



Royal College of  
Obstetricians &  
Gynaecologists

# Late Intrauterine Fetal Death and Stillbirth

Green-top Guideline No. 55  
October 2010



# Late Intrauterine Fetal Death and Stillbirth

This is the first edition of this guideline.

## 1. Purpose and scope

To identify evidence-based options for women (and their relatives) who have a late intrauterine fetal death (IUFD: after 24 completed weeks of pregnancy) of a singleton fetus. To incorporate information on general care before, during and after birth, and care in future pregnancies. The guidance is primarily intended for obstetricians and midwives but might also be useful for women and their partners, general practitioners and commissioners of healthcare.

This guideline does not include the management of multiple pregnancies with a surviving fetus, stillbirth following late fetocide, late delivery of fetus papyraceous or the management of specific medical conditions associated with increased risk of late IUFD. Recommendations about the psychological aspects of late IUFD are focused on the main principles of care to provide a framework of practice for maternity clinicians. The full psychological and social aspects of care have been reviewed by Sands (Stillbirth and neonatal death society).<sup>1</sup> The section on postmortem examination covers clinical aspects required for obstetricians and midwives caring for women who have suffered a stillbirth. More detail can be found in a Joint Report by the Royal College of Obstetricians and Gynaecologists (RCOG) and the Royal College of Pathologists.<sup>2</sup>

## 2. Background

The Perinatal Mortality Surveillance Report (CEMACH)<sup>3</sup> defined stillbirth as ‘a baby delivered with no signs of life known to have died after 24 completed weeks of pregnancy’. Intrauterine fetal death refers to babies with no signs of life in utero.

Stillbirth is common, with 1 in 200 babies born dead.<sup>3</sup> This compares with one sudden infant death per 10 000 live births.<sup>3</sup> There were 4037 stillbirths in the UK and Crown Dependencies in 2007, at a rate of 5.2 per 1000 total births. The overall adjusted stillbirth rate was 3.9 per 1000. Rates ranged from 3.1 in Northern Ireland to 4.6 in Scotland. Scotland had a significantly higher stillbirth rate than the other nations.<sup>3</sup> Overall, over one-third of stillbirths are small-for-gestational-age fetuses with half classified as being unexplained.<sup>3,4</sup> The 8th Annual Report of the Confidential Enquiries into Stillbirths and Deaths in Infancy (CESDI) identified suboptimal care as being evident in half of the pregnancies.<sup>5</sup>

The stillbirth rate has remained generally constant since 2000. It has been speculated that rising obesity rates and average maternal age might be behind the lack of improvement;<sup>4</sup> a systematic review identified these as the more prevalent risk factors for stillbirth.<sup>6</sup>

In addition to any physical effects, stillbirth often has profound emotional, psychiatric and social effects on parents, their relatives and friends.

## 3. Identification and assessment of evidence

This RCOG guideline was developed in accordance with standard methodology for producing RCOG Green-top Guidelines. A search was performed in the OVID database, which included Medline, Embase, the Cochrane Database of Systematic Reviews, the Cochrane Control Register of Controlled Trials (CENTRAL), the Database of Abstracts of Reviews and Effects (DARE) and the ACP Journal Club. The National Guidelines Clearing House, Sands publications, CEMACH reports, ISI Web, the Cochrane Methodology Register, the TRIP database and EBM Reviews – including Health Technology Assessment and the NHS Economic Evaluation Database – were also

searched. Search terms included 'stillbirth, intrauterine', 'fetal death, intrauterine', 'lactation suppression', 'induction of labour and intrauterine fetal death', 'intrauterine death' and 'intrauterine death and diagnosis'. The search was limited to 1 January 1980 to 5 June 2008 and to humans after 24 completed weeks of pregnancy. Duplicates were removed and filtered on Reference Manager for systematic reviews, randomised controlled trials, cohort studies, case-control studies and reviews. Six hundred and forty-nine manuscripts were obtained. Further documents were obtained by the use of free text terms and hand searches. The search was updated in June 2010 for vaginal birth after caesarean (VBAC) and induction of labour.

The levels of evidence and the grade of recommendations used in this guideline originate from the guidance by the Scottish Intercollegiate Guidelines Network Grading Review Group,<sup>7</sup> which incorporates formal assessment of the methodological quality, quantity, consistency and applicability of the evidence base. For the latter, we have used studies that report findings relevant to either stillbirths or deaths in utero. Findings of other studies have been extrapolated only after consideration of applicability.

## 4. Diagnosis

### 4.1 What is the optimal method for diagnosing late IUFD?

**Auscultation and cardiotocography should not be used to investigate suspected IUFD.**



**Real-time ultrasonography is essential for the accurate diagnosis of IUFD.**



**Ideally, real-time ultrasonography should be available at all times.**



**A second opinion should be obtained whenever practically possible.**



**Mothers should be prepared for the possibility of passive fetal movement. If the mother reports passive fetal movement after the scan to diagnose IUFD, a repeat scan should be offered.**



Auscultation of the fetal heart by Pinard stethoscope or Doppler ultrasound is insufficiently accurate for diagnosis. In a series of 70 late pregnancies in which fetal heart sounds were inaudible on auscultation, 22 were found to have viable fetuses.<sup>7</sup>

Evidence level 2+

Auscultation can also give false reassurance; maternal pelvic blood flow can result in an apparently normal fetal heart rate pattern with external Doppler.

Real-time ultrasound allows direct visualisation of the fetal heart. Imaging can be technically difficult, particularly in the presence of maternal obesity, abdominal scars and oligohydramnios, but views can often be augmented with colour Doppler of the fetal heart and umbilical cord.

In addition to the absence of fetal cardiac activity, other secondary features might be seen: collapse of the fetal skull with overlapping bones,<sup>8</sup> hydrops, or maceration resulting in unrecognisable fetal mass. Intrafetal gas (within the heart, blood vessels and joints) is another feature associated with IUFD that might limit the quality of real-time images.<sup>9,10</sup>

Evidence level 3

The ultrasound findings of severe maceration and gross skin oedema can be discussed with the parents.

Although evidence of occult placental abruption might also be identified, the sensitivity can be as low as 15%. Even large abruptions can be missed.<sup>10</sup>

Evidence level 3

After the diagnosis of late IUFD, mothers sometimes continue to experience (passive) fetal movement.

#### 4.2 What is the best practice for discussing the diagnosis and subsequent care?

**If the woman is unaccompanied, an immediate offer should be made to call her partner, relatives or friends.**



**Discussions should aim to support maternal/parental choice.**



**Parents should be offered written information to supplement discussions.**



Many strategies have been described for discussing bad news. Late IUFD poses particular difficulties as it is often sudden and unexpected. A crucial component is to determine the emotional feelings and needs of the mother and her companions.<sup>11</sup> This empathetic approach seeks to identify and understand women's thoughts and wishes but without trying to shape them. Women with an IUFD and their partners value acceptance and recognition of their emotions highly.<sup>12</sup>

Evidence level 3

Empathetic techniques, which can enhance recovery, can be learned and retained as a skill.<sup>13</sup>

Evidence level 4

Pregnancy loss can quickly result in vulnerability; imposing care can worsen the psychological impact.<sup>14</sup>

Evidence level 2++

A study of 808 families who had suffered an IUFD found that decisions about care varied widely from individual to individual.<sup>15</sup>

Evidence level 3

The developers concluded that carers should neither persuade parents nor make assumptions that would limit parental choice. Initial discussions can be used to emphasise choice in decision making.<sup>16</sup>

Evidence level 2

Continuity of caregiver and supplementary written information are valued by pregnant women with adverse events.<sup>17</sup>

Evidence level 3

### 5. Investigation of the cause of late IUFD

#### 5.1 What are the general principles of investigation?

**Clinical assessment and laboratory tests should be recommended to assess maternal wellbeing (including coagulopathy) and to determine the cause of death, the chance of recurrence and possible means of avoiding further pregnancy complications.**



**Parents should be advised that no specific cause is found in almost half of stillbirths.**



**Parents should be advised that when a cause is found it can crucially influence care in a future pregnancy.**



**Carers should be aware that an abnormal test result is not necessarily related to the IUFD; correlation between blood tests and postmortem examination should be sought. Further tests might be indicated following the results of the postmortem examination.**



**Systems that use customised weight charts and capture multiple contributing factors should be used to categorise late IUFDs.**



Tests aim to identify the cause of late IUFD and so provide the answer to the parents' question 'why?' In a study of 314 women, 95% stated that it was important emotionally to have an explanation of their baby's death.<sup>18</sup>

Evidence level 2+

Another important purpose of investigation is to assess maternal wellbeing and ensure prompt management of any potentially life-threatening maternal disease. This includes a detailed history of events during pregnancy and clinical examination for pre-eclampsia, chorioamnionitis and placental abruption. There is also a moderate risk of maternal disseminated intravascular coagulation (DIC): 10% within 4 weeks after the date of late IUID, rising to 30% thereafter. This can be tested for by clotting studies, blood platelet count and fibrinogen measurement.<sup>19</sup>

Evidence level 3

Tests should be repeated twice weekly in women who choose expectant management.

Evidence level 4

It is important to recognise that there is a distinction between the underlying cause of the death (the disease process), the mode of death (for example asphyxia) and the classification of the death (for example growth restriction). Conventional diagnostic systems fail to identify a specific cause in about half of IUIDs.<sup>3</sup> The proportion of unclassified late IUIDs can be significantly reduced with systems that use customised weight-for-gestational-age charts,<sup>20</sup> such as the relevant condition at death (ReCoDe) system,<sup>21</sup> or systems that capture multiple and/or sequential contributing factors, such as Tulip, Perinatal Society of Australia and New Zealand – Perinatal Death Classification (PSANZ-PDC) or Causes Of Death and Associated Conditions (CODAC).<sup>22</sup>

Evidence level 2++

Further research is required to determine the optimal classification method and tools.

An abnormal result might not be linked to the IUID but rather be simply an incidental finding; for example, factor V Leiden is present in about 5% of the general population and will often be an incidental finding.<sup>23</sup> Comprehensive investigation can be important even though one cause is particularly suspected. With a very obvious cause such as massive abruption, nonlethal fetal malformations might be identified at postmortem that would only have been revealed had the baby lived.

### 5.2 Are there any special recommendations for women with an IUID who are rhesus D-negative?

**Women who are rhesus D (RhD)-negative should be advised to have a Kleihauer test undertaken urgently to detect large fetomaternal haemorrhage (FMH) that might have occurred a few days earlier. Anti-RhD gammaglobulin should be administered as soon as possible after presentation.**

C

**If there has been a large FMH, the dose of anti-RhD gammaglobulin should be adjusted upwards and the Kleihauer test should be repeated at 48 hours to ensure the fetal red cells have cleared.**

C

**If it is important to know the baby's blood group; if no blood sample can be obtained from the baby or cord, RhD typing should be undertaken using free fetal DNA (ffDNA) from maternal blood taken shortly after birth.**

D

Major FMH is a silent cause of IUID and a Kleihauer test is recommended for all women to diagnose the cause of death (Table 1). In those women who are RhD-negative, the potentially sensitising bleed might have occurred days before the death is recognised, threatening the window for optimal timing of anti-RhD gammaglobulin administration (72 hours).<sup>24</sup> Anti-RhD gammaglobulin provides reduced benefit when given beyond 72 hours, up to 10 days after the sensitising event.<sup>25-27</sup>

Evidence level 2+

Persistent positivity of the Kleihauer is often because the baby's group is also RhD-negative, but might occur with very large RhD-positive FMHs. If it is important to distinguish between the two, the baby's blood group can be typed using conventional serology on cord blood. Typing with ffDNA from maternal blood is also available. In one series of 226 pregnancies with an informative result, fetal RhD status was correctly predicted in 223 women whose babies had not received intrauterine transfusions.<sup>28</sup>

Evidence level 3 extrapolated

In a series of 14 women with pre-eclampsia, one woman with an IUD had significantly higher levels of fDNA compared with women with live fetuses.<sup>29</sup>

### 5.3 What tests should be recommended to identify the cause of late IUD?

**Tests should be directed to identify scientifically proven causes of late IUD.**

**A**

Commonly associated antepartum conditions include congenital malformation, congenital fetal infection, antepartum haemorrhage, pre-eclampsia and maternal disease such as diabetes mellitus.<sup>3,4</sup> The common causes of intrapartum death include placental abruption, maternal and fetal infection, cord prolapse, idiopathic hypoxia-acidosis and uterine rupture.<sup>3,4</sup>

Evidence level 3

Transplacental infections associated with IUD include cytomegalovirus<sup>30</sup> (Evidence level 2+), syphilis<sup>31-34</sup> (Evidence level 1+) and parvovirus B19<sup>34,35</sup> (Evidence level 2++) as well as listeria<sup>36,37</sup> (Evidence level 2+), rubella<sup>38</sup> (Evidence level 3), toxoplasmosis<sup>33,34</sup> (Evidence level 2+), herpes simplex<sup>30</sup> (Evidence level 2+), coxsackievirus, leptospira, Q fever, and Lyme disease.<sup>39</sup> *Malaria parasitaemia* has also been associated with stillbirth (OR 2.3, 95% CI 1.3-4.1)<sup>40</sup> (Evidence level 2++).

Ascending infection, with or without membrane rupture, with *Escherichia coli*, *Klebsiella*, Group B *Streptococcus*, *Enterococcus*, mycoplasma/ureaplasma, *Haemophilus influenzae* and *Chlamydia* are the more common infectious causes in developed countries.<sup>32-34,41</sup>

Evidence level 2+

Other infections are either historical causes or common only in developing countries.<sup>39</sup>

Evidence level 1++

Table 1<sup>42-76</sup> summarises the diagnostic tests available, their indications and value and the evidence to support their use.

