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REVIEW ARTICLES

Saving Mothers' Lives: reviewing maternal deaths to make motherhood safer: 2006–8: a review

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Editor's key points

- The true UK maternal mortality rate fell to 11.39 per 100 000 maternities in 2006–8.
- Deaths from pulmonary embolism and obstetric haemorrhage decreased in 2006–8.
- Deaths from infection of the genital tract (sepsis) increased in 2006–8.
- Systemic sepsis requires early recognition, immediate treatment and multidisciplinary management.

Summary This review of the eighth report of the United Kingdom Enquiries into Maternal Deaths, Saving Mothers' Lives, is written primarily for anaesthetists and critical care specialists involved in both maternity and gynaecology services. Direct maternal deaths from systemic sepsis secondary to infection of the genital tract have increased. Systemic sepsis requires early recognition, immediate treatment and multidisciplinary management involving anaesthetists and critical care specialists. The incidence of deaths related to anaesthesia remains unchanged at seven in the three year period. Airway related problems unfortunately still cause maternal death. The role of early communication between obstetricians and anaesthesia and intensive care specialists is highlighted. The review summarizes the recommendations relating to anaesthesia and intensive care.

Keywords: anaesthesia; Confidential Enquiry; critical care; maternal mortality, sepsis

The eighth report of the United Kingdom Enquiries into Maternal Deaths, now known as Saving Mothers' Lives, was published in the *British Journal of Obstetrics and Gynaecology* in March 2011.[1] The data in this Report was collected by the Centre for Maternal and Child Enquiries and is summarized here with permission.

The Confidential Enquiries into Maternal Deaths have been in existence for almost 60 yr and they are the longest running continuous series of clinical audit in the world.

These large national enquiries, run over a 3 yr period, reduce the biases traditionally attributed to centre-based observational studies because case-selection is eliminated. The highest level of evidence comes from systematic reviews of randomized controlled trials, but these are simply not possible in relation to maternal deaths. However, we are all affected by the wisdom of hindsight and both the Central and Regional Clinical and Pathology Assessors, involved in the process of case assessment, attributing cause of death, and the detection of substandard care, are cognizant of this.

The international definition of the maternal mortality ratio is the number of *Direct* and *Indirect* deaths per 100 000 live births. For international comparison, the UK Maternal Mortality Ratio for 2006–8 is 6.69 [95% confidence interval (CI) 5.72–7.84] per 100 000 live births. This is calculated only from those *Direct* and *Indirect* maternal deaths notified on death certificates, the method used by all other countries. When making international comparisons, it is important to note that the criteria used by the UK assessors for *Indirect* deaths are far more inclusive than those used in other countries, for example, in the UK, all cases of cardiac disease, asthma, epilepsy, and most cases of suicide are coded as *Indirect*. The enhanced case ascertainment for maternal deaths is made possible through the UK wide network of carers and assessors in the maternity and gynaecology services, who identify these cases directly to the Centre for Maternal and Child Enquiries. Case ascertainment is also lower in the vast majority of other countries because of the lack of death certificate data.

Therefore, the true UK maternal mortality rate, calculated from all maternal mortality *Directly* or *Indirectly* due to pregnancy identified by this Enquiry, for 2006–8, was 11.39 (95% CI 10.09–12.86) per 100 000 maternities compared with the 13.95 (95% CI 12.45–15.64) per 100 000 maternities reported for the previous triennium, 2003–5. There has been a statistically significant decline in the overall UK maternal mortality rate for the years 2006–8 compared with the 2003–5 triennium ($P=0.02$).

The 2006–8 report shows, for the first time over many years, a small decline in the overall maternal mortality and also larger reductions in deaths from some *Direct* causes due to pregnancy, for example, pulmonary embolism and haemorrhage. However, deaths from infection of the genital tract (sepsis), largely from community-acquired Group A streptococcal disease, have increased. The overall rate has increased to 1.13 deaths (95% CI 0.77–1.67) per 100 000 maternities compared with 0.85 (95% CI 0.54–1.35) for

2003–5 (P=0.35). This has occurred at a time when the background population mortality rate from invasive Group A streptococcal infection, which is a notifiable disease, has also increased. This report was written before the H1N1 pandemic, so does not include deaths from this disease.

