertension.

## Messages for care of women with myocardial disease/cardiomyopathy

Previous Confidential Enquiry reports have emphasised the need to consider the diagnosis of cardiomyopathy when women present with breathlessness (Lewis 2007, Lewis, Cantwell et al. 2011). They have also emphasised the need for prompt and appropriate investigation including echocardiography (Lewis 2007, Lewis, Cantwell et al. 2011), and referral to the appropriate specialists (Lewis 2007). The review of the care of the women considered here identified the same messages.

When women present with objective signs of respiratory and/or cardiovascular compromise, such as orthopnoea, paroxysmal nocturnal dyspnoea, tachycardia and rising respiratory rate, it is important to make a substantive diagnosis by systematic investigation. As highlighted among the overall messages for care of women with cardiac disease, on several occasions once pulmonary embolism had been excluded no further attempt was made to reach a definitive diagnosis. A number of these women subsequently died from myocardial disease/cardiomyopathy.

Other important messages which were highlighted by the review of the care of women who died from myocardial disease/cardiomyopathy included messages that have been identified in the reviews of women who died from other causes. A rising respiratory rate should prompt further investigation, as it is a sensitive sign of deteriorating clinical condition. Relevant investigations and treatment should not be withheld due to pregnancy or breastfeeding. Several women with cardiomyopathy were not prescribed ACE inhibitors because they were breastfeeding despite the fact that ACE inhibitors can be used safely in breastfeeding women.

> A young super-morbidly obese woman collapsed at home in the third trimester. The paramedic crew had to discontinue cardiac resuscitation due to the difficulty getting the woman down some stairs due to her size. She died undelivered. A perimortem caesarean section was not performed on arrival in the Emergency Department because a fetal heart beat could not be heard.

This also illustrates the difficulties of managing morbidly obese women. As has been repeatedly noted in this Enquiry, perimortem caesarean section should be performed from 20 weeks of gestation (or if a woman is visibly pregnant if the gestation is unknown) to facilitate the woman's resuscitation, irrespective of the fetal condition.

## Pathology in myocardial disease/cardiomyopathy

The pathological aspects of the 27 women who died from myocardial disease/cardiomyopathy were reviewed in detail by MBRRACE-UK pathology assessors. Most women died following out of hospital cardiac arrest, days to months after delivery. The pathology in myocardial disease/cardiomyopathy can be blurred in terms of case definitions, with overlap into other categories. The hearts of twelve (44%) of the 27 women were reviewed by a cardiac pathologist.

### *Obesity cardiomyopathy*

There were two women with obesity cardiomyopathy; they had BMIs >45kg/m$^2$ and very large hearts (510gm, 665gm) with significant fat infiltration into the ventricular muscle.

> A morbidly obese multiparous woman was found dead in bed by her husband a month following an emergency caesarean section, having been up earlier caring for her children. She had a history of rheumatic fever as a child but no history of hypertension. Post-mortem examination revealed normal heart valves but left ventricular hypertrophy with fatty infiltration.

An obesity related cardiomyopathy is increasingly recognised, characterised by myocyte hypertrophy and left ventricular dilation (Hookana, Junttila et al. 2011). Obesity is an inflammatory state and has been shown to alter cardiac electrophysiology and prolong the QT interval on ECG. Obesity is also increasingly recognised in cases of sudden cardiac death outside of pregnancy (Hookana, Junttila et al. 2011, Adabag, Huxley et al. 2015).

### *Left ventricular hypertrophy (with or without fibrosis)*

Five women died who were found to have left ventricular hypertrophy with or without myocardial fibrosis at post mortem. Their body mass indices ranged from 22–34; their ventricular hypertrophy was thus not attributable to obesity.

There is a body of evidence which links left ventricular hypertrophy with ventricular arrhythmia and an increased risk of sudden cardiac death. Hypertrophied cardiac muscle is electrophysiologically different from and more arrhythmogenic than normal heart muscle (myocardium) and therefore hypertrophied myocardium is more susceptible to arrhythmias. In addition, left ventricular hypertrophy also results in myocardial fibrosis and an increase in the heterogeneity of interventricular conduction, providing a further means for the spread of a ventricular arrhythmia.

The true nature of idiopathic left ventricular hypertrophy with or without fibrosis is unclear, and it may represent an undefined emerging cardiomyopathy. There may be standard initiating factors such as hypertension that have been overlooked or have resolved. None of the women considered here had hypertension. None had DNA retained at autopsy for later analysis. It is important that the deaths of such women are clinico-pathologically categorised as systematically as possible, for without accurate documentation, including DNA analysis, their true pathogenesis and epidemiology cannot be evaluated.

### *Peripartum cardiomyopathy (PPCM)*

Nine women, all white, died of peripartum cardiomyopathy, having developed progressive heart failure in the last month of pregnancy or after delivery. The time of their deaths ranged from the day of delivery to 330 days post-partum (median 36 days); all died in hospital.

Seven of the women had an autopsy, and the cardiac pathology was typical for this disease: cardiac enlargement (median heart/body weight ratio 0.55), dilated chambers and non-specific myocardial irregular hypertrophy, i.e. a dilated cardiomyopathy. Two of the women were reviewed by a cardiac pathologist.

**Pathologists undertaking maternal autopsies where the clinical pathology points to cardiac disease should follow the protocols in the Royal College of Pathologists' autopsy guidelines for sudden deaths with likely cardiac pathology (Royal College of Pathologists 2015).**

### *Other cardiomyopathies*

There were only three women who died from other cardiomyopathies, although all were post-mortem diagnoses. Two had arrhythmogenic right ventricular cardiomyopathy (ARVCM) and one had hypertrophic cardiomyopathy (HOCM). These diseases are defined by their characteristic cardiac pathology at autopsy, and two had been referred to a cardiac pathologist; however, no DNA material was retained for genetic analysis.

## 3.5.4 Sudden arrhythmic cardiac death with a morphologically normal heart (SADS/MNH)

### Background

SADS/MNH is an emerging entity where people (usually under 50 years of age) collapse from cardiac arrest; some may survive with prompt resuscitation. Those who die come to autopsy and are found to have no gross or histopathological abnormality of the heart (or any other organ) to account for their death. Drug screens for cardio-active drugs (such as cocaine) are negative. Thus it is a diagnosis of exclusion within a compatible clinical scenario.

These deaths are presumed to be arrhythmic and the majority result from a malignant ventricular arrhythmia and are the end result of a complex interaction between an abnormal cardiac substrate and emotional, environmental or physiological triggers. The abnormal cardiac substrate, a subtle and histologically invisible abnormality of the conduction system and/or its interaction with the heart muscle cells, is genetically determined in a proportion of cases.

SADS/MNH was the commonest cause of cardiac death in this Enquiry, causing over a third (38%) of all cardiac deaths. SADS/MNH has been increasingly recognised as a cause of maternal death in the UK over recent years (Table 3.10), although few maternal mortality surveys from other high-income countries mention it (Hameed, Lawton et al. 2015).

**Table 3.10: Maternal deaths from SADS, UK 2003–14**

| Time period | Number of women who died during or up to six weeks after pregnancy | Maternal mortality rate per 100,000 maternities (95% CI) | Number of women who died more than six weeks and up to a year after pregnancy | Late maternal mortality rate per 100,000 maternities (95% CI) |
|---|---|---|---|---|
| 2003–5 | 3 | 0.1 (0.02 to 0.4) | N/A | N/A |
| 2006–8 | 10 | 0.4 (0.2 to 0.8) | N/A | N/A |
| 2009–14 | 36 | 0.8 (0.5 to 1.1) | 17 | 0.4 (0.2 to 0.6) |

N/A - detailed data on all late maternal deaths were not collected under CMACE

## The women who died

Fifty-three women (35% of all cardiac deaths reviewed) died from SADS/MNH, representing a maternal mortality rate during or up to one year after pregnancy of 1.03 per 100,000 in the UK and Ireland between 2009–14 (95% CI 0.8 to 1.4). Further information is presented only for the 52 women whose deaths were reviewed in detail.

### *Characteristics of the women*

Of the 52 women whose care was reviewed, 39 were Caucasian, 8 African/Afro-Caribbean, 3 Asian, and 2 belonged to other ethnic groups. The median parity of women who died was 1 (range 0–6), and median age 31 years (range 17–42). Their body size varied as much it does for all pregnant and postpartum women in UK; their median body mass index (BMI) was 27 (range 17–57).

### *Timing of death*

Twenty-one women died before delivery, at median gestation of 32 weeks (range 8–39). Post-partum, women died at a median of 6 weeks (range 1 hour to 39 weeks after delivery). The timing of women's deaths was spread fairly evenly over the antenatal period and into the following months (noting that the Enquiry includes deaths of women up to one year after the end of pregnancy). Importantly, there is an apparent clustering around the time of delivery at 40 weeks and the following week.

## Messages for care

Forty-two (81%) women had their cardiac arrest out of hospital: at home (including women who died during their sleep) or in the community. Ten women had a cardiac arrest in hospital, during delivery or up to a week post-partum. As expected for a fatal syndrome that happens suddenly and unexpectedly, there were few prodromal indications of the forthcoming collapse; most cardiac arrests happened out of the blue.

> A young Caucasian woman had a normal delivery of her third baby. Two weeks postpartum she collapsed at home but despite exemplary resuscitation could not be revived. Her autopsy was 'negative'; her BMI was normal, and her heart was normal weight. Review by a cardiac pathologist confirmed the likelihood that she died from SADS/MNH since all other possible causes had been excluded.

One woman, who died three months postpartum, had a father with known long QT syndrome. Another woman was documented to have had previous blackouts:

> A woman died a few months following the birth of her second child. She had a history of unexplained collapse which had been investigated in the past by a neurologist and no cause found. An ECG at that time had shown an abnormally prolonged QT interval of

475ms but she had not been referred for further investigation. It was unclear from the maternity notes whether the history of unexplained collapse and neurological investigation had been known about. The diagnosis of long QT syndrome was made on genetic testing at post mortem examination which had shown a morphologically normal heart.

Apart from these two women, there was nothing in the women's known medical histories or their antepartum, intrapartum or postpartum observations to indicate a risk of SADS/MNH.

### *Management*

A young woman from North Africa had a cardiac arrest during labour. Chest compressions and manual ventilation were commenced but no attempt was made to ascertain the woman's rhythm. She was moved to theatre for a perimortem caesarean section. She was intubated and the baby was delivered before the defibrillator pads were finally attached. She was found to be in ventricular fibrillation. Despite multiple shocks and a prolonged resuscitation attempt, she could not be resuscitated.

Early defibrillation is of utmost importance and each minute of delay in early defibrillation reduces the likelihood of survival (Larsen, Eisenberg et al. 1993). There was no attempt to determine the underlying cardiac rhythm of the woman described in the vignette above once she had sustained a cardiac arrest. The resuscitation attempt was overshadowed by the need for a perimortem caesarean section and was further delayed by the unnecessary transfer to theatre prior to the caesarean section being carried out. Both defibrillation and perimortem caesarean section are important elements of maternal resuscitation. If a woman has a shockable rhythm after cardiac arrest, delay in defibrillation will impact on her chance of survival. Transfer to theatre for perimortem caesarean section will cause further delay. Subsequently this woman was found to have a family history of sudden death. The woman's sister had died suddenly in adulthood. A family history of sudden death may be elicited by or from the general practitioner and emphasises the importance, as noted in the 2015 report, of making the GP aware of a woman's pregnancy and the GP informing maternity services about a woman's medical or mental health history.

**There is an immediate need to determine the cardiac rhythm at cardiac arrest. For [women in] cardiac arrest with a shockable rhythm (VF/pulseless VT) attempt defibrillation as soon as possible.**

**European Resuscitation Council guidelines 2015 (Soar, Nolan et al. 2015).**

**Women should be asked at booking whether a close relative has died from their heart stopping unexpectedly due to an abnormal rhythm.**

## Pathogenesis of SADS/MNH and management of the family after death of a relative

The current explanation of SADS/MNH deaths, as already noted, is that they are due to ion channelopathies, inheritable cardiac conditions. The different phenotypes include: long QT syndrome (LQTS), Brugada syndrome, catecholamine polymorphic ventricular tachycardia, progressive cardiac conduction defect, idiopathic ventricular fibrillation, and sodium channel disease [Behr 2009]. All these heart conditions are associated with a morphologically normal heart, that is, the heart appears normal on gross and histopathological examination. Wolff-Parkinson-White syndrome also should be added to this list since, though it is due to structurally abnormal conduction pathways in the atria, this is not identifiable at autopsy.

This maternal mortality rate of approximately 1 in 100,000 observed here is comparable to the annual rate of SADS/MNH deaths in non-pregnant adult women in the few comprehensive surveys available, from Denmark and Ireland (Margey, Roy et al. 2011, Winkel, Holst et al. 2011). Thus it appears that pregnancy does not affect the overall mortality rate. Women with most forms of long QT syndrome are at highest risk in the post-partum period, having had a reduced risk of an event during the actual pregnancy (Seth, Moss et al. 2007). The exact reason for this risk is unknown but the postpartum period is a time of emotional stress, altered sleeping patterns and profound reduction in oestrogen and progesterone and cardiac remodelling. In pregnant women already known to have a channelopathy, it has been shown that beta-blockers are protective in this period (Rashba, Zareba et al. 1998, Seth, Moss et al. 2007) and women should be informed about the importance of continuing these drugs.

These inherited abnormalities increase the risk of a malignant ventricular arrhythmia and of sudden cardiac death. In non-pregnant populations, one-third to one-fifth of 'post-mortem negative' sudden deaths in young adults are due to an identifiable channelopathy, mainly long QT syndrome, catecholaminergic polymorphic ventricular tachycardia and Brugada syndrome (Behr, Wood et al. 2003, Tan, Hofman et al. 2005). About 30% of SADS deaths are found with a relevant genetic abnormality on proband DNA testing (Semsarian, Ingles et al. 2015); when their first-degree relatives are examined in cardiac genetic clinics (with exercise, ECG and genetic analysis), up to half will be found to have a familial inherited cardiac condition phenotype (Papadakis, Raju et al. 2013).

First-degree relatives of women who die suddenly with a normal heart at post mortem, should be referred for clinical screening and genetic analysis. Currently only a minority of first-degree relatives are screened in cases of sudden adult death syndrome outside of pregnancy. One woman whose care was examined for the purposes of this Enquiry was diagnosed with long QT syndrome following genetic testing after death. It is important that intensive family follow-up is carried out after women die from SADS/MNH, to identify the potential for the same syndrome in their brothers, sisters and children.

