



# INVESTIGATION AND MANAGEMENT OF LATE FETAL INTRAUTERINE DEATH AND STILLBIRTH

## CLINICAL PRACTICE GUIDELINE

**Institute of Obstetricians and Gynaecologists, Royal College of Physicians of Ireland  
and**

**Directorate of Strategy and Clinical Programmes, Health Service Executive**

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## 1. Key Recommendations

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- Real-time ultrasonography is essential for the accurate diagnosis of Intra-uterine Fetal Death (IUFD).
- Discussions aim to support maternal/parental choice.
- Supportive care should be made available to all bereaved parents
- Recommendations about labour and birth should take into account the mother's preferences, her medical condition and previous intra-partum history.
- Management of IUFD may involve awaiting spontaneous labour or planned medical induction.
- Vaginal birth is the recommended mode of delivery for most women, but caesarean birth may need to be considered in individual cases.
- A combination of mifepristone and a prostaglandin preparation should be the first-line intervention for induction of labour.
- If a woman has had a previous caesarean section, a discussion as to the safety and benefits of induction of labour needs to be undertaken by a consultant obstetrician.
- Clinical assessment and evaluation is recommended to assess maternal wellbeing and to determine the cause of death, the chance of recurrence and of avoiding further pregnancy complications.
- Laboratory tests are recommended to rule out any maternal disease or risk factor that may have contributed to the IUFD / stillbirth.
- Fetal karyotyping should be considered in all cases.
- Parents should be offered a full postmortem examination of the baby.
- Postmortem examination should include external examination with birth weight, histology of relevant tissues and plain radiography (skeletal survey)
- Pathological examination of the cord, membranes and placenta is recommended in all cases of IUFD / stillbirth.
- Standardised checklists should be used to ensure that all appropriate care options are offered and that each response mark is recorded.
- A standardised dataset should be collected for all stillbirths.
- All stillbirths should be reviewed in a multi-professional meeting using a standardised approach.
- All term intra-partum deaths with no evidence of a major congenital anomaly should be investigated locally.
- Staff working with bereaved parents should be provided with an opportunity to develop their knowledge and understanding of perinatal loss, together with development of skills in working in this area.
- A system should be in place to give clinical and psychological support for staff involved with an IUFD/stillbirth.
- A follow-up appointment with the consultant obstetrician should be arranged and it should be clear who is responsible for making these arrangements.
- Women with a history of IUFD should attend a consultant-led hospital-based antenatal clinic in their next pregnancy and undergo increased antenatal surveillance.

## 2. Purpose and Scope

The purpose of this guideline is to assist all healthcare professionals in the diagnosis, investigation and management of late fetal intrauterine death (IUFD) and stillbirth.

The guidance is primarily intended as a resource for obstetricians and midwives but might also be useful for women and their partners, general practitioners and commissioners of healthcare.

### ***The objectives of the guideline are:***

- To standardise management of IUFD and stillbirth based on an evidence based best practice approach
- To provide an investigation protocol to help health care providers determine the cause of fetal death
- To incorporate information on general care before, during and after birth as well as care in future pregnancies
- To ensure best practice with respect to the treatment given to bereaved parents

### *The guideline does not include:*

- Management of multiple pregnancies with a surviving fetus
- Late delivery of fetus papyraceous
- Management of specific medical conditions associated with an increased risk of stillbirth or late IUFD

These guidelines are designed to guide clinical judgment and not replace it. In individual cases a healthcare professional may, after careful consideration, decide not to follow a guideline if it is deemed to be in the best interests of the woman.

### 3. Background

#### *The scale of the problem*

In the developed world, one in 200 infants is stillborn. This is a devastating outcome of pregnancy for parents and clinicians. Despite improvements in antenatal care, stillbirth remains 10 times more common than sudden infant death syndrome. More than 3.2 million stillbirths occur globally each year, yet stillbirths are largely invisible in global health indicators, policies and programmes [Stanton *et al.*, 2006]. In 2009, the stillbirth rate in England, Wales and Northern Ireland was 5.2 per 1000 total births, a rate that shows only a slight downward trend since 2000 [CMACE, 2011]. In Ireland, around 350 stillbirths are registered every year. The Irish Perinatal Statistics Report from 2008 notes that of the 75,587 births recorded, there were 358 stillbirths [ESRI, 2010; [Appendix 1](#)].

#### *Management of labour and delivery*

When a baby dies before birth, the options for care are either to wait for labour to start spontaneously or to induce labour. Most women (over 90%) begin to contract and labour within three weeks of IUID, but if labour does not begin, there is a risk of developing a disseminated intravascular coagulopathy (DIC) [Weiner, 1999], as well as intra-uterine infection if the membranes are ruptured. Other disadvantages of a long interval between fetal death and birth relate to greater emotional distress, and to the degree of information that can be obtained from a postmortem examination. It is usual clinical practice therefore to recommend medical induction, provided this can be safely undertaken.

Inducing labour in cases of IUID may involve the use of oxytocin or prostaglandins. The issues related to the type and dosage of induction agents are a little different for women who are having labour induced after IUID compared to induction of labour at term in the presence of a live fetus. While side effects (including uterine hyper-stimulation, nausea, vomiting, and diarrhoea) and safety (particularly rare complications such as uterine rupture) are important considerations for the woman, issues related to fetal wellbeing are not. Furthermore, it is necessary to consider the receptivity of the uterus to prostaglandin medication, especially at early gestational ages, where the use of low doses may be ineffective in inducing labour, or be associated with a long induction to delivery interval [Dodd and Crowther, 2010].

Misoprostol, a prostaglandin E1 analogue, is probably the most preferred agent because of its low cost, stability in room temperature and ease of administration. Mifepristone is a steroid compound, which competes with progesterone at the receptor level and is also widely used for termination of pregnancy. Mifepristone, administered before misoprostol, increases the sensitivity of the uterus to prostaglandins and ripens the cervix, thereby allowing lower doses of misoprostol to induce expulsion of the fetus. However, the optimum combination of mifepristone and misoprostol has not been established for induction of late intrauterine deaths [Dodd and Crowther, 2010, Wagaarachchi *et al.*, 2002].

### ***Psychological aspects of late IUFD / Stillbirth***

The recognition of perinatal loss as a significant bereavement is relatively new [Badenhorst and Hughes, 2007]. The substantial psychological impact of perinatal death on mothers and families has been extensively studied over the past 30 years, when it first became clear that the normal grief reactions to perinatal death did not differ greatly from those observed in other bereavement situations [Kennell, 1970]. The death of an infant is now recognised as one of the most stressful life events that an adult may experience [Fish, 1986]. A wide range of short and long-term negative outcomes for parents has been reported as a result of infant death [Hughes, 2003, Badenhorst and Hughes, 2007]. Factors which have been reported to increase the risk of adverse psychological outcomes for parents after a perinatal death include: perceived inadequate social support, traumatic circumstances surrounding the death, difficulties in coping with a crisis in the past, problematic relationships and the presence of other life crises.

Research has suggested that the role of practitioners in the handling of death and their interaction with the bereaved person following a loved one's death influences the intensity of grief. It is proposed that skilled, sensitive and caring treatment in the time surrounding pregnancy loss positively impacts on the grief experience of bereaved parents [Corbet-Owen and Kruger, 2001]. A number of studies have examined the factors considered to be important to bereaved parents following the death of their child, as well as aspects of care that they considered to be lacking. These findings implicate the importance of validation and acknowledgement of the physical and emotional aspects of their experience, empowerment and safety, collaborative decision-making, the sharing of knowledge, creation of memories and sensitive care [PSANZ, 2009].

Provision of an empathetic caring environment, and strategies to enable the mother, father and family to accept the reality of perinatal death, are now an accepted part of standard nursing/midwifery and social support in most of the developed world. Provision of interventions such as psychological support or counselling, or both, has been suggested to improve outcomes for families after a perinatal death

### ***Evaluation of causes of stillbirth***

Stillbirths deserve the same systematic evaluation as adult deaths. However, the optimal evaluation of stillbirth is controversial and is influenced by several medical factors, including the availability of perinatal pathology, as well as by personal beliefs and public concerns regarding fetal autopsy. The study of specific causes of stillbirth is also hindered by the absence of uniform protocols of investigation and lack of agreement on a definitive classification system.

The primary method for classification of stillbirth is according to the presumed cause of death or associated obstetric disorder. There are numerous classification systems and none is universally accepted [Silver *et al.*, 2007]. Original versions consisted of categories of congenital malformation and birth asphyxia, while more recent approaches have attempted to include abnormal fetal growth and placenta pathology, although it is controversial whether these conditions are causes of or risk factors for stillbirth [Fretts 2005; Smith and Fretts, 2007; Silver *et al.*, 2007].

Unexplained stillbirths account for 25 to 60% of total stillbirths. This wide variation in rates is both a reflection of the classification systems used to define stillbirth and the extent of postmortem assessment performed in each case [Fretts, 2005, Silver *et al*, 2007]. Further, an unexplained stillbirth may in fact be an un-investigated one. Postmortem examination may not be undertaken and the decision not to investigate can either be doctor or patient-mediated. Parents may have cultural or religious beliefs why autopsy is impermissible or doctors may feel that the clinical scenario or antenatal diagnosis suffices as an adequate explanation. These difficulties are further compounded by a lack of consensus regarding the number of tests needed and by the scarcity of uniform protocols of investigation [Silver *et al.*, 2007; Corabian *et al.*, 2007].

### ***Investigation of stillbirth***

The optimal evaluation of stillbirth is controversial. There is often debate regarding the attribution of a stillbirth to a particular underlying pathology, and lack of parental consent can restrict procedures such as autopsy. The cost of testing also has to be considered in most clinical settings. In general, the most common causes of stillbirth are investigated, as well as those conditions that might predispose couples to recurrent stillbirth. However, even identifying a sporadic cause has merit as it can bring closure for the parents and provide reassurance for the future [Silver *et al.*, 2007].

Histopathological examination of the fetus and placenta remain the most relevant investigations in understanding the events leading to intrauterine death. Evaluation of the placenta, membranes and umbilical cord can yield insight into different possible aetiologies of stillbirth [Silver *et al.*, 2007]. In addition, many of the broad categories of cause of death, including unexplained stillbirth, are thought to be related to placental function [Smith and Fretts, 2007]. About half of unexplained stillbirths have a birth weight less than the tenth percentile corrected for gestational age and parental characteristics [Froen *et al.*, 2004].

Following stillbirth, postmortem examination can reveal important information and findings at perinatal autopsy change the presumptive cause of death or yield additional information in 22-76% of cases [Gordijin *et al.*, 2002]. However, in the last decade, autopsy rates have fallen to around 40-50% of all stillbirths. While evidence supports all perinatal autopsies being performed by specialist perinatal pathologists, the majority of hospitals in the UK and Ireland do not have access to this. Concerns into the removal, retention and storage of fetal organs at postmortem examination in both the UK and Ireland have led to a significant change in public opinion about fetal autopsy. An Irish 25-year retrospective analysis from 1979 to 2003 reported a drop-off in postmortem rates from 90% in first half of the study to 50% by 2003 [Walsh *et al.*, 2008]. This has led to a search for alternatives to autopsy, including postmortem radiological imaging.

### ***“Stillbirths: the way forward in high income countries”***

The Lancet’s Stillbirths Series steering committee [Flenady *et al.*, 2011] concluded that:-

- Stillbirths in many high-income countries are potentially preventable.
- The proportion of unexplained stillbirths without adequate investigation is high.
- All parents should be offered a thorough investigation including a high quality autopsy and placental histopathology.

- Improvements in investigation and reporting practices, including consensus of definition and classification systems, is needed.
- Future research should focus on screening and interventions to reduce stillbirth associated with preterm birth, as well as a results of placental dysfunction.
- Parents have the greatest stake of all in the wellbeing of their baby, and must be part of the drive to reduce stillbirth.



## 4. Methodology

The literature reviewed during the development of this guideline included current local and national guidelines and their reference lists from the UK, Canada, USA, Australia and New Zealand.

A search was conducted of current international guidelines in the UK, USA, Canada, New Zealand and Australia.

In addition, Medline and the Cochrane Library were searched for literature published between 2000 and 2010. Articles were restricted to those published in English. The search words used were stillbirth, late fetal death, intra-uterine death, investigation, and management.

The principal guideline developer was Dr. Keelin O'Donoghue, Senior Lecturer, Obstetrics and Gynaecology, University College Cork and Cork University Maternity Hospital (CUMH). Ms. Anna Maria Verling (Chairperson, Miscarriage, Stillbirth and Neonatal Death Committee, CUMH) and Dr. Roisin O'Loughlin (SHO, CUMH) are acknowledged for their development of local guidelines and for assisting with review of this guideline.