The mortality rate for maternal deaths from all *Direct* causes of death was 4.67 (95% CI 3.86–5.64) for this triennium compared with the rate of 6.24 (95% CI 5.37–7.40) per 100 000 maternities given for the last report (P=0.02). There has been a significant decline in deaths from *Direct* causes since 1985.

The mortality rate for mothers' deaths from *Indirect* causes, that is, from pre-existing or new medical or mental health conditions aggravated by pregnancy such as heart disease or suicide, remains largely unchanged.

It is recognized that the study of 'near-miss'/severe maternal morbidity can provide valuable additional information to guide prevention and treatment of potentially life-threatening conditions. Maternal deaths represent the tip of the iceberg of disease; a much larger number of women suffer from severe maternal morbidity.

In this report, the latest results of two systems for severe morbidity or 'near-miss' surveillance are included. These are the United Kingdom Obstetric Surveillance System (UKOSS)[2] and the Scottish Confidential Audit of Severe Maternal Morbidity (SCASMM).[3]

This review of the 2006–8 report is written primarily for anaesthetists and critical care specialists involved in both maternity and gynaecology services and by necessity the full report is summarized. Issues of copyright unfortunately prevent the full publication of the Anaesthesia and Critical Care chapters of the report, which was allowed previously in the *British Journal of Anaesthesia*, because of prior publication of the full report in the *British Journal of Obstetrics and Gynaecology*. However, readers are encouraged to read and refer to the full report, which is published and accessible online (http://www.cmace.org.uk/Publications-Press-Releases/Report-Publications/Maternal-Mortality.aspx).

'Top ten' recommendations

Ten top recommendations are again made; some repeated from previous enquiries and the recommendations are not listed in the order of priority:

(1) Pre-pregnancy counselling for those with serious medical or psychiatric conditions should be offered.
(2) Professional interpretation services should be provided if communication in English is poor.
(3) Communications and referrals to specialist services in pregnancy should be prioritized as urgent.
(4) Women with potentially serious medical conditions require immediate and appropriate multidisciplinary specialist care.
(5) Clinical skills and training must be addressed: 'Back to basics'.
(6) Specialist clinical care and team working must identify and manage very sick women. The routine use of a national modified early obstetric warning score (MEOWS) chart for all pregnant or post-partum women, who become unwell and require either obstetric or gynaecology services, is again recommended. The management of pregnant or post-partum women, who present with an acute severe illness, requires a team approach including advice and help from anaesthetic and critical care services.
(7) Systolic hypertension above 150 mm Hg requires treatment.
(8) Genital tract infection/sepsis. There is an urgent need for a national clinical guideline to cover the identification and management of sepsis in pregnancy, labour, and the post-natal period. Until such time as a national guideline is developed, the guidelines for the management of acute sepsis developed and updated by the Surviving Sepsis Campaign should be used.
(9) Serious incident reporting. All maternal deaths must be subject to a high quality local review.
(10) Pathology. The standard of the maternal autopsy must be improved and the number of locations where they are performed should be reduced and specialist pathologists used.

Back to basics

A new chapter on 'Back to basics' is included in this report to aid learning and clinical practice. It includes common symptoms and conditions, which arise in pregnancy and when they should be taken seriously (red flagged) and action taken. The 'red flag' signs and symptoms for sepsis that should prompt referral for urgent hospital assessment are as follows:

- pyrexia $>38^{\circ}$C. A normal temperature does not exclude sepsis. Paracetamol and other analgesics may mask pyrexia, and this should be taken into account when assessing women who are unwell;
- sustained tachycardia >100 beats min^{-1};
- breathlessness (ventilatory frequency >20);
- abdominal or chest pain;
- diarrhoea, vomiting, or both;
- reduced or absent fetal movements, or absent fetal heart;
- spontaneous rupture of membranes or significant vaginal discharge;
- uterine or renal angle pain and tenderness;
- the woman is generally unwell or seems unduly anxious.