## Autopsy and investigative pathological aspects of SADS/MNH

SADS/MNH is a diagnosis of exclusion. The exclusion list in pregnant women is long and includes: venous thrombo-embolism, amniotic fluid embolism syndrome, asphyxia, sepsis, haemorrhage, stroke, acute anaphylaxis, toxicity by cardiac stimulant drugs, ischaemic heart disease, eclampsia and pre-eclampsia, hypertensive heart disease, valvular heart disease, pulmonary arterial hypertension, congenital heart disease, left ventricular hypertrophy with or without fibrosis, dilated cardiomyopathy (including peripartum cardiomyopathy (PPCM)), hypertrophic cardiomyopathy, arrhythmogenic right ventricular cardiomyopathy, and cor pulmonale.

Extensive histopathologic investigation is required to fully investigate these women's deaths, as well as, ideally, a full toxicological drug screen, estimation of mast cell tryptase for anaphylaxis, and review by a cardiac pathologist.

> A very obese young woman died a few weeks after her first delivery. She was found dead on the sofa in the morning, by her husband. A thorough autopsy, with histology and toxicology, found a normal heart and normal patent coronary arteries. However, the cause of death was then given as 'ischaemic heart disease due to atherosclerosis'. Evidently the pathologist was reluctant to consider SADS/MNH, or did not know of this condition.

Forty-seven of the women with SADS/MNH were known to have had an autopsy. In 33/47 autopsies (70%), there was a toxicology screen performed, all were negative. Only 11 autopsies also had mast cell tryptase analyses, again negative. Thirteen (28%) had blood or spleen kept for later genetic sequence analysis; LQTS was demonstrated in one woman. Reserved splenic DNA from any other women who died is not known to have been requested for analysis subsequently. In 31 women (66%), the heart pathology was reviewed by a cardiac pathologist with expertise in SADS/MNH, to confirm the normal morphology.

The women's heart sizes ranged from 247–505gm, but the more critical heart/body weight ratio (Gaitskell, Perera et al. 2011) had a median of 0.33% (range 0.26–0.55), i.e. within the normal range. In the classification of these women's deaths, care was taken to exclude hypertensive heart disease and other conditions such as idiopathic left ventricular hypertrophy with or without myocardial fibrosis. There were several instances of amniotic fluid embolism (AFE) being originally considered the cause of death, even though there was no evidence of AFE clinically or pathologically, and the deaths happened days after the woman's delivery. This again suggests reluctance on the part of pathologists to entertain the possibility of SADS/MNH as the cause of death.

The importance of determining if the woman who died had a morphologically normal heart, relates to the increased probability that her death was due to a genetically determined condition (a channelopathy) and it is of utmost importance that the first-degree relatives of these women are referred for investigation as a proportion will have the same potentially lethal condition.

Studies of non-pregnant individuals dying of SADS/MNH, using genetic sequencing, have found an identifable gene defect in 30–50% of cases, by examining first degree relatives of the person who died and/or their own DNA (Papadakis, Raju et al. 2013, Semsarian, Ingles et al. 2015). There is thus a need to reserve DNA material from all autopsies where SADS/MNH is a possible diagnosis. In this series, from the information available, only one

woman who died had a channelopathy directly proven, one had a known relative with LQTS (the commonest of the channelopathies) and only two women had a recorded history of previous palpitations. These low proportions are similar to those observed among the non-pregnant (Mellor, Raju et al. 2014).

## Messages for pathologists

- **It is vital that autopsy is undertaken systematically for robust diagnosis of SADS. All women who died from sudden cardiac arrest and who have a morphologically normal heart should have molecular studies performed at postmortem with the potential for family screening as there is a real possibility of identifying an inherited channelopathy. Tissue should be retained for genetics and families followed-up. Future sudden deaths amongst relatives may then be prevented.**

**The detailed pathological investigation of maternal deaths is making an important contribution to the growing understanding of the condition; this large series includes the first case of LQTS-related death in maternity in the UK.**

### 3.5.5 Pulmonary arterial hypertension

Regardless of the cause, pulmonary arterial hypertension in pregnancy carries an extremely poor prognosis; mortality remains at 20–30%, even if managed in an expert centre with modern selective pulmonary vasodilator therapy (Kiely, Condliffe et al. 2010). Women with pulmonary arterial hypertension should be counselled about the very high risk of pregnancy and given clear contraceptive advice as well as advice about interruption of any unintended pregnancy (Hemnes, Kiely et al. 2015).

Six women died from pulmonary arterial hypertension; it was associated with congenital heart disease in two.

> A woman with liver disease and portal hypertension had a planned pregnancy, and developed increasing breathlessness in the third trimester. She was discharged twice in two days from the Emergency Department after a CT scan excluded a pulmonary embolus. The CT scan showed a dilated right heart, but no action was taken. She presented unwell for a third time the following day and was admitted with hypotension and sinus tachycardia. She had an abnormal ECG that triggered medical review, and a bedside echo showed severe pulmonary arterial hypertension. She was transferred to the regional cardiothoracic centre but went into early labour and was delivered by emergency caesarean section. She had a placental abruption and massive postpartum haemorrhage with cardiac arrest from which she could not be resuscitated.

Although not common, there is a well-recognised association between portal hypertension and pulmonary arterial hypertension. Women with portal hypertension should be assessed for pulmonary arterial hypertension before pregnancy, and counselled appropriately. A recurring theme of the care of the women reviewed for this report is the reluctance to make a positive diagnosis to account for the presenting symptoms and signs, once pulmonary embolism is excluded.

**Pregnant or postnatal women with significant symptoms should not be discharged home without a diagnosis.**

An ethnic minority woman came to the UK as an adult and died two weeks after a normal vaginal delivery. She had an episode of unexplained collapse during her pregnancy for which she was not investigated. On the day of delivery she became breathless and hypotensive and was found to have continuous murmurs and an arterial oxygen saturation of 89%. Her ECG showed right ventricular hypertrophy. A CT scan excluded pulmonary embolus. An echocardiogram and cardiology review were requested; the echocardiogram was not performed for two days and the cardiology registrar refused to review the woman until the echocardiogram had been performed. The echocardiogram eventually confirmed severe pulmonary arterial hypertension. There followed a delay of a week before she was transferred to the regional pulmonary hypertension centre, where despite starting selective pulmonary vasodilator therapy, she continued to deteriorate and died.

This woman had a hereditary condition associated with pulmonary arterial hypertension. Had she been examined and assessed after her collapse during pregnancy, her diagnosis could have been secured and an earlier referral for expert pulmonary arterial hypertension treatment made. Any doctor who is asked to review a sick patient should attend without delay.

An ethnic minority woman moved to the UK as an adult. Her pregnancy was uneventful until the third trimester when she presented with breathlessness. She was cyanosed (arterial oxygen saturation 89%) with a high haemoglobin and thrombocytopenia. She was also hypertensive with proteinuria. She had abnormal heart sounds and her ECG was abnormal, triggering medical review and an echocardiogram, which confirmed severe pulmonary arterial hypertension. She was treated for pre-eclampsia and had a category 3 caesarean section the following day. On the first postpartum day she had episodes of cyanosis; a CT scan showed no pulmonary embolism, but she had ascites and hepatomegaly. She was transferred to ITU and discussed with the regional pulmonary hypertension centre. She became increasingly unstable and was transferred to a cardiothoracic centre for ECMO where she died some days later. At post mortem she was found to have had Eisenmenger syndrome secondary to a large patent ductus arteriosus.

Significant congenital heart disease is more likely to remain undiagnosed in people born in low resource countries, and may only present when they decompensate. Her cyanosis had been missed during her pregnancy as it is more difficult to detect in non-white women; this and her high haemoglobin and low platelet count were all due to her cyanotic heart disease.

A young woman with a repaired ventricular septal defect and persistent pulmonary arterial hypertension died 3 days after delivery. It is unclear whether she received pregnancy or contraception counselling from the paediatric cardiology services. She was referred to the specialist adult congenital heart unit for the first time when she found herself pregnant. She elected to continue her pregnancy and was offered care at a specialist pulmonary hypertension unit. She was delivered at 34 weeks after she became increasingly symptomatic. She was closely monitored post-delivery on ITU, but she collapsed suddenly and died the following day.

**All teenage girls with heart disease must receive age-appropriate pregnancy and contraceptive counselling**

Appropriate contraceptive and pregnancy counselling is particularly important for those with difficult social circumstances who are at high risk of teenage pregnancy, and most particularly those for whom pregnancy carries a high risk. This young woman's sudden death in the early post delivery period, heralded by a fall in platelet count, was typical of that of a woman with pulmonary arterial hypertension and occurred despite her exemplary post-delivery care.

## 3.5.6 Valvular heart disease

This section includes messages from both the Confidential Enquiry into Maternal Deaths and the Confidential Enquiry into Maternal Morbidity.

### Background

Women with valvular heart disease, who may have been asymptomatic prepregnancy, may develop symptoms for the first time in pregnancy due to their increased cardiac output. Stenotic valves are a significant risk factor in pregnancy as they represent an obstruction to the increased blood flow required in pregnancy. This can lead to ventricular failure, arrhythmias or hypoperfusion. Regurgitant lesions are less problematic, providing good ventricular function is maintained. In pregnant women in the UK aortic stenosis is usually congenital, and mitral stenosis usually rheumatic in origin. The number of women with rheumatic heart disease in the UK may be rising, due to higher levels of migration from Asia, Africa and Eastern Europe.

The presence of left heart obstruction and mechanical prosthetic valves have been shown to predict poor pregnancy outcome (Siu, Sermer et al. 2001, Drenthen, Boersma et al. 2010). It is believed that increasing numbers of women with prosthetic heart valves are embarking upon pregnancy, but optimal clinical management is hampered by a lack of good quality data about maternal mortality and rates of complications.

Deaths in women with valvular heart disease have formed a small proportion of the cardiac deaths in recent confidential enquiries, but these numbers may rise if more women with stenotic valve lesions or prosthetic valves become pregnant. For this reason, and in order to identify more generalisable messages for care, lessons identified from reviews of the care of 32 pregnant women with artificial heart valves who did not die in pregnancy are also included here.

### The women who died

**Table 3.11: Women who died from valvular heart disease, UK 1994–2014.**

| Type and cause of death | 1994–96 | 1997–99 | 2000–02 | 2003–05 | 2006–08 | 2009–14 |
|---|---|---|---|---|---|---|
| Stenosis or other valve dysfunction | 0 | 0 | 3 | 3 | 0 | 4 |
| Thrombosed valve | 1 | 0 | 0 | 0 | 2 | 4 |
| Infective endocarditis | 0 | 2 | 1 | 2 | 2 | 2 |
| Cerebrovascular accident | - | - | - | - | - | 1 |

Sources: CMACE, MBRRACE-UK

Eleven women died from valvular heart disease between 2009 and 2014. Two women had severe rheumatic mitral valve disease; two women died from endocarditis on native valves (one aortic, one tricuspid); the other 7 had mechanical prosthetic valves and died from valve dysfunction (n=2), valve thrombosis (n=4) and a cerebrovascular accident (CVA) (n=1). Three of the prosthetic valves were in the mitral position and four in the aortic position. A comparison with previous triennia is shown in Table 3.11.

### The women who survived

In addition to reviewing maternal deaths, a study of maternal morbidity relating to prosthetic valves in pregnancy was carried out, using the confidential enquiry methodology. The care of a stratified random sample of the women (n=32) reported to the UKOSS study of Prosthetic Heart Valves in Pregnancy (Vause, Clarke et al. 2016) was reviewed.

**Table 3.12: Characteristics of women with prosthetic heart valves whose care was examined in the morbidity enquiry**

| Characteristic | Number of women (n=32) |
|---|---|
| **Age** | Median 30.5 Range 18–42 |
| **Reason for valve replacement** | |
| *Congenital* | *17* |
| *Acquired* | *15* |
| **Valve position*** | |
| *Aortic* | *15* |
| *Mitral or systemic atrioventricular* | *20* |
| **Fetal outcome** | |
| *Miscarriage* | *3* |
| *Termination of pregnancy* | *1* |
| *Livebirth* | *26* |
| *Stillbirth* | *1* |
| *Not known* | *1* |
| **Mode of delivery (n=28 who delivered)** | |
| *Caesarean section* | *14* |
| *Vaginal delivery* | *13* |
| *Not known* | *1* |
| **Maternal complications** | |
| *Bleeding complication* | *11* |
| *CVA* | *2* |
| *Valve thrombosis* | *3* |

* three women had both mitral and aortic prosthetic valves

Although all of these women survived, half had serious maternal complications (Table 3.12). The most common complication was secondary haemorrhage including wound and vaginal haematomas which required return to theatre or secondary post partum haemorrhage requiring transfusion. Two women had thromboembolic CVAs and three had valve thromboses which were treated either by thrombolysis or surgically. The risks associated with pregnancy in a woman with a prosthetic heart valve must not be underestimated.

Improvements to care which may have made a difference to outcome were identified in almost a third of the women with valvular heart disease who survived. However, there was a clear difference in the care received by the women who died, two thirds of whom had improvements to care identified which may have made a difference to outcome (table 3.13).

**Table 3.13: Classification of care received amongst women with valvular heart disease who died and those who survived**

| | Women who died N (%) (n=11) | Women who survived N (%) (n=32) |
|---|---|---|
| Good care | 3 (27) | 17 (53) |
| Improvements to care which would have made no difference to outcome | 1 (9) | 5 (16) |
| Improvements to care which may have made a difference to outcome | 7 (64) | 10 (31) |

## Messages for the care of women with valvular heart disease

### *Pre-pregnancy care and contraception*

A woman who had previously undergone prosthetic valve replacement for rheumatic mitral valve disease became unexpectedly pregnant and requested termination of pregnancy. She was converted from warfarin to LMWH but initially the dose was inappropriately low, and only once daily. On the day before the termination she was admitted with breathlessness and coughing pink frothy sputum. She was tachycardic, tachypnoeic and hypoxic. In the intensive care unit ventilation was needed and she was treated for a chest infection with antibiotics and antivirals. A bedside echocardiogram performed to exclude endocarditis and evaluate cardiac function was thought to show right heart strain. The possibility of valve thrombosis was not considered. Four days after admission the echo was reviewed by a cardiologist and a thrombosed mitral valve diagnosed. The woman developed multi-organ failure and died two days later.