The guideline was peer-reviewed by Dr. Michael Gannon (Mullingar), Dr. Emma Kilgarriff (GP), Dr Eddie O'Donnell (Waterford) and Professor Michael Turner (HSE Obstetrics and Gynaecology Programme), the Institute of Obstetricians and Gynaecologists' Clinical Advisory Group, the HSE Obstetrics and Gynaecology Programme Working Group.

The guidelines were also reviewed by Féileacáin (Stillbirth and Neonatal Death Association of Ireland).

## 5. Glossary

### **Live birth**

Delivery of an infant, which, after complete separation from its mother, shows sign of life. Evidence of life includes breathing movements, presence of a heartbeat, pulsation of the cord or definite movement of voluntary muscles.

### **Neonatal death (NND)**

Death of a live born baby occurring before 28 completed days after birth.

**Early** 0-6 completed days.

**Late** 7-27 completed days.

### **Perinatal death**

Death of a fetus or a newborn in the perinatal period that commences at 24 completed weeks' gestation and ends before seven completed days after birth.

### **Stillbirth (SB)**

A baby delivered without signs of life after 23<sup>+6</sup> weeks of pregnancy.

### **Intra-uterine death (IUD)**

A baby who dies in utero

## 6. Clinical Guideline

### 6.1 Terminology

The World Health Organization (WHO) defines stillbirth as a "fetal death late in pregnancy" and allows each country to define the gestational age at which a fetal death is considered a stillbirth for reporting purposes. As a result, some countries define stillbirth as early as 16 weeks of gestation, whereas others use a threshold as late as 28 weeks.

According to the International Classification of Diseases, revision 10 (ICD-10), an early fetal death is death of a fetus weighing at least 500g (or if birth weight is unavailable then after 22 weeks gestation or with a crown-heel length of 25cm or more). A late fetal death is defined as death of a fetus weighing at least 1000g (or a gestational age of 28 weeks or a crown heel length of 35cm or more). Late fetal deaths are recommended by the WHO as the measure for international comparison.

The Perinatal Mortality Surveillance Report [CEMACE, 2011] defines stillbirth as 'a baby delivered without signs of life after 23<sup>+6</sup> completed weeks of pregnancy'. This definition was accepted by the Royal College of Obstetricians and Gynaecologists in their 2010 Green-top Guideline [RCOG Green-top Guideline No. 55, November 2010].

The National Perinatal Epidemiology Centre's perinatal death notification form defines stillbirth as "a baby delivered without signs of life from 24 weeks gestation and/or >500g".

The Stillbirths Registration Act (1994) applies "in relation to a child born weighing 500 grammes or more or having a gestational age of 24 weeks or more who shows no sign of life".

ACOG defines stillbirth as fetal death occurring during pregnancy at 20 weeks of gestation or later.

Intrauterine fetal death refers to babies with no signs of life in utero. There is general agreement between the above bodies on this definition.

In this guideline, stillbirth is taken to refer to a baby delivered without signs of life from 24 weeks gestation and IUFD is taken to refer to death in utero after 24 weeks gestation.

## 6.2 Diagnosis

### ***Diagnosis***

Real-time ultrasonography is essential for an accurate diagnosis of IUFD. This allows direct visualisation of the fetal heart, and views can be supplemented with colour Doppler of the heart and umbilical cord. Use of ultrasound also facilitates visualisation of other secondary features such as fetal hydrops, polyhydramnios, anhydramnios, overlapping skull bones and skin oedema [RCOG, 2010].

Auscultation of the fetal heart by Pinard Stethoscope or Doppler is inaccurate and this together with cardiotocography should not be used to investigate suspected IUFD.

Ideally, a second opinion should be obtained to confirm the diagnosis of IUFD. In addition, mothers ought to be prepared for the possibility of passive fetal movement, and where this is reported, a repeat ultrasound scan should be offered [RCOG, 2010].

When a diagnosis is confirmed, if a woman is unaccompanied, an offer should be made to call her partner/family/friends.

### ***Breaking the news***

Once a diagnosis has been firmly established the parents are told in a timely and unhurried manner in a private space. A doctor should advise parents of the death, with a midwife present.

Those giving the news should acknowledge the baby's death. If the parents have decided on a name for the baby it is important to use it. Staff should also be careful in using overly medicalised terminology when speaking to parents about their loss.

Parents need to be given the opportunity and space to talk about their loss. It has been shown that parents value acceptance and recognition of their emotions highly [McCreight, 2008]. Further guidance for staff to support them in their relationship with bereaved parents is available [SANDS, 2007].

### ***Follow-up***

Parents who experience adverse events value continuity of the caregiver. Discussions on further management should aim to support maternal/parental choice. Written information should be given to parents to supplement these discussions.

Supportive care for the parents and family should be made available. The general practitioner (GP) should be informed of the IUFD as soon as practicable after diagnosis.

The doctor / midwife dealing with the parents during initial diagnosis should give an appropriate contact number for the hospital. The parents need to be reassured that they can make contact at any time, if they need any further information or clarification.

### 6.3 Investigation

Clinical assessment and laboratory tests should be recommended to assess maternal wellbeing and to determine the cause of death, the chance of recurrence and possible means of avoiding further pregnancy complications [RCOG, 2010; PSANZ, 2009, BC Reproductive Care Program, 2000]. Even identification of a sporadic cause can bring emotional closure and facilitate parental recovery.

Parents should be made aware that:

1. No specific cause is found in almost half of stillbirths.
2. When a cause is found it can crucially influence care in a future pregnancy.
3. An abnormal test result is not necessarily related to the IUFD, so correlation between blood tests and postmortem examination should be sought.
4. Sometimes further investigation is necessary.

#### ***Investigations recommended for all stillbirths*** ([Appendix 2](#))

- At the time of diagnosis
  - Maternal and family history
  - Ultrasound scan +/- Amniocentesis
  - Maternal blood tests
  - Maternal toxicology
  - Maternal microbiology
- After delivery
  - External examination
  - Infant blood tests
  - Infant microbiology
  - Placenta, membrane and cord histopathology
  - Cytogenetic investigations
  - Postmortem examination
  - Postmortem Radiological imaging

#### ***Maternal and family history***

A detailed family history should be sought to identify a possible inherited cause to explain the stillbirth. A comprehensive maternal medical and social history should be taken.

This should explore:

- Previous fetal losses
- Elevated blood pressure
- History of bleeding
- Recent illness or viral exposure
- Medications during pregnancy
- Substance use
- History of fetal movements
- Antenatal investigations
- Fetal ultrasounds and fetal growth

### ***Ultrasound +/- Amniocentesis***

At the time of ultrasound confirmation of IUFD, the ultrasound should include examination for possible fetal abnormalities, fetal biometry and assessment of amniotic fluid volume [PSANZ, 2009].

The option of amniocentesis after IUFD should be discussed. Parents will need to be given time to consider this, and supported through the procedure. Amniocentesis can provide cytogenetic results, especially if the mother chooses expectant management, but patient acceptability and safety (i.e. infection) of amniocentesis has not been specifically investigated in the setting of IUFD [Saal *et al.*, 1987; Khare *et al.*, 2005]. A report on a large series of third-trimester amniocentesis suggested this is an acceptable option, with a low complication rate, although a 10% cytogenetic culture failure rate was reported [O'Donoghue *et al.*, 2005].

Amniotic fluid collected by amniocentesis prior to the onset of labour can provide an uncontaminated specimen for microbiological assessment. It is the only sample where the detection of pathogens such as E-Coli will be of value, especially if no autopsy is performed. This is due to potential contamination during vaginal birth where findings from cultures of natural orifices and the placenta/membranes are often discredited [PSANZ, 2009].

### ***Maternal blood tests***

Laboratory tests should be recommended to out rule any maternal disease or risk factor that may have contributed to the IUFD / stillbirth.

#### Full blood examination

A full blood examination can assist in detection of: infection as a cause of the fetal death; maternal anaemia which may indicate conditions such as thalassemia; low platelet levels - a marker for pre-eclampsia; autoimmune diseases such as systemic lupus erythematosus (SLE) and Idiopathic Thrombocytopenia Purpura (ITP); and elevated platelet levels may indicate thrombocythemia [PSANZ, 2009].

#### Maternal coagulation testing

Testing maternal coagulation and plasma fibrinogen are not indicated to find a cause for the IUFD, but rather because of the association between IUFD and maternal coagulopathy. Maternal sepsis, placental abruption and pre-eclampsia, all possible causes of IUFD, increase the chance of maternal DIC. These tests are also relevant if regional anaesthesia is requested during labour [RCOG, 2010].

#### Serology for Cytomegalovirus, Toxoplasma, Parvovirus B19, Rubella and Syphilis

Serology for Cytomegalovirus, Toxoplasma and Parvovirus B19 should be undertaken following an IUFD. Rubella and Syphilis should also be included if they have not already been undertaken during the antenatal period. Where test results are positive, a microbiologist or infectious disease specialist should be consulted regarding further testing and treatment required [PSANZ, 2009].

Maternal-fetal transmission of Toxoplasmosis is dependent on the time of maternal infection. The earlier the fetus acquires the infection the more severe the consequences,

however maternal-fetal transmission is more likely to occur later in pregnancy. Disseminated Toxoplasma may cause fetal death [Goldenberg RL and Thompson C, 2003].

Parvovirus (B19) causes severe fetal anaemia, non-immune hydrops and fetal death [Goldenberg RL and Thompson C, 2003; Tolfvenstam *et al.*, 2001]. It was found to be the cause of death in 10% of all non-malformed fetal deaths occurring between 10 and 24 weeks of gestation referred for pathological examination [Wright *et al.*, 1996]. 1%-3% of susceptible pregnant women will develop serologic evidence of infection in pregnancy, of which the transmission rate to the fetus is 17%-33% (16-18). The spontaneous loss rate of fetuses affected by Parvovirus B19 after 20 weeks gestation is 2.3% [Crane *et al.*, 2002]. Of note, hydrops is not necessarily a feature of parvovirus related late IUFD [RCOG, 2010].

Rubella is associated with a wide variety of fetal abnormalities and also infects the placenta, enhancing the risk of stillbirth. However due to widespread vaccination, congenital rubella infection in developed countries is extremely rare [Goldenberg RL and Thompson C, 2003].

Whether CMV actually causes stillbirth and, if so, the mechanism by which it does so is not clear [Goldenberg RL and Thompson C, 2003]. However, a prospective study of more than 10,000 women found an increase in fetal loss associated with infection in early pregnancy [Griffiths PD and Baboonian C, 1984].

#### Blood group and antibody screen

A blood group and antibody screen should be performed to exclude haemolytic disease due to maternal sensitisation to red cell antigens, for example Rh D and Kell [Moise, 2004].

#### Kleihauer-Betke test

A Kleihauer-Betke test to detect fetomaternal haemorrhage should be performed following the diagnosis of an IUFD, and preferably prior to delivery. Limited evidence suggests that post delivery Kleihauer may still be useful [RCOG, 2010; PSANZ, 2009, Biankin *et al.*, 2003].

The incidence of massive fetomaternal haemorrhage is <0.1%. However the incidence in otherwise unexplained cases of fetal death has been estimated to be as high as 14% [Laube DW and Schauburger CW, 1982]. The diagnosis of a significant fetomaternal haemorrhage is confirmed by quantification of fetal erythrocytes in maternal blood performed by the Kleihauer test. The general consensus is that 50ml constitutes a significant haemorrhage, with various studies using limits ranging from 30- 150ml; these levels are gestation dependent [PSANZ, 2009].

The time period over which the haemorrhage occurs will have a direct impact upon the mortality associated with it, according to whether the fetus was able to compensate for the loss in blood volume. However, as it is not currently possible to assess this, a loss of 20% of total fetal blood volume should be considered severe enough to cause fetal mortality [WiSSP, 2004].

#### Renal Function Tests including Uric Acid

Elevated uric acid levels early in the third trimester in pre-eclamptic women have been

associated with perinatal death and it is therefore recommended to evaluate the contribution of pre-eclampsia to the death [PSANZ, 2009].

Abnormal renal function is an indicator of possible SLE, which is associated with a significant increase in fetal morbidity and mortality. Uric acid is the most sensitive laboratory indicator of pre-eclampsia and is a better predictor of perinatal outcome than blood pressure [PSANZ, 2009; Redman *et al.*, 1976].

### Liver Function and Bile acid Tests

Mild liver test abnormalities are a possible marker for obstetric cholestasis. Obstetric cholestasis (OC) was initially associated with a significant increase in the perinatal mortality rate, ranging from 3%-20%, as well as a five-fold increased incidence in intra-partum fetal distress and pre-term labour [Fisk NM and Storey GN, 1988]. When more recent studies are considered, the perinatal mortality rate from OC is 11/1000, and the additional risk of stillbirth from OC over the general population remains undetermined [RCOG, 2011]

Abnormalities in liver function are also a marker for viral hepatitis, cytomegalovirus, and toxoplasmosis. Abnormal liver function has also been associated with acute fatty liver of pregnancy and HELLP syndrome (**H**aemolysis, **E**levated **L**iver function, **L**ow **P**latelets) [PSANZ, 2009].