Pre-eclampsia and eclampsia

The number of deaths from pre-eclampsia/eclampsia has remained fairly constant over the past six triennia. Owing to the number of deaths secondary to cerebral haemorrhage and eclampsia, it is recommended that systolic hypertension >150 mm Hg is treated urgently and effectively. Hypertension should be avoided by abandoning the routine use of ergometrine in the management of the third-stage of labour. I.M.

oxytocin, not Syntometrine®, should be the routine drug for active management of the third stage of labour.[4]

Severe pre-eclampsia requires immediate control and regular, frequent monitoring of arterial pressure with high dependency care. Anaesthetic services and, on occasions, critical care services should be involved in management at an early stage.

Obstetric haemorrhage

There has been a welcome decline in the number of deaths from obstetric haemorrhage; post-partum haemorrhage due to uterine atony remains the most common cause.

Detection of concealed haemorrhage is vital. All women delivered by Caesarean section should have regular observations for at least 24 h after delivery recorded on a MEOWS chart. Abnormal scores should be investigated and acted upon without delay. Women known to be at risk of major haemorrhage, for example, those with placenta accreta and those who decline blood products, should be delivered in maternity units with access to critical care, interventional radiology, and cell salvage.

Circulatory collapse can happen suddenly in haemorrhage, and management should be multidisciplinary. The management of circulatory collapse due to haemorrhage includes surgery, i.v. fluid, blood and blood products, and cardiovascular monitoring. Fluid resuscitation and inotropic support should be used cautiously before surgical control of the haemorrhage.

The symptoms and signs of hypovolaemia are more difficult to recognize if there is any of the following:

- language difficulty;
- obesity;
- pre-eclampsia;
- brown/black skin;
- β-blockade.

Amniotic fluid embolism

Amniotic fluid embolism (AFE) continues to rank as a major cause of *direct* maternal death. However, AFE is no longer regarded as a condition leading to certain death. High-quality supportive care can result in good outcomes for both mother and baby, particularly if the collapse occurs within the labour suite or operating theatre and resuscitation is prompt.

Genital tract sepsis

The main reason for the increase in maternal mortality from sepsis in this triennium is deaths caused by community-acquired β-haemolytic streptococcus Lancefield Group A (*Streptococcus pyogenes*). Most women had signs and symptoms of severe sepsis by the time they presented to hospital. If sepsis is suspected in the community, urgent referral and transfer to hospital is needed. In hospital, high-dose i.v. broad-spectrum antibiotics should be started immediately without waiting for the results of microbiology or other investigations. Blood cultures and cultures from any possible sites of infection should be taken before the first dose of antibiotics is given, provided that this does not delay antibiotic administration.

Once infection becomes systemic, the woman's condition can deteriorate extremely rapidly over a period of a few hours. Circulatory collapse can happen suddenly in sepsis, and the cornerstone is multidisciplinary management.

Women with sickle-cell disease are at increased risk of infection as a result of poor splenic function.

All units should have an effective and robust system in place to ensure peri-abortion antibiotic prophylaxis. Infection must be suspected and actively ruled out when women who have had a recent termination of pregnancy or spontaneous miscarriage have a pyrexia, persistent bleeding, or abdominal pain.

There is an urgent need for a national clinical guideline to cover the identification and management of sepsis in pregnancy, labour, and the post-natal period. This should be available for all maternity units, emergency departments, general practitioners, and community midwives. Until such time as a national guideline is developed, the guidelines for the management of acute sepsis developed and updated by the Surviving Sepsis Campaign[5] should be used.

Cardiac disease

Cardiac disease remains not only the most common cause of *indirect* maternal death but the most common cause overall. Aortic dissection, myocardial infarction (MI), ischaemic heart disease (non-MI), sudden adult death syndrome (SADS), and peripartum cardiomyopathy are the more common acquired causes of death from cardiac disease. Ten women died of SADS during this triennium compared with three in the last report. Six of them were obese.