**Table 1. Tests recommended for women with a late IUD**

Test	Reason(s) for test	Evidence level	Reference(s)	Additional comments
Maternal standard haematology and biochemistry including CRPs and bile salt	Pre-eclampsia and its complications	3	3, 19, 42	Platelet count to test for occult DIC (repeat twice weekly)
	Multi-organ failure in sepsis or haemorrhage			
	Obstetric cholestasis			
Maternal coagulation times and plasma fibrinogen	DIC	3	19	Not a test for cause of late IUD Maternal sepsis, placental abruption and pre-eclampsia increase the probability of DIC Especially important if woman desires regional anaesthesia
Kleihauer	Lethal fetomaternal haemorrhage	2	25, 43	Fetomaternal haemorrhage is a cause of IUD <sup>43</sup>
	To decide level of requirement for anti-RhD gammaglobulin			
				Kleihauer should be recommended for all women, not simply those who are RhD-negative (ensure laboratory aware if a woman is RhD-positive) Tests should be undertaken before birth as red cells might clear quickly from maternal circulation In RhD-negative women, a second Kleihauer test also determines whether sufficient anti-RhD has been given

**Table 1 (continued).** Tests recommended for women with a late IUFD

Test	Reason(s) for test	Evidence level	Reference(s)	Additional comments
<b>Maternal bacteriology:</b> <ul style="list-style-type: none"> <li>● blood cultures</li> <li>● midstream urine</li> <li>● vaginal swabs</li> <li>● cervical swabs</li> </ul>	Suspected maternal bacterial infection including <i>Listeria monocytogenes</i> and <i>Chlamydia</i> spp.	1++	32–34, 39 41, 44, 45	<p><b>Indicated in the presence of:</b></p> <ul style="list-style-type: none"> <li>● maternal fever</li> <li>● flu-like symptoms</li> <li>● abnormal liquor (purulent appearance/offensive odour)</li> <li>● prolonged ruptured membranes before late IUFD</li> </ul> <p>Abnormal bacteriology is of doubtful significance in the absence of clinical or histological evidence of chorioamnionitis<sup>46</sup> (Evidence level 3)</p> <p>In one study, amniotic fluid culture was positive in only 1 of 44 women with IUFD despite evidence of chorioamnionitis in a further 9 women<sup>47</sup> (Evidence level 3)</p> <p>Also used to direct maternal antibiotic therapy</p>
<b>Maternal serology:</b> <ul style="list-style-type: none"> <li>● viral screen</li> <li>● syphilis</li> <li>● tropical infections</li> </ul>	Occult maternal–fetal infection	2+	30, 32–35, 48	<p>Stored serum from booking tests can provide baseline serology</p> <p>Parvovirus B19, rubella (if nonimmune at booking), CMV, herpes simplex and <i>Toxoplasma gondii</i> (routinely)</p> <p>Hydrops not necessarily a feature of parvovirus-related late IUFD</p> <p>Treponemal serology – usually known already</p> <p>Others if presentation suggestive, e.g. travel to endemic areas</p>
<b>Maternal random blood glucose</b>	Occult maternal diabetes mellitus	3	49, 50	<p>Rarely a woman will have incidental type 1 diabetes mellitus, usually with severe ketosis</p> <p>Women with gestational diabetes mellitus return to normal glucose tolerance within a few hours after late IUFD has occurred</p>
<b>Maternal HbA<sub>1c</sub></b>	Gestational diabetes mellitus	2+	3, 4, 51–53	<p>Most women with gestational diabetes mellitus have a normal HbA<sub>1c</sub></p> <p>Need to test for gestational diabetes mellitus in future pregnancy</p> <p>Might also indicate occult type 1 and type 2 diabetes</p>
<b>Maternal thyroid function</b>	Occult maternal thyroid disease	3	54, 55	TSH, FT4 and FT3
<b>Maternal thrombophilia screen</b>	Maternal thrombophilia	1++	56–58	<p><b>Indicated</b> if evidence of fetal growth restriction or placental disease</p> <p>The association between inherited thrombophilias and IUFD is weak, and management in future pregnancy is uncertain<sup>56,58</sup></p> <p>Most tests are not affected by pregnancy – if abnormal, repeat at 6 weeks</p> <p>Antiphospholipid screen repeated if abnormal</p>
<b>Anti-red cell antibody serology</b>	Immune haemolytic disease	3	59–62	<b>Indicated</b> if fetal hydrops evident clinically or on postmortem
<b>Maternal anti-Ro and anti-La antibodies</b>	Occult maternal autoimmune disease	3	63	<b>Indicated</b> if evidence of hydrops, endomyocardial fibro-elastosis or AV node calcification at postmortem
<b>Maternal alloimmune antiplatelet antibodies</b>	Alloimmune thrombocytopenia	3	64	<b>Indicated</b> if fetal intracranial haemorrhage found on postmortem

**Table 1 (continued).** Tests recommended for women with a late IUFD

Test	Reason(s) for test	Evidence level	Reference(s)	Additional comments
<b>Parental bloods for karyotype</b>	Parental balanced translocation Parental mosaicism	3	65–67	<b>Indicated if:</b> <ul style="list-style-type: none"> <li>● fetal unbalanced translocation</li> <li>● other fetal aneuploidy, e.g. 45X (Turner syndrome)</li> <li>● fetal genetic testing fails and history suggestive of aneuploidy (fetal abnormality on postmortem, previous unexplained IUFD, recurrent miscarriage)</li> </ul>
<b>Maternal urine for cocaine metabolites</b>	Occult drug use	1++	68	With consent, if history and/or presentation are suggestive
<b>Fetal and placental: microbiology</b> <ul style="list-style-type: none"> <li>● fetal blood</li> <li>● fetal swabs</li> <li>● placental swabs</li> </ul>	Fetal infections	2+ 3	33, 34, 69	More informative than maternal serology for detecting viral infections  Cord or cardiac blood (if possible) in lithium heparin  Written consent advisable for cardiac bloods  Need to be obtained using clean technique
<b>Fetal and placental tissues for karyotype (and possible single-gene testing):</b> <ul style="list-style-type: none"> <li>● deep fetal skin</li> <li>● fetal cartilage</li> <li>● placenta</li> </ul>	Aneuploidy Single gene disorders <b>See section 5.4 on sexing</b>	2+	70–74	<b>Absolutely contraindicated</b> if parents do not wish (written consent essential)  Send several specimens – cell cultures might fail  Culture bottles must be kept on labour ward in a refrigerator – stored separately from formalin preservation bottles  Genetic material should be stored if a single-gene syndrome is suspected
Postmortem examination: <ul style="list-style-type: none"> <li>● external</li> <li>● autopsy</li> <li>● microscopy</li> <li>● X-ray</li> <li>● placenta and cord</li> </ul>	<b>See section 5.6</b>		3, 4, 75, 76	<b>Absolutely contraindicated</b> if parents do not wish (written consent essential)  External examination should include weight and length measurement  IUGR is a significant association for late IUFD

Some tests should be taken before birth. Tests below the bold line are fetal. Shaded tests are selective.

AV = atrioventricular; CMV = cytomegalovirus; CRP = C-reactive protein; DIC = disseminated intravascular coagulation; FT3 = free triiodothyronine; FT4 = free thyroxin index; HbA1c = glycated haemoglobin; IUFD = intrauterine fetal death; IUGR = intrauterine growth restriction; RhD = rhesus D; TSH = thyroid-stimulating hormone

#### 5.4 What precautions should be taken when sexing the baby?

**Parents can be advised before birth about the potential difficulty in sexing the baby, when appropriate.**



**Two experienced healthcare practitioners (midwives, obstetricians, neonatologists or pathologists) should inspect the baby when examining the external genitalia of extremely preterm, severely macerated or grossly hydropic infants.**



**If there is any difficulty or doubt, rapid karyotyping should be offered using quantitative fluorescent polymerase chain reaction (QF-PCR) or fluorescence in situ hybridisation (FISH).**



Females can be mistaken for males, and vice versa. Errors in fetal sexing can result in severe emotional harm for parents. Some practitioners who have incorrectly determined the sex on external inspection probably had no doubt at the time. Extreme prematurity, maceration and hydrops can all make the diagnosis difficult. If the sex cannot be determined clinically or if there is any difficulty or

Evidence level 3



doubt, the genetic sex can be tested rapidly on skin (or placental) tissue, even of macerated babies.<sup>77</sup>

Evidence level 3

QF-PCR with additional Y chromosome markers can provide a highly accurate result within two working days in more than 99.9% of samples.<sup>78</sup> Sexing can also be performed rapidly and reliably by FISH.<sup>9</sup> If these techniques fail, sex can be determined on cell culture or at postmortem, but these methods can take longer.

Evidence level 2++ extrapolated from prenatal and level 2++

If the genital sex is not clear and the parents do not wish for postmortem testing in any form, they might wish to judge the sex themselves for registration purposes, perhaps based on an earlier scan, or ask the midwife or doctor to make a judgement. Other parents might choose not to sex the baby and give a neutral name. Stillborn babies can be registered as having indeterminate sex (see section 8.4).

### 5.5 *What is best practice guidance for cytogenetic analysis of the baby?*

**Written consent should be taken for any fetal samples used for karyotyping.**



**Samples from multiple tissues should be used to increase the chance of culture.**



**More than one cytogenetic technique should be available to maximise the chance of informative results.**



**Culture fluid should be stored in a refrigerator and thawed thoroughly before use.**



Karyotyping is important as about 6% of stillborn babies will have a chromosomal abnormality.<sup>80-82</sup>

Evidence level 3

Some abnormalities are potentially recurrent and can be tested for in future pregnancies. Culture potentially provides the greatest range of genetic information (trisomies, monosomies, translocations, major deletions and marker chromosomes). Microdeletions have to be requested specifically, usually according to the result of any postmortem examination. If all cultures fail, QF-PCR can be performed on extracted DNA.<sup>83,84</sup>

Evidence level 2+ extrapolated

Many laboratories are moving towards DNA-based methods for routine chromosome analysis, avoiding the need for cell culture. It is a reliable (<0.01% failure rate), efficient and cheap technique for detecting common aneuploidies.<sup>78</sup> It provides slightly less detailed limited genetic information and is unreliable for the detection of translocations and marker chromosomes.

Evidence level 2++ extrapolated

A range of tissue types can be used (see below), but all cell cultures can fail.<sup>71,85</sup>

Evidence level 3

Contamination with bacteria is an avoidable reason for failure to obtain results.<sup>78</sup>

Evidence level 2++ extrapolated

Culture fluid containing antibiotics can reduce this risk. Perinatal specimens suitable for karyotyping include skin, cartilage and placenta. Skin specimens are associated with a higher rate of culture failure (~60%), twice that of other tissues, including placenta. Placenta usually has the advantages of being the most viable tissue and of more rapid cell culture, but the disadvantages of maternal contamination and placental pseudomosaicism.<sup>86</sup> The next best is cartilage, e.g. patella, but cartilage is harder to sample.<sup>87</sup> Amniocentesis can also provide cytogenetic results if the mother chooses expectant management,<sup>1,71,73,74</sup> but patient acceptability and safety (infection) of amniocentesis has not been investigated in this setting.

Evidence level 3

Placental biopsy (approximately 1 cm diameter) should be taken from the fetal surface close to the cord insertion (to avoid tissue of maternal origin<sup>2</sup>). Skin biopsy should be deep to include underlying muscle<sup>2</sup> (about 1 cm in length from the upper fleshy part of the thigh). The skin can be closed with wound adhesive strips and tissue adhesives, but this is less successful when the baby is severely macerated.

5.6 *What is the guidance on perinatal postmortem examination for maternity clinicians?*

Parents should be offered full postmortem examination to help explain the cause of an IUD.

C

Parents should be advised that postmortem examination provides more information than other (less invasive) tests and this can sometimes be crucial to the management of future pregnancy.

C

Attempts to persuade parents to choose postmortem must be avoided; individual, cultural and religious beliefs must be respected.

✓

Written consent must be obtained for any invasive procedure on the baby including tissues taken for genetic analysis. Consent should be sought or directly supervised by an obstetrician or midwife trained in special consent issues and the nature of perinatal postmortem, including retention of any tissues for clinical investigation, research and teaching.

D

Parents should be offered a description of what happens during the procedure and the likely appearance of the baby afterwards. This should include information on how the baby is treated with dignity and any arrangements for transport. Discussions should be supplemented by the offer of a leaflet.

✓

Postmortem examination should include external examination with birth weight, histology of relevant tissues and skeletal X-rays.

✓

Pathological examination of the cord, membranes and placenta should be recommended whether or not postmortem examination of the baby is requested.

D

The examination should be undertaken by a specialist perinatal pathologist.

D

Parents who decline full postmortem might be offered a limited examination (sparing certain organs), but this is not straightforward and should be discussed with a perinatal pathologist before being offered.

✓

Less invasive methods such as needle biopsies can be offered, but these are much less informative and reliable than conventional postmortem.

D

Ultrasound and magnetic resonance imaging (MRI) should not yet be offered as a substitute for conventional postmortem.

D

MRI can be a useful adjunct to conventional postmortem.

D

It is essential to offer conventional postmortem examination to all parents but in a way that allows free choice; it is now agreed that the quality of the consent process is paramount and not the rate of uptake.<sup>2</sup>

The 8th CESDI report recommended that all practitioners who discuss postmortems with parents have a responsibility to understand the process so that consent is fully informed. It was also recommended that the consent form should include sections on the purpose of the postmortem; the extent of the examination; possible organ/tissue retention and purpose; what should happen to tissues/organ after postmortem; and research and education.<sup>5</sup>

Evidence level 4

Postmortem examination of the baby and placenta has the highest diagnostic yield of all investigations.<sup>69</sup> Postmortem examination might reveal the cause(s) and time of death, inform discussions of relevance to the risk of recurrence and provide information for any medico-legal proceedings.<sup>80-82</sup> A study of 1477 stillbirths demonstrated that autopsy alone provided a classification of death in 45.9% of cases. When combined with other diagnostic tests, it offered information relevant to recurrence risk in 40.1% of cases and to management of next pregnancy in 51%. Important information that affected management of next pregnancy was elicited in 10% of stillborn infants with no recognisable cause of death from other clinical or laboratory investigations.<sup>88</sup> In an analysis of 168 perinatal deaths, an autopsy was not requested in 26.2% and was uninformative in 24.2%. Of the 94 examinations that provided a conclusive autopsy, in 55.3% the pathological diagnosis confirmed the clinical diagnosis, but in 44.7% the findings changed or significantly added to it.<sup>89</sup>

Evidence level 3

Postmortem may also identify coincidental structural anomalies. About one-tenth of stillborn babies have congenital malformations, some of which are not related to the cause of death but can help plan future care.<sup>3,4</sup>

There are published standards for the conduct of perinatal autopsies. Autopsies must include external examination and measurement of the baby.<sup>2</sup>

Evidence level 4

Independently of full autopsy, placental pathology is useful and should be offered even if a post-mortem examination of the baby is declined. A retrospective review of 120 autopsy reports of stillborn babies and placentas showed that in 88% a major contributor to death was found in the placentas.<sup>76</sup>

Evidence level 3

More restricted conventional postmortem examinations can be undertaken, but these are of very limited value unless there is a specific question about the organs the parents will allow to be examined. Limited postmortems are technically difficult and run the risk that the pathologist can inadvertently fail to comply with parents' wishes. For example, if permission to examine the heart is given, the parents have to be aware that in order to do this not only the heart but also the thymus and lungs need to be removed from the baby's body.