Pregnancy is very high risk in women with prosthetic valves and therefore reliable contraception is extremely important. All healthcare professionals must provide women with prosthetic valves appropriate advice about contraception, and revisit this issue at each appointment. This will often be cardiologists, haematologists and the GP as these are the healthcare professionals such women are most likely to encounter outside of pregnancy.

**Pregnancy is very high risk in women with prosthetic valves and therefore all healthcare professionals should provide women with advice about appropriate, reliable contraception.**

**Clear guidance on contraceptive choices for women with cardiac disease is available (Faculty of Sexual and Reproductive Healthcare Clinical Effectiveness Unit 2014).**

### *Multidisciplinary care planning*

A women who had a metallic prosthetic aortic valve and root replacement for congenital aortic stenosis had a planned pregnancy, following pre-pregnancy counselling. During the pregnancy she had multidisciplinary care, and regular review by senior clinicians, with intensive monitoring of her anticoagulation. During her pregnancy her heart valve function deteriorated. A multidisciplinary care plan including obstetric, cardiac, anaesthetic and haematological elements was generated and modified as the pregnancy progressed. She underwent successful elective caesarean delivery at term with an excellent outcome.

The level of complexity of this woman's pregnancy was recognised and changes in her condition responded to appropriately. Developing individualised, multidisciplinary care plans requires good organisation, an effective administrative structure and the investment of a significant amount of time.

**A written multidisciplinary care plan, which the woman is involved in generating, and which is modified when necessary as the pregnancy progresses, facilitates good communication and consistent management. The care plan should include postnatal management and follow up.**

### *Anticoagulation*

All six women with prosthetic valves who died used low molecular weight heparin throughout pregnancy as their anticoagulant, but one woman was using an inappropriately low dose once daily initially, one was poorly compliant and one woman had no monitoring of the adequacy of her anticoagulation (Anti Xa levels). In women with prosthetic valves, thrombotic complications are more likely in association with subtherapeutic Anti Xa levels,

either due to non compliance, or due to subtherapeutic dosing (McLintock, McCowan et al. 2009). In the UKOSS national study of pregnancy outcomes in women with prosthetic heart valves, 71% used LMWH throughout pregnancy (Vause, Clarke et al. 2016).

Guidelines regarding monitoring of LMWH in women with prosthetic valves vary with a lack of consistency on frequency of monitoring, target ranges and the timing of the post dose (peak) anti Xa level, but stress the need for twice daily dosing to ensure less variation in anticoagulant activity over the 24 hour period, and the need to check Anti Xa levels to assess the adequacy of anticoagulation (European Society of Gynecology, Association for European Paediatric Cardiology et al. 2011, Nishimura, Otto et al. 2014).

Both the European Society of Cardiology guidelines and the American College of Cardiology/American Heart Association guidelines favour the use of oral anticoagulation in the second and third trimesters, but suggest that if LMWH is used it should be given 'twice daily (with dose adjustment according to weight and target anti-Xa level 4–6 hours post-dose 0.8–1.2 U/mL.' Many women with prosthetic valves in the UK choose to use LMWH throughout pregnancy, in view of the fetal risks associated with warfarin. There is an urgent need for evidence to guide the counselling of women about the maternal and fetal risks associated with the different anticoagulant regimens.

A woman with congenital heart disease had a prosthetic aortic valve replacement 5 years prior to her pregnancy. She presented very early in pregnancy and was referred immediately to a tertiary hospital with obstetric-cardiac and obstetric-haematology services, where she was seen the next day. She was converted from warfarin to LMWH before 6 weeks of pregnancy and had an echocardiogram which confirmed good valvular and ventricular function. When a first trimester ultrasound was performed a non viable pregnancy was diagnosed. She had uneventful surgical management under a general anaesthetic.

Although this woman miscarried, review of her care demonstrated excellent referral pathways and the value of close multidisciplinary working. To enable women to convert from warfarin to LMWH before 7 weeks' gestation and avoid the risk of teratogenicity, the referral system must function seamlessly. The woman and all relevant health care professionals need to understand the importance of early presentation and how to access appropriate care.

### *Valve thrombosis*

In several women, including women who died, the possibility of valve thrombosis was not considered, with infection and pulmonary embolism being preferred diagnoses, despite clear signs such as the absence of valve clicks on auscultation.

A woman who spoke very little English had a mechanical mitral valve replacement as a child. She also had aortic regurgitation and left ventricular dilatation. During pregnancy she was prescribed once daily LMWH and there was no monitoring of Anti Xa levels. She did not see an obstetrician until mid-pregnancy, and did not see a consultant (obstetrician or cardiologist) or have an echocardiogram until the third trimester. LMWH was stopped prior to induction of labour. She had a vaginal delivery and was discharged home the following day on LMWH. The onus was placed on the woman to make her own anticoagulant clinic appointment. Two weeks postnatally she was admitted with a mitral valve thrombosis which was treated successfully with thrombolysis, but two weeks later she suffered a thromboembolic stroke.

In contrast to the woman described in the previous vignette, clinicians caring for this woman did not appear to appreciate the level of risk faced by this woman, and she was not referred for tertiary care. There was no senior input until late in her pregnancy, and even then areas were identified where her care could clearly have been improved. The management of her anticoagulation in particular could have been improved throughout pregnancy, around the time of delivery and postnatally. It is unrealistic to expect a woman who had just had a baby, and spoke very little English to make her own anticoagulant clinic appointment following discharge from hospital.

**Women with prosthetic valves in pregnancy are at extremely high risk of complications, and should be referred to specialist centres at the earliest possible opportunity. They need expert obstetric, haematology, cardiology and anaesthetic input.**

**New onset of cardiorespiratory symptoms and/or absence of valve clicks in women with prosthetic heart valves should prompt careful echocardiography and early review by a senior cardiologist to exclude the possibility of valve thrombosis.**

**Management of anticoagulation following delivery is challenging. Women should be kept in hospital until their treatment has been stabilised and arrangements for outpatient follow up have been made.**

A woman who had a prosthetic mitral valve replacement was told that when she became pregnant she should change from warfarin to enoxaparin 1.5g/kg once daily. She conceived a few months later and saw her midwife in early pregnancy. She first saw an obstetrician in the mid-second trimester. In the third trimester she attended the Emergency Department with shortness of breath and haemoptysis. Her saturations were 91% on air. She was admitted to a medical ward with a presumptive diagnosis of pneumonia or pulmonary embolism and treated with antibiotics and her LMWH dose was increased. Her condition continued to deteriorate and she was transferred to a high dependency unit. A transthoracic echocardiogram showed right heart strain but no valve thrombosis, and a CTPA was negative. Her condition worsened and she was intubated and transferred to intensive care in another hospital where a diagnosis of fetal death in utero was made and a transoesophageal echocardiogram showed a valve thrombosis. She underwent surgery and the metallic valve was replaced with a bioprosthetic (tissue) valve.

The dose of LMWH suggested to this woman was inappropriately low. Although she presented to her midwife in the first trimester there was then a delay of nine weeks before she was seen by an obstetrician. Women with prosthetic valves are extremely high risk and need to be able to access care from a team with appropriate expertise as soon as their pregnancy is confirmed. This woman remained on once daily dose of LMWH, resulting in inadequate anticoagulation. She did not see a cardiologist or anaesthetist until she was admitted in the third trimester. As with the woman who died described above, prosthetic valve thrombosis was not considered in the initial differential diagnosis. When she had surgery the mechanical prosthetic valve was replaced with a bioprosthetic (tissue) valve, presumably in anticipation of the woman wanting further pregnancies. If her plans for pregnancy had been discussed with her prior to her initial surgery, she may have chosen to have a tissue valve, rather than a mechanical valve at that point, and avoided the complications she experienced. The advantage of a bioprosthesis (tissue valve) is that there is no need for long term anticoagulation, and the risks involved in pregnancy are much lower. The disadvantage of a bioprosthesis is that it will deteriorate and require further, higher risk, redo surgery to replace it after 5–10 years.

The AHA/ACC guidelines state that *'All patients referred for a valve operation before pregnancy should receive prepregnancy counselling by a cardiologist with expertise in managing patients with valvular heart disease during pregnancy about the risks and benefits of all options for operative interventions, including mechanical prosthesis, bioprosthesis and valve repair' (Nishimura, Otto et al. 2014)*. Whilst this recommendation is helpful, an obstetrician should also be involved in the consultation.

**All women of childbearing age referred for a valve operation before pregnancy should receive prepregnancy counselling by a team (cardiologist, obstetrician and relevant others) with expertise in managing patients with valvular heart disease during pregnancy about the risks and benefits of all options for operative interventions, including mechanical prosthesis, bioprosthesis and valve repair.**

This woman was transferred safely and appropriately to a higher level of care and survived once the correct diagnosis had been made and appropriate management instigated. Women who have significant medical conditions (e.g. significant cardiac disease, pre-eclampsia, sepsis), and who require inter-hospital transfer in pregnancy or the peripartum period, are at risk of serious complications during or after such a transfer.

There are established guidelines for the transfer of non-obstetric patients (Association of Anaesthetists of Great Britain and Ireland 2009) that apply equally in the critically ill mother. A crucial early decision is the possible requirement for a midwife and/or an anaesthetist to accompany the woman, to allow appropriate deployment of staff remaining in the base hospital or calling in extra staff. Ideally, women who require close haemodynamic monitoring (e.g. women with aortic dissection or heart failure) should have invasive blood pressure monitoring during transfer; this provides more precise assessment than non-invasive methods and should always be considered.

Inter-hospital referral of a sick pregnant or postpartum woman should be directed by the principle 'one transfer to definitive care'. As noted in chapter 6, it is unlikely to be appropriate to move a sick antenatal woman to a facility without on-site obstetric cover.

#### *Antibiotic prophylaxis*

> A woman with congenital heart disease was known to have moderate aortic regurgitation and a ventriculoseptal defect. She had a normal vaginal delivery. She was not given any intrapartum antibiotics. Three weeks postnatally she was diagnosed as having endometritis and an echo showed endocarditis with severe aortic regurgitation. There was good input from the microbiologist into her care, but she deteriorated and was eventually too sick to be transferred to a cardiac surgical unit and died.

Current NICE guidelines state that antibiotic prophylaxis against infective endocarditis should not be offered for gynaecological and obstetric procedures or childbirth (National Institute for Health and Care Excellence 2008b). This is based on one small study of bacteraemia rates at elective caesarean section. The NICE guidelines also state that the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual woman, in consultation with the woman. Some women, following discussion of the risks and benefits, may therefore choose to have antibiotic prophylaxis because of the serious nature of endocarditis and the low risk of anaphylaxis. These issues should be discussed with women with valvular heart disease prior to delivery.

### 3.5.7 Congenital heart disease

A total of 11 women with structural congenital heart disease died and are included in other sections.

- Five died from aortic dissection; two had complex aortic repairs with significant residual disease, and three were found to have bicuspid aortic valve at post mortem, one in the context of undiagnosed Loeys Dietz syndrome.
- Three women with congenital heart disease and mechanical valves died, two from valve thrombosis.
- Two had pulmonary arterial hypertension, one with a late repair of a ventricular septal defect and one with undiagnosed Eisenmenger syndrome secondary to a patent arterial duct.
- One woman with a small ventricular septal defect and bicuspid aortic valve died from endocarditis.

There was an additional late death, nearly a year post delivery, in a woman with complex congenital heart disease who died of multi-organ failure after an out of hospital cardiac arrest. A further 17 women with prosthetic heart valves whose care was examined in the Confidential Enquiry into Maternal Morbidity had congenital heart lesions leading to their valve replacement.

There are increasing numbers of adult survivors of congenital heart disease who are well enough to contemplate pregnancy. The relatively small number of maternal deaths in women with complex congenital heart disease (and none in this report with repaired tetralogy of Fallot, a systemic right ventricle or a single ventricle circulation) may be a reflection of good pre pregnancy counselling and contraception and antenatal and perinatal care.

## 3.6 Conclusions

Cardiac disease remains the leading cause of maternal death in the UK. There were clear messages for improvements in basic care identified by the assessors, including in particular awareness of the significance of symptoms such as raised respiratory rate, chest pain, persistent tachycardia and orthopnoea, and the need for multi-disciplinary team working. The significance of a history of heart disease should not be overlooked. Overall, improvements in care were identified for 50% of the women who died from cardiac disease (Table 3.14), and in just over a third this may have made a difference to the outcome. However, the care of women varied according to their underlying condition. Improvements in care which may have made a difference to outcome were identified in 49% of women who died from causes other than sudden arrhythmic death syndrome. Improvements in care that may have made a difference to outcome were identified in 31% of women with artificial heart valves who had a pregnancy and survived. The overall care of the women who died from SADS/MNH was mostly felt to be good, however, in the absence of genetic diagnosis and subsequent screening of the families of most of the women who died from SADS/MNH, there remain opportunities for prevention of other sudden deaths. Further research is needed to investigate the apparent rising rate of maternal mortality due to SADS/MNH.

**Table 3.14: Classification of care received by women who died from a cardiac cause and for whom case notes were available for an in-depth review, UK and Ireland, 2009–14**

| | Ischaemic deaths (n=34) N (%) | Valvular heart disease (n=11) N (%) | Essential hypertension (n=5) N (%) | Myocardial disease/ cardiomyopathy (n=22) N (%) | SADS/ MNH (n=52ł) N (%) | Aortic dissection (n=21) N (%) | Others (n=7) N (%) | Total (n=152)* N (%) |
|---|---|---|---|---|---|---|---|---|
| Classification of care received | | | | | | | | |
| Good care | 21 (62) | 3 (27) | 0 (0) | 7 (32) | 41 (79) | 3 (14) | 1 (14) | 76 (50) |
| Improvements to care which would have made no difference to outcome | 5 (15) | 1 (9) | 1 (20) | 6 (27) | 6 (11) | 3 (14) | 0 (0) | 22 (14) |
| Improvements to care which may have made a difference to outcome | 8 (23) | 7 (64) | 4 (80) | 9 (41) | 5 (10) | 15 (71) | 6 (86) | 54 (36) |

*Excludes 37 late cardiac deaths identified from the records of the ONS and NRS for which no information was available.