Peripartum cardiomyopathy should be suspected in women in late pregnancy or within 6 months of delivery if they have symptoms of breathlessness, oedema, or orthopnoea and signs of tachypnoea and tachycardia. A chest X-ray and an echocardiogram are indicated. Women with peripartum cardiomyopathy should be managed by cardiologists with expertise in this condition and their care should be discussed with the regional cardiac transplant centre.

Deaths from anaesthesia

There were seven women who died from problems directly associated with anaesthesia in this triennium (2006–8). The number of *Direct* deaths from anaesthesia over the past eight UK reports has remained relatively unchanged with an average of two deaths per annum.

Thankfully, deaths from airway-related causes have decreased from the high incidence seen in the 1960s, when anaesthetic deaths were much more common and such deaths were first discussed in a separate chapter. Anaesthesia is clearly not a disease; it is an intervention and all anaesthetic deaths may be considered iatrogenic and potentially preventable. Striving for absence of deaths from airway-related causes is achievable, as in 1994–6,

when there was only one anaesthetic death due to a combined spinal and epidural anaesthesia.

In this triennium, two women died from failure to ventilate the lungs, four from postoperative complications, and one from leukoencephalitis.

Management of failed intubation/ventilation is a core anaesthetic skill that should be rehearsed and assessed regularly.[6] In managing a rare but critical situation, it is important to fully implement an accepted drill and maintain priorities. The drill should not be complex and must be practised regularly. The anaesthetist must avoid natural behaviour patterns of fixation and denial where tracheal intubation is seen as the goal rather than oxygenation of the lungs. Simulation training may improve performance in the management of life-threatening emergencies.

The woman who died from failure to ventilate the lungs at induction of general anaesthesia had a working epidural in labour when it was decided to perform a category 2 Caesarean section. After a delay, the urgency of Caesarean section was subsequently escalated to category 1 because of fetal bradycardia. If the epidural had been topped up at the time it was decided she was to have a Caesarean section, general anaesthesia may not have been required.

Epidural analgesia that has been working well in labour should be topped up to provide full surgical anaesthesia without delay once the decision to perform an emergency operative delivery is made.

Four women died after complications in the postoperative period. The assessors judged the most likely cause of death in these women from the information available.

One death was related to opioid toxicity in a woman receiving patient-controlled analgesia but by the time this was known, the patient-controlled analgesia machine, the syringe, and its contents had been discarded and not available for inspection and analysis.

A second death due to acute circulatory failure may have been due to blood incompatibility after a blood transfusion.

One woman died from cardiac arrest while recovering from general anaesthesia for a surgical abortion. After the event, it transpired that the woman was a regular substance abuser. She had been given Syntometrine® i.v. which may have caused the cardiac arrest in view of the cardiac pathology secondary to substance abuse found at autopsy.

A fourth woman probably aspirated stomach contents on emergence from general anaesthesia after an emergency Caesarean section. A category 1 Caesarean section was thought to be indicated because of antepartum haemorrhage from a known placenta praevia, but the bleeding settled and she was cardiovascularly stable. She had eaten a full meal in hospital immediately before this decision. General anaesthesia was therefore considered to be a reasonable choice, but there was no documented discussion about whether a category 1 Caesarean section was actually indicated or time could be allowed for the stomach to empty. In the presence of a full stomach, the management of extubation is as critical as intubation. The patient should be fully awake and able to protect her airway before extubation. In this case, the stomach was presumed to contain gastric contents, and had not been decompressed with a wide-bore orogastric tube before extubation.[7]

Acute haemorrhagic disseminated leukoencephalitis, a very rare hyperacute and usually fatal form of acute disseminated encephalomyelitis, was found at autopsy in a woman who died some days after an uneventful spinal anaesthetic for Caesarean section. Autopsy also revealed an empyema in the spinal canal. An autoimmune pathology is likely and it was considered that the spinal empyema triggered this very rare autoimmune disease. This emphasizes the necessity for strict asepsis when performing spinal or epidural anaesthesia.

Deaths to which anaesthesia contributed

In addition to the seven women who died from anaesthesia, the assessors considered that in a further 18 deaths, anaesthetic management contributed to the outcome. Women with severe acute illness or significant co-morbidity present a major challenge to obstetric, anaesthetic, and midwifery services, particularly when the maternity service is already stretched with peak activity in its normal workload.