Evidence level 4

Medical imaging can act as an adjunct to full postmortem, particularly of the brain and spinal cord. In one series, 100 stillborn babies underwent a postmortem MRI, limited to the brain and spinal cord. In 54, there was a complete agreement between the MRI and autopsy findings. In 24, the MRI added valuable information to the autopsy, but if MRI had been the only investigation, essential information would have been lost in 17% of the perinatal deaths.<sup>90</sup>

Evidence level 2+

X-rays can show skeletal defects that are difficult to identify or categorise on dissection.<sup>91</sup>

Evidence level 3

Some parents are less uncomfortable with the notion of noninvasive or minimally invasive testing. Clinically useful information might be obtained from less invasive methods including transcutaneous tissue biopsy, body-cavity aspiration and medical imaging, particularly whole-body X-ray.<sup>2</sup> Currently, these techniques, alone or in combination, are of limited availability, and are significantly less informative than conventional postmortem.<sup>2</sup>

Evidence level 4

MRI is currently being evaluated (MaRIAS trial) but is not yet suitable for clinical service. Ultrasound has been used to visualise fetal brain, cardiac, lung and renal development when consent to autopsy has been withheld, but the use of ultrasound in such a context has not been subject to rigorous evaluation.<sup>92</sup>

Evidence level 3

## 6. Labour and birth

### 6.1 What are the recommendations for timing and mode of birth?

Recommendations about labour and birth should take into account the mother's preferences as well as her medical condition and previous intrapartum history.

C

Women should be strongly advised to take immediate steps towards delivery if there is sepsis, pre-eclampsia, placental abruption or membrane rupture, but a more flexible approach can be discussed if these factors are not present.

D

Well women with intact membranes and no laboratory evidence of DIC should be advised that they are unlikely to come to physical harm if they delay labour for a short period, but they may develop severe medical complications and suffer greater anxiety with prolonged intervals. Women who delay labour for periods longer than 48 hours should be advised to have testing for DIC twice weekly (Table 1).

D

If a woman returns home before labour, she should be given a 24-hour contact number for information and support.

✓

Women contemplating prolonged expectant management should be advised that the value of postmortem may be reduced.

D

Women contemplating prolonged expectant management should be advised that the appearance of the baby may deteriorate.

✓

Vaginal birth is the recommended mode of delivery for most women, but caesarean birth will need to be considered with some.

✓

More than 85% of women with an IUD labour spontaneously within three weeks of diagnosis.<sup>93,94</sup> If the woman is physically well, her membranes are intact and there is no evidence of pre-eclampsia, infection or bleeding, the risk of expectant management for 48 hours is low.<sup>95-96</sup> There is a 10% chance of maternal DIC within 4 weeks from the date of fetal death and an increasing chance thereafter.<sup>19</sup>

Evidence level 3

A Swedish study of 380 women with stillbirth and 379 controls with a live healthy child showed that an interval of 24 hours or more from the diagnosis of death in utero to the start of labour was associated with an increased risk of moderately severe anxiety or worse (OR 4.8, 95% CI 1.5-15.9).<sup>97</sup>

Vaginal birth can be achieved within 24 hours of induction of labour for IUD in about 90% of women.<sup>98</sup> Vaginal birth carries the potential advantages of immediate recovery and quicker return to home. Caesarean birth might occasionally be clinically indicated by virtue of maternal condition. The woman herself might request caesarean section because of previous experiences or a wish to avoid vaginal birth of a dead baby. Vaginal birth was described as emotionally distressing by 47% of 314 women with an intrauterine death compared with just 7% of 322 matched controls.<sup>18</sup>

Evidence level 2+

This demands a careful and sensitive discussion and joint decision making. The implications of caesarean delivery for future childbearing should be discussed.<sup>99</sup>

### 6.2 How should labour be induced for a woman with an unscarred uterus?

A combination of mifepristone and a prostaglandin preparation should usually be recommended as the first-line intervention for induction of labour.

D

**Misoprostol can be used in preference to prostaglandin E2 because of equivalent safety and efficacy with lower cost but at doses lower than those currently marketed in the UK.**

**B**

**Women should be advised that vaginal misoprostol is as effective as oral therapy but associated with fewer adverse effects.**

**A**

In a study of a case series of 96 women with a late IUD, the combination of mifepristone and misoprostol gave an average duration of labour of 8 hours. The addition of mifepristone appeared to reduce the time interval by about 7 hours compared with published regimens not including mifepristone, but there was no other apparent benefit.<sup>98</sup>

Evidence level 3

A single 200 mg dose of mifepristone is appropriate for this indication.

A randomised controlled trial comparing intravenous oxytocin alone with intravaginal misoprostol (a prostaglandin E1 analogue) for induction of labour in women with an IUD showed that misoprostol was more effective.<sup>100</sup>

Evidence level 1+

Two randomised controlled trials comparing prostaglandin E2 with low-dose misoprostol for women with a live fetus found misoprostol to be efficacious in cervical ripening and labour induction. The studies demonstrated a similar maternal safety profile for both groups.<sup>101,102</sup>

Evidence level 1+ extrapolated

For third- (and second-) trimester IUD, a systematic review found that vaginal misoprostol for induction of labour appears equally effective as gemeprost but is much cheaper.<sup>103</sup>

Evidence level 1+

The average cost per treatment is also much lower for misoprostol than for prostaglandin E2.<sup>102,104</sup>

Evidence level 1+ extrapolated

The use of misoprostol for induction of labour in women with IUD has been endorsed by NICE.<sup>94</sup> NICE recommended that the choice and dose of vaginal prostaglandins should 'take into account the clinical circumstances, availability of preparations and local protocols'. A review of misoprostol use for late IUD recommended that the dose should be adjusted according to gestational age (100 micrograms 6-hourly before 26<sup>+6</sup> weeks, 25-50 micrograms 4-hourly at 27<sup>+0</sup> weeks or more, up to 24 hours).<sup>105</sup>

Evidence level 3

Misoprostol use in pregnancy is off-label in the UK,<sup>106</sup> and the doses used in these studies are not currently marketed in Britain. Two phase III trials have recently been completed for lower-dose formulations for induction of labour.<sup>101,102</sup> The current 200 microgram tablet can be divided in half by pharmacists or dissolved in water and administered as measured aliquots.<sup>107</sup>

Two randomised controlled trials compared oral and vaginal misoprostol. In the first, the mean induction to birth interval was shorter with vaginal use by 7.9 hours ( $P < 0.05$ ) and there was a reduced need for oxytocin augmentation.<sup>108</sup> In the other, there was no difference in mean induction to birth interval for gestations of more than 28 weeks.<sup>109</sup> In both studies the systemic adverse effects (diarrhoea, vomiting, shivering and pyrexia) were more common with oral misoprostol.

Evidence level 1+

*6.3 What is best practice for induction of labour for a woman with a history of lower segment caesarean section (LSCS)?*

**A discussion of the safety and benefits of induction of labour should be undertaken by a consultant obstetrician.**

**D**

**Mifepristone can be used alone to increase the chance of labour significantly within 72 hours (avoiding the use of prostaglandin).**

**A**

**Mechanical methods for induction of labour in women with an IUD should be used only in the context of a clinical trial.**

A

**Women with a single lower segment scar should be advised that, in general, induction of labour with prostaglandin is safe but not without risk.**

C

**Misoprostol can be safely used for induction of labour in women with a single previous LSCS and an IUD but with lower doses than those marketed in the UK.**

C

**Women with two previous LSCS should be advised that in general the absolute risk of induction of labour with prostaglandin is only a little higher than for women with a single previous LSCS.**

C

**Women with more than two LSCS deliveries or atypical scars should be advised that the safety of induction of labour is unknown.**

D

A randomised controlled trial of oral mifepristone alone (200 mg three times a day for 2 days) was compared with placebo in women with an IUD. Labour occurred within 72 hours in significantly more women in the mifepristone group (63% versus 17%,  $P < 0.001$ ).<sup>110</sup>

Evidence level 1+

Use of mifepristone in this context is off-label.<sup>106</sup> Mifepristone 600 mg once daily for 2 days can also be used.<sup>106</sup>

Evidence level 4

A transcervical balloon catheter technique was used to induce labour for a small series of 37 women with a live fetus and an unfavourable cervix who had previously undergone a caesarean section. There were no complications and 79% achieved vaginal birth.<sup>111</sup>

Evidence level 3

In another large retrospective study of women with one previous caesarean section, induction of labour with mechanical methods resulted in uterine rupture rates (5 in 862, 0.58%) that were significantly lower than with prostaglandins (18 in 1130, 1.59%) and similar to spontaneous labour (51 in 9239, 0.55%).<sup>112</sup>

Evidence level 2+

Mechanical methods of induction might increase the risk of ascending infection in the presence of IUD.<sup>113</sup>

Evidence level 1++

No studies were found on the safety and effectiveness of induction of labour after IUD in women with a single caesarean section scar. In general maternity care, the RCOG Green-top Guideline on VBAC recommends that women should be informed that there is a higher risk of uterine rupture with induction of labour with prostaglandins.<sup>114</sup> The more frequent serious risks of induction of labour with VBAC relate to the fetus, however. In the National Institute of Child Health (NICH) study of 17 898 women with a live fetus undergoing VBAC, the maternal morbidity associated with VBAC (including induced and augmented labours) was a higher risk of endometritis (OR 1.62, CI 1.40–1.87), blood transfusion (OR 1.71, CI 1.41–2.08) and scar dehiscence/rupture (0.7%). There was no evidence of an increased rate of hysterectomy or maternal death. Of a subset of 4708 women who had had labour induced, 48 had scar problems (1%).<sup>115</sup>

Evidence level 2++

The Society of Obstetricians and Gynaecologists of Canada recommended that misoprostol is contraindicated in women with previous caesarean delivery because of a high rate of uterine rupture.<sup>116</sup> A more recent narrative review of induction of labour for late IUD concluded that misoprostol can be used safely at lower doses for women with a previous caesarean (25–50 micrograms).<sup>105</sup>

Evidence level 4

Misoprostol is off-label for this indication, however, and is not currently marketed in the UK at the doses recommended. These lower doses can be prepared in-house by dissolving a 200 microgram tablet in water.<sup>107</sup>

No studies were found on the safety of induction of labour in women with two caesarean births and IUFD. A retrospective cohort database study of 3970 women with a live fetus and two previous LSCS compared outcome with those for 20 175 women who had undergone a single procedure. Thirty percent of labours were induced in both groups. The chance of successful vaginal birth was almost identical (~75%). The chance of major maternal morbidity, including rupture, was higher in the multiple LSCS group, but the absolute risk remained low: 3.23% overall (rupture 1.8%) versus 2.12% overall (rupture 0.9%, adjusted OR 1.61, 95% CI 1.11–2.33).<sup>117</sup>

Evidence level 2++

Another retrospective multicentre study of 975 women with two previous LSCS and 16 915 with one LSCS reported similar results: uterine rupture rates of 0.9% versus 0.7% ( $P=0.37$ ), hysterectomy 0.6% versus 0.2% ( $P=0.23$ ) and transfusion 3.2% versus 1.6% ( $P<0.001$ ). Induction of labour (all types combined) was a significant risk factor for rupture (1% rate for induction versus 0.7–0.9% overall; OR 1.78, 95% CI 1.24–2.56 in univariate analysis; OR 2.71–2.8, 95% CI 1.56–5.22 in multivariate models).<sup>118</sup>

No studies were found into the safety of induction of labour in women with three or more caesarean sections and IUFD. VBAC is not ordinarily recommended for women with three previous caesarean sections, previous uterine rupture or upper segment incisions.<sup>114</sup>

Evidence level 4

In a prospective study of 89 women who attempted VBAC after three or more caesareans, including 29 inductions of labour, there were no cases of uterine rupture or of major maternal morbidity, but the upper 95% confidence interval for zero incidence extends to 4% (calculated by guideline developers).<sup>119</sup>

Evidence level 2+

No data were found on the maternal safety of VBAC with an IUFD in the presence of atypical uterine scars.

#### 6.4 *What are considered suitable facilities for labour?*

**Women should be advised to labour in an environment that provides appropriate facilities for emergency care according to their individual circumstances.**



**Maternity units should aim to develop a special labour ward room for well women with an otherwise uncomplicated IUFD that pays special heed to emotional and practical needs without compromising safety. This can include a double bed for her partner or other companion to share, away from the sounds of other women and babies.**



**Care in labour should be given by an experienced midwife.**



The physical priorities of women with an IUFD vary greatly according to their individual clinical findings.

#### 6.5 *What are the recommendations for intrapartum antimicrobial therapy?*

**Women with sepsis should be treated with intravenous broad-spectrum antibiotic therapy (including antichlamydial agents).**



**Routine antibiotic prophylaxis should not be used.**



**Intrapartum antibiotic prophylaxis for women colonised with group B streptococcus is not indicated.**



Infection is a common association of late IUD and the mother can develop severe sepsis from a wide range of bacteria, including severe systemic chlamydial infection.<sup>120</sup> Regardless of the primary cause of death, the fetus can act as a focus for severe secondary sepsis, including gas-forming clostridial species, which can result in severe DIC.<sup>121,122</sup> In one study, 3.1% of women with an IUD developed signs of sepsis during induction of labour.<sup>98</sup>

Evidence level 3

It has been suggested that artificial rupture of membranes may facilitate ascending infection, but no studies were found on this aspect of care. It should be remembered that prostaglandins, given to induce labour, are associated with pyrexia.<sup>123</sup>

Evidence level 1+

No studies were found on routine intrapartum antibiotic prophylaxis in this specific circumstance.