Information on care grading was not available for one woman for whom detailed records were not available


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# 4. Caring for women with hypertensive disorders of pregnancy

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## 4.1 Key messages

Mortality from pre-eclampsia is reducing but aspects of care can still be improved.

Women with risk factors for pre-eclampsia and those who develop hypertension or proteinuria in pregnancy should have a plan for an appropriate schedule of checks (with more visits than those for low risk pregnant women). New onset hypertension or proteinuria needs prompt referral with clear communication between health professionals.

Monitor blood pressure and urinalysis at each antenatal attendance in both primary and secondary care and make sure results from tests are followed-up. Keep blood pressure in all women to below 150/100, with urgent treatment to achieve this in women with severe hypertension.

If women have a blood pressure over 140mmHg systolic or 90mmHg diastolic on 2 occasions in labour or immediately after birth they should be considered for transfer to a Consultant unit.

Staff should be aware that agitation and restlessness may be a sign of an underlying problem in women with hypertension.

Whilst intubation may be required for airway control, maternal stabilisation and blood pressure control is vital prior to intubation in order to minimise maternal risk.

Neuroimaging should be performed urgently in any woman with hypertension or pre-eclampsia who has focal neurology or who has not recovered from a seizure.

## 4.2 Background

The Confidential Enquiry into Maternal Death has considered eclampsia, pre-eclampsia, haemolysis elevated liver enzymes low platelet syndrome (HELLP), elevated liver enzymes low platelet syndrome (ELLP) and liver disorders associated with pregnancy (acute fatty liver of pregnancy, AFLP) together in one group since 2003–2005. Guidance on the management of hypertension in pregnancy was produced by NICE in 2010 (National Institute for Health and Care Excellence 2010b) and identified that one in ten women in pregnancy were affected by pregnancy-associated hypertensive disorders. Pregnancy-associated hypertension is associated with both maternal and fetal morbidity. A UKOSS study in 2005–2006 (Knight *et al*. 2007) identified a rate of eclampsia of 26.8 per 100,000 maternities (95% CI 23.3–30.7 per 100,000), compared to a rate of 49 per 100,000 maternities (95% CI 45–54 per 100,000) in a survey from 1992 (Douglas and Redman 1994). HELLP or ELLP syndrome occurs in 2.3 per 100,000 maternities (Fitzpatrick, Hinshaw et al. 2014) and AFLP occurs in 5.0 per 100,000 maternities (95% CI 3.8 to 6.5 per 100 000) (Knight, Nelson-Piercy et al. 2008). Each of these variants of the syndrome of pre-eclampsia are associated with increased risks of maternal and perinatal morbidity and mortality. Improving the care of women with these complications in line with national guidance would be expected to improve mortality and morbidity. The present report demonstrates an ongoing improvement in mortality from hypertensive disorders but nonetheless improvements in care which may have made a difference to the outcome were identified.

# 4.3 Summary of the key findings 2009–2014

## The women who died

There has been a significant decrease in the mortality rate from hypertensive disorders of pregnancy in the period between 2009–11 and 2012–14. In this six-year period 14 women died in the UK and Ireland; 11 died between 2009–2011 (0.42 per 100,000 maternities, 95% CI 0.21 to 0.76) whereas only 3 died between 2012–2014 (0.11 per 100,000 maternities, 95% CI 0.02 to 0.34) (p=0.005 when comparing 2009–11 with 2012–14). In each of the previous six-year periods 37 women died. This is a positive reflection on the standard and provision of care for women with hypertensive disorders of pregnancy. In this report (as in previous reports) intracranial haemorrhage was the most common cause of death followed by hepatic complications (Table 4.1). Reassuringly no women died in relation to inappropriate fluid management (pulmonary oedema and renal failure).

**Table 4.1: Causes of death among women who died from hypertensive disorders of pregnancy (1997–2014)**

| | 1997–2002§ | 2003–8§ | 2009–14¶ |
|---|---|---|---|
| Intracranial Haemorrhage | 16 | 18 | 7* |
| Eclampsia/cerebral oedema | 0 | 6 | 3 |
| Pulmonary oedema | 3 | 0 | 0 |
| Hepatic rupture | 2 | 1 | 0 |
| Hepatic Necrosis/HELLP | 9 | 5 | 4* |
| AFLP | 7 | 7 | 1 |
| Total | 37 | 37 | 14* |

*One woman died due to both intracranial bleed and HELLP syndrome.

§ Figures for UK only

¶ Figures for UK and Ireland

## Risk Factors

**Table 4.2: The socio-demographic characteristics of women who died from hypertensive disorders of pregnancy, UK and Ireland, 2009–14**

| Characteristics | N=14 Number (%) |
|---|---|
| **Socio-demographic** | |
| *Age (years)* | *Median=35, range 18 to 38* |
| *<35* | *6 (43)* |
| *≥ 35* | *8 (57)* |
| **Parity** | |
| *Nulliparous* | *11 (79)* |
| *Multiparous* | *3 (21)* |
| **Ethnicity** | |
| *White* | *8 (57)* |
| *Non-white* | *6 (43)* |
| **Woman's region of birth** | |
| *United Kingdom/Ireland* | *6 (43)* |
| *Outside UK/Ireland* | *7 (50)* |
| *Missing* | *1 (7)* |
| **Socioeconomic status (Index of Multiple Deprivation)** | |
| *First - third quintile (Not deprived)* | *7 (50)* |
| *Fourth/fifth quintile (Deprived)* | *5 (36)* |
| *Missing* | *2 (14)* |

The characteristics of the women who died are shown in table 4.2. All three multiparous women who died had a history of hypertensive and related disorders in previous pregnancies. Twelve out of the 14 women (86%) who died had one or more medical comorbidity; two women had pre-existing essential hypertension. The median BMI of women who died was 24 kg/m$^2$ (range 19 to 33 kg/m$^2$), six women had a BMI of ≥25 kg/m$^2$. Most women died during the postnatal period 1 to 42 days after delivery (Table 4.3). The gestational age at delivery ranged from 28 to 41 weeks with seven women giving birth at <37 completed weeks of gestation.

**Table 4.3: Timing of maternal deaths from hypertensive disorders of pregnancy, UK and Ireland, 2009–14**

| Time period of deaths in the pregnancy care pathway | N=14 Number (%) |
|---|---|
| Antenatal period or on day of delivery | 3 (21) |
| Postnatal 1 to 42 days after delivery | 10 (71) |
| Postnatal >42 days after delivery | 1 (7) |

# 4.4 Overview of care and lessons to be learned

## Antenatal care

A low risk woman had a normal blood pressure at booking but did not have her urine tested. She had a high risk test for Downs Syndrome and was referred to fetal medicine. The fetus was small (3rd centile), and extensive fetal investigations were performed but no maternal checks. At 21 weeks she was found unresponsive with slurred speech, severe hypertension and 4+ proteinuria. She never regained consciousness and died from her intracranial bleed.

A woman in her fourth pregnancy, with a history of HELLP syndrome in her second pregnancy requiring ICU admission, had a borderline raised blood pressure at 35 and 37 weeks. She had not taken aspirin. She was admitted at 39 weeks with a headache and vomiting and a systolic blood pressure of over 200mmHg. She was treated promptly with antihypertensives but she developed HELLP syndrome and an intracranial bleed 5 hours after delivery.

One of the main functions of antenatal care is to screen women for pre-eclampsia with a blood pressure and urine check at every visit, in whatever setting, including fetal medicine, particularly if there is an underlying concern about the pregnancy which may be linked to hypertensive disorders. However in five women no blood pressure was recorded at booking and in a number of instances the urine was not checked at each visit. In women with a past history of pre-eclampsia aspirin should be considered, and there should be greater surveillance when there is either borderline hypertension or proteinuria. New onset proteinuria always requires careful review and this is even more important in women with intermittent hypertension. All women should be educated about the features of pre-eclampsia and who to call if those features appear.

A woman in her first pregnancy had repeated severe hypertension on home monitoring but had a normal blood pressure in clinic with no proteinuria. In the third trimester she developed proteinuria and a urine sample was sent to the laboratory for a protein-creatinine ratio. The result was not followed up and the woman was returned to midwifery care. Two weeks later she was found dead at home with signs of having had an eclamptic fit. Death was certified as due to eclampsia.

This woman's care shows the importance of ensuring the results of investigations are followed-up. This requires a system to be in place to identify abnormal investigations and ensure they are acted upon. A recurrent raised blood pressure at home which normalises with health care professionals should lead to a careful assessment and consideration of an increased schedule of assessments.

**Blood pressure measurement and urinalysis for protein should be carried out at each antenatal visit to screen for pre eclampsia.**

**NICE Guideline CG62 Antenatal Care (National Institute for Health and Care Excellence 2008a)**

**Advise women at high risk of pre-eclampsia to take 75 mg of aspirin daily from 12 weeks until the birth of the baby. Women at high risk are those with any of the following:**

- **hypertensive disease during a previous pregnancy**
- **chronic kidney disease**
- **autoimmune disease such as systemic lupus erythematosis or antiphospholipid syndrome**
- **type 1 or type 2 diabetes**
- **chronic hypertension.**

**Advise women with more than one moderate risk factor for pre-eclampsia to take 75 mg of aspirin daily from 12 weeks until the birth of the baby. Factors indicating moderate risk are:**

- **first pregnancy**
- **age 40 years or older**
- **pregnancy interval of more than 10 years**
- **body mass index (BMI) of 35 kg/m$^2$ or more at first visit**
- **family history of pre-eclampsia**
- **multiple pregnancy.**

**NICE Guideline CG107 Hypertension in Pregnancy (National Institute for Health and Care Excellence 2010b).**

**Women with risk factors for pre-eclampsia and those who develop hypertension or proteinuria in pregnancy should have a plan for an appropriate schedule of checks. NICE recommends twice weekly visits for women who present with pregnancy induced hypertension prior to 32 weeks.**

**NICE Guideline CG107 Hypertension in Pregnancy (National Institute for Health and Care Excellence 2010b).**

**New onset hypertension or proteinuria needs careful assessment and referral to secondary care with an appropriate follow up plan.**

## Appropriate escalation

When women have been identified as having pre-eclampsia it is important to ensure senior review and that a plan is in place for ongoing care. However the plan must be adapted if circumstances change and a multidisciplinary approach to decision-making is required. The use of MEWS charts and close fluid balance with 1:1 care is appropriate for women with severe disease. The development of multisystem problems or other complications, such as haemorrhage, can be challenging and the advice of colleagues from tertiary centres or other specialities can be important in making the correct decisions.

> A woman was seen at the antenatal clinic at 30 weeks' gestation with 3+ proteinuria. Her blood pressure was not recorded. At 32 weeks she presented feeling unwell and with decreased fetal movements. She had 3+ proteinuria and BP 210/140. She was reviewed by a junior doctor and treated with nifedipine. She was transferred to the antenatal ward. One to one care was not provided. Her blood pressure was not recorded until three hours later. No MEWS chart was completed. She died from an intracranial haemorrhage.

There should be policies in place to support and encourage midwives to seek more senior obstetric review if they have concerns about the clinical management of women by junior doctors.

## Control of hypertension

A woman was admitted in labour with a blood pressure of 170/90. She did not have urinalysis done and her blood pressure was not rechecked until she had a neurological event three hours later. At this point her blood pressure was 180/100 with 4+ proteinuria. She was given magnesium sulphate and transferred to theatre for caesarean section under general anaesthesia. No antihypertensives were given prior to intubation nor was fentanyl given until after delivery of the baby. She did not recover from her general anaesthetic and was found to have had a large intracranial bleed.

An important message from previous reports has been the urgent need to control severe hypertension (National Institute for Health and Care Excellence 2010b). In five of the women who died there was a delay in responding to severe hypertension with subsequent intracranial haemorrhage. This is particularly important before the provision of general anaesthesia and whilst magnesium sulphate does reduce blood pressure, and should be given promptly, it should not be seen as an adequate anti-hypertensive agent for women with severe hypertension. Two women had general anaesthesia prior to adequate maternal stabilisation, which is likely to have caused a surge in blood pressure and may have contributed to the intracranial haemorrhage. Invasive monitoring should be considered early in deteriorating or at risk women, especially in morbidly obese women where non-invasive blood pressure readings can be erroneous and in women with severe preeclampsia requiring intravenous vasodilators.

**Keep blood pressure in all women to below 150/100, with urgent treatment to achieve this in women with severe hypertension.**

**NICE Guideline CG107 Hypertension in pregnancy (National Institute for Health and Care Excellence 2010b)**

**Whilst intubation may be required for airway control, maternal stabilisation and blood pressure control is vital prior to intubation in order to minimise maternal risk.**

The women who died were not always in a consultant-led setting at the time they became unwell.

A healthy low risk woman in her first pregnancy was delivered in a freestanding midwifery unit. Following delivery she developed a severe headache and moderate hypertension. Opiate analgesia was verbally prescribed. Over the following three hours she had severe hypertension but she was not transferred to the consultant unit until she had neurological signs. On arrival in the consultant unit her blood pressure was normal but she had lost airway control and CT scan performed shortly after her transfer showed a large intracranial bleed.

This woman's death emphasises the need for clear understanding of criteria for transfer from low risk to high risk birth settings.

**If women have a blood pressure over 140mmHg systolic or 90mmHg diastolic on two occasions 30 minutes apart in labour or immediately after birth they should be considered for transfer to a Consultant unit.**

**NICE Guideline CG190 Intrapartum Care (National Institute for Health and Care Excellence 2014a)**

## Investigating women with eclampsia or neurological signs

Five women were admitted with neurological symptoms and hypertension. In some of these women it was not possible for the reviewers to determine whether they had an intracranial bleed secondary to hypertension or if they were hypertensive secondary to an intracranial bleed (though all had proteinuria or abnormal liver function suggesting pre-eclampsia). A number of these women had severe recalcitrant hypertension that responded poorly to initial attempts at control.

> A woman in her late thirties woke her husband overnight calling out in her sleep followed by a seizure. Following this she was unable to move her left arm. She was admitted but despite appropriate care continued to have seizures. Over the next day on the intensive care unit she continued to have a left sided hemiparesis and intermittent headaches. CT scan performed 36 hours after she presented showed a right-sided intracranial haemorrhage. She died a week later from multi-organ failure.