### Thyroid Function Tests

Pregnancy is associated with physiological changes in the thyroid function, which may result in thyroid disorders. Thyroid disorders during pregnancy have been associated with adverse health outcomes for both the mother and child, including increased risk of miscarriage, gestational hypertension, low birth weight and fetal death [Feki *et al.*, 2008]. Recent reports have focused on the correlation of subclinical hypothyroidism and adverse pregnancy outcome [Benhadi *et al.*, 2000].

### HbA1c

The increased risk of fetal morbidity and mortality with maternal diabetes is well known [Engel *et al.*, 2008]. A stillbirth rate of 35 per 1000 births to type 2 diabetic mothers has been reported [Cundy *et al.*, 2000]. Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance of variable severity with the onset or first recognition during pregnancy. There is some evidence to indicate that uncontrolled GDM is associated with increased perinatal mortality; however the majority of women with GDM have a normal HbA1c [Aberg *et al.*, 1997; RCOG, 2010]. *HbA1c* monitors glycaemia over the previous 3 months by reflecting the average glucose concentration over the life of the red cells and therefore may provide information to aid in the consideration of the contribution of diabetes to the fetal death. If the *HbA1c* level is raised, fasting blood glucose should be tested and if abnormal a Glucose Tolerance Test performed 6-8 weeks postnatally [PSANZ, 2009].

### Investigation for Thrombophilia

Testing for Anticardiolipin antibodies, Lupus anticoagulant and APC resistance are recommended for all women at the time of IUFD.



Ideally, further investigation for thrombophilia should be undertaken 8-12 weeks postnatally where a fetal death is associated with fetal growth restriction, pre-eclampsia, maternal thrombosis and/or maternal family history of thrombosis, remains unexplained following the core investigations or where tests for thrombophilia were positive at the time of the IUFD. These tests include fasting homocysteine levels, Protein C and S deficiency, the Prothrombin gene mutation and the anti-thrombin II deficiency [PSANZ, 2009; RCOG 2010]. Local protocols may apply regarding the timing of testing for thrombophilia.

Anticardiolipin antibodies and Lupus anticoagulant should be repeated postnatally if found to be positive at the time of the IUFD and the Factor V Leiden mutation should be tested if APC resistance was positive at birth.

Thrombophilias are multigenic disorders caused by inherited and acquired defects resulting in a predisposition to thrombosis [Alonos *et al.*, 2002]. Antiphospholipid antibodies are the most important causes of acquired thrombophilias. In pregnancy, thrombophilic disorders are associated with an increased risk of venous thromboembolism, pre-eclampsia, placental abruption, early and late fetal demise, recurrent pregnancy loss and fetal growth restriction [Alfirevic *et al.*, 2002; Saade GR and McLintock C, 2002]. However, accurate estimates of strength of the associations for adverse pregnancy outcome and inherited thrombophilic disorders are problematic due to small numbers and heterogeneity of the available studies [Alfirevic *et al.*, 2002]. Recent systematic reviews have demonstrated a statistically significant increase in the risk of stillbirth associated with APC resistance, Factor V Leiden mutation, Protein C deficiency, Protein S deficiency, Prothrombin G20210 mutation and MTHFR [Saade GR and McLintock C, 2002; Rey *et al.*, 2003; Dudding TE and Attia J, 2004, PSANZ, 2009].

Ideally the identification of thrombophilia following an unexplained stillbirth would result in intervention in future pregnancies to reduce the risk. Although the evidence is unclear, there is some evidence to suggest that antithrombotic therapy may reduce adverse pregnancy outcome for women with thrombophilia [McLintock *et al.*, 2001].

### Parental karyotypes

Parental bloods for karyotype are indicated if a fetal balanced translocation is identified. These tests should also be performed if fetal genetic testing fails and there is a history suggestive of fetal aneuploidy e.g fetal abnormality or a history of a previous unexplained IUFD or recurrent pregnancy loss [RCOG, 2010; Sikkema-Raddatz *et al.*, 2000].

### Maternal autoantibody testing

Testing for occult maternal autoimmune disease may be indicated in certain circumstances. These include where fetal hydrops is evident clinically or at postmortem (test anti-red cell antibody serology), or where endomyocardial fibroelastosis or AV node calcification is found at postmortem (test maternal anti-Ro or anti-La antibodies). Maternal alloimmune antiplatelet antibodies should be tested where fetal intracranial haemorrhage is found or fetal thrombocytopaenia detected [RCOG, 2010].

### ***Maternal Toxicology***

Illicit drug use accounts for a proportion of stillbirths [Silver *et al.*, 2007]. Maternal urine should be analysed for cocaine metabolites, if the history or presentation are suggestive [Lutiger *et al.*, 1991]. The RCOG Green-top guideline lists a maternal toxicology screen as a recommended test - as long as maternal consent is obtained and where history and/or presentation are suggestive [RCOG, 2010].

### ***Maternal microbiology***

Infectious and microbiological investigation should be performed where infection is suspected as an aetiology (maternal fever, abnormal liquor, flu-like symptoms, prolonged rupture of membranes) or where the cause of stillbirth is not obvious [RCOG, 2010, Moyo *et al.*, 1996]. Tests to be performed include maternal blood cultures, mid-stream urine analysis, vaginal and cervical swabs [RCOG, 2010].

McDonald *et al* identified that although 70% of women with mid-gestation spontaneous abortions were asymptomatic for infection, micro-organisms were identified from the placenta and/or fetus in 62% of women studied and histological chorioamnionitis was present in 69%. Among 51 women with intact membranes, 28 were culture-positive, with the most frequent isolate being Group B Streptococcus (GBS). In this study, GBS was the most significant pathogen associated with the fetal deaths, and was often the sole pathogen recovered [McDonald HM and Chambers HM, 2000]. The detection of GBS is optimised with the use of a perianal swab in conjunction with a low vaginal swab and the use of specific culture media [Jones *et al.*, 2004].

### ***External examination***

A perinatal pathologist, neonatologist or paediatrician should perform a detailed external examination of the baby where possible, irrespective of whether a postmortem is being performed or not. A comprehensive external examination of the baby is an essential component of the investigation of a stillbirth [PSANZ, 2009, BC Reproductive Care Program, 2000; Magee 2001]. A report on a large case series suggested that approximately 25% of stillborn infants were found on clinical examination to have demonstrable abnormalities and also indicated that lack of external examination would have resulted in approximately 4% of diagnoses being missed [WiSSP, 2004].

A detailed external examination of the baby is also a component of a full postmortem. As the perinatal pathologist is the most appropriate person to carry out the external examination, parents who have declined a full postmortem should be asked to consent for the baby to be examined by a pathologist. In circumstances where it is not possible for a pathologist to perform the examination, or where a perinatal pathologist is not available, then a neonatologist or paediatrician should conduct the examination [PSANZ, 2009].

The external examination should aim to answer at least three questions [Magee, 2001]:

1. Does the infant display a detectable anomaly?
2. Is growth appropriate?
3. Is maceration present, and if so, how severe?

### ***Infant blood tests***

A blood sample should be collected from the infant for investigation of the presence of infection, to assess other haematological parameters for karyotyping (if not already performed) and a routine Guthrie test [PSANZ, 2009].

A cord blood sample should be collected after delivery where possible; if this is not possible, cardiac puncture can be performed. This blood sample will provide a potentially uncontaminated sample for microbiological culture and assessment of fetal inflammatory response. If a sample of blood is obtained it should also be sent for chromosomal analysis, and haematological assessment (full blood count, nucleated red cell count, group and antibody screen).

### ***Infant microbiology***

Surface swabs for aerobic and anaerobic bacterial culture cultures should be taken from the ear and throat of all stillbirths. Intrauterine infections have been reported to represent the cause of death in 15%-24% of cases of stillbirths when premature rupture of membranes is included. Infection may be subclinical in the mother, hence the importance of investigating all incidences of fetal death where a cause is not obvious [PSANZ, 2009]. Fetal microbiological investigations may be more informative than maternal serology for detecting viral infections. [RCOG, 2010]

### ***Analysis of the placenta, cord and membranes***

At time of delivery, the clinician should undertake:

- A detailed macroscopic examination of the placenta and cord and should document the findings
- Placental swabs between the amnion and chorion using aseptic technique for aerobic and anaerobic bacterial cultures
- Sampling of amnion and placental tissue for karyotyping if required.

Pathological examination of the cord, membranes and placenta should be recommended whether or not postmortem examination of the baby is requested. Following a stillbirth, the placenta, membrane and cord should be sent to the perinatal pathologist fresh and unfixed for macroscopic and histological examination.

The placenta should be examined in all cases of intrauterine death. Examination of the placenta reduces the proportion of unexplained stillbirths [Heazell and Martindael, 2009]. In one review of 146 autopsies performed on macerated and non-macerated stillbirths, significant findings were identified in the placenta in 53% of cases [Magee, 2001]. Another review of placentas from stillbirths identified histologic abnormalities in 98% of cases (the findings supporting the prior clinical impression in 77% of cases, being contradictory to prior impressions in 11% of cases, and being the sole contributor to explaining death in a further 11% of cases) [Rayburn *et al.*, 1985]. In addition to a probable cause of death, placental examination in cases of stillbirth may provide an audit of antenatal clinical judgment by providing clinic-pathologic correlation and/or lead to an improved management of subsequent pregnancies by diagnosing conditions that may recur or be preventable or treatable in subsequent pregnancies [Magee, 2001].

## ***Cytogenetic investigations***

Karyotyping is important as about 6% of stillborn babies will have a chromosomal abnormality [Genest *et al.*, 1992]. Some abnormalities are potentially recurrent and can be tested for in future pregnancies. Written consent should be taken for any fetal samples used for karyotyping [RCOG, 2010].

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, but this provides less detailed genetic information.

Ideally, more than one cytogenetic technique should be available to maximise the chance of informative results [RCOG, 2010; PSANZ, 2009]. Cytogenetic investigation of pregnancy loss can now be routinely performed by MLPA (multiplex ligation-dependent probe amplification). This technique has a higher success rate than karyotyping – 85-95% - as well as reduced reporting time (12 days). Karyotyping will still be performed where this can provide relevant information that investigation by MLPA may not provide. Parental follow up will be required in a proportion of cases. Local guidelines and laboratory service agreements will determine the technique used, the laboratory involved, the sample requirements and the reporting times.

A range of tissue types can be used, but all cell cultures can fail. Samples from multiple tissues should be used to increase the chance of culture [RCOG, 2010]. Perinatal specimens suitable for karyotyping include skin, cartilage and placenta. Skin specimens are associated with a higher rate of culture failure, 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 [Schreck *et al.*, 1990].

Placental biopsy (approximately 1 cm diameter) should be taken from the fetal surface close to the cord insertion (to avoid tissue of maternal origin). Skin biopsy should be deep to include underlying muscle (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 [RCOG, 2010].

The rate of successful chromosome analysis using amniocentesis in cases of IUFD ranges from 82%-92%. In contrast, the success rate for placental chromosome analysis is approximately 60% and approximately 30% for skin. The total time from fetal death until biopsies can be processed is often long, and the chances of succeeding with a chromosomal analysis decreases with time. Amniocentesis reduces the elapsed time between fetal death and sample collection, and the samples are easier to handle and for the laboratory to process Ahlenius *et al.*, 1995; Neiger R and Croom CS, 1990].

## ***Postmortem examination***

Parents should be offered a full postmortem examination of the stillborn infant to help explain the cause of an IUFD / stillbirth. The value of post-mortem examination after stillbirth is well documented. It provides additional information in up to 65% of cases of IUFD and

may also alleviate parental anxiety about antenatal care, as well as being essential for research to investigate the aetiology of stillbirth [Stock et al., 2010; Gordijn et al., 2002].

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. Parents should be given time to make this decision. However, attempts to persuade parents to choose postmortem must be avoided; individual, cultural and religious beliefs must be respected [RCOG, 2010].

The examination should ideally be undertaken by a specialist perinatal pathologist [RCOG, 2010].

Postmortem examination should include external examination with birth weight, histology of relevant tissues and skeletal X-rays. Parents can also be offered a limited postmortem examination, sparing certain parts of the body e.g. the brain.

Each pathology department should have a stillbirth postmortem protocol to include consideration of the following: external examination, internal examination (dissection procedure), weights and measurements, tissue histology (special stains and frozen sections), ancillary studies (cytogenetic studies, molecular and biochemical studies, viral/bacterial studies) and placental examination [Magee, 2001].