No studies were found on the use of antibiotics for the prevention of maternal infection in women with a late IUD. Intrapartum antibiotic prophylaxis for carriers of group B streptococcus is primarily intended to reduce the risk of neonatal infection. A large prospective study of group B streptococcus carriers in the USA showed that 2.0% of women developed postpartum endometritis.<sup>124</sup>

Evidence level 3

### 6.6 Are there any special recommendations for pain relief in labour?

**Diamorphine should be used in preference to pethidine.**

D

**Regional anaesthesia should be available for women with an IUD.**

D

**Assessment for DIC and sepsis should be undertaken before administering regional anaesthesia.**

D

**Women should be offered an opportunity to meet with an obstetric anaesthetist.**



Analgesia is particularly important for women with an IUD. A study of 314 women with an IUD and 322 with a live fetus revealed that labour and delivery were assessed as physically insufferably hard by 17% of the affected women compared with 10% of controls. Analgesia was more frequently used during labour for stillbirth.<sup>18</sup>

Evidence level 2+

All usual modalities should be available including regional anaesthesia and patient-controlled anaesthesia. Diamorphine and morphine have greater analgesic qualities and longer duration of action than pethidine. They were rated more highly by labouring women in the National Birthday Study.<sup>125</sup> DIC increases the chance of subdural and epidural haematomata with regional anaesthesia.<sup>126,127</sup>

Evidence level 3

Maternal sepsis can result in epidural abscess formation.

### 6.7 What are the recommendations for women labouring with a scarred uterus?

**Women undergoing VBAC should be closely monitored for features of scar rupture.**

D

**Oxytocin augmentation can be used for VBAC, but the decision should be made by a consultant obstetrician.**

B

Fetal heart rate abnormality, usually the most common early sign of scar dehiscence, does not apply in this circumstance. Other clinical features include maternal tachycardia, atypical pain, vaginal bleeding, haematuria on catheter specimen and maternal collapse.<sup>114</sup>

Evidence level 4

No studies were found into the safety and effectiveness of oxytocin augmentation in VBAC with IUD. Women with previous caesarean section and a live fetus who need augmentation of labour have a 73.9% of achieving vaginal delivery.<sup>128</sup>

Evidence level 2++



The RCOG Green-top Guideline on VBAC recommends that the decision to augment with oxytocin should be discussed with a consultant.<sup>114</sup>

Evidence  
level 4

## 7. Puerperium

### 7.1 Where should women receive care before returning home?

**Women should be cared for in an environment that provides adequate safety according to individual clinical circumstance.**



**Women with no critical care needs should ideally be able to choose between facilities which provide adequate privacy.**



Some women have acute medical problems after birth, e.g. sepsis, pre-eclampsia, etc., with continuing critical care needs. Women without acute medical issues who do not want to return home immediately might wish to receive care within the hospital but away from the maternity unit if such a facility is available.

### 7.2 What are the criteria for thromboprophylaxis?

**Women should be routinely assessed for thromboprophylaxis, but IUD is not a risk factor.**



**Heparin thromboprophylaxis should be discussed with a haematologist if the woman has DIC.**



Established guidelines should be followed for thromboprophylaxis.<sup>129</sup> Given the association of late IUD with obesity, advanced maternal age, infection and maternal disease,<sup>3,4,6,130,131</sup> it is likely that many women with an IUD fall into the moderate- or high-risk categories.

### 7.3 What are the options for suppression of lactation?

**Women should be advised that almost one-third of those that choose nonpharmacological measures are troubled by excessive discomfort.**



**Women should be advised that dopamine agonists successfully suppress lactation in a very high proportion of women and are well tolerated by a very large majority; cabergoline is superior to bromocriptine.**



**Dopamine agonists should not be given to women with hypertension or pre-eclampsia.**



**Estrogens should not be used to suppress lactation.**



Suppression of lactation is of psychological importance for some women following IUD. Up to one-third of women who use simple measures such as a support brassière, ice packs and analgesics experience severe breast pain.<sup>132</sup>

Evidence  
level 1++

A placebo-controlled randomised controlled trial showed that bromocriptine inhibited lactation in more than 90% of women with few adverse effects.<sup>133</sup> A second randomised controlled trial found bromocriptine to be significantly more effective than breast binders.<sup>134</sup>

Evidence  
level 1+

A double-blind randomised controlled trial of 272 women requesting lactation suppression compared a single dose of cabergoline (1 mg) with bromocriptine (2.5 mg twice daily) for 14 days. The two regimens had very similar effectiveness, but cabergoline was simpler to use and had significantly lower rates of rebound breast activity and adverse events.<sup>135</sup>

Evidence  
level 1++

Dopamine agonists are contraindicated in women with hypertension or pre-eclampsia.<sup>136</sup> They can increase blood pressure and have been associated with intracerebral haemorrhage.<sup>137</sup> Estrogen is of unproven benefit for lactation suppression and it increases thromboembolic risk.<sup>138</sup>

Evidence level 3

#### 7.4 *Who should be informed of events?*

**All key staff responsible for care of the woman during pregnancy and afterwards should be informed of events.**



**All existing appointments should be cancelled – maternity units should keep a list of likely departments that need to be contacted.**



All key staff groups must be informed to ensure cancellation of existing appointments and continuity of follow-up. This includes the community midwives, health visitor, antenatal class coordinator and general practitioner. Other existing carers such as psychiatrists, secondary care specialists and drug workers should also be contacted. It should also include voluntary groups who distribute free items to new mothers, but specific details should not be released to maintain confidentiality. Appointments for antenatal clinics (hospital and community), ultrasound scans and preoperative assessment should be cancelled.

## 8. Psychological and social aspects of care

### 8.1 *What psychological problems can follow late IUF?*

**Carers must be alert to the fact that mothers, partners and children are all at risk of prolonged severe psychological reactions including post-traumatic stress disorder but that their reactions might be very different.**



Perinatal death is associated with increased rates of admission owing to postnatal depression.<sup>139</sup> Unresolved normal grief responses can evolve into post-traumatic stress disorder.<sup>140,141</sup> Women with poor social support are particularly vulnerable.<sup>142</sup>

Evidence level 3

Partners of women with an IUF can also suffer from severe grief responses, but the prevalence of such psychological disorders in partners is not precisely known. Men demonstrate less guilt, anxiety and depression than women themselves, but they can also develop post-traumatic stress disorder.<sup>143</sup> Discordant grief reactions between partners are more common after IUF than after neonatal death and this is a risk factor for prolonged and abnormal grief reactions.<sup>144</sup>

Evidence level 2+

Parental relationships have a 40% higher risk of dissolving after stillbirth compared with live birth.<sup>145</sup>

### 8.2 *What is best practice for use of interventions that might aid psychological recovery?*

**Carers should be aware of and responsive to possible variations in individual and cultural approaches to death.**



**Counselling should be offered to all women and their partners.**



**Other family members, especially existing children and grandparents, should also be considered for counselling.**



**Debriefing services must not care for women with symptoms of psychiatric disease in isolation.**



**Parents should be advised about support groups.**



**Bereavement officers should be appointed to coordinate services.**

**D**

Some parents develop prolonged psychological problems after stillbirth. This appears to be much more likely if professional support is not given,<sup>146</sup> but there is a paucity of evidence from randomised trials that address the benefits and pitfalls of psychological interventions after perinatal death.<sup>147</sup>

Evidence level 1+/1++

An interview survey of women after an IUD found that many wanted their carers to understand and acknowledge the nature of perinatal grief.<sup>148</sup>

Evidence level 2+

Guilt is a common emotion but is not necessarily voiced.<sup>149</sup> Carers should carefully seek to identify false assumptions made by parents and communicate these to counsellors.

Other members of the family can also be severely affected by bereavement. A 10-year study of 843 parents who experienced a stillbirth, newborn death or sudden unexpected death in infancy included extended family members; primarily grandparents, but also existing children. The most common response of grandparents was a profound need to protect their own child. The study found that grandparents need information on how they can help their children recover from their loss, how long grief lasts and the differences between men's and women's grief responses. Existing children often felt a need to help the family heal.<sup>150</sup>

Evidence level 3

Their grief responses are influenced by their ability to conceptualise death and their parents' responses.<sup>151</sup>

Evidence level 2+

Child-parent relationships can be adversely affected if the parents have great difficulty coping with their loss. Some parents wish to have guidance on how to explain the death to siblings and how to help them mourn.

Some UK maternity units have developed debriefing services for parents who have experienced traumatic events in relation to childbirth. One systematic review analysed eight random-allocation trials. There was no evidence of benefit in six studies and possible evidence of harm in a seventh. The authors emphasised the essential need to differentiate between parents who perceive their experience of childbirth as emotionally traumatic and those who develop symptoms of depression or post-traumatic stress disorder (for whom specific psychiatric treatment might be required).<sup>152</sup>

Evidence level 1+

Support groups, such as Sands (Stillbirth and neonatal death society), have been developed to offer help to both partners. In an observational study of 23 women who attended pregnancy loss groups, interviews showed that the primary focus for women was the need to seek recognition and acceptance of their grief.<sup>12</sup> The introduction of bereavement support officers has been shown to improve the management of perinatal loss.<sup>153</sup>

Evidence level 3

*8.3 What is the evidence for seeing, holding, naming and mementos?*

**Carers should avoid persuading parents to have contact with their stillborn baby, but should strongly support such desires when expressed.**

**C**

**Parents who are considering naming their baby should be advised that after registration a name cannot be entered at a later date, nor can it be changed.**



**If parents do decide to name their baby, carers should use the name, including at follow-up meetings.**



**Parents should be offered, but not persuaded, to retain artefacts of remembrance.**

**C**

Maternity units should have the facilities for producing photographs, palm and foot prints and locks of hair with presentation frames.



Verbal consent should be sought from the parents and information governance regulations should be complied with for clinical photography.



If the parents do not wish to have mementos, staff should offer to store them securely in the maternal case record for future access.



It should be explained that clothes on a macerated baby might become stained.



Many parents expressly wish to see and hold their baby.<sup>15</sup>

Evidence level 3

A study of 309 women found an overall beneficial effect, in terms of better sleep and less chance of getting a headache, after having a stillborn baby.<sup>154</sup>

However, another study showed that practices that actively promoted contact with the stillborn baby are associated with worse outcomes. Women who had held their stillborn baby were more depressed than those who only saw the baby, while those who did not see the baby were least likely to be depressed (39% versus 21% versus 6%,  $P=0.03$ ). Women who had seen their stillborn baby had greater anxiety ( $P=0.02$ ) and more symptoms of post-traumatic stress disorder than those who had not ( $P=0.02$ ), and their next-born babies were more likely to show disorganised attachment behaviour (42% versus 8%,  $P=0.04$ ).<sup>14</sup>

Evidence level 2+

Some parents may wish to name their baby, but others may decide not to do so. Either option is allowable in law, but once the stillbirth has been registered, names cannot be added or changed (Births and Deaths Registration Act 1953; amended by the Still-Birth (Definition) Act 1992).<sup>155</sup>

Keeping mementoes has not been associated with adverse outcomes,<sup>14</sup> and qualitative studies have shown that many parents value them highly.<sup>97,156</sup>

Evidence level 3

#### 8.4 What are the legal requirements for medical certification of stillbirth?

**Obstetricians and midwives should be aware of the law related to stillbirth.**



The following practice guidance is derived from statute and code of practice.

- Stillbirth must be medically certified by a fully registered doctor or midwife; the doctor or midwife must have been present at the birth or examined the baby after birth. (Statute)
- HM Coroner must be contacted if there is doubt about the status of a birth. (Statute)
- Police should be contacted if there is suspicion of deliberate action to cause stillbirth. (Statute)
- Fetal deaths delivered later than 24 weeks that had clearly occurred before the end of the 24th week do not have to be certified or registered. (Code of Practice)
- The baby can be registered as indeterminate sex awaiting further tests. (Code of Practice)
- The parents are responsible in law for registering the birth but can delegate the task to a healthcare professional. (Statute)

The current law on stillbirth registration is set out in the Births and Deaths Registration Act 1953 (amended by the Still-Birth (Definition) Act 1992).<sup>155</sup> The legal definition of stillbirth is: any child expelled or issued forth from its mother after the 24th week of pregnancy that did not breathe or show any other signs of life.

Legal advisors for the Department of Health and the Office for National Statistics have agreed that a fetus that is expelled after 24 weeks of pregnancy, provided it was no longer alive at the 24th week of pregnancy (this fact being either known or provable from the stage of development reached by the dead fetus), does not fall within

the category of births to be registered as a stillbirth under the above Acts. This interpretation is also accepted by the General Register Office for Scotland and the General Register Office for Northern Ireland.<sup>155</sup> When the gestational age is not known before the birth, with unbooked pregnancies for example, the decision about the status of the birth should be made on the basis of the stage of development of the baby on examination.

The doctor or midwife attending the stillbirth is required to issue a Medical Certificate of Stillbirth that enables the birth to be registered. The cause and sequence of medical events leading to the IUD should be given in as much detail as possible. Nonspecific terms such as anoxia, prematurity and so on should be avoided. Certification should not be delayed for the results of the postmortem.

The mother (or father if the couple were married at the time of birth) is responsible for registering the stillbirth, normally within 42 days (21 days in Scotland) but with a final limit of 3 months for exceptional circumstances. This responsibility can be delegated to health professionals, including a midwife or doctor present at the birth or a bereavement support officer. The person registering the birth has to be able to provide the following:

- the place and date of birth of the baby
- if the parents wish to name the baby, the name and surname
- the sex of the baby (but can be registered as indeterminate and later changed if tests show a clear result)
- the names, surnames, places of birth and occupations of the parents
- the mother's maiden name (if applicable)
- in Scotland, the marriage certificate of the parents is required.

The Registrar of Births will meet with the parents in private. The birth is entered onto the Stillbirth Register, which is separate from the standard Register of Births. The parents are then issued with a Certificate of Stillbirth and the documentation for burial or cremation. A certificate for cremation cannot be issued before the registration.