Clinical examination of women with neurological symptoms and hypertension should include a full neurological examination including fundoscopy. There should be awareness of agitation and restlessness as a sign of an underlying problem. Neuroimaging should be considered early in women with atypical eclampsia. This includes those with multiple fits, those with only mildly increased blood pressure or proteinuria and those who do not become fully conscious within an hour of their fit (including those who are kept sedated/anaesthetised). Whilst most of these women will have normal neurological anatomy, in some, treatable intracranial pathology may be diagnosed.

Staff did not always recognise symptoms of cerebral irritation despite the woman showing signs of altered behaviour: agitation, drowsiness, restlessness, disorientation and confusion. Medical and midwifery staff need to be aware of the signs and symptoms and treatment of hypertensive disorders in pregnancy. Altered conscious level should be considered a red flag and a reason for this should be established by early senior input. All staff are responsible for ensuring the appropriate grade of medical staff reviews the woman. Staff should be aware that agitation and restlessness may be a sign of an underlying problem in women with hypertension.

**Neuroimaging should be performed urgently in any woman with hypertension or pre-eclampsia who has focal neurology or who has not recovered from a seizure.**

## Fluid Management

Although no women died directly due to fluid overload there were instances when fluid boluses were given inappropriately. The absence of deaths related to fluid related problems emphasises the benefits of close fluid balance and a general approach of fluid restriction in pre-eclampsia.

## Liver disease

Three women died in association with abnormal liver function. In one of these women the diagnosis of acute fatty liver of pregnancy was not considered despite a relatively modest rise in blood pressure and extremely abnormal liver function tests. Transfer to the regional liver unit was late. Whilst raised transaminases are an obvious sign of liver impairment, levels can appear to improve whilst the liver function continues to deteriorate (due to hepatic necrosis). Prothrombin time (INR) is a sensitive measure of liver function as the failing liver is unable to continue to synthesise coagulation factors, so it is important to continue to check the prothrombin time even when liver transaminases appear to be decreasing. A rising prothrombin time may be a marker of deteriorating liver function.

> A woman was admitted at 32 weeks' gestation with hypertension and proteinuria. Three days later she developed increased hypertension and abdominal pain with rising transaminases. She was delivered by caesarean section due to fetal concerns. Over the next 12 hours she developed liver and renal failure and was transferred to ICU. She died despite maximal care.

Pre-eclampsia is an unpredictable disease and can progress very rapidly. A multidisciplinary approach to care by senior clinicians is required. In the presence of organ failure intensive care and sometimes referral to tertiary care may be required. Women with severe disease often deteriorate in the postnatal period so close observation is still required in the days immediately after birth.

## 4.5 Conclusions

**Table 4.4: Classification of care received by women who died as a result of hypertensive disorders of pregnancy, UK and Ireland (2009–14)**

| | N=14 Number (%) |
|---|---|
| **Classification of care received** | |
| Good care | 1 (7) |
| Improvements to care which would have made no difference to outcome | 0 (0) |
| Improvements to care which may have made a difference to outcome | 13 (93) |

Deaths from the hypertensive disorders of pregnancy have significantly reduced. This is a sign of generally improving care for women. However the assessors felt that improvements in care may have made a difference to outcome for 93% of women who died (Table 4.4). Basic assessments are not always being performed routinely therefore the lessons to be learned continue to be relevant. Women should have a blood pressure and urine check at each health care contact in both primary and secondary care in pregnancy, as well as after delivery if she is unwell. There should be an increased schedule of care for women with risk factors and new hypertension or proteinuria requires secondary care review and appropriate follow up. There should be a prompt response to severe hypertension and senior involvement in the care of women with severe pre-eclampsia. Fluid restriction remains a corner stone of good clinical care in severe pre-eclampsia but women with severe disease need multidisciplinary team care with senior involvement and close monitoring.

# 5. Lessons for Early Pregnancy Care

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## 5.1 Key messages

Women of reproductive age presenting to the Emergency Department collapsed, in whom a pulmonary embolism is part of the differential diagnosis, should have a Focused Assessment with Sonography in Trauma (FAST) scan to exclude intra-abdominal bleeding from a ruptured ectopic pregnancy before thrombolysis is given. This should be done especially in the presence of anaemia.

Women of reproductive age presenting in a state of shock and collapse in the community, with no obvious cause, should be transferred to a hospital Emergency Department without delay for urgent assessment and treatment.

A diagnosis of ectopic pregnancy should be considered in any woman of reproductive age presenting to the emergency department with collapse, acute abdominal/pelvic pain or gastrointestinal symptoms, including diarrhoea, vomiting and dizziness, regardless of whether or not she is known to be pregnant. A bedside pregnancy test should be performed in these women.

A woman with a suspected ectopic pregnancy and deteriorating symptoms, should be seen by a senior gynaecologist as a matter of urgency.

The full range of clinical and investigatory services required to assess women with early pregnancy emergencies should be available throughout the whole week.

Providers and commissioners of care must ensure that there are safe pathways to transfer women from non-NHS facilities offering termination of pregnancy to local NHS services when complications arise.

## 5.2 Background

Early pregnancy complications are common and account for the largest proportion of emergency work performed in gynaecology departments throughout the UK. This group of conditions includes all types of miscarriage, ectopic pregnancies, trophoblastic disease and complications arising from treatments for these conditions. Estimates of the rate of miscarriage in clinically recognised pregnancies up to 20 weeks' gestation range from 8 to 20% (Wilcox, Weinberg et al. 1988, Wang, Chen et al. 2003).

Ectopic pregnancies have an incidence of approximately 11 per 1,000 pregnancies (Lewis, Cantwell et al. 2011), which means that each year in the UK nearly 12,000 women have ectopic pregnancies diagnosed. Major risk factors for ectopic pregnancy include a previous ectopic pregnancy and tubal damage from either surgery or infection. Other risk factors include intrauterine contraceptive devices, smoking, infertility, infertility treatment and younger or older maternal age.

Therefore, both miscarriage and ectopic pregnancies are common and dealt with every day of the week in UK hospitals. Nevertheless, women still experience severe morbidity and some will die as a result of these conditions or their complications.

## 5.3 Summary of the key findings 2009–2014

### The women who died

In 2009–2014, 191 women died at less than 24 weeks' gestation in the UK and Ireland whilst still pregnant or after their pregnancy ended at less than 24 weeks (Table 5.1). Twelve of these women died from early pregnancy-associated causes. Nine of the 12 women died as a direct result of an ectopic pregnancy and three women died from complications following termination or attempted termination of pregnancy including one self-attempted abortion. The care of other women who died in early pregnancy or following miscarriage is discussed in other chapters in this and previous reports. A woman who died due to HELLP syndrome complicating a molar pregnancy is discussed in the pre-eclampsia chapter in this report. A woman who had an ischaemic cardiac death following termination in a non-NHS setting is included in the cardiac chapter. Two women died following pulmonary embolism complicating the management of their second trimester miscarriage and were discussed in the thrombosis chapter of the 2015 report (Knight, Tuffnell et al. 2015). Three women died due to sepsis associated with miscarriage and were discussed in the sepsis chapter of the 2014 report (Knight, Kenyon et al. 2014). Of note, there were no maternal deaths associated with ovarian hyperstimulation syndrome reported to the Enquiry between 2009–14.

**Table 5.1: Causes of death amongst women who died at less than 24 weeks' gestation whilst still pregnant or after their pregnancy ended at less than 24 weeks (2009–14), UK and Ireland**

| Cause of death | Number of women | Percentage of women |
|---|---|---|
| **Amniotic Fluid Embolism** | 1 | 0.5 |
| **Anaesthetic deaths** | 1 | 0.5 |
| **Pre-eclampsia and eclampsia** | 1 | 0.5 |
| **Sepsis** | 19 | 10.0 |
| **Thrombosis and thromboembolism** | 22 | 11.5 |
| **Cardiac disease** | 24 | 12.6 |
| **Mental health problems** | 24 | 12.6 |
| *Early pregnancy-related causes* | *12* | *6.3* |
| *Ectopic pregnancy* | *9* | *4.8* |
| *Legal termination of pregnancy* | *2* | *1.0* |
| *Self-attempted abortion* | *1* | *0.5* |
| **Haemorrhage** | 2 | 1.1 |
| **Neurology** | 22 | 11.5 |
| **Indirect deaths** | 29 | 15.1 |
| **Unascertained** | 1 | 0.5 |
| **Coincidental deaths** | 33 | 17.3 |
| **Total** | **191** | **100** |

The characteristics of the 12 women who died from early-pregnancy related causes are shown in Table 5.2. Six of the 12 women had social problems including drug use and/or social isolation that may have contributed to their death. Four women were from abroad, one of whom spoke no English. Two other women from overseas did not appear to know that they could seek the help of the NHS. Half of the women died whilst still pregnant and half after the end of pregnancy (Table 5.3).

**Table 5.2: The socio-demographic characteristics of women who died from complications during early pregnancy, UK and Ireland, 2009–14**

| Characteristics | N=12 Number (%) |
|---|---|
| **Age (in years)** | Median=33, Range 26 to 43 |
| *<35* | *7 (58)* |
| *≥ 35* | *5 (42)* |
| **Parity** | |
| *Nulliparous* | *0* |
| *Multiparous* | *8 (67)* |
| *Missing* | *4 (33)* |
| **UK/Irish citizen** | |
| *Yes* | *7 (58)* |
| *No* | *4 (33)* |
| *Missing* | *1 (8)* |
| **Ethnicity** | |
| *White* | *4 (33)* |
| *Black or other minority ethnic group* | *6 (50)* |
| *Missing* | *2 (17)* |
| **Woman's region of birth** | |
| *United Kingdom/ Ireland* | *3 (25)* |
| *Outside UK* | *4 (33)* |
| *Missing* | *5 (42)* |

**Table 5.3: Timing of maternal deaths due to complications during early pregnancy, UK and Ireland, 2009–14**

| Time period of deaths in the pregnancy care pathway | N=12 Number (%) |
|---|---|
| Antenatal period/ still pregnant | 6 (50) |
| On the day of termination/ pregnancy loss or within 42 days | 5 (42) |
| Postnatal 43–90 days | 1 (8) |

## 5.4 Overview of care and lessons to be learned

### Ectopic Pregnancy

The majority of the women died due to ectopic pregnancy, and this is the main focus of the chapter. The reported prevalence of ectopic pregnancy is 6–16% among women who attend an Emergency Department with first trimester bleeding or pain or both (Murray, Baakdah et al. 2005). In 98% of these women, the pregnancy will be sited in the fallopian tube with the remainder distributed variously in the ovary, cervix or structures within the abdomen (Bouyer, Coste et al. 2002).

#### The Collapsed Woman

Severe bleeding from an ectopic pregnancy, especially in women who are haemodynamically unstable, requires immediate surgical intervention to stop the haemorrhage. No other treatment will suffice and time spent attempting resuscitation rather than surgical intervention to 'turn off the tap' increases the risk of cardiac arrest and death.

### *Ectopic pregnancy versus pulmonary embolism in maternal collapse*

Paramedics were called to a woman who was found collapsed at her home. She was cold, clammy, pale and shocked with no cardiac output. She was given CPR and transferred to the Emergency Department after two hours, with a presumed diagnosis of pulmonary embolism. Blood tests in the Emergency Department found that she was severely acidotic and had a haemoglobin of 6.9g/dl. She was thrombolysed for the presumed diagnosis of pulmonary embolism. A computerized tomography (CT scan) ruled out a pulmonary embolism but found a large amount of blood in the abdomen. At subsequent surgery a ruptured bleeding ectopic pregnancy was discovered. She died the following day from multi-organ failure.

Eight out of nine women in this six year period who died as a result of ectopic pregnancy presented in a state of haemodynamic collapse. If lives are to be saved it is critical to get the diagnosis right. Pulmonary embolism (PE) was considered as the most likely diagnosis in four women despite all four having severe anaemia. Three of the women were thrombolysed and in the fourth it was considered. There was evidence that the clinicians were affected by a fixation error in all of these cases. Thrombolysis quite clearly was only going to worsen the situation and make resuscitative efforts with fluid or blood useless. A pregnancy test carried out on each of these women might have alerted the clinical team to the possibility of ectopic pregnancy as the cause of collapse.

In 2009–2013 (Knight, Tuffnell et al. 2015) 12 of the women who died from PE died in the first trimester before antenatal booking. Presentation was mixed varying from collapse to chest pain, dyspnoea and/or leg pain. A positive computerised tomography pulmonary artery (CTPA) or ventilation / perfusion (V/Q) scan will confirm the diagnosis of PE and these women can then be anti-coagulated and if necessary be given thrombolytic therapy. Shock or collapse is an unusual presentation of PE with an estimate of around 8% outside of pregnancy (Stein, Beemath et al. 2007).

Maternal deaths are often used as a reference point for generating a differential diagnosis of maternal collapse. Although the 2009–14 data now indicate that thrombosis is almost twice as common as haemorrhage as a cause of maternal mortality, including the first six weeks after pregnancy, the balance of risk may not be the same in early pregnancy (Nelson-Piercy *et al.* 2015). Given that ectopic pregnancy is extremely rare outside of the first trimester in instances of collapse, ectopic pregnancy must be considered high on the list of differentials when women collapse in early pregnancy, particularly when found to be anaemic. When PE is suspected definitive testing with either a CTPA or a bedside echocardiogram, in addition to a pregnancy test, should be obtained prior to a decision about thrombolysis. Another diagnostic aid is the Focused Assessment with Sonography in Trauma (FAST) scan, which can be performed at the bedside with relatively simple ultrasound equipment. A FAST scan is very useful in identifying intraperitoneal haemorrhage in hypotensive patients (Wherrett, Boulanger et al. 1996). Most Emergency Departments have the equipment and expertise to perform these examinations and it is important that they are utilised when working out the diagnosis in a collapsed, shocked woman, especially where pregnancy is known or suspected.

**Women of reproductive age presenting to the Emergency Department collapsed, in whom a pulmonary embolism is suspected, should have a Focused Assessment with Sonography in Trauma (FAST) scan to exclude intra-abdominal bleeding from a ruptured ectopic pregnancy especially in the presence of anaemia.**

## Making the Clinical Diagnosis

It can be difficult to make the diagnosis of an ectopic pregnancy, particularly in the absence of collapse. The symptoms in the early stages of the disease process are often vague and the physical signs can be subtle. One population-based study found that 18% of ectopic pregnancies presented with rupture (Job-Spira, Fernandez et al. 1999). As with all diagnoses, the condition has to be considered in the differential diagnosis in order that appropriate investigations and management can be pursued. In five of the nine women who died from ectopic pregnancy, the diagnosis was never considered.