## Consent

### **What should be discussed in seeking consent for a postmortem examination**

1. Why the postmortem examination is required and why it would be helpful to the clinicians and to the family.
2. That the examination will be carried out according to best practice guidelines and professional standards with care and respect for the body of the infant.
3. Parents have the right to refuse a postmortem examination.
4. What a postmortem examination entails. Parents have the option to decline detailed - as opposed to general – information.
5. That hospital postmortem examinations can be full or limited, and that a limited postmortem may lead to an incomplete assessment or not clarify a diagnosis.
6. The possibility of removal and retention of organs and tissues and the reasons why this may be required.
7. What happens to organs and tissues that have been removed and retained.
8. Storage of organs and tissues retained at postmortem examination.
9. Other uses to which retained organs and tissues can be put – e.g. research, education and training.
10. Where and when the postmortem will take place, and an estimation of how long it will take.
11. Implications of postmortem examination on funeral arrangements.
12. Options for the ultimate disposition of organs not returned to the body prior to the funeral.
13. When the postmortem results may be available.
14. Options in relation to communication of the postmortem results.

[Adapted from the Code of Practice for Post Mortem Services, 2010].

Written consent must be obtained for any invasive procedure on the baby including tissues taken for genetic analysis ([Appendix 3](#)).

The way in which the postmortem examination is discussed with the parents is extremely important. In all cases postmortem examination of the baby should be discussed with parents by senior medical staff (Consultant and/or Registrar) in a sensitive manner. The medical staff seeking consent must have knowledge of the procedures involved. An improvement in postmortem rates has been demonstrated when senior staff are involved in counselling [Stock et al., 2010].

Parents should be given clear, honest and objective information [Code of Practice for Post Mortem Services, 2010]. 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 – but parents should be advised that they may find the terminology distressing [RCOG, 2010].

Parents should be given time to receive information and make decisions, the opportunity to ask questions, and should be allowed privacy for discussion between themselves. Parents need to feel comfortable to discuss their fears around the procedure and have the confidence to ask staff for guidance. Emotional or psychological support during this time may also be helpful [Code of Practice for Post Mortem Services, 2010].

The possible retention of organs and /or tissues must be discussed, along with the reasons why organs/tissues may be retained. The various options in relation to the sensitive disposal of organs/tissues after examination should be explored. Specific consent must be obtained for the removal and /or retention of organs or tissues for any reason [Madden, 2005; Code of Practice for Post Mortem Services, 2010].

If, after discussion, parents decline postmortem examination this decision should be documented in the maternal chart.

If, after discussion, including provision of an explanatory leaflet outlining postmortem examination, parents agree to a postmortem examination, written consent is obtained and the 'request for postmortem' form completed in full. If possible, the mother should be encouraged to sign, particularly where her surname differs from the father, as discrepancies in surnames can lead to difficulties in the carrying out of the postmortem.

The postmortem consent form outlines the exact nature of a postmortem examination, any limitations made by the parents are recorded and then a parent and one of the senior medical staff sign it. If the Consultant or Registrar has specific issues to be dealt with in the post-mortem, they should bring these to the attention of the relevant Pathologist.

### Making arrangements

Parents should be advised of the local arrangements for postmortem examination. In some hospitals, this will involve the baby being transported to another hospital for the procedure, and this must be made clear to the parents.

Following consent for postmortem examination, the mortician is contacted to arrange a time

of examination in the Pathology Department.

If X- rays have been carried out they should be sent with the baby when being sent for postmortem. In some units, the skeletal survey will be performed in the radiology department en route to the pathology department.

The completed postmortem request form with clinical details and signed, fully completed postmortem consent form accompany the baby's body to the Pathology Department.

Detailed local arrangements should exist to confirm the baby's identity, ensure the remains are transported with dignity, and to confirm the baby's return to the parents after the postmortem. Parents should be advised of baby's return as early as possible, and can be given time with baby after the return from the postmortem examination.

### Communication

Postmortem and placental examinations are performed to uncover a cause of death and/or identify factors that could influence the management of future pregnancies. It is necessary therefore that the pathologist (a) generate a timely and informative report; (b) communicate autopsy findings to health care providers; and (c) participate in a regular review of stillbirths [Magee, 2001].

A preliminary autopsy report (comprising a short but relevant history, a list of gross findings in infant and/or placenta, a list of tests whose results are awaited, such as cytogenetics and viral studies), and an estimated date for release of the final report should be issued within 48 hours of the autopsy procedure. Guidelines for turnaround times for the full report are available, with 3 months being the suggested maximum [Magee, 2001].

### ***Postmortem radiological imaging***

Parents who decline an autopsy should be asked for consent to undertake a full body X-ray. A skeletal survey (plain radiography) may detect abnormalities (mainly skeletal), which may not be detected on an external examination. The Wisconsin Stillbirth Service Program estimated that approximately 20% of unselected stillborn infants had abnormalities detectable on X-Ray [WiSSP, 2004].

Ultrasound and magnetic resonance imaging (MRI) should not yet be offered as a substitute for conventional postmortem examination [RCOG, 2010].

Magnetic resonance imaging (MRI) can be a useful adjunct to conventional postmortem for the evaluation of stillborn fetuses [Griffiths *et al.*, 2005; Cohen *et al.*, 2008]. MRI was chosen for its excellent soft tissue contrast and representation of the central nervous system (CNS), an area that presents problems for pathologists. Initial studies reported detailed anatomical depiction of most organ systems, but the depiction of abnormalities outside the CNS was inferior to formal autopsy. Other problems include limited availability of MR in many centres and the length of time per scan.

Computerised tomography (CT) represents another non-invasive alternative to fetal autopsy. To date, postmortem CT has been confined to use in adult forensic examination, where it gives excellent spatial resolution for most organs, particularly skeletal views, and is

better at forensic reconstruction than MRI [Dirnhofer *et al.*, 2006]. The proposed advantages of CT over MR postmortem imaging include depiction of fractures and gross tissue injury, as well as the fast acquisition time (5-10 minutes for whole-body CT) which leads to minimal intrusion on the working schedule of a clinical radiology department. Further, with the use of multi-detector CT (MDCT), images can be reconstructed in any plane, which helps to elucidate complex anatomical structures.

A recent study confirmed the feasibility of MDCT in the investigation of third trimester stillbirth. MDCT image quality was acceptable and the examination demonstrated a range of anatomic and pathologic findings. Initially, the value of CT may also be as an important adjunct to conventional postmortem examination, especially where postmortem rates are low, in the setting of congenital malformation, and where the resource of MRI is not available. [O'Donoghue *et al.*, 2011]. Targeted biopsy under imaging control may add to the sensitivity and specificity of postmortem imaging and allow histological diagnosis.



## Status of Current Evaluation for the Cause of Stillbirth

Generally accepted tests	Useful in some cases	Uncertain utility	Developing technologies
<ul style="list-style-type: none"> <li>• Medical and obstetric history</li> <li>• Maternal haematology and biochemistry</li> <li>• Post-mortem examination</li> <li>• Radiological investigations</li> <li>• Placental evaluation</li> <li>• Maternal bacteriology</li> <li>• Karyotype</li> <li>• Kleihauer-Betke test</li> <li>• Blood group and antibody screen</li> <li>• Liver function and bile acid testing</li> <li>• Parvovirus serology</li> <li>• Toxicology screen</li> </ul>	<ul style="list-style-type: none"> <li>• Lupus anticoagulant</li> <li>• Anti-cardiolipin antibodies</li> <li>• Factor V Leiden mutation</li> <li>• Prothrombin G20210A mutation</li> <li>• Screen for Protein C, Protein S and Anti-thrombin III deficiency</li> <li>• Rubella and Syphilis testing (if not done antenatally)</li> <li>• Maternal autoantibodies</li> <li>• Parental karyotypes</li> </ul>	<ul style="list-style-type: none"> <li>• Thyroid function tests, TSH</li> <li>• TORCH serology</li> <li>• Placental cultures</li> <li>• Testing for other thrombophilias</li> <li>• Glyco-haemoglobin (HbA1c)</li> </ul>	<ul style="list-style-type: none"> <li>• Comparative genomic hybridisation</li> <li>• Testing for single-gene disorders</li> <li>• Nucleic acid based testing for infection</li> <li>• MR and CT imaging</li> </ul>

[From Silver *et al.*, 2007; PSANZ, 2009; RCOG, 2010]

## 6.4 Labour and delivery

### **Management**

The management of the birth is discussed as soon after diagnosis as feasible, and options are explored with parents regarding timing of the birth. Recommendations about labour and birth should take into account the mother's preferences as well as her medical condition and previous intra-partum history. Clear explanations of procedures should be communicated to the parents in a sensitive manner.

Management may involve awaiting spontaneous labour or planned induction.

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 [RCOG, 2010].

The management plan should be clearly documented in the chart in consultation with the parents. This should include their wishes with regard to the bereavement and loss team. The midwife who is dealing with the family should inform Bed Management, Delivery Suite and the relevant ward, to ensure that an appropriate space is made available.

### **Expectant management**

More than 85% of women with an IUFD labour spontaneously within three weeks of diagnosis. 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 [NICE, 2008].

However, there is a 10% chance of maternal DIC within 4 weeks from the date of fetal death and an increasing chance thereafter [Parasnis *et al.*, 1992]. Women who delay labour for periods longer than 48 hours should therefore be advised to have testing for DIC twice weekly. They should also be advised that they could develop severe medical complications and suffer greater anxiety with prolonged intervals [RCOG, 2010].

Women contemplating prolonged expectant management should be advised that the value of subsequent postmortem examination might be reduced and that the appearance of the baby might deteriorate [RCOG, 2010].

### **Medical induction**

Vaginal birth is the recommended mode of delivery for most women, but caesarean section will need to be considered in some cases [RCOG, 2010].

Vaginal birth can be achieved within 24 hours of induction of labour for IUFD in about 90% of women [Wagaarachchi. *et al.*, 2002]. Vaginal birth carries the potential advantages of immediate recovery and quicker return to home.

A combination of mifepristone and a prostaglandin is recommended as the 1<sup>st</sup> line intervention for induction of labour. Wagaarachchi *et al* found that the combined use of

mifepristone and misoprostol was not only safe but also had an average time to delivery interval less than any of the other induction regimes in use.

A single 200mg dose of mifepristone is appropriate for induction after IUFD.

Misoprostol can be used in preference to prostaglandin E2 because of equivalent safety and efficacy with lower cost [RCOG, 2010]. The use of vaginal misoprostol in the termination of second and third trimester of pregnancy is as effective as other prostaglandin preparations (including cervagem, prostaglandin E2 and prostaglandin F2alpha), and more effective than oral administration of misoprostol. [Dodd and Crowther, 2010].

A review of misoprostol use for late IUFD recommended that the dose should be adjusted according to gestational age (100 micrograms 6-hourly before 26 weeks; 25–50 micrograms 4-hourly at 27 weeks or more) [Gómez Ponce de León, 2007]. The National Institute has endorsed this recommendation for Health and Clinical Excellence [NICE, 2008], although the 2010 Cochrane Review on the use of Misoprostol in IUFD concluded that the differing treatment regimens analysed appeared comparable for the common reported outcomes.

There remains wide variation in the dose, frequency and route of administration of misoprostol used in the setting of IUFD. While concerns about fetal safety are not relevant, issues of side effects for the mother remain. In addition, important information regarding maternal safety, and in particular the occurrence of rare outcomes such as uterine rupture, remains limited [Dodd and Crowther, 2010].

A suggested protocol for medical induction of labour after IUFD is set out in [Appendix 4](#).

Caesarean birth might occasionally be clinically indicated by virtue of the maternal condition. The woman herself might request caesarean section because of previous experiences or a wish to avoid vaginal birth of a dead baby. This demands a careful and sensitive discussion and joint decision-making [RCOG, 2010]. The implications of caesarean delivery for future childbearing should be discussed [NICE, 2004].

### ***Previous caesarean section***

If a woman has had a previous caesarean section, a discussion as to the safety and benefits of induction of labour needs to be undertaken by a consultant obstetrician [RCOG, 2010].

Mifepristone can be used alone (at a dose of 600mg) to increase the chance of labour significantly within 72 hours (avoiding the use of prostaglandin).

Women with a single lower segment scar should be advised that, in general, induction of labour with prostaglandin is safe but not without risk. The RCOG Green-top guideline (2010) concludes that misoprostol can be 'safely' used for induction of labour in women with a single previous CS and an IUFD, while acknowledging the paucity of studies on the safety and effectiveness of induction of labour after IUFD in women with a single caesarean section scar. 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 [RCOG, 2007].

In contrast, the Society of Obstetricians and Gynaecologists of Canada recommended that misoprostol be contraindicated in women with previous caesarean delivery because of a high rate of uterine rupture [SOGC, 2005]. A more recent review of induction of labour for late IUFD concluded that misoprostol could be used safely at lower doses for women with a previous caesarean (25–50 micrograms) [Gómez Ponce de León, 2007]. This latter recommendation has been endorsed by NICE [NICE, 2008]. Misoprostol is not currently marketed at these lower doses.

Women with two previous CS 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 CS [RCOG, 2010]. Women with more than two CS deliveries or atypical scars should be advised that the safety of induction of labour is unknown [RCOG, 2010]. Unless there is a pressing need to induce labour, caution should be exercised in using oxytocic agents in the presence of a uterine scar.