If the couple were not married at the time of the birth, the father's details can be added only if one of the following is fulfilled:

- the mother and father go to the register office and sign the stillbirth register together or
- where the father is unable to go to the register office with the mother, the father may make a statutory declaration acknowledging his paternity, which the mother must produce to the Registrar (this form can be obtained from any Registrar of Births) or
- where the mother is unable to go to the register office with the father, the mother might make a statutory declaration acknowledging the father's paternity, which the father must produce to the Registrar (this form can be obtained from any Registrar of Births).

If information about the father is not recorded initially, it is possible for the birth to be re-registered to include his details later.

Most local authorities have websites on the registering of stillbirth. There are no fees for registration, but additional certificates do carry a charge (£3.50 per copy as of January 2010).

HM Coroner does not normally have jurisdiction over stillbirth, even if the cause of death is not known, but contact should be made for an apparently fresh stillbirth not attended by a healthcare professional. HM Coroner also has discretion to be involved if the death followed a criminal act such as common assault and can then request for any postmortem to be expedited. Twenty-one stillbirths were referred to HM Coroner Services for England and Wales in 2007 and 13 in 2008. If there is suspicion of actions taken deliberately to cause a stillbirth, the police service should be contacted.

#### 8.5 *What are the recommendations for spiritual guidance, burial, cremation and remembrance?*

**Maternity units should have arrangements with elders of all common faiths and nonreligious spiritual organisations as a source of guidance and support for parents.**



The legal responsibility for the child's body rests with the parents but can be delegated to hospital services. C

Parents should be allowed to choose freely about attendance at a funeral service. C

A leaflet about the options should be available. ✓

Maternity units should provide a book of remembrance for parents, relatives and friends. ✓

Carers should offer parents the option of leaving toys, pictures and messages in the coffin. ✓

Parents might wish to seek guidance from a spiritual leader or religious elder. Funeral options including burial and cremation should be discussed with parents, taking into account religious and cultural considerations. Practical issues should be discussed with the parents, at a time and to an extent that suits them.

Having a funeral service for the infant was associated with slower resolution of women's psychological distress in one study.<sup>157</sup> Evidence level 2+

An observational study found that most women appreciate rapid arrangements for the funeral or cremation.<sup>158</sup> Evidence level 3

Some parents choose to leave messages, toys and photographs in the coffin.

If the parents request cremation they have to complete Cremation Form 3 (application for cremation of remains of a stillborn child). Together with a copy of the Stillbirth Certificate (known also as Cremation Form 9), they submit CF3 to the Medical Referee, who issues Cremation Form 10 (authorisation to cremate a stillborn child). Cremation Form 2 is the equivalent of CF3 for retained body parts of a stillborn child when the body has already been cremated.

### 8.6 *What advice should be given about fertility?*

**Information about fertility and contraception should be offered to mothers before returning home.** C

Mothers are vulnerable to psychological disorders when conception occurs soon after the loss.<sup>141,143</sup> With suppression of lactation, ovulation returns more quickly. This can be as early as day 18.<sup>159</sup> Evidence level 2+

Some women might not be aware that they might conceive before their first menstrual period.

## 9. Follow-up

### 9.1 *What are the options for follow-up meetings?*

**The wishes of the woman and her partner should be considered when arranging follow-up.** ✓

**Before the visit, it is essential to ensure that all available results are readily to hand.** ✓

There is no evidence to support home visits over clinic follow-up, or to indicate the optimum timing and frequency of such appointments, but it is recognised that some parents find it very distressing to return to the unit where their baby was stillborn. If practicable, the option of home visits should be offered to parents. Office consultation has the potential advantages over clinic follow-up of preventing waits and allowing flexible duration. Six to eight weeks is common practice for the timing of the appointment, when the placental and the postmortem histology results usually become available, but a flexible approach is appropriate according to the needs of the parents and the range of tests performed.

## 9.2 What are the recommendations for the content of the follow-up appointment?

**Parents should be advised about the cause of late IUFD, chance of recurrence and any specific means of preventing further loss.**



**Women should be offered general prepregnancy advice, including support for smoking cessation.**



**Women should be advised to avoid weight gain if they are already overweight (body mass index over 25) and to consider weight loss.**



**An offer should be made to discuss the potential benefit of delaying conception until severe psychological issues have been resolved.**



**Carers should be aware that while mothers tend to experience greater anxiety when conception occurs soon after a fetal loss, partners are more likely to suffer anxiety if conception is delayed.**



**Parents can be advised that the absolute chance of adverse events with a pregnancy interval less than 6 months remains low and is unlikely to be significantly increased compared with conceiving later.**



**The meeting should be documented for the parents in a letter that includes an agreed outline plan for future pregnancy.**



Women might wish to keep a written log of questions and comments. Some women/couples might wish to use this to help set the agenda themselves at the start of the meeting. As well as an opportunity to ask about the physical and emotional wellbeing of the mother and her partner, the meeting allows parents time to discuss the results of tests and the likely cause of late IUFD. The meeting can also focus on the prognosis and options for future pregnancies. The discussion should cover general preparation for pregnancy: lifestyle, folic acid supplementation and rubella vaccination. Parents often desire an open, honest discussion with an opportunity to make comments and the chance to raise any concerns they might have. If care has been suboptimal, parents might want this to be acknowledged, lessons to be learned and care in the future to be improved.

Vulnerability to depression and anxiety in the next pregnancy is related to time since stillbirth, with more recently bereaved women at significantly greater risk than controls.<sup>160</sup> In contrast to mothers' vulnerability to psychological disorder when conception occurs soon after the loss, fathers tend to experience greater problems when pregnancy is delayed.<sup>161</sup>

Evidence level 2+

Two medium-sized studies focusing on women with previous stillbirth have not shown any association between inter-pregnancy interval and pregnancy outcome.<sup>162,163</sup>

Evidence level 2++

Recent larger studies and a meta-analysis<sup>164,165</sup> of the general maternity population suggested that there is a higher rate of adverse events with shorter inter-pregnancy intervals but the absolute risk remained low. Inter-pregnancy intervals shorter than 6 months were associated with increased risks of preterm birth, low birth weight and small-for-gestational-age babies (adjusted OR [95% CI] 1.40 [1.24-1.58], 1.61 [1.39-1.86] and 1.26 [1.18-1.33], respectively).<sup>164</sup>

Evidence level 1++ extrapolated

The odds ratio for stillbirth for women who smoke is 1.6 (95% CI 1.2-2.3). Women who stop smoking have equivalent stillbirth rates to women who have never smoked.<sup>166</sup>

Evidence level 2+

In two large studies, the odds ratio for stillbirth for women with a prepregnancy body mass index (BMI) over 30 kg/m<sup>2</sup> ranged from 1.4 to 2.6 (Evidence level 2+)<sup>131,167</sup> and in a systematic review it was 2.1-2.8.<sup>6</sup>

Evidence level 1++

Another study of 151 025 women, including 666 with stillbirth, showed that the risk of adverse outcomes in the next pregnancy increased linearly for women who gained three or more BMI units after birth compared with women whose BMI did not change by more than one unit between pregnancies. The increased risk included stillbirth for women with a BMI over 25 before the weight increase (OR 1.63, 95% CI 1.20–2.21).<sup>168</sup>

Evidence level 2++

## 10. Pregnancy following unexplained stillbirth

### 10.1 What recommendations should be made for pregnancy following unexplained late IUD?

**The history of stillbirth should be clearly marked in the case record and carers should ensure they read all the notes thoroughly before seeing the woman.**



**Women with a previous unexplained IUD should be recommended to have obstetric antenatal care.**



**Women with a previous unexplained IUD should be recommended to have screening for gestational diabetes.**



**For women in whom a normally formed stillborn baby had shown evidence of being small for gestational age, serial assessment of growth by ultrasound biometry should be recommended in subsequent pregnancies.**



Small studies<sup>169</sup> have shown no difference in stillbirth recurrence, but a large retrospective study of 947 women and 261 384 controls showed that women with a history of stillbirth (but otherwise low-risk) had a 12-fold increased risk of intrapartum stillbirth (95% CI 4.5–33.7).<sup>170</sup> A study that compared outcomes in the second pregnancy for 364 women with previous stillbirth versus 33 715 with previous live birth showed an increased risk of pre-eclampsia (OR 3.1, 95% CI 1.7–5.7) and placental abruption (OR 9.4, 95% CI 4.5–19.7).<sup>171</sup>

Evidence level 2+

Another study of 71 315 women showed that there was an increased risk of ischaemic placental disease (OR 1.6, 95% CI 1.2–2.1), fetal distress (OR 2.8, 95% CI 1.7–4.5), chorioamnionitis (OR 2.3, 95% CI 1.5–4.3), extreme preterm birth (OR 4.2, 95% CI 1.8–9.9) and early neonatal mortality (OR 8.3, 95% CI 3.7–18.6) in pregnancies after stillbirth versus pregnancies after live birth.<sup>162</sup>

Evidence level 2++

The increased risk was independent of recurrent maternal conditions and fetal congenital anomalies.<sup>172</sup>

An observational study of 316 consecutive pregnancies in women with a history of unexplained stillbirth revealed a rate of gestational diabetes four times higher than expected.<sup>173</sup> A significant proportion of unexplained IUDs are reclassified as fetal growth restriction when customised charts and different classification systems are used.<sup>20,21</sup>

Evidence level 2+

There are no prospective outcome studies of serial sonography in the next pregnancy after an IUD, but it is a prudent action that can provide reassurance to most women and partners. The optimum timing and frequency of scans are not known.

### 10.2 What recommendations should be made for the management of future delivery after unexplained stillbirth?

**Previous unexplained IUD is an indication to recommend birth at a specialist maternity unit.**



**Previous IUD related to a known nonrecurrent cause merits individual assessment for place of birth.**





**Maternal request for scheduled birth should take into account the gestational age of the previous IUFD, previous intrapartum history and the safety of induction of labour.**



A large retrospective study of 947 women after an IUFD and 261 384 controls showed that history of stillbirth conferred a greater risk of subsequent early IUFDs between 20 and 28 weeks (HR 10.3, 95% CI 6.1–17.2) than of late IUFDs (over 29 weeks) (HR 2.5, 95% CI 1.0–6.0).<sup>170</sup> There have been no studies that adequately tested fetal benefit from intervention by routine induction of labour. A study of intrapartum events in 364 pregnancies following unexplained stillbirth has shown higher rates for induction of labour (OR 3.2, 95% CI 2.4–4.2). This was associated with higher rates of instrumental delivery (OR 2.0, 95% CI 1.4–3.0) and emergency caesarean deliveries (OR 2.1, 95% CI 1.5–3.0) compared with controls.<sup>171</sup> Others have shown similar findings.<sup>173</sup>

Evidence level 2+

These complications were probably iatrogenic, the result of obstetric intervention.<sup>174</sup>

Evidence level 3

*10.3 What recommendations should be made for maternal care after the next birth?*

**Carers should be vigilant for postpartum depression in women with a previous IUFD.**



**Carers should be aware that maternal bonding can be adversely affected.**



The birth of a healthy baby does not compensate for a previous loss and can trigger a resurgence of grief; women might feel happy one moment and sad the next. Depression in the third trimester is highly predictive of depression one year after subsequent birth, particularly for women who conceive within less than 12 months from an IUFD.<sup>160</sup> Unresolved maternal grief may result in disorganisation of attachment with future babies.<sup>175</sup>

Evidence level 2+

## 11. Clinical governance

*11.1 Are there any risk management standards for IUFD?*

**Maternity units should be aware of specific standards for IUFD and stillbirth.**



National Health Service Litigation Authority risk management maternity standards include expectations for care specific to intrauterine death and stillbirth. These vary from edition to edition.

*11.2 What are the standards for documentation?*

**Standardised checklists can be used to ensure that all appropriate care options are offered and that the response to each is recorded.**



**Consent for perinatal postmortem examination should be documented using the nationally recommended form.**



**All stillbirths should be reviewed in a multiprofessional meeting using a standardised approach to analysis for substandard care and means of future prevention. Results of the discussion should be recorded in the mother's case record and discussed with the parents.**



**All stillbirths should be reported to the Centre for Maternal and Child Enquiries (CMACE).**



*11.3 Information leaflets*

All women (and partners) should be offered leaflets that provide information on the following issues:

- named carers
- local contact points

- postmortem - nature, benefits and choice
- expectations for physical recovery
- lactation suppression
- registering the birth including web addresses of local authority site
- details of national and local parent support groups, e.g. Sands
- guidance on fertility and contraception
- plan for follow-up.

#### 11.4 What is best practice for care of staff?

**A system should be in place to give clinical and psychological support for staff involved with an IUID.**



**Occupational Health should be contacted for advice if there are particular concerns about fitness to work.**



In a survey of 804 doctors' experiences and attitudes in dealing with perinatal death, 75% of respondents reported that caring for a patient with a stillbirth took a large emotional toll on them personally. Nearly one in ten obstetricians reported they had considered giving up obstetric practice because of the emotional difficulty in caring for a woman with a stillbirth. Talking informally with colleagues (87%) or friends/family (56%) had been the most common strategies used by doctors to cope. Confidentiality is important. Improved bereavement training can help staff care for grieving families but can also help staff cope with their own emotions.<sup>176</sup>

Evidence level 2+

#### 11.5 What are important auditable standards?

- Proportion of stillbirths reported as a clinical incident (requirement for the Clinical Negligence Scheme for Trusts).
- Completion of investigations for the cause of late IUID.
- Proportion of parents offered postmortem examination.
- Proportion of parents declining full postmortem who were offered alternative tests.
- Proportion of parents who have postmortem consent undertaken by an appropriately trained obstetrician or midwife.
- Proportion of women offered suppression of lactation.
- Proportion of women given fertility and contraceptive advice.
- Proportion of parents offered follow-up with a senior obstetrician.
- Proportion of women and families offered counselling follow-up.

#### 11.6 What are the important aspects of training?

- Seminars on the causes and care of late IUID.
- Skills training for the ultrasound diagnosis of late IUID.
- Training for discussions with parents about late IUID.
- Training on the postmortem examination, including consent.
- Additional training in IUID for bereavement counsellors.
- Quarterly multidisciplinary clinic-pathology meetings for critical analysis of stillbirths.
- Role play of follow-up appointments for obstetric trainees.