Ectopic pregnancies usually cause noticeable symptoms from 6 to 8 weeks after the last menstrual period. While this is not an absolute rule and the symptoms can have their onset outside of this gestational period, it is important to take a good menstrual history in women of reproductive age who present with vague abdominal or pelvic symptoms. Where it is not possible to take a direct history due to the clinical condition of the women, a bedside pregnancy test must be carried out to exclude pregnancy; this may necessitate catheterisation to obtain a urine sample. The most commonly reported symptoms of ectopic pregnancy are abdominal and or pelvic pain, amenorrhoea and vaginal bleeding, but less commonly the presenting symptoms are gastrointestinal, such as diarrhoea and vomiting, urinary, rectal pressure from blood in the pouch of Douglas or shoulder tip pain. In approximately 7% of cases the woman may be completely asymptomatic (National Institute for Health and Care Excellence 2012). Atypical symptoms should not therefore distract from the possibility that an ectopic pregnancy may be the cause of a woman's illness. Where there is difficulty or uncertainty in arriving at a definitive diagnosis, it is important for the woman to be personally reviewed by a senior doctor.

A woman in her twenties who was a known drug user presented to her local Emergency Department with seven weeks of amenorrhoea and mild lower abdominal pains. She did not have any vaginal bleeding. After the initial assessment, the diagnosis was unclear; she was instructed to take analgesia for the pain and sent home with an appointment for an ultrasound scan of her pelvis three days later. She returned to the Emergency Department after 24 hours with increasing abdominal pain and diarrhoea. She was given morphine for her pain and rehydrated with intravenous fluids. The junior doctor carried out a vaginal examination and found the woman to be "very tender". She was discussed with the gynaecology registrar who, without seeing the woman, advised that an ectopic was unlikely due to the diffuse nature of her pain and that it was more likely to be gastroenteritis. She was again sent home and advised to keep the existing ultrasound scan appointment. The next day, 48 hours after her initial presentation, she collapsed at home and had a cardiac arrest. She was resuscitated by the paramedics and transferred to the Emergency Department two and a half hours after her arrest. She was taken to theatre for a laparotomy and management of her ruptured ectopic. In theatre she had a further cardiac arrest and died.

This woman's death illustrates several points. She initially presented with vague symptoms, but knew she was pregnant. There was still the possibility of an intra-uterine pregnancy, hence the request for an ultrasound scan of her pelvis. When she returned to the Emergency Department the next day the symptoms and physical signs were now strongly suggestive of an ectopic pregnancy despite the telephone opinion of the gynaecology registrar. The return visit to the Emergency Department, need for opiates and IV fluids were all 'red flag' signs that should have triggered a further assessment and an urgent ultrasound scan. Furthermore, following her collapse, there was a substantial delay from identifying the problem in the community and transporting her to hospital for definitive surgery, the only effective intervention to stop the bleeding and save her life.

**A woman with a suspected ectopic pregnancy and deteriorating symptoms should be urgently seen by a senior gynaecologist.**

**Repeated presentation with abdominal and/or pelvic pain, or pain requiring opiates in a woman know to be pregnant should be considered 'red flag' signs.**

## Investigations for ectopic pregnancy

### *Urinary pregnancy testing and serum hCG measurements*

In most instances, symptoms and signs alone are not enough to make the diagnosis of an ectopic pregnancy and further investigations are required to narrow down the differential. In five of the nine women who died from ectopic pregnancy the diagnosis was not considered. Instead alternative diagnoses, which are less common in women of reproductive age, were felt to be more likely. A urinary pregnancy test is a rapid and effective way of confirming if a woman is pregnant. When there is diagnostic uncertainty a pregnancy test should be performed. It will alert clinicians to the possibility of an ectopic pregnancy at the very least and may change the approach to the management of these women.

**A diagnosis of ectopic pregnancy should be considered in any woman of reproductive age presenting to the emergency department with collapse, acute abdominal/pelvic pain or gastrointestinal symptoms, particularly diarrhoea, vomiting and dizziness, regardless of whether or not she is known to be pregnant. A bedside pregnancy test should always be performed in these women, if necessary catheterising to obtain urine.**

In the less acute situation a quantitative serum hCG can guide the clinician in making the diagnosis.

Normally the serum hCG rises by at least 60% in 48 hours and doubles by 72 hours. Women with a decline in serum hCG of <50% or a rise of <65% must have an assessment including a transvaginal ultrasound, in an early pregnancy service, within 24 hours. However, thresholds or threshold rises and falls in the level of serum hCG cannot be relied upon to diagnose an ectopic pregnancy and it remains a controversial area.

### *Ultrasound Scanning*

A transvaginal ultrasound scan is the imaging modality of choice and should be carried out by a clinician with expertise in gynaecological scanning. While both transabdominal and transvaginal ultrasound scans have high specificities, transvaginal ultrasound has higher sensitivities for diagnosing an ectopic and therefore is the imaging modality of choice (National Institute for Health and Care Excellence 2012). Finding an intrauterine pregnancy, a gestational sac with a yolk sac or embryo, on transvaginal ultrasound virtually excludes the diagnosis of an ectopic pregnancy. Women who opt for a transabdominal scan must be told of its limitations in diagnosing ectopic pregnancies.

**Offer women who attend an early pregnancy assessment service (or out-of hours gynaecology service if the early pregnancy assessment service is not available) a transvaginal ultrasound scan to identify the location of the pregnancy and whether there is a fetal pole and heartbeat.**

**If a transvaginal ultrasound scan is unacceptable to the woman, offer a transabdominal ultrasound scan and explain the limitations of this method of scanning.**

**NICE Guideline CG154 Ectopic pregnancy (National Institute for Health and Care Excellence 2012)**

It is important to remember that quantitative beta hCG and transvaginal ultrasound assist in making the diagnosis of an ectopic pregnancy only after a full clinical assessment has been performed. All information needs to be weighed in the balance when making the diagnosis. Where there is still a diagnostic dilemma on how to proceed, it is important to involve a senior clinician in the decision making process, preferably with their direct clinical review of the woman concerned.

Ultimately, it may be necessary to resort to performing a laparoscopy as a diagnostic (and if needed therapeutic) procedure when there is real doubt about the diagnosis.

## Service Organisation

Many early pregnancy problems are now managed more conservatively than in the past. This necessitates an increase in the follow up of these women to ensure that if complications develop they are detected early and patient safety is maintained. Consequently Early Pregnancy Assessment Services (EPAS) should run daily with access to the full range of haematological, biochemical and imaging services. Once the investigations are performed a senior gynaecologist must review their results and the clinical presentation.

**The full range of clinical and investigatory services required to assess women with early pregnancy emergencies should be available throughout the whole week.**

Eight of the nine women who died from ectopic pregnancy as well as one other woman who died collapsed in the community and were attended to by the paramedic services. In several instances the time spent by paramedics in the community attempting resuscitation, was considered by the assessors to be too long to be of any practical benefit to these women. For resuscitation and treatment to be life-saving in collapsed women with ruptured ectopic pregnancies, the bleeding must be stopped and the only way to do this is surgically. Therefore it is important that

paramedic services review the management of the collapsed / shocked woman in the community. A 'scoop and run' policy is the best approach for shocked women of reproductive age, so that in those with an ectopic pregnancy the bleeding can be stopped as rapidly as possible.

**Women of reproductive age who present in the community in a state of shock and/or collapse with no obvious cause should be transferred to a hospital Emergency Department without delay for urgent assessment and treatment.**

**Paramedic services should review protocols for the management in the community of the collapsed/ shocked woman of reproductive age.**

### Termination of Pregnancy

Two women died following legal termination of pregnancy. Both terminations were initiated in a non-NHS setting, which is where the vast majority of terminations take place in the UK. In one woman staff were not made aware of a history of multiple caesarean sections and a repeatedly unsuccessful medical approach for a second trimester termination was pursued. The use of powerful uterotonic agents to stimulate a medical termination of pregnancy in women with a scarred uterus is hazardous. The risk of uterine rupture in women who have had a prior caesarean section is 28 per 10,000 (0.28%; 95%CI 0.08–1.00%) compared to 4 per 10,000 (0.04%; 95%CI 0.01–0.20%) in women with an intact uterus (Goyal 2009). These women must not be left to inexperienced doctors to manage alone without direct senior review and supervision. If the medical termination is not successful a thorough assessment should be made after each course of treatment. Women must be made aware of the consequences of a ruptured uterus, including the implications for their future fertility, as well as the risk of death. Dilatation and evacuation is an alternative method of undertaking a termination with low risks and should be considered if there is a prolonged failure to achieve medical termination in the second trimester. It is also important that pathways are in place to allow for urgent transfer and overnight admission if it is needed for ongoing care after any termination procedure.

**Providers and commissioners of care must ensure that there are safe pathways of care to transfer women from non-NHS facilities offering termination of pregnancy to local NHS services when complications arise.**

## 5.5 Conclusions

The assessors concluded that five of the 12 women (42%) considered in this chapter received good care (Table 5.4). However, for the remaining seven women (58%) they identified improvements in care which may have made a difference to the outcome. Whilst very few women died from early pregnancy complications in the period 2009–2014, they largely died as a result of common conditions that are highly amenable to medical or surgical treatments. The presenting symptoms and physical signs can be confusing especially when a woman presents collapsed and in a state of clinical shock. In women of reproductive age simple bedside tests, a urinary pregnancy test and a FAST scan, are valuable aids in making the correct diagnosis. They will also guard against giving potentially dangerous treatments, such as thrombolysis, to women who have intra-abdominal bleeding from a ruptured ectopic pregnancy. Women of reproductive age who are found collapsed in the community from an unknown cause need rapid transfer to hospital. Resuscitation by paramedics in the community will not stop a woman bleeding to death from a ruptured ectopic pregnancy. Definitive surgical intervention is the only way to arrest the bleeding and avoid death in these situations.

**Table 5.4: Table 5.4: Classification of care received by women who died as a result of early pregnancy complications, UK and Ireland (2009–14)**

| | N=12 Number (%) |
|---|---|
| **Classification of care received** | |
| Good care | 5 (42) |
| Improvements to care which would have made no difference to outcome | 0 |
| Improvements to care which may have made a difference to outcome | 7 (58) |

# 6. Messages for Critical Care

Rupert Gauntlett on behalf of the MBRRACE-UK critical care chapter-writing group

Chapter writing group members: David Churchill, Rupert Gauntlett, Malcolm Griffiths, Linda Ibbetson, Vijay Jagannathan, Marian Knight, Annette Lobo, Laura Magee, Sue Orchard, Roshni Patel, Frank Schroeder, Judy Shakespeare, Mike Weiss, Sarah Wheatly, Adrian Wills.

## 6.1 Key messages

Early recognition of critical illness, prompt involvement of senior clinical staff and authentic multi-disciplinary team working remain the key factors in providing high quality care to sick pregnant and postpartum women.

Reduced or altered conscious level is not an early warning sign; it is a red flag which indicates established illness.

Critical care support can be initiated in a variety of settings. Critical care outreach nurses can work in partnership with midwives to provide care before transfer to the critical care unit. Delay caused by bed pressures in a critical care unit is not a reason to postpone critical care.

Key investigations must not be delayed because of pregnancy.

Inter-hospital referral of a sick pregnant or postpartum woman should be directed by the principle 'one transfer to definitive care'. It is unlikely to be appropriate to move a sick antenatal woman to a facility without on-site obstetric cover.

Severe respiratory failure in pregnant and postpartum women should trigger early referral to an ECMO centre.

Obstetricians and obstetric anaesthetists must remain closely involved in the clinical management of women with obstetric specific conditions such as pre-eclampsia. These conditions are rarely seen on the general critical care unit but are common problems on the labour ward.

Pregnancy can make the differential diagnoses of critical illness more complex. There must be a balance between appropriate clinical suspicion and a conclusive diagnosis; not all hypertension is pre-eclampsia and shortness of breath is not always a pulmonary embolism.

When critical care staff have any involvement in a maternal death, it is imperative that they are included in case reviews, root cause analysis and serious incident investigations.

## 6.2 Background

When a pregnant or postpartum woman dies in hospital, critical care specialists are frequently involved either as part of a resuscitation team or in providing multi-organ support in the final days of life. Maternal death remains a rare event and the purpose of this chapter is to bring together common lessons to improve maternal critical care.

The last chapter concerning critical care in a confidential enquiry report was published in March 2011 and covered the deaths for the triennium 2006-2008. Since then the single most significant issue in maternal critical care was the H1N1 influenza pandemic of 2009–10. In common with previous outbreaks of influenza, pregnant women were disproportionately represented and a significant number of women were treated with extra-corporeal membrane oxygenation (ECMO). The maternal and fetal outcomes for this cohort have been reported elsewhere (Yates, Pierce et al. 2010, Pierce, Kurinczuk et al. 2011).

Critical care is one of the few areas of maternal morbidity where there is excellent data on pregnant and postpartum women who survive their illness. The Case Mix Programme database run by The Intensive Care National Audit and Research centre (ICNARC) provides detailed information from critical care units in England, Wales and Northern Ireland. The Scottish Intensive Care Society Audit Group (SICSAG) collate similar information in Scotland.

In December 2013 ICNARC and the OAA published data on 6793 obstetric admissions to critical care over a four-year period ending in December 2012 (Intensive Care National Audit and Research Centre 2013). The report confirmed the pattern of admission seen in many smaller epidemiological studies of obstetric critical care. The majority of women are admitted postpartum following major obstetric haemorrhage. A much smaller number of women are admitted during their pregnancy, the reasons for admission in this group are more heterogeneous but pneumonia predominates. The outcome data following admission to intensive care provide reassurance that the majority of women will survive critical illness during and after pregnancy (Table 6.1).