### ***Care on admission to the hospital***

The admission should be planned and the parents prioritised on their arrival and taken directly to the relevant ward or clinical area. The parents should be accommodated in a room on their own - where possible in a location within the hospital away from antenatal or postnatal wards.

An individual midwife should be allocated to the family. This midwife should welcome the family, orientate them to the ward and provide additional supportive care during their stay in the hospital. The consultant or registrar should then reassess the woman, and review the care plan with the couple and the allocated midwife.

Appropriate support services should be contacted in relation to the parents' admission, including members of the hospital bereavement and loss team (personnel involved will vary locally). Pastoral care is also offered to the family.

Unnecessary disruption should be avoided during the time on the ward and contact with additional staff minimised.

### ***Care on admission to the Labour Ward***

The midwife on ward should liaise with Labour Ward prior to transfer. On arrival, the parents should be introduced to the Midwifery and Medical Team and the Care Plan is reviewed with the parents.

Staff should try to ensure a quiet environment for the parents during this time. 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 [RCOG, 2010].

### ***Intra-partum management***

An experienced midwife should give care in labour. During labour the parents should have the opportunity to spend time on their own if that is what they wish.

Routine antibiotic prophylaxis should not be used. Women with sepsis should be treated with intravenous broad-spectrum antibiotic therapy. Intra-partum antibiotic prophylaxis for women colonised with group B streptococcus is not indicated. Infection is a common association of late IUFD and the mother can develop severe sepsis from a wide range of bacteria. Regardless of the primary cause of death, the fetus can act as a focus for severe secondary sepsis, which can result in DIC. In one study, 3.1% of women with an IUFD developed signs of sepsis during induction of labour [Wagaarachchi *et al*, 2002]. There are no data on the routine use of intra-partum antibiotics for the prevention of maternal infection in the setting of IUFD [RCOG, 2010].

Analgesia in labour is particularly important for women with an IUFD. All usual modalities should be available including regional anaesthesia and patient-controlled anaesthesia [RCOG, 2010]. Diamorphine should be used in preference to pethidine. Regional anaesthesia should be available for women with an IUFD; however, assessment for DIC and sepsis should be undertaken before administering regional anaesthesia. Women should be offered an opportunity to meet with an obstetric anaesthetist [RCOG, 2010].

Women undergoing VBAC should be closely monitored for features of scar rupture. Oxytocin augmentation can be used for VBAC, but a consultant obstetrician should make the decision [RCOG, 2010]. 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 [RCOG, 2007]. There are no reports on the safety and effectiveness of oxytocin augmentation in VBAC with IUFD.

### **Birth**

The parents will never forget this time, and the aim is to sensitively ensure it is as positive an experience as possible. If an assisted delivery is required, the obstetrician must handle this sensitively, and adequate analgesia should be maintained throughout.

Certain fetal scenarios e.g. macrosomia or hydrops may increase the time spent in labour and increase the risk of dystocia. It is estimated that around 3% of stillborn babies weigh more than 4kg [CMACE, 2009]. Because of this, a longer passive second stage of labour has been advocated in the setting of IUFD. This aims to ensure good descent of the fetal head and prevent CS at full dilatation. Destructive procedures such as craniotomy, decapitation, and cleidectomy were common many years ago to enable vaginal delivery of a dead baby that had become obstructed in the pelvis during labour. These procedures have almost completely disappeared from obstetrics in the developed world, although are still rarely carried out in the developing world, where abdominal delivery poses a significant risk to the mother. However, some authors make the case for skilled practitioners to continue to perform these operations in certain cases [Steel *et al.*, 2009].

Post partum haemorrhage also needs to be anticipated, particularly where there was pre-existing polyhydramnios or where labour has been either precipitate or prolonged. A senior obstetrician should therefore be either available or in attendance at delivery. Active management of the third stage of labour, using oxytocics to ensure adequate uterine tone, should also be advocated.

At birth, the parents should be provided the opportunity if appropriate to:

- Cut the cord
- Have the baby delivered into mother's arms
- Spend time alone with the baby
- Get to know their baby
- Facilitate mother and baby skin to skin contact
- Take and have a variety of photographs taken

Parents are often ill-prepared for the appearance of their baby, especially where death occurred several days before delivery. Staff should gently explain to the parents what their baby might look like after birth.

The parents may need to be gently guided in carrying out these tasks for their baby. The midwife will also facilitate this in the way she models the care of the baby as she would with a living baby. The way in which the midwife interacts with the baby using the same respect and importance that she would with a living baby will have a profound influence on the parent's reaction to their baby.

## **6.5 Post-natal care**

### ***Care on the ward after delivery***

One midwife should be allocated to care for the parents and the baby.

Parents should be allocated a room on their own after delivery. The partner should be offered open visiting and facilitated to stay with the mother at night.

Parents need to be advised in relation to rooming with the baby and the need for the baby to be placed occasionally in quiet room.

### ***Lactation***

Mothers need to be advised on what to expect regarding lactation and how to suppress or manage this. Suppression of lactation is of psychological importance for some women following IUFD. One third of those who choose non-pharmacological measures to achieve this are troubled by excessive discomfort.

If suppression is necessary, dopamine agonists are 1<sup>st</sup> line agents to suppress lactation. Cabergoline is superior to bromocriptine (Cabergoline 1mg od for 14 days). Dopamine agonists should not be given to women with hypertension or pre-eclampsia. Oestrogens should not be used to suppress lactation [RCOG, 2010].

### ***Thromboprophylaxis***

Women should be routinely assessed for thromboprophylaxis as per local protocols and established guidelines, but IUFD is not a risk factor on its own [RCOG, 2010].

### ***Who should be informed of the stillbirth?***

- General Practitioner
- Hospital chaplain
- Social worker
- Public health nurse
- Bereavement officer
- All existing antenatal appointments should be cancelled

Ideally, a telephone call should be made to the GP as soon as reasonable after the diagnosis of IUFD and after stillbirth - a letter or email from the hospital may not be received in time prior to a bereaved mother or father presenting to their GP.

### ***Discharge***

Before discharge, the woman should be reviewed by a senior obstetrician.

Parents should be provided with written information on supportive care (from support groups as well as local pregnancy loss services) and contact information for follow-up.

The chart should be retained in the hospital and safely stored. Results of postmortem examination and placental pathology, and results of blood tests should be filed in a timely manner. The chart will be needed for review at the hospital multi-disciplinary meeting and for perinatal audit, as well as for completion of perinatal death notification forms.

In some units, it is practice to attach a sticker to the chart to indicate that a perinatal death has occurred and alert staff to the patients' history. This is a discreet way of ensuring that health care professionals who come into contact with the bereaved parents are aware of the previous stillbirth and treat the couple with sensitivity.

The parents should be aware that a follow-up appointment with the consultant obstetrician will be arranged and it should be clear who is responsible for making these arrangements. Subsequent clinic appointments should take place in a quiet and undisturbed location within the hospital, for example at the end of a gynaecology clinic.

Follow up arrangements are also made with the GP.

### ***Birth registration***

Parents are advised on the registration requirements and procedure before discharge.

The medical certificate is an essential requirement but if a postmortem examination is to be carried out, the medical certificate cannot be completed until those results are available and this may take several months.

When the parents attend for follow up to receive the results, the medical certificate may then be completed by the obstetrician and given to the registrar so that the parents may apply for registration of their stillborn baby.

### ***Burial / Cremation***

Parents should be given information regarding burial and cremation and be allowed to make choices. Some parents will make their own burial arrangements at a family plot or choose cremation.

If parents are considering a hospital burial they need to be made aware that shared plots are used, and should be given information on the relevant cemetery. If parents decide on hospital burial, or cremation, the services of the hospital's Undertakers are offered. Written consent for hospital burial is completed and placed in the chart, while a copy is also given to the parents. Local guidelines apply regarding this process.

Pastoral Care is offered to all families by the Hospital Chaplains. Parents are offered a Religious Service in conjunction with the Hospital Chaplain or their chosen Religious Leader, which the Chaplain will assist in facilitating.



## 6.6 Supportive Care

Ideally, a bereavement officer / team should be appointed to coordinate services for parents who have experienced an IUFD. The midwife caring for the parents should link with appropriate services including Funeral Director, Chaplain, bereavement and loss officer / team.

Parents should be invited to meet with Chaplain or their chosen religious leader.

Staff should gently support parents' wishes in having contact with their stillborn baby.

Parents are to be supported in parenting their baby, e.g. holding, dressing, bathing, and getting to know their baby.

Parents should be helped to retain artefacts of remembrance.

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

Photographs are precious to bereaved parents, especially those taken soon after birth. Guidance on taking pictures at this difficult time is available from support groups.

Footprints, handprints and lock of hair (if available) are then taken for a memories booklet, with the parents' consent.

Counselling should be offered to all women and partners. Other family members should be considered for counselling. Posttraumatic stress disorder is prevalent in parents in this situation. Perinatal death is also associated with increased rates of admission with post-natal depression. Women with poor social support are particularly vulnerable. Parental relations have a 40% higher risk of dissolving after stillbirth compared with a live birth.

Parents should be advised about local and national support groups (e.g. A Little Lifetime Foundation, Feileacain, etc.).

Finally, excellence in clinical care needs to be matched with the same attention to emotional support. Ancillary guidelines for staff in appropriately communicating with bereaved parents are available [SANDS, 2007].

## 6.7 Follow up

It has been shown that parents value [Badenhorst and Hughes, 2007]:

- Efforts to find out how they are coping
- Full and frank information given sensitively to enable them to build up a cohesive picture of what happened and assess their future options.
- Reassurance where possible.

A follow-up appointment with the consultant obstetrician should be organised when results of postmortem tests are available.

Parents should have an appropriate contact number for the obstetric team during this time. The parents need to be reassured that they can make contact at any time.

At follow-up, parents should be advised about the cause of late IUFD, chance of recurrence and any specific means of preventing further pregnancy loss.

General pre-pregnancy advice should also be included in the consultation: smoking cessation, weight loss as appropriate, pre-conceptual folic acid therapy.

Support services including pastoral care and bereavement counselling should also be offered. Parents may choose to make contact with these services at their discretion over time.

Mothers who suffer perinatal death may not have the same access to routine care where they can discuss their physical needs in the postnatal period. Close liaison between hospital, general practice and support services is important. Relevant issues of care include suppression of lactation, contraception, gynaecological complications and sexual difficulties [Badenhorst and Hughes, 2007].

## 6.8 Pregnancy after stillbirth

### ***Recurrence of stillbirth***

In Ireland in 2008, 98.3% of total births to multiparous women recorded no previous stillbirths – but 1.7% recorded at least at 1 previous stillbirth, consistent with data from other years [ESRI 2010].

Small studies have shown no difference in stillbirth recurrence, but a large retrospective study of 947 women and 261384 controls showed that women with a history of stillbirth (but otherwise low-risk) had a 12-fold increased risk of intra-partum stillbirth (95% CI 4.5–33.7) [Sharma *et al.*, 2007]. 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) [Black *et al.*, 2008].

The ACOG Practice Bulletin reports the risk of recurrent stillbirth after 20 weeks of gestation as 7.8 to 10.5 per 1000 births. Most of this risk occurs before 37 weeks of gestation. However, the risk for subsequent stillbirth for women with a previous live born, growth-restricted infant delivered before 32 weeks of gestation is double the risk for women with a previous stillbirth [ACOG, 2009].

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 [Robson *et al.*, 2001]. A significant proportion of unexplained IUFDs are reclassified as fetal growth restriction when customised charts and different classification systems are used [Gardosi *et al.*, 2005].

### ***Management of pregnancy after stillbirth***

The history of stillbirth should be clearly marked in the case record and caregivers should ensure they read all the previous notes thoroughly before seeing the woman at the booking visit.

Women with this history should attend a consultant-led hospital-based antenatal clinic - [RCOG, 2010] and should have early access to combined antenatal care [Monari and Facchinetti, 2009].

Women should be advised about smoking cessation; ceasing smoking in the first trimester seems sufficient to reduce the risk of stillbirth [Monari and Facchinetti, 2009].

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 (e.g. 4 weekly from 24 weeks) [Monari and Facchinetti, 2009].

Screening should be carried out for gestational diabetes [Monari and Facchinetti, 2009]. Maternal request for scheduled birth should take into account the gestational age of the previous IUFD, previous intra-partum history and the safety of induction of labour.

Caregivers should be vigilant for postpartum depression in women with a previous IUFD. The birth of a healthy baby does not compensate for a previous loss and can trigger a resurgence of grief.

Carers should be aware that maternal bonding in a pregnancy after stillbirth could be adversely affected. 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. Unresolved maternal grief may result in disorganisation of attachment with future babies [Badenhorst and Hughes, 2007].