## 12. Future research

### 12.1 What are the recommendations for future research?

- The optimal system for classification of stillbirth.
- Safety and efficacy of methods for induction of labour with a previous caesarean section.
- The optimal dose of misoprostol for induction of labour according to gestational age.
- The diagnostic power and accuracy of MRI for postmortem investigation.
- The optimal psychological care of women and their partners.
- A comparison of hospital and home follow-up appointments.

## References

- Schott J, Henley A, Kohner N. *Pregnancy Loss and the Death of a Baby: Guidelines for professionals*. 3rd ed. London: Bosun Press, on behalf of Sands (stillbirth and neonatal death society); 2007.
- Royal College of Obstetricians and Gynaecologists and Royal College of Pathologists. *Fetal and perinatal pathology: Report of a Joint Working Party*. London: RCOG Press; 2001 [http://www.rcog.org.uk/files/rcog-corp/uploaded-files/WPRFetalPathology2001.pdf].
- Confidential Enquiry into Maternal and Child Health (CEMACH). *Perinatal Mortality 2007: United Kingdom*. CEMACH: London, 2009 [http://www.cmace.org.uk/getattachment/1d2c0ebc-d2aa-4131-98ed-56bf8269e529/Perinatal-Mortality-2007.aspx].
- Confidential Enquiry into Maternal and Child Health (CEMACH). *Perinatal Mortality 2006: England, Wales and Northern Ireland*. CEMACH: London, 2008 [http://www.cmace.org.uk/getattachment/4cc984be-9460-4cc7-91f1-532c9424f76e/Perinatal-Mortality-2006.aspx].
- Confidential Enquiry into Stillbirths and Deaths in Infancy. 8th Annual Report. London: Maternal and Child Health Research Consortium; 2001 [http://www.cmace.org.uk/getattachment/8ce7dc4e-6d7d-47cc-8cee-7c0867941606/8th-annual-report.aspx].
- Fretts RC. Etiology and prevention of stillbirth. *Am J Obstet Gynecol* 2005;193:1923-35.
- Harbour R, Miller J. A new system for grading recommendations in evidence based guidelines. *BMJ* 2001;323:334-6.
- Zeit RM. Sonographic demonstration of fetal death in the absence of radiographic abnormality. *Obstet Gynecol* 1976;48 1 Suppl:49S-52S.
- Weinstein BJ, Platt LD. The ultrasonic appearance of intravascular gas in fetal death. *J Ultrasound Med* 1983;2:451-4.
- McCully JG. Gas in the fetal joints: a sign of intrauterine death. *Obstet Gynecol* 1970;36:433-6.
- Lalor JG, Begley CM, Devane D. Exploring painful experiences: impact of emotional narratives on members of a qualitative research team. *J Adv Nurs* 2006;56:607-16.
- McCreight BS. Perinatal loss: a qualitative study in Northern Ireland. *Omega (Westport)* 2008;57:1-19.
- Buckman R. Communications and emotions. *BMJ* 2002;325:672.
- Hughes P, Turton P, Hopper E, Evans CD. Assessment of guidelines for good practice in psychosocial care of mothers after stillbirth: a cohort study. *Lancet* 2002;360:114-8.
- Rand CS, Kellner KR, Revak-Lutz R, Massey JK. Parental behavior after perinatal death: twelve years of observations. *J Psychosom Obstet Gynaecol* 1998;19:44-8.
- Fox R, Pillai M, Porter H, Gill G. The management of late fetal death: a guide to comprehensive care. *Br J Obstet Gynaecol* 1997;104:4-10.
- Lalor JG, Devane D, Begley CM. Unexpected diagnosis of fetal abnormality: women's encounters with caregivers. *Birth* 2007;34:80-8.
- Rådestad I, Nordin C, Steineck G, Sjögren B. A comparison of women's memories of care during pregnancy, labour and delivery after stillbirth or live birth. *Midwifery* 1998;14:111-7.
- Parasnis H, Rajee B, Hinduja IN. Relevance of plasma fibrinogen estimation in obstetric complications. *J Postgrad Med* 1992;38:183-5.
- Vergani P, Cozzolino S, Pozzi E, Cuttin MS, Greco M, Ornaghi S, et al. Identifying the causes of stillbirth: a comparison of four classification systems. *Am J Obstet Gynecol* 2008;199:319.e1-4.
- Gardosi J, Kady SM, McGeown P, Francis A, Tonks A. Classification of stillbirth by relevant condition at death (ReCoDe): population based cohort study. *BMJ* 2005;331:1113-7.
- Flenady V, Frøen JF, Pinar H, Torabi R, Saastad E, Guyon G, et al. An evaluation of classification systems for stillbirth. *BMC Pregnancy Childbirth* 2009;9:24.
- Rees DC, Cox M, Clegg JB. World distribution of factor V Leiden. *Lancet* 1995;346:1133-4.
- Fox R. Preventing RhD haemolytic disease of the newborn. RhD negative women who have intrauterine death may need anti-D immunoglobulin. *BMJ* 1998;316:1164-5.
- Royal College of Obstetricians and Gynaecologists. Green-top Guideline No. 22. *Anti-D immunoglobulin for Rh prophylaxis*. London: RCOG; 2002 [http://www.rcog.org.uk/womens-health/clinical-guidance/use-anti-d-immunoglobulin-rh-prophylaxis-green-top-22].
- Lee D, Contreras M, Robson SC, Rodeck CH, Whittle MJ. Recommendations for the use of anti-D immunoglobulin for Rh prophylaxis. British Blood Transfusion Society and the Royal College of Obstetricians and Gynaecologists. *Transfus Med* 1999;9:93-7.
- The estimation of fetomaternal haemorrhage. BCSH Blood Transfusion and Haematology Task Forces. *Transfus Med* 1999;9:87-92.
- Finning K, Martin P, Daniels G. A clinical service in the UK to predict fetal Rh (Rhesus) D blood group using free fetal DNA in maternal plasma. *Ann NY Acad Sci* 2004;1022:119-23.
- Zhong XY, Steinborn A, Sohn C, Holzgreve W, Hahn S. High levels of circulatory erythroblasts and cell-free DNA prior to intrauterine fetal death. *Prenat Diagn* 2006;26:1272-3.
- Syridou G, Spanakis N, Konstantinidou A, Piperaki E, Kafetzis D, Patsouris E, et al. Detection of cytomegalovirus, parvovirus B19 and herpes simplex viruses in cases of intrauterine fetal death: association with pathological findings. *J Med Virol* 2008;80:1776-82.
- Zhang XM, Zhang RN, Lin SQ, Chen SX, Zheng LY. [Clinical analysis of 192 pregnant women infected by syphilis]. *Zhonghua Fu Chan Ke Za Zhi* 2004;39:682-6. Article in Chinese.
- Osman NB, Folgosa E, Gonzales C, Bergström S. Genital infections in the aetiology of late fetal death: an incident case-referent study. *J Trop Pediatr* 1995;41:258-66.
- Moyo SR, Hägerstrand I, Nyström L, Tswana SA, Blomberg J, Bergström S, et al. Stillbirths and intrauterine infection, histologic chorioamnionitis and microbiological findings. *Int J Gynaecol Obstet* 1996;54:115-23.
- Moyo SR, Tswana SA, Nyström L, Bergström S, Blomberg J, Ljungh A. Intrauterine death and infections during pregnancy. *Int J Gynaecol Obstet* 1995;51:211-8.
- Tolfvenstam T, Papadogiannakis N, Norbeck O, Petersson K, Broliden K. Frequency of human parvovirus B19 infection in intrauterine fetal death. *Lancet* 2001;357:1494-7.
- Smerdon WJ, Jones R, McLauchlin J, Reacher M. Surveillance of listeriosis in England and Wales, 1995-1999. *Commun Dis Public Health* 2001;4:188-93.
- Smith B, Kemp M, Ethelberg S, Schiellerup P, Bruun BG, Gerner-Smidt P, et al. *Listeria monocytogenes*: maternal-foetal infections in Denmark 1994-2005. *Scand J Infect Dis* 2009;41:21-5.
- Andrade JQ, Bunduki V, Curti SP, Figueiredo CA, de Oliveira MI, Zugaib M. Rubella in pregnancy: intrauterine transmission and perinatal outcome during a Brazilian epidemic. *J Clin Virol* 2006;35:285-91.
- Goldenberg RL, Thompson C. The infectious origins of stillbirth. *Am J Obstet Gynecol* 2003;189:861-73.
- Poespoprodjo JR, Fobia W, Kenangalem E, Lampah DA, Warikar N, Seal A, et al. Adverse pregnancy outcomes in an area where multidrug-resistant *Plasmodium vivax* and *Plasmodium falciparum* infections are endemic. *Clin Infect Dis* 2008;46:1374-81.
- Tolockiene E, Morsing E, Holst E, Herbst A, Ljungh A, Svenningsen N, et al. Intrauterine infection may be a major cause of stillbirth in Sweden. *Acta Obstet Gynecol Scand* 2001;80:511-8.
- Glantz A, Marschall HU, Mattsson LA. Intrahepatic cholestasis of pregnancy: Relationships between bile acid levels and fetal complication rates. *Hepatology* 2004;40:467-74.

43. Biankin SA, Arbuckle SM, Graf NS. Autopsy findings in a series of five cases of fetomaternal haemorrhages. *Pathology* 2003;35:319-24.
44. Thorp JM Jr, Katz VL, Fowler LJ, Kurtzman JT, Bowes WA Jr. Fetal death from chlamydial infection across intact amniotic membranes. *Am J Obstet Gynecol* 1989;161:1245-6.
45. Jain A, Nag VL, Goel MM, Chandrawati, Chaturvedi UC. Adverse foetal outcome in specific IgM positive Chlamydia trachomatis infection in pregnancy. *Indian J Med Res* 1991;94:420-3.
46. Benedetto C, Tibaldi C, Marozio L, Marini S, Masuelli G, Pelissetto S, et al. Cervicovaginal infections during pregnancy: epidemiological and microbiological aspects. *J Matern Fetal Neonatal Med* 2004;16 Suppl 2:9-12.
47. Blackwell S, Romero R, Chaiworapongsa T, Kim YM, Bujold E, Espinoza J, et al. Maternal and fetal inflammatory responses in unexplained fetal death. *J Matern Fetal Neonatal Med* 2003;14:151-7.
48. Syridou G, Skevaki C, Kafetzis DA. Intrauterine infection with parvovirus B19 and CMV: implications in early and late gestation fetal demise. *Expert Rev Anti Infect Ther* 2005;3:651-61.
49. Aberg A, Rydhström H, Källén B, Källén K. Impaired glucose tolerance during pregnancy is associated with increased fetal mortality in preceding sibs. *Acta Obstet Gynecol Scand* 1997;76:212-7.
50. Engel PJ, Smith R, Brinsmead MW, Bowe SJ, Clifton VL. Male sex and pre-existing diabetes are independent risk factors for stillbirth. *Aust N Z J Obstet Gynaecol* 2008;48:375-83.
51. Günter HH, Scharf A, Hertel H, Hillemanns P, Wenzlaff P, Maul H. [Perinatal morbidity in pregnancies of women with preconceptional and gestational diabetes mellitus in comparison with pregnancies of non-diabetic women. Results of the perinatal registry of Lower Saxony, Germany]. *Z Geburtshilfe Neonatol* 2006;210:200-7. Article in German.
52. Günter HH, Tzialidou I, Scharf A, Wenzlaff P, Maul H, Hillemanns P. [Intrauterine fetal death in pregnancies of women with preconceptional and gestational diabetes mellitus and of women without glucose tolerance disorders. Results of the perinatal registry of Lower Saxony, Germany]. *Z Geburtshilfe Neonatol* 2006;210:193-9. Article in German.
53. Keshavarz M, Cheung NW, Babae GR, Moghadam HK, Ajami ME, Shariati M. Gestational diabetes in Iran: incidence, risk factors and pregnancy outcomes. *Diabetes Res Clin Pract* 2005;69:279-86.
54. Cove DH, Johnston P. Fetal hyperthyroidism: experience of treatment in four siblings. *Lancet* 1985;1:430-2.
55. Allan WC, Haddow JE, Palomaki GE, Williams JR, Mitchell ML, Hermos RJ, et al. Maternal thyroid deficiency and pregnancy complications: implications for population screening. *J Med Screen* 2000;7:127-30.
56. Kist WJ, Janssen NG, Kalk JJ, Hague WM, Dekker GA, de Vries JJ. Thrombophilias and adverse pregnancy outcome - A confounded problem! *Thromb Haemost* 2008;99:77-85.
57. Gonen R, Lavi N, Attias D, Schliamser L, Borochowitz Z, Toubi E, et al. Absence of association of inherited thrombophilia with unexplained third trimester intrauterine fetal death. *Am J Obstet Gynecol* 2005;192:742-6.
58. Alfirevic Z, Roberts D, Martlew V. How strong is the association between maternal thrombophilia and adverse pregnancy outcome? A systematic review. *Eur J Obstet Gynecol Reprod Biol* 2002;101:6-14.
59. Wikman A, Edner A, Gryfelt G, Jonsson B, Henter JI. Fetal hemolytic anemia and intrauterine death caused by anti-M immunization. *Transfusion* 2007;47:911-7.
60. Furukawa K, Nakajima T, Kogure T, Yazaki K, Yoshida M, Fukaishi T, et al. Example of a woman with multiple intrauterine deaths due to anti-M who delivered a live child after plasmapheresis. *Exp Clin Immunogenet* 1993;10:161-7.
61. Cannon M, Pierce R, Taber EB, Schucker J. Fetal hydrops fetalis caused by anti-D in a mother with partial D. *Obstet Gynecol* 2003;102:1143-5.
62. Howard H, Martlew V, McFadyen I, Clarke C, Duguid J, Bromilow I, et al. Consequences for fetus and neonate of maternal red cell allo-immunisation. *Arch Dis Child Fetal Neonatal Ed* 1998;78:F62-6.
63. Nield LE, Silverman ED, Taylor GP, Smallhorn JF, Mullen JB, Silverman NH, et al. Maternal anti-Ro and anti-La antibody-associated endocardial fibroelastosis. *Circulation* 2002;105:843-8.
64. Kjeldsen-Kragh J, Killie MK, Tomter G, Golebiowska E, Randen I, Hauge R, et al. A screening and intervention program aimed to reduce mortality and serious morbidity associated with severe neonatal alloimmune thrombocytopenia. *Blood* 2007;110:833-9.
65. Pauli RM, Reiser CA. Wisconsin Stillbirth Service Program: II. Analysis of diagnoses and diagnostic categories in the first 1,000 referrals. *Am J Med Genet* 1994;50:135-3.
66. Tsenghi C, Metaxotou-Stavridaki C, Strataki-Benetou M, Kalpini-Mavrou A, Matsaniotis N. Chromosome studies in couples with repeated spontaneous abortions. *Obstet Gynecol* 1976;47:463-8.
67. Sikkema-Raddatz B, Bouman K, Verschuuren-Bemelmans CC, Stoepker M, Mantingh A, Beekhuis JR, et al. Four years' cytogenetic experience with the culture of chorionic villi. *Prenat Diagn* 2000;20:950-5.
68. Lutiger B, Graham K, Einarson TR, Koren G. Relationship between gestational cocaine use and pregnancy outcome: a meta-analysis. *Teratology* 1991;44:405-14.
69. Martinek IE, Vial Y, Hohlfield P. [Management of in utero foetal death: Which assessment to undertake?]. *J Gynecol Obstet Biol Reprod (Paris)* 2006;35:594-606. Article in French.
70. Thein AT, Abdel-Fattah SA, Kyle PM, Soothill PW. An assessment of the use of interphase FISH with chromosome specific probes as an alternative to cytogenetics in prenatal diagnosis. *Prenat Diagn* 2000;20:275-80.
71. Smith A, Bannatyne P, Russell P, Ellwood D, den Dulk G. Cytogenetic studies in perinatal death. *Aust N Z J Obstet Gynaecol* 1990;30:206-10.
72. Tabet AC, Aboura A, Dauge MC, Audibert F, Coulomb A, Batallan A, et al. Cytogenetic analysis of trophoblasts by comparative genomic hybridization in embryo-fetal development anomalies. *Prenat Diagn* 2001;21:613-8.
73. Saal HM, Rodis J, Weinbaum PJ, DiMaggio R, Landrey TM. Cytogenetic evaluation of fetal death: the role of amniocentesis. *Obstet Gynecol* 1987;70:601-3.
74. Khare M, Howarth E, Sadler J, Healey K, Konje JC. A comparison of prenatal versus postnatal karyotyping for the investigation of intrauterine fetal death after the first trimester of pregnancy. *Prenat Diagn* 2005;25:1192-5.
75. Heazell AE, Martindale EA. Can post-mortem examination of the placenta help determine the cause of stillbirth? *J Obstet Gynaecol* 2009;29:225-8.
76. Kidron D, Bernheim J, Aviram R. Placental findings contributing to fetal death, a study of 120 stillbirths between 23 and 40 weeks gestation. *Placenta* 2009;30:700-4.
77. Derom C, Vlietinck R, Derom R, Boklage C, Thiery M, Van den Berghe H. Genotyping of macerated stillborn fetuses. *Am J Obstet Gynecol* 1991;164:797-800.
78. Cirigliano V, Voglino G, Cañadas MP, Marongiu A, Ejarque M, Ordoñez E, et al. Rapid prenatal diagnosis of common chromosome aneuploidies by QF-PCR. Assessment on 18000 consecutive clinical samples. *Mol Hum Reprod* 2004;10:839-46.
79. Choolani M, Ho SS, Razvi K, Ponnusamy S, Baig S, Fisk NM, et al. FastFISH: technique for ultrarapid fluorescence in situ hybridization on uncultured amniocytes yielding results within 2 h of amniocentesis. *Mol Hum Reprod* 2007;13:355-9.
80. Genest DR. Estimating the time of death in stillborn fetuses: II. Histologic evaluation of the placenta; a study of 71 stillborns. *Obstet Gynecol* 1992;80:585-92.
81. Genest DR, Singer DB. Estimating the time of death in stillborn fetuses: III. External fetal examination; a study of 86 stillborns. *Obstet Gynecol* 1992;80:593-600.