**Table 6.1: Outcomes for female admissions to critical care aged 16–50 years reported as 'currently pregnant' or 'recently pregnant' on admission to the critical care unit**

| Female admissions aged 16–50 years | | Currently pregnant | Recently pregnant |
|---|---|---|---|
| **Number of admissions** | | 1,188 | 5,605 |
| **Critical care unit mortality, deaths (%) [95% CI]** | | 20 (1.7) [1.1, 2.6] | 73 (1.3) [1.0, 1.6] |
| **Acute hospital mortality*, deaths (%) [95% CI]** | | 30 (2.7) [1.9, 3.8] | 97 (1.8) [1.5, 2.2] |
| **Location of death, n (% of deaths)** | Original critical care unit admission | 19 (63.3) | 67 (69.1) |
| | Subsequent critical care unit admission† | 7 (23.3) | 22 (22.7) |
| | Acute hospital – following discharge from critical care‡ | 4 (13.3) | 8 (8.2) |

* Excluding readmissions to the critical care unit within the same acute hospital stay.

† Following transfer to another critical care unit or readmission to the original critical care unit.

‡ May include some deaths in other critical care units not participating in the CMP.

Reproduced with permission from: Female admissions (aged 16–50 years) to adult, general critical care units in England, Wales and Northern Ireland reported as 'currently pregnant' or 'recently pregnant'. 1 January 2009 to 31 December 2012. Report from the Intensive Care National Audit & Research Centre.

Doctors who have become intensive care specialists through training in anaesthesia will have experience of working on the labour ward in the role of a junior obstetric anaesthetist. Critical care in the UK is now an independent speciality. The future medical workforce is predicted to include a larger number of specialists who have trained exclusively in intensive care medicine or whose dual speciality is not anaesthesia (Centre for Workforce Intelligence 2015). These doctors may have no post-graduate experience of working on the labour ward and therefore caring for pregnant and postpartum women.

## 6.3 Summary of the key findings 2009–14

The care of 144 women who received critical care prior to their death between 2009 and 2014 was assessed for the purposes of this chapter. The characteristics of the women and the causes of their deaths are summarised in tables 6.2, 6.3 and 6.4. During this period, which included the H1N1 influenza pandemic, the largest group of women (n=45) died from sepsis, of whom 22 died from influenza, 10 died from pregnancy-related infections and 13 died from pneumonia (not influenza-related) and other infections.

**Table 6.2: The characteristics of women whose critical care was assessed, UK and Ireland, 2009–14**

| Characteristics | Total (n=144) Frequency (%) |
|---|---|
| **Age** | |
| *<20* | *5 (3)* |
| *20–24* | *16 (11)* |
| *25–29* | *40 (28)* |
| *30–34* | *36 (25)* |
| *35–39* | *34 (24)* |
| *≥ 40* | *13 (9)* |
| **Parity** | |
| *0* | *60 (42)* |
| *1 to 2* | *57 (40)* |
| *≥3* | *25 (17)* |
| *Missing* | *2 (1)* |
| **Ethnicity** | |
| *White European* | *100 (69)* |
| *Asian* | *28 (19)* |
| *African/Caribbean* | *9 (6)* |
| *Others* | *6 (4)* |
| *Missing* | *1 (1)* |
| **Socioeconomic status (Index of Multiple Deprivation)** | |
| *First quintile (Least deprived)* | *16 (11)* |
| *Second quintile* | *15 (10)* |
| *Third quintile* | *26 (18)* |
| *Fourth quintile* | *35 (24)* |
| *Fifth quintile (Most deprived)* | *41 (28)* |
| *Missing* | *11 (8)* |
| **Body mass index (kg/m2)** | |
| *<18.5* | *5 (3)* |
| *18.5–24* | *52 (36)* |
| *25–29* | *40 (28)* |
| *≥ 30* | *37 (26)* |
| *Missing* | *10 (7)* |
| **Any pre-existing medical problem (excluding obesity)** | |
| *Yes* | *108 (75)* |
| *No* | *34 (24)* |
| *Missing* | *2 (1)* |

**Table 6.3: Timing of death of women whose critical care was assessed, UK and Ireland, 2009–14**

| Time period of deaths in the pregnancy care pathway | Total (n=144) Frequency (%) |
|---|---|
| Antenatal period/ still pregnant | 9 (6) |
| Postnatal on day of delivery | 14 (10) |
| Postnatal 1 to 42 days after delivery | 95 (66) |
| Postnatal 43–364 days | 26 (18) |

**Table 6.4: Causes of death of women whose critical care was assessed, UK and Ireland, 2009–14**

| Cause of death | Total (n=144) Frequency (%) |
|---|---|
| Amniotic fluid embolism | 5 (3) |
| Early pregnancy death | 3 (2) |
| Pre-eclampsia and eclampsia | 8 (6) |
| Haemorrhage | 6 (4) |
| Neurological | 16 (11) |
| Thrombosis and thromboembolism | 6 (4) |
| Sepsis | 45 (31) |
| Deaths from psychiatric cause | 1 (1) |
| Cardiac disease | 23 (16) |
| Other indirect deaths | 19 (13) |
| Anaesthetic death | 1 (1) |
| Coincidental | 10 (7) |
| Unascertained | 1 (1) |

## 6.4 Overview of care and lessons to be learned

On review it is clear that many of the women who died received excellent critical care and died from an overwhelming disease process despite best treatment.

A woman with a history of depression, intravenous drug abuse and hepatitis C was admitted to hospital following an overdose in the third trimester. She became unconscious with hypoxic respiratory failure. An emergency caesarean delivery was performed and she was managed on the intensive care unit with appropriate treatments and escalating organ support. An echocardiograph demonstrated tricuspid endocarditis but despite maximal therapy she died of overwhelming sepsis on day six of her admission.

A woman collapsed in cardiac arrest immediately after giving birth to her second child. There had been no significant problems in her antenatal period, labour or vaginal delivery. Resuscitation was initiated rapidly and performed to a high standard by a team including two consultants. Return of spontaneous circulation was achieved within 10 minutes and followed by rapid initiation of invasive monitoring and organ support. A diagnostic CT scan was performed just over one hour from the initial collapse and revealed a massive subarachnoid haemorrhage. Brain stem death was confirmed the following day.

There is increasing recognition of the lessons that can be learned from good practice.

**When high quality care has been provided, even if a woman dies, it is important to learn from the things that went well as well as from those elements that might have been improved.**

**(Hollnagel, Wears et al. 2015)**

The need to repeat previously identified priorities is a salutary feature of confidential enquiry reports. In 2011 clinicians were encouraged to go 'back to basics' to ensure that the fundamental elements of good care were consistently provided (Lewis, Cantwell et al. 2011). For critical care this means timely identification of the sick pregnant or postpartum woman and rapid involvement of senior staff and this is still an essential improvement to care identified from the cases reviewed here.

## Early recognition of critical illness and prompt involvement of senior clinical staff

In 2007 a key recommendation of the Confidential Enquiry into Maternal Deaths (Lewis 2007) was to adopt a national modified early warning chart into obstetric practice. A wide variety of early warning systems are now in use but a national evidence-based standard has not emerged.

Early warning systems rely on a phase of partial decompensation in physiology as a window of opportunity to intervene and prevent deterioration. We are still learning how well this model works in the obstetric population who usually have the physiological reserve to compensate for problems until a point of abrupt deterioration.

A key feature of early warning systems is the link between recording abnormal observations and action. In the case of sick pregnant and postpartum women, it is vital that response algorithms alert senior staff at an early stage.

The early identification of sepsis is currently a high priority in all healthcare settings and remains a particular focus of concern in maternity. Red flags for sepsis have been defined (Box 6.1) and a maternity sepsis toolkit has recently been developed alongside new NICE guidance (National Institute for Health and Care Excellence 2016b).

**Box 6.1: Maternal sepsis red flags**

**Any one of the following features represents a 'red flag' in a sick pregnant or postpartum woman with suspected infection**

- Responds only to voice or pain/ unresponsive
- Systolic B.P ≤ 90 mmHg (or drop >40 from normal)
- Heart rate > 130 per minute
- Respiratory rate ≥ 25 per minute
- Needs oxygen to keep $SpO_2$ ≥92%
- Non-blanching rash, mottled/ ashen/ cyanotic
- Not passed urine in last 18 hours
- Urine output less than 0.5 ml/kg/hr
- Lactate ≥2 mmol/l

**UK Sepsis Trust Inpatient Maternal Sepsis Tool (UK Sepsis Trust 2016)**

(Note that additional tools cover Out of hours/telephone triage, community midwifery, pre-hospital/ambulance services, Emergency Departments and general practice.)

**Take into account that women who are pregnant, have given birth or had a termination of pregnancy or miscarriage in the past 6 weeks are in a high risk group for sepsis. In particular, women who:**

- **have impaired immune systems because of illness or drugs**
- **have gestational diabetes or diabetes or other comorbidities**
- **needed invasive procedures (for example, caesarean section, forceps delivery, removal of retained products of conception)**
- **had prolonged rupture of membranes**
- **have or have been in close contact with people with group A streptococcal infection, for example, scarlet fever**
- **have continued vaginal bleeding or an offensive vaginal discharge.**

**NICE guideline NG51 Sepsis: recognition, diagnosis and early management (National Institute for Health and Care Excellence 2016b)**

A woman with a background history of type 2 diabetes mellitus, obesity and hepatitis C in her first pregnancy was admitted in the third trimester with a three week history of worsening shortness of breath and a dry cough. She was admitted via the emergency department on a Friday evening and assessed by the on-call obstetric team. The differential diagnosis was infection or pulmonary embolism and appropriate treatment was initiated for both of these possibilities, however there was no review by a consultant obstetrician and no referral for a medical opinion.

Over the next two days the woman remained intermittently breathless and low oxygen saturations were documented. On Monday she was transferred to the radiology department for a V/Q scan. She was not accompanied by medical staff and a positioning wedge was not used. Around 20 minutes into the scan she had a pulseless electrical activity cardiac arrest. Full resuscitation, including a perimortem caesarean section, was performed but return of spontaneous circulation was not achieved for about 25 minutes.

The woman was transferred to intensive care where she remained for 11 days. She did not regain consciousness and EEG and CT scan findings suggested a severe hypoxic-ischaemic brain injury from which she died; her baby survived.

The first consultant review of this woman did not occur until 60 hours after admission. The possibility of a cardiac cause for breathlessness was not included on the initial list of differential diagnoses. Early consultant involvement and referral for medical review may have produced a more comprehensive list of possible diagnoses. Simple cardiac investigations, such as an ECG, were not performed. It was also noted that the early warning chart was not used correctly. Oxygen saturations were recorded in the area of the chart that should have been used to record respiratory rate.

**Any woman presenting with severe shortness of breath should have the same baseline medical investigations that would be expected with the same presentation outside of pregnancy.**

Modified obstetric early warning systems set up in response to the 2007 key recommendation should be reviewed to ensure that they remain fit for purpose. The review should consider how developments in modern information technology, near patient testing and sepsis red flags should influence the development of obstetric early warning systems.

## Authentic multidisciplinary team working

A woman with a known thrombophilic condition was correctly assessed antenatally as high-risk and received regular input from senior staff across multiple disciplines throughout her pregnancy until she was admitted for induction. A plan was in place for both antenatal and postnatal thromboprophylaxis. Once she was admitted for induction there was very little senior input. Her induction was delayed and she did not receive thromboprophylaxis during this time. Postnatally the plan made for thromboprophylaxis was not followed. She was readmitted three days after discharge with a venous sinus thrombosis. On ITU, there was no evidence of senior review from any specialty over the following four days before she died.

No single specialist has all the skills to care for a critically ill pregnant or postpartum woman. At the very least an intensive care doctor will need to draw on the skills and knowledge of an obstetrician and usually the clinical team will be much larger including obstetric anaesthetists, midwives, nurses, specialist physicians and surgeons as well as other allied medical professionals.

The importance of team working has been championed by the Confidential Enquiry reports and has been identified as a key factor by subsequent enquiries into serious failings in maternity services (Kirkup 2015). Strategies to improve team working, skills drills and simulation have been repeatedly promoted. Inadequacy of team working is frequently identified in case reviews. GMC guidance is clear; doctors must work 'collaboratively with colleagues, respecting their skills and contributions' and must be aware of how their own behaviour influences others within the team (General Medical Council 2014). Too often internal hospital reports into maternal deaths demonstrate close scrutiny of clinical decisions but little attention to clinical behaviours. Team working should be seen as an important clinical skill and an inability to collaborate well with colleagues is as serious as any other clinical concern.

A multi-disciplinary approach does not negate the requirement to have a team leader. This role is normally taken by the obstetrician for women on delivery suite and the critical care consultant for women admitted to intensive care. Team members must be collaborative, flexible and prepared to accept that their views may not always predominate. The importance of being able to remain constructive in disagreement and accepting of polite criticism cannot be overstated.

**You must work collaboratively with colleagues, respecting their skills and contributions.**

**You must be aware of how your behaviour may influence others within and outside the team.**

**(General Medical Council 2014)**

**Those who work together should train together. Multi-professional learning should be a core part of all training for doctors, nurses and midwives, so that they understand and respect each other's skills and perspectives.**

**Multi-professional training should be a standard part of continuous professional development, both in routine situations and in emergencies.**

**(The National Maternity Review 2015)**

A woman with a known abdominal tumour presented with abdominal pain and vomiting in the third trimester, and concerns about reduced fetal movement. She was transferred from obstetrics to urology and an MRI scan was arranged which revealed a new complex mass in the right upper quadrant. The urologists arranged a transfer to an oncology unit at a specialist hospital. By the time she arrived at the oncology unit she was very unwell, an ultrasound showed a necrotic looking mass in contact with the fundus of the uterus. The oncology team wondered if this might represent a placenta accreta and a second transfer took place on the same day to the obstetric unit of a third hospital.

She had an emergency caesarean section the following morning but the baby was stillborn. At operation faecal peritonitis was identified. She was transferred to the critical care unit where she died three days later from sepsis.

One day before this woman had a stillborn baby and an intra-operative cardiac arrest she was transferred between hospitals not once, but twice. The clinicians involved did not achieve adequate cross-speciality communication and did not appear aware of the limits of their knowledge.

In complex and rare conditions time must be found to hold an early multi-disciplinary meeting to plan pregnancy and delivery care. The purpose of this meeting is to understand the different perspectives of the professionals involved and formulate a plan for the most likely clinical scenarios that might arise during the pregnancy. It is not clear that the decision to transfer to the oncology centre was carefully evaluated in the context of an on-going pregnancy with recent concern about reduced fetal movement. As a general rule, critically sick pregnant women should not be transferred to health care facilities without on-site obstetric cover.