## 6.9 Perinatal Death Notification Form

From 2011, perinatal death notification forms should be completed for all cases of stillbirth [[Appendix 5](#)]. These should be filled out using the information available in the maternity case notes, the postmortem report and the placental histology report, and submitted (electronically) to the National Perinatal Epidemiology Centre (NPEC).

Queries regarding the Perinatal Death Notification Form should be addressed to NPEC:-

Tel: (0) 21 4205017

Fax: (0) 21 4205025

E-mail: [npec@ucc.ie](mailto:npec@ucc.ie)

## 6.10 Legal requirements, Registration and the Role of the Coroner

The legal definition of stillbirth is “any child expelled or issued forth from its mother after the 24<sup>th</sup> week of pregnancy that did not breathe or show any signs of life”.

Fetal deaths delivered later than 24 weeks that had clearly occurred before the end of the 24<sup>th</sup> week do not have to be certified or registered.

A Coroner must be contacted if there is a doubt about the status of the birth [Coroners Acts 1962 and 2005].

The relevant authorities should be contacted if there is a suspicion of deliberate action to cause stillbirth.

The parents are responsible in law for registering the birth but can delegate the task to a healthcare professional.

### ***Stillbirths Registration Act (1994)***

This Act applies in relation to a child born weighing 500 grammes or more or having a gestational age of 24 weeks or more who shows no sign of life.

The functions of an tArd-Chláraitheoir, superintendent-registrars and registrars under the Births and Deaths Registration Acts, 1863 to 1987, include the registration of stillbirths.

Each Registrar is obliged to establish and maintain a register of stillbirths.

The Information recorded in the register is set out as follows:-

- Date and Place of Birth.
- Sex of Child
- Weight.
- Gestational Age
- Forename and Surname of Child.
- Mother's Forename and Surname, Address and Occupation.
- Any former Surname(s) of Mother.
- Father's Forename and Surname, Address and Occupation.
- Any former Surname(s) of Father.
- Signature, Qualification and Address of Informant.
- When Registered.

The Act sets out the legal requirements for notification and registration of stillbirths:-

- The mother or the father of a stillborn child may, within forty-two days after the birth, give the registrar of the district in which the stillbirth occurred the information specified and sign the register in the presence of the registrar, and the registrar shall register the stillbirth accordingly and sign the register.
- The required particulars shall comprise the details indicated in the Schedule to this Act and a medical certificate signed by a registered medical practitioner, who has attended

the birth or has examined the child, stating, in the opinion of the medical practitioner, the weight and gestational age of the child and naming, where applicable, the hospital in which the birth occurred or which had care of the mother following the birth.

- Where the registration takes place as the result of particulars provided by the mother or the father of the child, the registrar shall, within two weeks of registration, notify the hospital named in the certificate or the medical practitioner who signed it, where no hospital is named, that such registration has taken place.
- Where no such notification is received by the hospital or by the medical practitioner within three months of the stillbirth, it shall be the duty of the hospital (by an authorised member of its staff) or, where no hospital is involved, of the medical practitioner who attended the birth or examined the child to give to the registrar within four months of the stillbirth, the required particulars of the stillbirth and sign the register in the presence of the registrar, and the registrar shall register the stillbirth accordingly and sign the register.
- A medical practitioner who attends a stillbirth or examines the child shall provide the required medical certificate to the mother or the father of the stillborn child, where either parent expresses a wish to inform the registrar of a stillbirth.
- Where a medical certificate is provided to the mother or the father of the child and the hospital or the medical practitioner is not notified that registration has taken place as the result of information given to the registrar by the parents, a duplicate of that certificate may be used for registration purposes.
- If the medical practitioner is not fully satisfied that the birth was a stillbirth, the medical practitioner shall refer the matter to the Coroner.
- If, in the course of duty, a Coroner finds that a body is that of a stillborn child, the Coroner shall, within one month of so finding, notify the registrar of the details, so far as the Coroner can ascertain them, of the stillbirth indicated in the Schedule, and the registrar shall register the stillbirth accordingly and sign the register.

### ***Coroner's post-mortem examination***

A Coroner in Ireland is an independent office holder charged with the legal responsibility [Coroners Acts 1962 and 2005] for the investigation of sudden, unexplained, violent and unnatural deaths in his or her district. This may require a post mortem examination, sometimes followed by an inquest.

A Coroner's postmortem examination is compulsory under the law and consent is not required. Parents should therefore not be approached for consent.

The postmortem is carried out by a pathologist, who acts as the Coroner's agent for this purpose. Pathologists and /or facilities at hospitals operated or funded by the HSE may be used for the purpose of Coroners' post mortems. Coroners are entitled and obliged by law to direct the retention of organs and ante-mortem samples in the context of establishing the cause of death.

No doctor may certify a death which is due directly or indirectly to any unnatural cause. The Coroner's inquiry is concerned with establishing whether or not the death was due to natural or unnatural causes. The general rule is that all sudden, unexplained, violent deaths and any death which is due directly or indirectly to any unnatural cause must be reported to the Coroner. If a doctor has any doubt in the matter, he or she should contact the District Coroner.

The Dublin City Coroner has also determined that the following deaths are reportable by Maternity Hospitals in Dublin City. Local requirements should be ascertained by other hospitals by contacting the Coroner for the district in which the hospital or institution is located [Code of Practice for Postmortem Services, 2010].

- All maternal deaths
- Infant death occurring as either stillbirth / intrapartum / neonatal / post- neonatal death where any of the following arise:
  - Questions of criminal offence
  - Concealment of birth
  - Want of attention at birth / possible infanticide
  - Procured abortion
- Trauma (accidental / non-accidental)
- Allegation of malpractice (which may have contributed to the cause of death) or any concerns relating to death
- Certain stillbirths (where the medical practitioner is not fully satisfied that the birth was a stillbirth or there are any other concerns)
- Certain deaths in hospital
  - Post diagnostic/therapeutic/instrumental procedure (where the procedure may be a factor in the causation of death.)
  - Adverse drug reaction
  - Certain healthcare acquired infections
- Maternal drug addiction (that may have contributed to death)
- Unnatural death (antepartum, intrapartum, neonatal, post neonatal)
- Domiciliary delivery



## 6.11 Clinical Governance

Maternity units should be aware of specific standards for diagnosis, management, investigation and follow-up of cases of IUFD / stillbirth

Standardised checklists are recommended to ensure that all appropriate care options are offered and that each response mark is recorded. An example is shown in [Appendix 6](#).

Parents should be provided with written information leaflets on the following issues:-

- Postmortem examination
- Expectations for physical recovery
- Lactation suppression
- Birth registration
- Details of local and national support groups
- Plan for follow-up

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

A standardised dataset should be collected for all stillbirths.

Perinatal death notification forms should be completed for all cases of stillbirth and cases reported to the National Perinatal Epidemiology Centre.

All stillbirths should be reviewed in a multi-professional meeting using a standardised approach to analysis for substandard care and means of future prevention.

All term intra-partum deaths with no evidence of a major congenital anomaly should be fully investigated locally with a view to identifying whether there were avoidable factors and to identify any areas where future care can be improved. The rate of intrapartum fetal death is a perinatal outcome, which is particularly sensitive to the standard of intrapartum management [Walsh et al., 2008].

Staff working with bereaved parents should be provided with an opportunity to develop their knowledge and understanding of perinatal loss, together with development of skills in working in this area.

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

### ***Perinatal Audit***

Perinatal audit has been described as: “The systematic, critical analysis of the quality of perinatal care, including the procedures used for diagnosis and treatment, the use of resources and the resultant outcome and quality of life for women and their babies” [Flennady *et al.*, 2011].

Although high-level evidence is not available, a review of before-and-after studies in low-income and middle-income countries showed a 30% reduction in perinatal mortality

associated with the introduction of perinatal audit [Pattinson *et al.*, 2005]. Studies in high-income countries also indicate benefit.

The Lancet's Stillbirths Series steering committee [Flenady *et al.*, 2011] recommended these essentials for high quality perinatal audit:-

- Complete registration and comprehensive documentation for each stillbirth
- Allocated motivated multidisciplinary personnel
- Training in audit methodology and communication skills for participants
- An independent chairperson
- Analysis of what went well
- Analysis of what should have been done differently
- Analysis of the substandard care factor
- Definition of improvements in care that need to be made
- Implementation of improvements
- Checking that change has occurred
- Keeping the goal in mind: to improve the quality of care

## 6.12 Future Research

The RCOG Green-top guideline No.55 lists 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.

The Lancet's Stillbirths Series steering committee [Flenady *et al.*, 2011] lists stillbirth research priorities in discovery science, epidemiology, and development and delivery:

### ***Research priorities in discovery science***

- The effects of peri-conceptual environment, including nutrition and micronutrient status, on embryonic development
- Development of repositories of well phenotyped human samples from stillbirths or other related conditions and matched controls, with clear arrangements for access, and appropriate ethical and other legal permissions in place
- Characterising the fetal response to an adverse intrauterine environment to develop improved means of clinical assessment of fetal wellbeing
- Defining pathophysiological pathways leading to stillbirth associated with maternal disease, in particular type 1 and type 2 diabetes mellitus
- Defining pathophysiological pathways leading to increased rates of growth restriction and decreased rates of pre-eclampsia among smokers
- Development of improved statistical, biometric, and bioinformatic technologies for data interpretation and clinical prediction of outcome
- The effect of maternal obesity, with or without insulin resistance, on fetal and placental development
- The role of normal and abnormal coagulation in normal and abnormal pregnancy
- Understanding the fetal or placental function and control of the timing of parturition in post-dates pregnancy
- Discovery-based analysis (expression array or high throughput sequencing, proteomics, and metabolomics) of samples from well characterised complicated pregnancies and matched control

### ***Research priorities in epidemiology***

- What factors contribute to the excess in stillbirth rates in minority populations?
- What maternal lifestyle consumptions (caffeine, alcohol, cannabis) are associated with stillbirth and what are their relation with other relevant disorders and causes of stillbirth?
- What care factors relating to health-care professional practice, care setting, and the mother and family are associated with potentially avoidable stillbirth?
- How relevant is antenatal detection of fetal growth restriction to the prevention of stillbirth?
- What is the contribution of other maternal bacterial infections in pregnancy (e.g., group B streptococcal infection, bacterial vaginosis) to stillbirth?

- What is the optimum investigation protocol for stillbirth to identify causes and relevant conditions in terms of yield, utility, and costs?
- What approaches can be used to enhance accuracy of data on stillbirth rates using existing health systems datasets?
- What is the optimum model for clinical perinatal mortality audit and how can this be implemented on a population-based scale?
- Can a universal shortlist of less than ten categories of cause of stillbirth be used while linking to the present complex systems for stillbirth cause-of-death classification in high income countries? Would such a classification system meet the needs for comparability globally and still be useful for surveillance and public health decision-making in varying settings?
- What factors affect under-reporting of stillbirth in disadvantaged communities and can these be reduced?

### ***Research priorities in development and delivery***

- How can smoking cessation programmes be most effectively implemented as part of routine antenatal care?
- In pregnancies with established intrauterine growth restriction, what is the optimum mode and timing of birth to reduce stillbirth and neonatal and infant mortality and severe morbidity?
- In high-risk pregnancies, does fetal umbilical artery Doppler ultrasound reduce the risk of stillbirth, neonatal and infant mortality, and major morbidity?
- What is the role of fetal growth monitoring with growth curves adjusted according to individual characteristics in detection of abnormalities in fetal growth and reduction of stillbirth, neonatal and infant mortality, and morbidity; and which characteristics, if any, result in optimal performance of such an approach?
- For disadvantaged populations, how can access to optimum antepartum and birthing care be improved?
- How can perinatal audit and facility quality improvement be most effectively undertaken to reduce stillbirth rates?
- What is the role of screening in early pregnancy with markers of placental function in reduction of the risk of stillbirth, neonatal and infant death, and major morbidity?
- For women who report decreased fetal movements, what is the optimum management to reduce the risk of stillbirth in term and preterm pregnancies?
- What characteristics of antenatal care are associated with a reduction in the risk of stillbirth?
- In pregnancies with impaired fetal growth, what regimens of fetal surveillance are associated with a reduction in adverse pregnancy outcome including stillbirth, neonatal and infant mortality, and major morbidity?

## 7 Key performance indicators

1. Completion of investigations for the cause of late IUFD
2. Proportion of parents offered postmortem examination
3. Proportion of parents declining postmortem who were offered alternative tests
4. Proportion of parents who have postmortem consent undertaken by an appropriately trained senior obstetrician
5. Proportion of women offered follow-up with a senior obstetrician
6. Proportion of women and families offered counselling follow-up

## 8. References and Recommended Reading

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## 9. Useful resources

### A Little Lifetime Foundation

A Little Lifetime Foundation (formerly ISands), providing information and support to bereaved parents and families since 1983. Working with Health Care Professionals and Others to develop good practices in the area of Infant death. A Little Lifetime Foundation is a registered charity with support and services provided by volunteers.