Workload

Many case reports highlighted the fact that providing good high dependency care was difficult when the maternity service was already very busy with normal activity at a peak. A number of case reports highlighted that peak labour ward activity coincided with the emergency admission of a pregnant woman with an acute, severe illness. This produces difficulties in providing the appropriate level of high dependency care to a pregnant woman admitted with an acute, severe illness to the labour ward or during early pregnancy to a gynaecological ward. When staffing levels are based on average activity, there needs to be a clear contingency plan for all disciplines to obtain further skilled assistance.

Failure to consult with anaesthetic or critical care services

There were 12 cases of severe pregnancy-induced hypertension or sepsis where obstetricians or gynaecologists failed to consult with anaesthetic or critical care services sufficiently early, which the assessors considered might have contributed to the deaths.

Anaphylaxis

A woman died after suffering an unexpected acute anaphylactic reaction to an antibiotic given during labour. She was not known to be allergic to the drug before this. The anaesthetist was busy in theatre at the time. The failure to initiate perimortem Caesarean section on the labour ward within 4 min of cardiac arrest to deliver the fetus may have contributed to the unsuccessful maternal resuscitation.[8] Acute anaphylaxis requires an immediate medical response including treatment with epinephrine. A formal anaphylaxis protocol,[9]

similar to a cardiopulmonary resuscitation chart, should be immediately available for all clinical staff to follow. These charts are already available in every operating theatre.[10]

Obesity

A national study of the most morbidly obese women (BMI 50 kg m^{-2} or greater) was undertaken through UKOSS.[11] This identified an estimated prevalence of 87 such women per 100 000 maternities. These women were at increased risk of severe morbidity including pre-eclampsia, gestational diabetes, and requiring intensive care unit admission. Obese women were also more likely to have interventions which put them at risk of severe morbidity, including Caesarean delivery (adjusted odds ratio 3.50, 95% CI 2.72–4.51) and general anaesthesia (adjusted odds ratio 6.35, 95% CI 2.63–15.3).

Critical care

The first chapter on Critical Care issues in maternal deaths was in the 1991–3 triennial report. Critical care is typically a consequence of severe maternal morbidity rather than a cause of maternal death. More than half of all the women who die each triennium spend some time in a critical care unit. Critical care has a major role in prevention of maternal death in those women who suffer a 'near-miss' or severe maternal morbidity.

In Scotland,[3] during the triennium 2006–8, the rate of severe maternal morbidity was 5.88 per 1000 births (95% CI 5.52–6.25). The most frequent reason (47%) for critical care admission was for massive obstetric haemorrhage (>1.5 litre).

The most frequent 'uncategorized' reason for admission was for a cardiac condition, both congenital and acquired (12% of critical care admissions).

The critical care admission rate was 1.44 (95% CI 1.27–1.63) per 1000 births.

Early referral to critical care specialists and the provision of critical care outreach services are invaluable in preventing severe maternal morbidity progressing to maternal death.

The management of maternal sepsis, whether it occurs in early pregnancy, late pregnancy, or the puerperium and arises in the genital tract or elsewhere, is considered in detail in the critical care chapter in the report and is summarized here.

Maternal sepsis

The increasing use of MEOWS and collaboration between outreach teams and obstetrics and gynaecology will go some way to improving earlier detection of maternal sepsis.

The complex effects of sepsis explain why effective treatment has proved elusive but the 'Surviving Sepsis Campaign'[5] remains the best-evidenced package of treatment for sepsis. Time is of the essence in initiating treatment, and should start well before admission to critical care. Early and prompt referral to a critical care specialist is paramount and patient management should be discussed at a senior clinical level even if immediate admission is either not yet required or impossible due to bed availability.

There is increasing evidence that early protocol-based resuscitation improves outcome[12] and should be initiated when the diagnosis of severe sepsis or septic shock is strongly suspected.