## Reduced or altered conscious level

A change in conscious level in a pregnant or postpartum woman should trigger urgent clinical review. Subtle alterations in mental state and abnormal behaviour may be more difficult to interpret but it is vital that such changes are not ascribed to anxiety; it may be the only sign of a serious illness.

A primiparous woman presented in the third trimester with a history of headache and vomiting. On admission she was found to have severe hypertension and proteinuria. She was transferred to the labour ward high dependency area and received magnesium sulphate and intravenous anti-hypertensive drugs. An abnormal CTG prompted an emergency caesarean section. This took place in the early hours of the morning, approximately 18 hours after her initial presentation. An effective regional block had to be supplemented by general anaesthesia when the woman became agitated before the start of surgery.

Initial post-operative recovery seemed to be uneventful but within 24 hours of delivery the woman was found to be unresponsive with a GCS of 8/15. A CT scan was performed which revealed multiple areas of sub-cortical white matter oedema and signs of raised intracranial pressure (ICP). She was transferred to a neurosurgical centre and ICP monitoring was commenced. In the first nine hours of admission the ICP rose sharply and despite a decompressive craniectomy, she deteriorated and died.

This woman's blood pressure was labile but periods of significant hypertension could have been managed more aggressively. The early involvement of senior staff might have improved this aspect of management. She had at least two signs which almost certainly indicated cerebral irritation/oedema. On the day of admission the woman became 'agitated and restless' and during the caesarean section she was 'agitated/anxious and appeared confused and disorientated' prompting the conversion of a regional technique to general anaesthesia. Despite these incidents brain imaging did not occur for several hours after the second incident. False reassurance was taken from the apparent return to normal neurology and it was not until she became unrousable that an urgent CT scan was arranged.

**Reduced or altered conscious level is not an early warning sign; it is a red flag indicating established illness.**

## Critical care support

Most UK critical care units run close to full capacity and delays to admission whilst beds are being created are commonplace. Critical care support can be initiated in a variety of settings including operating theatres and recovery/post-operative care units and it is important to make a distinction between delays to initiating critical care support and delays to admission.

Obstetric anaesthetists working in liaison with critical care colleagues are well placed to provide initial resuscitation and stabilisation, whilst bed management takes place. Critical care outreach nurses can work in partnership with midwives to provide care before transfer to the critical care unit.

**Admission to Intensive Care must occur within 4 hours of making the decision to admit.**

**The Faculty of Intensive Care Medicine and The Intensive Care Society Guidelines for the provision of intensive care services (The Faculty of Intensive Care Medicine and The Intensive Care Society 2015)**

A multiparous woman in her third trimester was referred from primary care with a short history of cough and difficulty breathing. On admission there were minor delays in recognition of the severity of her illness, involvement of senior medical staff and commencement of appropriate therapy but in general her initial assessment and treatment was good. She was found to be profoundly hypoxaemic but transfer to the high dependency unit was not achieved until almost 12 hours later. Chest x-ray revealed a severe bilateral pneumonia and subsequent tests were positive for H1N1.

Delay to transfer to a high dependency care facility (because of lack of availability of beds) is a cause for concern. Consideration of moving the woman to a theatre or recovery area to initiate critical care supportive treatment should always occur if beds are not immediately available.

**Critical care support can be initiated in a variety of settings. Critical care outreach nurses can work in partnership with midwives to provide care before transfer to the critical care unit. Delay caused by bed pressures in a critical care unit is not a reason to postpone critical care.**

Access to clinical investigations for sick pregnant and postpartum women must be the same between obstetric facilities and general medical admissions. Unit location and out of hours access to tests should not be allowed to prejudice the care that a woman receives.

## Investigations

Urgent echocardiography is an important tool in the assessment of the collapsed or critically sick pregnant or postpartum woman to make diagnoses and prevent inappropriate treatment. Skills in focussed echocardiography are becoming more widespread amongst critical care specialists and may have a particular role to play in distinguishing critical presentations of pulmonary embolism and peripartum cardiomyopathy. Focussed echo is no substitute for a full examination by an operator familiar with the normal cardiac changes of pregnancy but should become a standard for emergency assessment of the collapsed pregnant or postpartum woman.

A woman presented to the emergency department three days postpartum with chest pain, shortness of breath and palpitations. She was seen by junior medical staff who treated her for both a chest infection and a possible pulmonary embolism. She failed to improve with treatment and continued to complain of difficulty breathing. Echocardiography was not available out of hours and a cardiology referral was deferred until echocardiography had been performed. She was not referred to the obstetric team. A few days after she was admitted she collapsed in cardiac arrest. The resuscitation team considered the possibility of a massive PE and gave thrombolysis; return of spontaneous circulation was achieved after 80 minutes. A post-arrest echocardiogram revealed a severe dilated cardiomyopathy and full critical care support (including discussion with the regional cardio thoracic centre) was initiated. However, she had a second cardiac arrest from which she could not be resuscitated. Post-mortem findings were consistent with multi-organ failure caused by peripartum cardiomyopathy.

Early involvement of a consultant obstetrician might have led to a wider list of differential diagnoses being considered. The early warning score raised the appropriate alarms but the responding doctors missed opportunities to revise the diagnosis. Echocardiography was indicated in this woman on the basis of her presenting symptoms, however it was not undertaken in a timely manner.

**Key investigations must not be delayed because of pregnancy or time of the day or day of the week.**

**Pregnancy can make the differential diagnoses of critical illness more complex. There must be a balance between appropriate clinical suspicion and a conclusive diagnosis; not all hypertension is pre-eclampsia and shortness of breath is not always a pulmonary embolism.**

Management of suspected massive pulmonary embolism should follow the guidelines set out by the European Society of Cardiology. Neither pregnancy, caesarean section delivery or the immediate postpartum state are absolute contraindications to thrombolysis (Knight, Kenyon et al. 2014). An emergency echo showing signs of right ventricular strain and occasionally visualisation of clot in the cardiac chambers can increase confidence in diagnosis and aid the decision to thrombolyse a pregnant or postpartum woman, however, evidence is limited (Konstantinides, Torbicki et al. 2014).

**If life-threatening pulmonary embolism is suspected, the on-call medical team should be contacted immediately. An urgent portable echocardiogram or CTPA within 1 hour of presentation should be arranged. If massive PE is confirmed, or in extreme circumstances prior to confirmation, immediate thrombolysis should be considered.**

**RCOG Green-top guideline 37b Thromboembolic disease in pregnancy and the puerperium: acute management (Royal College of Obstetricians and Gynaecologists 2015)**

## Inter-hospital referral

Inter-hospital transfer of a critically sick pregnant or postpartum woman entails hazards and risks above the normal. Women should not be transferred to obtain an expert opinion; clinicians are more mobile than critically ill patients. Transfers to achieve an upgrade of care in specialist units or for particular interventions are justified. It is important to recognise however, that when individual clinicians are working at the limit of their experience it can be easy to over-estimate the benefits of a transfer.

Transfer training programmes and written guidance on the transfer of critically sick pregnant or postpartum women are lacking. Ambulance trusts have considerable experience of transferring women in active labour into healthcare facilities and between midwifery care and obstetric units however there is no widespread understanding about how best to transfer a pregnant or recently pregnant woman who is critically ill. A need to develop consensus guidance in this area has already been identified in Ireland (Health Service Executive 2014).

An additional hazard in transfer is loss of information between care providers. In some reviews undertaken for the purposes of this chapter this was noted to result in duplication of imaging investigations and loss of important elements of the medical history.

A woman with a rare benign tumour which is known to act in a malignant manner in pregnancy had multiple admissions throughout pregnancy with pain, vomiting, diarrhoea and fever. Care focussed on treating her pain without identifying its cause although she did improve after an initial course of antibiotics. She was cared for in three different hospitals with some time spent investigating a fourth transfer. This resulted in loss of her original obstetric documentation and details of investigations in the preceding weeks which could have highlighted an increasing concern. Her peritonitis was diagnosed at emergency caesarean delivery but both mother and baby died.

**Inter-hospital referral of a sick pregnant or postpartum woman should be directed by the principle 'one transfer to definitive care'. It is unlikely to be appropriate to move a sick antenatal woman to a facility without on-site obstetric cover.**

**Evidence-based guidelines on appropriate transfer of the critically-ill pregnant or postpartum woman are lacking. Such guidance needs to be developed.**

There is now evidence that even for complex interventions involving multiple teams of specialists, outcomes can be improved by centralisation (National Peer Review Programme 2014). With less than 400 critically ill pregnant women in the UK each year, evidence is needed as to whether sick pregnant women could also benefit from service rationalisation.

## Transfer to respiratory ECMO centres

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

**Saving Lives, Improving Mothers' Care 2014 (Knight, Kenyon et al. 2014)**

A primigravid women in her third trimester presented to the obstetric unit at the height of the influenza A/H1N1 pandemic with a 7 day history of cough. She was prescribed amoxicillin and discharged home. Two days later she was referred to the Emergency Department by her GP with a diagnosis of presumed H1N1. On arrival in the Emergency Department she was found to have type 1 respiratory failure and referred to critical care. In critical care the diagnosis of H1N1 was confirmed. She required increasing levels of respiratory and inotropic support but died three weeks later. At no point was referral to an ECMO centre considered.

The period covered by this chapter includes women who died in the H1N1 influenza pandemic of 2009–10. This strain and other influenza viruses remain a serious threat to pregnant women, causing life threatening respiratory failure. Public health surveillance and targeted vaccination programmes are central to the prevention of influenza but in severe disease the role of extra-corporeal membrane oxygenation (ECMO) is now well established (Peek, Mugford et al. 2009, Noah, Peek et al. 2011). There are five adult respiratory ECMO centres in England and one in Scotland. Clinicians in all of these centres have developed expertise in caring for pregnant women with severe respiratory failure although not all of the sites are co-located with obstetric services.

Lung protective ventilation strategies and early referral to an ECMO centre are vital for women with life-threatening respiratory failure. All units operate similar referral criteria (see box 6.2) and these should be familiar to critical care physicians on all units which might admit a pregnant or postpartum woman. It is important to note that survival after ECMO decreases significantly in proportion to the length of prior mechanical ventilation (Brogan, Thiagarajan et al. 2009).

**Box 6.2: Referral criteria for ECMO**

Referrals to the service should only be made by adult intensive care units for patients who are critically ill and already receiving lung protective mechanical ventilation

Providers will accept patients referred to the service who:

- have potentially reversible severe respiratory failure
- have failed optimal conventional intensive care management
- have severe but potentially reversible severe respiratory failure, defined as a Murray score ≥ 3.0, or uncompensated hypercapnoea with a pH < 7.20 despite optimal conventional treatment. Reversibility will be based on expert clinical opinion.

The Murray score uses four variables to assess the acuity of lung injury:

- oxygenation
- radiographic findings
- level of positive end expiratory pressure (PEEP) used in mechanical ventilation
- lung compliance.

**2013/14 NHS standard contract for extra corporeal membrane oxygenation service for adults with respiratory failure (NHS England 2013a)**

## Management of obstetric-specific conditions on the critical care unit

**Obstetricians, midwives and obstetric anaesthetists must remain closely involved in the clinical management of women with obstetric specific conditions such as pre-eclampsia. These conditions are rarely seen on the general critical care unit but are common problems on obstetric wards. It is also essential that pregnant and postpartum women on the critical care ward receive routine antenatal and postnatal care.**

Obstetricians, midwives and obstetric anaesthetists are experienced in the management of obstetric specific conditions such as severe pre-eclampsia as well as management of normal pregnancy and the puerperium. It is important that when a woman is admitted to the general critical care unit all the available expertise is utilised.

The situation of pre-eclampsia complicated by a major obstetric haemorrhage should be recognised as high risk. It is sometimes difficult for critical care practitioners to remain mindful of the targets for hypertension which merit treatment in an obstetric population but would be normal for other patients under their care.

**In women with severe hypertension who are in critical care, aim to keep systolic blood pressure below 150mmHg and diastolic blood pressure between 80 and 100 mmHg**

**NICE Guideline CG107 Hypertension in pregnancy (National Institute for Health and Care Excellence 2010b)**

A primigravid woman was admitted preterm with severe pre-eclampsia and delivered by caesarean section three days later. After delivery she continued to deteriorate, developing renal and hepatic failure. She was appropriately referred to critical care, however, in the critical care unit she was given a fluid challenge by the critical care registrar which precipitated pulmonary oedema. She died a few days later from multi-organ failure in relation to her HELLP syndrome.

Although this woman did not die due to fluid overload there were also other instances when fluid boluses were given inappropriately. Close fluid balance and a general approach of fluid restriction is important in pre-eclampsia and highlights the importance of ongoing involvement of obstetricians, midwives and obstetric anaesthetists.

### Case reviews

High standards in risk management are a feature of many maternity service providers. When a maternal death occurs it is particularly important to seek contributions from staff outside the obstetric and midwifery teams for alternative perspectives.

There were a number of instances where critical care staff who were closely involved in providing care to the women who died were not fully included in subsequent case reviews and enquiries. Sharing experience and learning the lessons from a maternal death must include participation of all those involved.

It is also good practice for critical care staff to include the obstetric team in discussion about treatment withdrawal, death certification and post-mortem decisions.

When critical care staff have any involvement in a maternal death, it is imperative that they are included in case reviews, root cause analysis and serious incident investigations.

## 6.5 Conclusions

The survival rate amongst pregnant and postpartum women admitted to general critical care units remains high (>98%) (Intensive Care National Audit and Research Centre 2013) and even amongst the women who die, many receive a very high standard of care.

The relative rarity of an obstetric admission to the critical care unit continues to provoke particular levels of anxiety. The current trends in critical care training make it less likely that the practitioners of the future will have post-graduate experience working on the labour ward and this will need to be compensated for by a greater effort to work collaboratively with obstetricians and obstetric anaesthetists particularly in women admitted with conditions unique to pregnancy.

The H1N1 influenza pandemic resulted in a surge of pregnant women with severe respiratory failure and it is important that the lessons learned (close adherence to lung protective ventilation strategies and early discussions with centres that provide respiratory ECMO) are not forgotten both for pregnant and postpartum women with seasonal influenza and in any future influenza epidemic or pandemic.

Finally, when a maternal death occurs it is vital that members of the critical care team who have played a part in the woman's care should be included in the local investigation and enquiry processes that follow. Their perspective and insight may be crucial in identifying improvements in care for the future.

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