Website: [www.isands.ie](http://www.isands.ie)

### Féileacáin

Féileacáin (Stillbirth and Neonatal Death Association of Ireland – SANDAI) is a newly formed organisation (charitable status pending) that aims to offer support to anyone affected by the death of a baby during pregnancy or shortly after. The organisation was formed by a group of bereaved parents who have now come together to formally offer support to other parents and families who find themselves in a similar situation.

Website: [www.feileacain.ie](http://www.feileacain.ie)

### Stillbirth and Neonatal Death Society (SANDS)

The UK Stillbirth and Neonatal Death Charity, established by bereaved parents in 1981. The core aims are (1) To support anyone affected by the death of a baby; (2) To work in partnership with health professionals to improve the quality of care and services offered to bereaved families; and (3) To promote research and changes in practice that could help to reduce the loss of babies' lives.

Website: [www.uk-sands.org](http://www.uk-sands.org)

### Child Bereavement Trust (CBT)

The UK's leading charity that supports families and educates professionals, both when a child dies and when a child is bereaved.

Website: [www.childbereavement.org.uk](http://www.childbereavement.org.uk)

### International Stillbirth Alliance (ISA)

A non-profit coalition of organizations dedicated to understanding the causes and prevention of stillbirth. ISA's mission raise awareness of stillbirth and to promote global collaboration in the prevention of stillbirth and provision of appropriate care for parents whose baby is stillborn.

Website: [www.stillbirthalliance.org](http://www.stillbirthalliance.org)

## 10. Qualifying statements

These guidelines have been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. Clinical material offered in this guideline does not replace or remove clinical judgment or the professional care and duty necessary for each pregnant woman. Clinical care carried out in accordance with this guideline should be provided within the context of locally available resources and expertise.

This Guideline does not address all elements of standard practice and assumes that individual clinicians are responsible to:

- Discuss care with women in an environment that is appropriate and which enables respectful confidential discussion.
- Advise women of their choices and ensure informed consent is obtained.
- Meet all legislative requirements and maintain standards of professional conduct.
- Apply standard precautions and additional precautions as necessary, when delivering care.
- Document all care in accordance with local and mandatory requirements.

## 11. Implementation Strategy

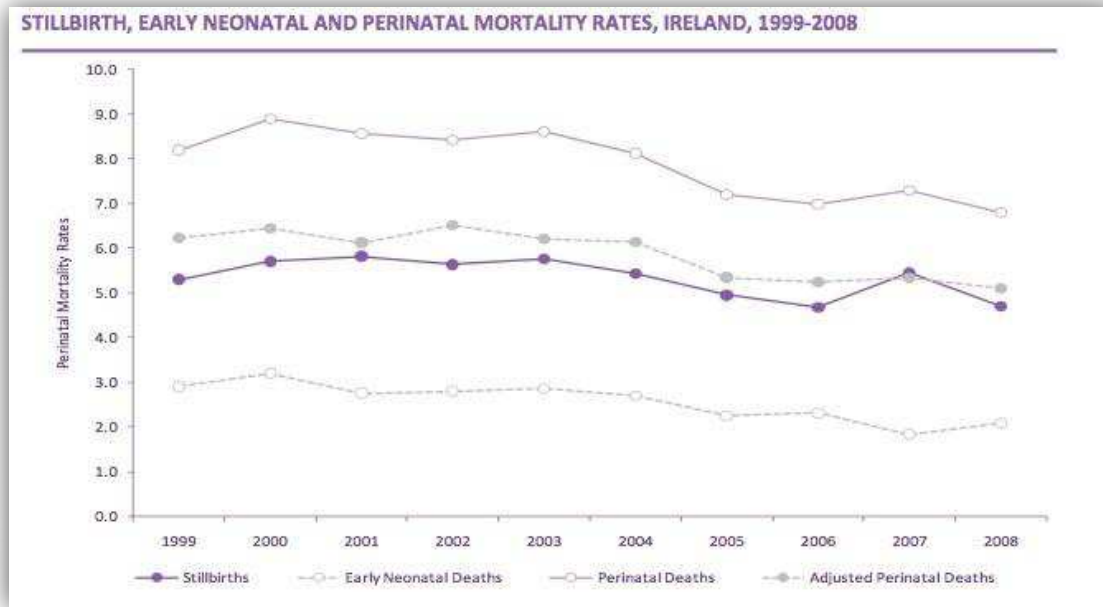
- Distribution of guideline to all members of the Institute and to all maternity units.
- Implementation through the HSE Obstetric and Gynaecological Programme's local implementation boards.
- Distribution to other interested parties, including general practitioners, parent and support groups, regulatory and educational training bodies.

## 12. Appendix List

1. Stillbirth, early neonatal and perinatal mortality rates, Ireland 1999-2008
2. Checklist for investigation of IUFD/ stillbirth
3. Consent to postmortem form
4. Suggested algorithm for induction of labour after IUFD
5. Perinatal death notification manual, NPEC, 2011
6. Checklist for management of IUFD / stillbirth

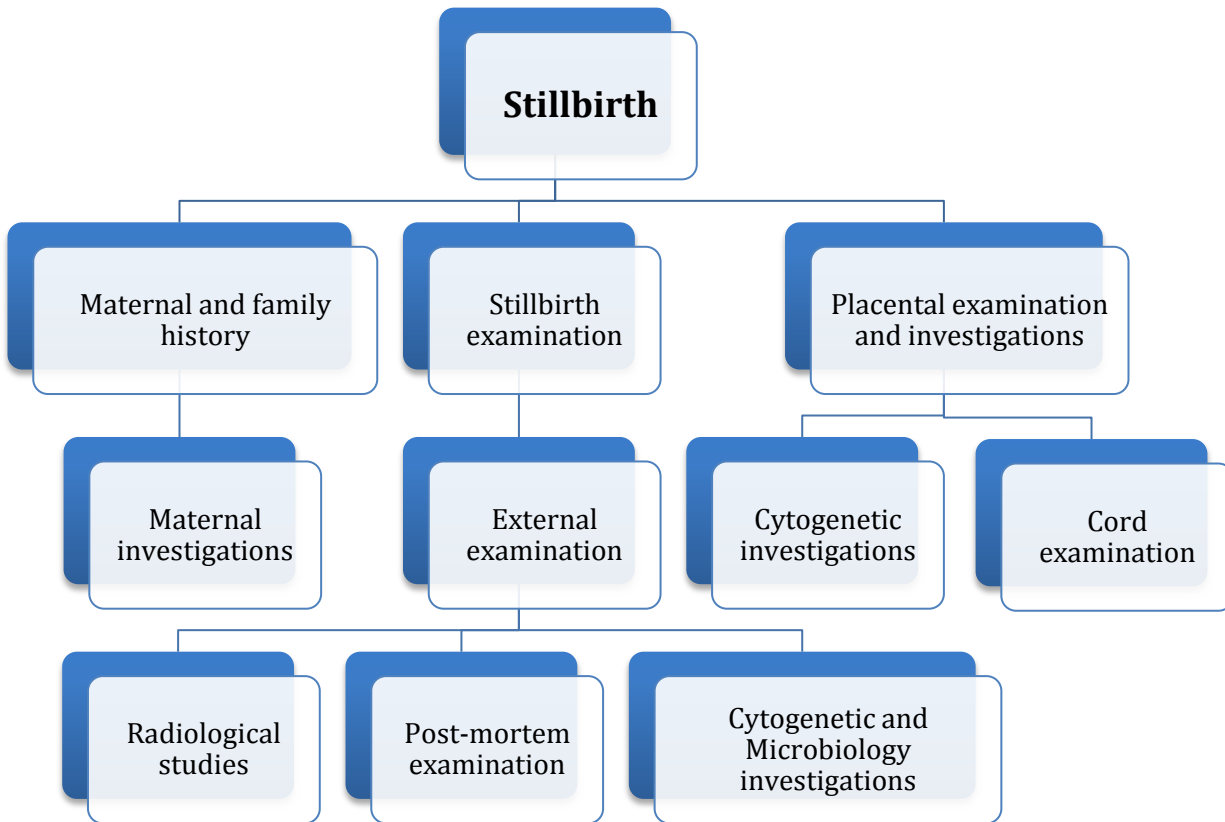
## Appendix 1

Stillbirth, early neonatal and perinatal mortality rates, Ireland 1999-2008  
 ESRI, 2010




## Appendix 2

Algorithm for investigation of stillbirth





### Appendix 3


  <b><u>POST MORTEM CONSENT FORM</u></b>	<b>Affix addressograph label to EACH page</b>
I have been given the post mortem information booklet and I have been given an opportunity to discuss the post mortem examination with a doctor.	<b>Yes</b> <input type="checkbox"/>
I understand that the post mortem examination is carried out to verify the cause of death and: <ul style="list-style-type: none"> <li>• Involves taking small samples of tissues (blocks and slides) for examination, along with medical photographs and x-rays, all of which are retained as part of the healthcare record. <span style="float: right;"><b>Yes</b> <input type="checkbox"/></span></li> <li>• Information will be used for medical audit and education purposes. <span style="float: right;"><b>Yes</b> <input type="checkbox"/></span></li> <li>• If the examination is limited a full explanation of an illness may not be obtained. <span style="float: right;"><b>Yes</b> <input type="checkbox"/></span></li> <li>• Involves the temporary removal of all organs from the body. Some organs may remain outside the body for a few days to complete the examination, but these will be returned to the body before it is released for the funeral. <span style="float: right;"><b>Yes</b> <input type="checkbox"/></span></li> <li>• In exceptional circumstances it may be considered necessary to retain (after release of the body) an organ for detailed examination to be completed. The reason for this will be explained to me and I will be asked to sign a separate consent form to allow this to happen. <span style="float: right;"><b>Yes</b> <input type="checkbox"/></span></li> </ul>	
I consent to the following examination being performed: (a) 'Full' hospital post mortem examination with no limitations <p style="text-align: center;"><b>OR</b></p> (b) Limited post mortem examination. The limitations imposed on the post mortem examination are: _____ _____	<b>Yes</b> <input type="checkbox"/>  <b>(OR)</b>  <b>Yes</b> <input type="checkbox"/>
I agree that the blocks and slides may be used for research purposes, which are approved by the Hospital's Research Ethics Committee.	<b>Yes</b> <input type="checkbox"/> <b>No</b> <input type="checkbox"/>

I \_\_\_\_\_ hereby give my consent to the performance of a post mortem examination on the body of baby \_\_\_\_\_. Date \_\_\_\_\_  
**Signature of Parent/Next of Kin** \_\_\_\_\_ Relationship to the Deceased \_\_\_\_\_

I confirm that I have spoken with \_\_\_\_\_ the parent/next of kin of \_\_\_\_\_ and that I have explained to them the content of this form and that the consent to post mortem examination has been given on an informed basis. **Doctor's Name (Print)** \_\_\_\_\_  
 Signature \_\_\_\_\_ Medical Council No. \_\_\_\_\_ Date \_\_\_\_\_ Time \_\_\_\_\_

**Pathology Department** - the consent form has been reviewed before undertaking the post mortem by:  
 Pathologist \_\_\_\_\_ Medical Council No. \_\_\_\_\_ Date \_\_\_\_\_ Time \_\_\_\_\_  
 A.P.T. \_\_\_\_\_ Date \_\_\_\_\_ Time \_\_\_\_\_

PA 1064A (Mar 2011) **White copy** - Pathology Record, **Yellow copy** - Parent/Next of Kin, **Blue copy** - Mother/Baby Healthcare Record

	<p><b><u>CONSENT FORM FOR THE RETENTION OF ORGAN(S)</u></b></p>
<p><b>Name of Deceased</b> _____ <b>PM Number</b> _____</p> <p><b>Address</b> _____</p> <p>_____</p> <p>_____</p> <p>_____</p>	

The retention of [name the organ(s)] \_\_\_\_\_ is requested on the basis of (state rationale) \_\_\_\_\_

I \_\_\_\_\_ hereby give my consent for the Rotunda Hospital to retain the organ(s) as outlined above. Date \_\_\_\_\_

**Signature of Parent/Next of Kin** \_\_\_\_\_ **Relationship** \_\_\_\_\_

I confirm that I have explained the reason for the retention of organ(s).

**Doctor's Name (Print)** \_\_\_\_\_ **Medical Council No.** \_\_\_\_\_

**Signature** \_\_\_\_\_ **Date** \_\_\_\_\_

Once all the investigations have been completed, the organ(s) will be released by the Rotunda hospital. The hospital will pay for the grave opening /cremation fees.