82. Genest DR, Williams MA, Greene MF Estimating the time of death in stillborn fetuses: I. Histologic evaluation of fetal organs; an autopsy study of 150 stillborns. *Obstet Gynecol* 1992;80:575-84.
83. Diego-Alvarez D, Garcia-Hoyos M, Trujillo MJ, Gonzalez-Gonzalez C, Rodriguez de Alba M, Ayuso C, *et al.* Application of quantitative fluorescent PCR with short tandem repeat markers to the study of aneuploidies in spontaneous miscarriages. *Hum Reprod* 2005;20:1235-43.
84. Zou G, Zhang J, Li XW, He L, He G, Duan T. Quantitative fluorescent polymerase chain reaction to detect chromosomal anomalies in spontaneous abortion. *Int J Gynaecol Obstet* 2008;103:237-40.
85. Kyle PM, Coghlan P, Matthews J, de Ryke R, Reid R. Accuracy of prenatal diagnosis in a tertiary fetal medicine unit. *N Z Med J* 2009;122:50-61.
86. Schreck RR, Falik-Borenstein Z, Hirata G. Chromosomal mosaicism in chorionic villus sampling. *Clin Perinatol* 1990;17:867-88.
87. Gelman-Kohan Z, Rosensaft J, Ben-Hur H, Haber A, Chemke J. Cytogenetic analysis of fetal chondrocytes: a comparative study. *Prenat Diagn* 1996;16:165-8.
88. Michalski ST, Porter J, Pauli RM. Costs and consequences of comprehensive stillbirth assessment. *Am J Obstet Gynecol* 2002;186:1027-34.
89. Saller DN Jr, Lesser KB, Harrel U, Rogers BB, Oyer CE. The clinical utility of the perinatal autopsy. *JAMA* 1995;273:663-5.
90. Cohen MC, Paley MN, Griffiths PD, Whitby EH. Less invasive autopsy: benefits and limitations of the use of magnetic resonance imaging in the perinatal postmortem. *Pediatr Dev Pathol* 2008;11:1-9.
91. Cernach MC, Patricio FR, Galera MF, Moron AF, Brunoni D. Evaluation of a protocol for postmortem examination of stillbirths and neonatal deaths with congenital anomalies. *Pediatr Dev Pathol* 2004;7:335-41.
92. Furness ME, Weckert RC, Parker SA, Knowles S. Ultrasound in the perinatal necropsy. *J Med Genet* 1989;26:368-72.
93. Goldstein DP, Reid DE. Circulating fibrinolytic activity - a precursor of hypofibrinogenemia following fetal death in utero. *Obstet Gynecol* 1963;22:174-80.
94. National Institute for Health and Clinical Excellence. Clinical guideline no. 70: *Induction of labour*. London: National Institute for Health and Clinical Excellence; 2008 [http://www.nice.org.uk/nicemedia/pdf/CG070NICEGuideline.pdf].
95. Silver RM. Fetal death. *Obstet Gynecol* 2007;109:153-67.
96. Goldstein DP, Johnson JP, Reid DE. Management of intrauterine fetal death. *Obstet Gynecol* 1963;21:523-9.
97. Rådestad I, Steineck G, Nordin C, Sjögren B. Psychological complications after stillbirth - influence of memories and immediate management: population based study. *BMJ* 1996;312:1505-8.
98. Wagaarachchi PT, Ashok PW, Narvekar NN, Smith NC, Templeton A. Medical management of late intrauterine death using a combination of mifepristone and misoprostol. *BJOG* 2002;109:443-7.
99. National Collaborating Centre for Women's and Children's Health. Clinical guideline: *Caesarean section*. London: RCOG Press; 2004 [http://www.gserver.nice.org.uk/nicemedia/pdf/CG013fullguideline.pdf].
100. Nakintu N.A comparative study of vaginal misoprostol and intravenous oxytocin for induction of labour in women with intra uterine fetal death in Mulago Hospital, Uganda. *Afr Health Sci* 2001;1:55-9.
101. Calder AA, Loughney AD, Weir CJ, Barber JW. Induction of labour in nulliparous and multiparous women: a UK, multicentre, open-label study of intravaginal misoprostol in comparison with dinoprostone. *BJOG* 2008;115:1279-88.
102. Prager M, Eneroth-Grimfors E, Edlund M, Marions L.A randomised controlled trial of intravaginal dinoprostone, intravaginal misoprostol and transcervical balloon catheter for labour induction. *BJOG* 2008;115:1443-50.
103. Dodd JM, Crowther CA. Misoprostol versus cervagem for the induction of labour to terminate pregnancy in the second and third trimester: a systematic review. *Eur J Obstet Gynecol Reprod Biol* 2006;125:3-8.
104. Jain JK, Mishell DR Jr. A comparison of intravaginal misoprostol with prostaglandin E2 for termination of second-trimester pregnancy. *N Engl J Med* 1994;331:290-3.
105. Gómez Ponce de León R, Wing D, Fiala C. Misoprostol for intrauterine fetal death. *Int J Gynaecol Obstet* 2007;99 Suppl 2:S190-S193.
106. British Medical Association and Royal Pharmaceutical Society of Great Britain. *British National Formulary (BNF) 58*. London: BMJ Publishing Group Ltd and RPS Publishing; 2009.
107. How to dilute 200 mcg of misoprostol in 200ml water. In: Weeks A, Fiala C, editors. *Misoprostol in Obstetrics and Gynaecology*. 2010 [http://misoprostol.org/File/about.php].
108. Nyende L, Towobola OA, Mabina MH. Comparison of vaginal and oral misoprostol, for the induction of labour in women with intra-uterine foetal death. *East Afr Med J* 2004;81:179-82.
109. Chittacharoen A, Herabutya Y, Punyavachira P.A randomized trial of oral and vaginal misoprostol to manage delivery in cases of fetal death. *Obstet Gynecol* 2003;101:70-3.
110. Cabrol D, Dubois C, Cronje H, Gonnet JM, Guillot M, Maria B, *et al.* Induction of labor with mifepristone (RU 486) in intrauterine fetal death. *Am J Obstet Gynecol* 1990;163:540-2.
111. Khotaba S, Volfson M, Tarazova L, Odeh M, Barenboym R, Fait V, *et al.* Induction of labor in women with previous cesarean section using the double balloon device. *Acta Obstet Gynecol Scand* 2001;80:1041-2.
112. Al-Zirqi I, Stray-Pedersen B, Forsén L, Vangen S. Uterine rupture after previous caesarean section. *BJOG* 2010;117:809-20.
113. Boulvain M, Kelly A, Lohse C, Stan CM, Irion O. Mechanical methods for induction of labour. *Cochrane Database Syst Rev* 2001;(4):CD001233. DOI: 10.1002/14651858.CD001233.
114. Royal College of Obstetricians and Gynaecologists. Green-top Guideline No. 45: *Birth after previous caesarean birth*. London: RCOG; 2007 [http://www.rcog.org.uk/files/rcog-corp/uploaded-files/GT45BirthAfterPreviousCaesarean.pdf].
115. Landon MB, Hauth JC, Leveno KJ, Spong CY, Leindecker S, Varner MW, *et al.* Maternal and perinatal outcomes associated with a trial of labor after prior cesarean delivery. *N Engl J Med* 2004;351:2581-9.
116. Society of Obstetricians and Gynaecologists of Canada. SOGC clinical practice guidelines. Guidelines for vaginal birth after previous caesarean birth. Number 155 (Replaces guideline number 147), February 2005. *Int J Gynaecol Obstet* 2005;89:319-31.
117. Macones GA, Cahill A, Pare E, Stamilio DM, Ratcliffe S, Stevens E, *et al.* Obstetric outcomes in women with two prior cesarean deliveries: is vaginal birth after cesarean delivery a viable option? *Am J Obstet Gynecol* 2005;192:1223-8, discussion 1228-9.
118. Landon MB, Spong CY, Thom E, Hauth JC, Bloom SL, Varner MW, *et al.* Risk of uterine rupture with a trial of labor in women with multiple and single prior cesarean delivery. *Obstet Gynecol* 2006;108:12-20.
119. Cahill AG, Tuuli M, Obido A, Stamilio D, Macones G. Vaginal birth after caesarean for women with three or more prior caesareans: assessing safety and success. *BJOG* 2010;117:422-7.
120. Flanagan PG, Westmoreland D, Stallard N, Stokes IM, Evans J. Ovine Chlamydiosis in pregnancy. *Br J Obstet Gynaecol* 1996;103:382-5.
121. Catanzarite V, Schibanoff JM, Chinn R, Mendoza A, Weiss R. Overwhelming maternal sepsis due to a gas-forming *Escherichia coli* chorioamnionitis. *Am J Perinatol* 1994;11:205-7.
122. Braun U, Bearth G, Dieth V, Corboz L. [A case of disseminated intravascular coagulation (DIC) in a cow with endometritis and fetal death]. *Schweiz Arch Tierbeilkd* 1990;132:239-45. Article in German.
123. Van Mensel K, Claerhout F, Debois P, Keirse MJ, Hanssens M. A randomized controlled trial of misoprostol and sulprostone to end pregnancy after fetal death. *Obstet Gynecol Int* 2009;2009:496320.