Diagnosis of septic shock

Septic shock is defined as tissue hypoperfusion (hypotension persisting after initial fluid challenge or a blood lactate concentration ≥4 mmol $litre^{-1}$). Blood cultures and cultures from other possible sites should be taken ideally before the first dose of antibiotics is given, provided that this does not delay antibiotic administration. Diagnostic imaging should be arranged as soon as possible.

Antibiotic therapy

I.V. antibiotic therapy should be started as early as possible and certainly within the first hour of recognition of septic shock or severe sepsis without septic shock.

Initial resuscitation

For the first 6 h of resuscitation, attempts should be made to achieve the following goals:

- central venous pressure (CVP): 8–12 mm Hg,
- mean arterial pressure (MAP) ≥ 65 mm Hg,
- urine output ≥0.5 ml kg^{-1} h^{-1},
- central venous (superior vena cava) or mixed venous oxygen saturation ≥70% or ≥ 65%, respectively.

Fluid therapy

I.V. fluids should be given rapidly to achieve a target CVP of at least 8 mm Hg (12 mm Hg in ventilated patients). If the CVP increases without significant haemodynamic improvement, then fluid administration should be slowed.

Vasopressors

In severe sepsis, the target mean arterial pressure of ≥65 mm Hg may not be achieved by fluid infusion alone due to vasodilatation caused by nitric oxide release. Norepinephrine or dopamine should be used to increase the systemic vascular tone as soon as central venous access has been established.

Inotropes

Dobutamine is recommended as the inotrope of choice where there is evidence of a reduced cardiac output in the presence of elevated cardiac filling pressures.

Corticosteroids

The use of high-dose corticosteroid therapy no longer has a place in the management of sepsis. There is some evidence to support the use of low-dose hydrocortisone (<300 mg per day) in septic patients unresponsive to fluid and vasopressors. Therapy should be weaned off as soon as vasopressors are no longer required.

Recombinant human-activated protein C

The current recommendation is that activated protein C should be reserved for patients with a high risk of death (Acute Physiology and Chronic Health Evaluation II scores of $\geq$25). The risks of bleeding outweigh its benefits in less seriously ill groups which is a particular concern in postoperative sepsis.

Haemoglobin and platelets

Haemoglobin concentration should be kept between 7 and 9 g dl^{-1}. Platelets should be administered to keep the count above 5×10^9 $litre^{-1}$ at all times and at $\geq50\times10^9$ $litre^{-1}$ if surgery is required.

The recognition and management of any severe, acute illness in a pregnant woman, not just severe sepsis, requires multidisciplinary teamwork. An anaesthetist, a critical care specialist, or both should be involved early. Obstetric and gynaecology services, particularly those without an on-site critical care unit, must have a defined local guideline to obtain rapid access to, and help from, critical care specialists. The delivery of protocol-driven treatment for life-threatening illnesses can save lives but needs to be started well before admission to a critical care unit.

Serious incidents

When a serious incident occurs, all equipment and drugs should be retained *in situ* for inspection and analysis until the cause of the incident is determined. Most maternal deaths within hospital now initiate a full serious incident hospital enquiry, the reports of which were available to the regional and central assessors. These reports are still of variable quality and clearly completed in-house and therefore open to bias. Hospital managers are again asked to consider whether unbiased external input would assist in this process and ensure greater objectivity. No review was undertaken in 20% of maternal deaths.

The future

The Republic of Ireland joined the Enquiry in January 2009 and its contribution will be included from then. The National Patient Safety Agency has recently undertaken a competitive tendering process for the future provision of the National Confidential Enquiries and another body may undertake the Confidential Enquiries into Maternal Deaths in a different format from 2009. It is hoped that this reorganization and funding issues do not jeopardize this world-class continuous audit, which has such an international impact on maternal health since the early days of the National Health Service in the UK.

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Conflict of interest

J.H.M. was a Clinical Research Fellow sponsored by Astra Pharmaceuticals (now AstraZeneca) in 1979 and has undertaken consultancy work and one sponsored lecture tour since. T.H.C.-B. is a shareholder in Sphere Medical Ltd and is a member of its medical advisory board.

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