I request the following option for the sensitive disposal of the retained organ(s): **(Please tick one option only)**

1. The Rotunda hospital will bury the retained organ(s) in the Angels' Remembrance Garden, Glasnevin Cemetery.	<b>Yes</b> <input type="checkbox"/>
2. The Rotunda hospital will bury the retained organ(s) in the private family grave.	<b>Yes</b> <input type="checkbox"/>
3. I will make personal arrangements for the burial of the retained organ(s).	<b>Yes</b> <input type="checkbox"/>
4. The Rotunda hospital will cremate the retained organ(s) and the ashes of the casket will not be returned.	<b>Yes</b> <input type="checkbox"/>

**Signature of Parent/Next of Kin** \_\_\_\_\_ **Date** \_\_\_\_\_

I confirm that I have explained the options available for the return of the retained organ(s).

**Name (Print)** \_\_\_\_\_ **Medical Council No.** \_\_\_\_\_

**Signature** \_\_\_\_\_ **Date** \_\_\_\_\_

## Appendix 4

### Medical Induction of labour after IUFD

#### On the day of diagnosis of IUFD

Mifepristone 200mg PO

#### 36-48 hours after diagnosis

24-34 weeks Misoprostol 200mcg PV followed by 200mcg PO 3 hourly x 4 doses

>34 weeks Misoprostol 100mcg PV followed by 100mcg PO 3 hourly x 4 doses

A second course may be started after 24 hours and with medical review

NB: Particular caution needs to be taken when considering induction of labour in women with a previous uterine scar.

## Appendix 5

### Appendix 5



## NATIONAL PERINATAL EPIDEMIOLOGY CENTRE

### REFERENCE MANUAL

## For completion of Perinatal Death Notification Forms

If you have any queries regarding the Perinatal Death Notification Form, please contact us at the National Perinatal Epidemiology Centre

Tel: (0)21 420 5017  
Fax: (0)21 420 5025  
E-mail: [npec@ucc.ie](mailto:npec@ucc.ie)

1. Please complete the notification form using the information available on the maternity case notes, the post mortem report and the placental histology report.
2. In the absence of a post mortem, please refer to the death certificate.
3. 'Not known' codes should be used as sparingly as possible.
4. Please complete all dates in the format DD/MM/YY; and all times using the 24hr clock e.g. 17.45.
5. Guidance for completion of Question 6.6:  
Termination of Pregnancy refers to all cases where the pregnancy is medically ended in the interest of the maternal health, with the expected outcome of fetal or early neonatal death.
6. Guidance for completion of Sections 11 and 12:  
Definitions for Cause of Death are outlined on the following pages. Associated subcategories which will help you choose the relevant conditions associated with the death, are also included.

<b>Guidance and Definitions for Completion of Section 11</b>	
<b>CAUSE OF DEATH - STILLBIRTH AND NEONATAL DEATH</b>	
<b>DEFINITION OF TERMS</b>	<b>Subcategory</b>
<b>1. MAJOR CONGENITAL ANOMALY.</b> Any genetic or structural defect arising at conception or during embryogenesis incompatible with life or potentially treatable but causing death	Central nervous system Cardiovascular system Respiratory system Gastro-intestinal system Musculo-skeletal anomalies Multiple anomalies Chromosomal disorders Metabolic diseases Urinary tract Other
<b>2. HYPERTENSIVE DISORDERS OF PREGNANCY.</b>	Pregnancy induced hypertension Pre-eclampsia HELLP syndrome Eclampsia
<b>3. ANTEPARTUM OR INTRAPARTUM HAEMORRHAGE.</b> After 20 w gestation, whether revealed or not. If associated with PET, APH will be a secondary diagnosis. Ignore minor degrees of haemorrhage (e.g. 'shows', cervical polyps etc). Recurrent bleeding of uncertain origin followed by preterm labour should not be ignored.	Praevia Abruptio Uncertain
<b>4. MECHANICAL.</b> Any death attributed to uterine rupture, deaths from birth trauma or intrapartum asphyxia associated with problems in labour such as cord compression, malpresentation, shoulder dystocia etc. Antepartum deaths associated with cord entanglement in the absence of strong circumstantial evidence that cord compression caused death should be classified as having no associated factor.	<b>Cord Compression</b> Prolapse cord Cord around neck Other cord entanglement or knot <b>Uterine Rupture</b> Before labour During labour <b>Mal-presentation</b> Breech / Transverse Face / Compound Other <b>Shoulder dystocia</b>
<b>5. MATERNAL DISORDER.</b> Specify hypertensive disease present before pregnancy or any other maternal disease or condition sufficient to jeopardise the baby such as diabetes, cardiac disease etc. Infection is classified separately.	Pre-existing hypertensive disease Diabetes Other endocrine conditions Thrombophilias Obstetric cholestasis Drug misuse Uterine anomalies Connective tissue disorders / Other
<b>6. INFECTION.</b> Confirmed by microbiology / placental histology. Specify maternal infections sufficient to have compromised the baby which may be associated with congenital infection of the baby. Trans-placental transmission may have occurred such as CMV, toxoplasmosis etc. Specify only those ascending infections that are a significant factor in death. Chorioamnionitis sufficient to cause preterm birth may be specified for some neonates but evidence of fetal infection may be required as an explanation of stillbirth.	<b>Maternal infection</b> Bacterial / Viral diseases Syphilis / Group B Streptococcus Protozoal Other <b>Ascending infection</b> Chorioamnionitis Other
<b>7. SPECIFIC FETAL CONDITIONS.</b> Document only those specific conditions arising in the fetal period.	Twin-twin transfusion Feto-maternal haemorrhage Non-immune hydrops Iso-immunisation Other
<b>8. SPECIFIC PLACENTAL CONDITIONS.</b> Specific placental conditions sufficient to cause death or be associated with fetal compromise such as IUGR. These will often be secondary to other maternal conditions e.g. PET. Cord problems associated with compression will normally be classified under 'Mechanical'	Placental infarction Retroplacental haemorrhage Thrombosis in fetal circulation Chorioamnionitis Villitis Fetal vasculitis Massive perivillous fibrin deposition Vasa praevia / Velamentous insertion Other
<b>9. INTRA-UTERINE GROWTH RESTRICTION DIAGNOSIS MADE.</b> IUGR may be suspected antenatally by abdominal circumference (AC) less than the centile threshold used to define IUGR locally, or decreased AC growth velocity, +/- oligohydramnios.	Suspected antenatally Observed at delivery Observed at post mortem
<b>10. ASSOCIATED OBSTETRIC FACTORS.</b> Factors recorded as Other Associated Obstetric Factors will be important clinical or pathological features of the pregnancy or baby but will not be an explanation of the death; they will often be secondary to other maternal or fetal conditions. Birth trauma and/or Intrapartum asphyxia should normally be classified primarily by the underlying cause (e.g Mechanical ). Birth Trauma and/or other antenatal/intra-partum factors can be recorded here either as a secondary factor or when there is no underlying explanation.	<b>Birth Trauma</b> Intracranial haemorrhage Birth injury to scalp Fracture Other <b>Intrapartum fetal blood sample &lt;7.25</b> <b>Other</b> Polyhydramnios Oligohydramnios Premature rupture of membranes Spontaneous premature labour Other
<b>11. NO ANTECEDENT OR ASSOCIATED OBSTETRIC FACTORS.</b> Deaths with no explanation or significant associated factor.	
<b>12. UNCLASSIFIED.</b> Cases where little or nothing is known about pregnancy or delivery and which cannot be fitted into any of the above categories. Use as sparingly as possible.	

**Guidance and Definitions for Completion of Section 12:****CAUSE OF DEATH – NEONATAL DEATH ONLY**

The following definitions and associated subcategories will help you choose the relevant neonatal conditions causing and associated with death.

<b>DEFINITION OF TERMS</b>	<b>Subcategory</b>
<b>MAJOR CONGENITAL ANOMALY.</b> Any genetic or structural defect arising at conception or during embryogenesis incompatible with life or potentially treatable but causing death.	Central nervous system Cardiovascular system Respiratory system Gastro-intestinal system Musculo-skeletal system Multiple anomalies Chromosomal disorders Metabolic disorders Urinary tract Other
<b>PRE-VIABLE.</b> Babies (less than 22 weeks) who are non-viable at birth because of gestation but who show signs of life.	
<b>RESPIRATORY DISORDERS.</b> Severe pulmonary immaturity will encompass those babies where structural lung immaturity is so gross as to mean ventilatory support is unsustainable at the outset, usually babies between 22 – 24w gestation. Surfactant Deficient Lung Disease may include babies with clinical or pathological evidence of hyaline membrane disease.	Severe pulmonary immaturity Surfactant deficiency lung disease Pulmonary hypoplasia Meconium aspiration syndrome Primary persistent pulmonary hypertension Chronic lung disease / BPD Other (includes pulmonary haemorrhage)
<b>GASTRO-INTESTINAL DISEASE.</b> Many babies with NEC will have associated sepsis which may be given as a secondary cause.	Necrotising enterocolitis (NEC) Other
<b>NEUROLOGICAL DISORDER.</b> HIE includes those babies with severe hypoxic-ischaemic brain injury before birth. If possible, please specify if HIE was primarily of intrapartum or antepartum origin. Specify periventricular leukomalacia only if this is a significant factor in the infant death. Birth Trauma will usually be classified here.	Hypoxic-ischaemic encephalopathy (HIE) Intraventricular/Periventricular haemorrhage Other
<b>INFECTION.</b> Where possible specify the location of infection and whether due to bacteria, virus, fungus or other specific organism. If infection was the main cause of death please specify whether infection is congenital (i.e. acquired ante or intrapartum acquired) or neonatal in origin.	Generalised (sepsis) Pneumonia Meningitis Other
<b>INJURY / TRAUMA.</b> Post natal trauma only including iatrogenic injury. 'Birth Trauma' will usually be classified under neurological disorder e.g. HIE; the obstetric classification identifying the timing of the injury.	
<b>OTHER SPECIFIC CAUSES.</b> Death due to specific fetal and neonatal conditions such as isoimmunisation or unexplained hydrops. Neonatal conditions will include aspiration, unexplained pulmonary haemorrhage.	Malignancies/Tumours Specific conditions
<b>SUDDEN UNEXPECTED DEATHS.</b> SIDS should conform to the accepted definition. Unascertained are those unexpected deaths that are not explained despite a full investigation including autopsy, but do not conform to the accepted definition of SIDS.	Sudden Infant Death Syndrome (SIDS) Infant deaths – cause unascertained
<b>UNCLASSIFIED.</b> Cases where little or nothing is known about the pregnancy or delivery and which cannot be fitted into any of the above categories. Please use this category as sparingly as possible.	

**Please return all completed forms to:**

**The National Perinatal Epidemiology Centre  
Department of Obstetrics and Gynaecology  
5<sup>th</sup> Floor  
Cork University Maternity Hospital  
Wilton  
Cork**

## Appendix 6



Feidhmeannacht na Seirbhíse Sláinte  
Health Service Executive

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### Checklist: Intrauterine Death / Stillbirth

<b>Baby's name</b>
<b>Consultant</b>

<b>EDD</b>
<b>Gestation</b>

	Signature	Date
Parents given time to see and hold baby		
Memories booklet completed / given to parents		
'A little lifetime' booklet given to parents		

Ensure Consultant Obstetrician meets parents	
Chaplain informed – if requested	
B & L officer / team informed – if requested	
Public health nurse informed – if verbal consent given	
Social worker informed – if requested	
GP informed - by Obstetric team	

Information sheet on post-mortem given to parents and explained by Obstetric team	
<i>Signature:</i>	
If PM appropriate, consent obtained and Form completed	
<i>Signature:</i>	
If PM performed, request Form completed	
<i>Signature:</i>	
Skeletal survey of baby performed	
Original forms sent to Pathology	
Photocopy of forms filed in mother's chart	

If Coroner's case:	
Coroner's information leaflet given to parents	
Coroner's office informed by Obstetric team	

	Signature	Date
Placenta sent to Pathology Dept. (in formalin) if no PM		
Placenta sent to Pathology Dept. if PM performed		
If amniocentesis done before delivery, result obtained		
If cytogenetic analysis indicated, placental sample or skin biopsy sent (in saline)		
Morphological examination of baby (if no PM)		
Swabs for C & S taken: Placenta / Eye / Ear / HVS		

Notification of birth form completed / sent to Records	
Medical Certificate completed – PM not performed	
Medical Certificate completed – when PM available	
Information leaflet on registration given to parents	

Record book in prayer room / chapel filled in when:	
1. Baby goes for / returns from PM	
2. On discharge of baby home / for burial	

Coffin and Name plate ordered (if requested)	
Appropriate service in hospital / home arranged	
Burial in family plot	
Burial by hospital in Cemetery (map given)	
Cremation	
Consent obtained and signed	

Maternal blood group checked (Anti-D given if indicated)	
<i>Signature:</i>	
Maternal bloods for investigation of stillbirth taken (see separate checklist)	
<i>Signature:</i>	
GP letter filled in, sent, and copies filed in chart	
Histology reports returned and filed in chart	

ALERT stickers attached to chart	
Antenatal clinic informed - to cancel appointments	
Follow up arranged with Consultant and / or Bereavement & Loss Service	
<i>Signature:</i>	