124. Krohn MA, Hillier SL, Baker CJ. Maternal peripartum complications associated with vaginal group B streptococci colonization. *J Infect Dis* 1999;179:1410-5.
125. Chamberlain G, Wraight A, Steer P, editors. *Pain and its relief in childbirth: the results of a national survey conducted by the National Birthday Trust*. Edinburgh: Churchill Livingstone; 1993.
126. Okuda Y, Kitajima T. Epidural hematoma in a parturient who developed disseminated intravascular coagulation after epidural anesthesia. *Reg Anesth Pain Med* 2001;26:383-4.
127. Lao TT, Halpern SH, MacDonald D, Huh C. Spinal subdural haematoma in a parturient after attempted epidural anaesthesia. *Can J Anaesth* 1993;40:340-5.
128. Landon MB, Leindecker S, Spong CY, Hauth JC, Bloom S, Varner MW, et al.; National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. The MFMU Cesarean Registry: factors affecting the success of trial of labor after previous cesarean delivery. *Am J Obstet Gynecol* 2005;193:1016-23.
129. Royal College of Obstetricians and Gynaecologists. Green-Top Guideline No. 37: *Reducing the risk of thrombosis and embolism during pregnancy and the puerperium*. London: RCOG; 2009 [http://www.rcog.org.uk/files/rcog-corp/GT37ReducingRiskThrombo.pdf].
130. Arendas K, Qiu Q, Gruslin A. Obesity in pregnancy: pre-conceptional to postpartum consequences. *J Obstet Gynaecol Can* 2008;30:477-88.
131. Kristensen J, Vestergaard M, Wisborg K, Kesmodel U, Secher NJ. Pre-pregnancy weight and the risk of stillbirth and neonatal death. *BJOG* 2005;112:403-8.
132. Spitz AM, Lee NC, Peterson HB. Treatment for lactation suppression: little progress in one hundred years. *Am J Obstet Gynecol* 1998;179:1485-90.
133. Bhardwaj N. Inhibition of puerperal lactation: evaluation of bromocriptine and placebo. *Aust N Z J Obstet Gynaecol* 1979;19:154-7.
134. Shapiro AG, Thomas L. Efficacy of bromocriptine versus breast binders as inhibitors of postpartum lactation. *South Med J* 1984;77:719-21.
135. Single dose cabergoline versus bromocriptine in inhibition of puerperal lactation: randomised, double blind, multicentre study. European Multicentre Study Group for Cabergoline in Lactation Inhibition. *BMJ* 1991;302:1367-71.
136. British Medical Association and Royal Pharmaceutical Society of Great Britain. *British National Formulary (BNF) 54*. London: BMJ Publishing Group Ltd and RPS Publishing; 2007.
137. Iffy L, Zito GE, Jakobovits AA, Ganesh V, McArdle JJ. Postpartum intracranial haemorrhage in normotensive users of bromocriptine for ab lactation. *Pharmacoepidemiol Drug Saf* 1998;7:167-71.
138. Niebyl JR, Bell WR, Schaaf ME, Blake DA, Dubin NH, King TM. The effect of chlorotrianisene as postpartum lactation suppression on blood coagulation factors. *Am J Obstet Gynecol* 1979;134:518-22.
139. National Institute for Health and Clinical Excellence. NICE clinical guideline 45: *Antenatal and postnatal mental health. Clinical management and service guidance*. London: NICE; 2007 [http://www.nice.org.uk/nicemedia/pdf/CG045NICEGuidelineCorrected.pdf].
140. Hughes P, Turton P, McGauley GA, Fonagy P. Factors that predict infant disorganization in mothers classified as U in pregnancy. *Attach Hum Dev* 2006;8:113-22.
141. Turton P, Hughes P, Evans CD, Fainman D. Incidence, correlates and predictors of post-traumatic stress disorder in the pregnancy after stillbirth. *Br J Psychiatry* 2001;178:556-60.
142. Lake ME, Johnson TM, Murphy J, Knuppel RA. Evaluation of a perinatal grief support team. *Am J Obstet Gynecol* 1987;157:1203-6.
143. Badenhorst W, Hughes P. Psychological aspects of perinatal loss. *Best Pract Res Clin Obstet Gynaecol* 2007;21:249-59.
144. Schaap AH, Wolf H, Bruinse HW, Barkhof-van de Lande S, Treffers PE. Long-term impact of perinatal bereavement. Comparison of grief reactions after intrauterine versus neonatal death. *Eur J Obstet Gynecol Reprod Biol* 1997;75:161-7.
145. Gold KJ, Sen A, Hayward RA. Marriage and cohabitation outcomes after pregnancy loss. *Pediatrics* 2010;125:e1202-7.
146. Forrest GC, Standish E, Baum JD. Support after perinatal death: a study of support and counselling after perinatal bereavement. *Br Med J (Clin Res Ed)* 1982;285:1475-9.
147. Flenady V, Wilson T. Support for mothers, fathers and families after perinatal death. *Cochrane Database Syst Rev* 2008;(1):CD000452. DOI: 10.1002/14651858.CD000452.pub2.
148. Säflund K, Sjögren B, Wredling R. The role of caregivers after a stillbirth: views and experiences of parents. *Birth* 2004;31:132-7.
149. Hsu MT, Tseng YF, Banks JM, Kuo LL. Interpretations of stillbirth. *J Adv Nurs* 2004;47:408-16.
150. DeFrain J. Learning about grief from normal families: SIDS, stillbirth, and miscarriage. *J Marital Fam Ther* 1991;17:215-32.
151. Dowden S. Young children's experiences of sibling death. *J Pediatr Nurs* 1995;10:72-9.
152. Rowan C, Bick D, Bastos MH. Postnatal debriefing interventions to prevent maternal mental health problems after birth: exploring the gap between the evidence and UK policy and practice. *Worldviews Evid Based Nurs* 2007;4:97-105.
153. Appleton R, Gibson B, Hey E. The loss of a baby at birth: the role of the bereavement officer. *Br J Obstet Gynaecol* 1993;100:51-4.
154. Rådestad I, Surkan PJ, Steineck G, Cnattingius S, Onelöv E, Dickman PW. Long-term outcomes for mothers who have or have not held their stillborn baby. *Midwifery* 2009;25:422-9.
155. Royal College of Obstetricians and Gynaecologists. Good Practice Guideline No. 4: *Registration of stillbirths and certification for pregnancy loss before 24 weeks of gestation*. London: RCOG; 2005 [http://www.rcog.org.uk/files/rcog-corp/uploaded-files/GoodPractice4RegistrationStillbirth2005.pdf].
156. Samuelsson M, Rådestad I, Segesten K. A waste of life: fathers' experience of losing a child before birth. *Birth* 2001;28:124-30.
157. Hughes P, Turton P, Hopper E, McGauley GA, Fonagy P. Factors associated with the unresolved classification of the Adult Attachment Interview in women who have suffered stillbirth. *Dev Psychopathol* 2004;16:215-30.
158. Trulsson O, Rådestad I. The silent child - mothers' experiences before, during, and after stillbirth. *Birth* 2004;31:189-95.
159. Kremer JA, van der Heijden PF, Schellekens LA, Thomas CM, Brownell J, Rolland R. Postpartum return of pituitary and ovarian activity during lactation inhibition with the new dopamine agonist CV 205-502 and during normal lactation. *Acta Endocrinol (Copenh)* 1990;122:759-65.
160. Hughes PM, Turton P, Evans CD. Stillbirth as risk factor for depression and anxiety in the subsequent pregnancy: cohort study. *BMJ* 1999;318:1721-4.
161. Turton P, Badenhorst W, Hughes P, Ward J, Riches S, White S. Psychological impact of stillbirth on fathers in the subsequent pregnancy and puerperium. *Br J Psychiatry* 2006;188:165-72.
162. Getahun D, Lawrence JM, Fassett MJ, Strickland D, Koebnick C, Chen W, et al. The association between stillbirth in the first pregnancy and subsequent adverse perinatal outcomes. *Am J Obstet Gynecol* 2009;201:378.e1-6.
163. DaVanzo J, Hale L, Razzaque A, Rahman M. Effects of interpregnancy interval and outcome of the preceding pregnancy on pregnancy outcomes in Matlab, Bangladesh. *BJOG* 2007;114:1079-87.
164. Conde-Agudelo A, Rosas-Bermúdez A, Kafury-Goeta AC. Birth spacing and risk of adverse perinatal outcomes: a meta-analysis. *JAMA* 2006;295:1809-23.
165. Smith GC, Pell JP, Dobbie R. Interpregnancy interval and risk of preterm birth and neonatal death: retrospective cohort study. *BMJ* 2003;327:313.

166. Wisborg K, Kesmodel U, Henriksen TB, Olsen SF, Secher NJ. Exposure to tobacco smoke in utero and the risk of stillbirth and death in the first year of life. *Am J Epidemiol* 2001;154:322-7.
167. Sebire NJ, Jolly M, Harris JP, Wadsworth J, Joffe M, Beard RW, et al. Maternal obesity and pregnancy outcome: a study of 287,213 pregnancies in London. *Int J Obes Relat Metab Disord* 2001;25:1175-82.
168. Villamor E, Cnattingius S. Interpregnancy weight change and risk of adverse pregnancy outcomes: a population-based study. *Lancet* 2006;368:1164-70.
169. Lurie S, Eldar I, Glezerman M, Sadan O. Pregnancy outcome after stillbirth. *J Reprod Med* 2007;52:289-92.
170. Sharma PP, Salihu HM, Kirby RS. Stillbirth recurrence in a population of relatively low-risk mothers. *Paediatr Perinat Epidemiol* 2007;21 Suppl 1:24-30.
171. Black M, Shetty A, Bhattacharya S. Obstetric outcomes subsequent to intrauterine death in the first pregnancy. *BJOG* 2008;115:269-74.
172. Heinonen S, Kirkinen P. Pregnancy outcome after previous stillbirth resulting from causes other than maternal conditions and fetal abnormalities. *Birth* 2000;27:33-7.
173. Robson S, Chan A, Keane RJ, Luke CG. Subsequent birth outcomes after an unexplained stillbirth: preliminary population-based retrospective cohort study. *Aust N Z J Obstet Gynaecol* 2001;41:29-35.
174. Robson S, Thompson J, Ellwood D. Obstetric management of the next pregnancy after an unexplained stillbirth: an anonymous postal survey of Australian obstetricians. *Aust N Z J Obstet Gynaecol* 2006;46:278-81.
175. Hughes P, Turton P, Hopper E, McGauley GA, Fonagy P. Disorganised attachment behaviour among infants born subsequent to stillbirth. *J Child Psychol Psychiatry* 2001;42:791-801.
176. Gold KJ, Kuznia AL, Hayward RA. How physicians cope with stillbirth or neonatal death: a national survey of obstetricians. *Obstet Gynecol* 2008;112:29-34.

## APPENDIX

Clinical guidelines are 'systematically developed statements which assist clinicians and women in making decisions about appropriate treatment for specific conditions'. Each guideline is systematically developed using a standardised methodology. Exact details of this process can be found in Clinical Governance Advice No.1: *Development of RCOG Green-top Guidelines* (available on the RCOG website at <http://www.rcog.org.uk/guidelines>). These recommendations are not intended to dictate an exclusive course of management or treatment. They must be evaluated with reference to individual patient needs, resources and limitations unique to the institution and variations in local populations. It is hoped that this process of local ownership will help to incorporate these guidelines into routine practice. Attention is drawn to areas of clinical uncertainty where further research might be indicated.

The evidence used in this guideline was graded using the scheme below and the recommendations formulated in a similar fashion with a standardised grading scheme.

Classification of evidence levels	Grades of recommendations
1++ High-quality meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a very low risk of bias	<b>A</b> At least one meta-analysis, systematic review or randomised controlled trial rated as 1++ and directly applicable to the target population; or  A systematic review of randomised controlled trials or a body of evidence consisting principally of studies rated as 1+ directly applicable to the target population and demonstrating overall consistency of results
1+ Well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias	<b>B</b> A body of evidence including studies rated as 2++ directly applicable to the target population, and demonstrating overall consistency of results; or  Extrapolated evidence from studies rated as 1++ or 1+
1- Meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a high risk of bias	<b>C</b> A body of evidence including studies rated as 2+ directly applicable to the target population and demonstrating overall consistency of results; or  Extrapolated evidence from studies rated as 2++
2++ High-quality systematic reviews of case-control or cohort studies or high-quality case-control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal	<b>D</b> Evidence level 3 or 4; or  Extrapolated evidence from studies rated as 2+
2+ Well-conducted case-control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal	
2- Case-control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal	
3 Non-analytical studies, e.g. case reports, case series	
4 Expert opinion	
	<b>Good practice point</b>   Recommended best practice based on the clinical experience of the guideline development group



This guideline was produced on behalf of the Guidelines Committee of the Royal College of Obstetricians and Gynaecologists by:

**Dr D Siassakos MRCOG, Bristol; Dr R Fox MRCOG, Taunton; Dr T Draycott FRCOG, Bristol;**  
and **Mrs C Winter RM, Bristol.**

and peer reviewed by:

RCOG Consumers' Forum; British Association of Perinatal Medicine; British Maternal and Fetal Medicine Society; Mr D I Fraser MRCOG, Norwich; Mr R B Beattie FRCOG, Cardiff; Dr A C G Breeze MRCOG, Nottingham; Professor E S Draper, Professor of Perinatal and Paediatric Epidemiology, University of Leicester; Dr P Cox, Consultant Perinatal Pathologist, Birmingham Women's Hospital; The Child Bereavement Charity; Centre for Maternal and Child Enquiries; Mrs J Frohlich, Deputy Head of Midwifery, Ashford and St Peter's NHS Trust, Chertsey; Professor G C S Smith MRCOG, Cambridge; Professor J Gardosi, Director, Perinatal Institute; Dr A E P Heazell MRCOG, Manchester; Dr A G Howatson, Consultant Paediatric and Perinatal Pathologist, Royal Hospital for Sick Children, Glasgow, Scotland; Dr I Jeffrey, Perinatal Pathology Service, St George's Hospital, London; Sands; Dr E J Treloar MRCOG, Bristol; Royal College of Paediatrics and Child Health; Obstetric Anaesthetists' Association.

Committee lead peer reviewers were: Mrs C E Overton FRCOG, Dr J Thomas MRCOG, Dr S K Surendran FRCOG and Dr P Owen MRCOG.

The final version is the responsibility of the Guidelines Committee of the RCOG.

The guideline review process will commence in 2013 unless evidence requires earlier review.

#### DISCLAIMER

The Royal College of Obstetricians and Gynaecologists produces guidelines as an educational aid to good clinical practice. They present recognised methods and techniques of clinical practice, based on published evidence, for consideration by obstetricians and gynaecologists and other relevant health professionals. The ultimate judgement regarding a particular clinical procedure or treatment plan must be made by the doctor or other attendant in the light of clinical data presented by the patient and the diagnostic and treatment options available within the appropriate health services.

This means that RCOG Guidelines are unlike protocols or guidelines issued by employers, as they are not intended to be prescriptive directions defining a single course of management. Departure from the local prescriptive protocols or guidelines should be fully documented in the patient's case notes at the time the relevant decision is taken.