#### RCOG GREEN-TOP GUIDELINES



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### Care of late intrauterine fetal death and stillbirth

Green-top Guideline No. 55

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This is the second edition of this guideline. The first edition was published in 2010 under the same title.

#### **Key recommendations**

- A combination of mifepristone and a prostaglandin preparation should usually be recommended as the first-line intervention for induction of labour (Grade B).
- A single 200 milligram dose of mifepristone is appropriate for this indication, followed by:
  - 24<sup>+0</sup>-24<sup>+6</sup> weeks of gestation 400 micrograms buccal/sublingual/vaginal/ oral of misoprostol every 3 hours;
  - 25<sup>+0</sup>-27<sup>+6</sup> weeks of gestation 200 micrograms buccal/sublingual/vaginal/ oral of misoprostol every 4 hours;
  - from 28<sup>+0</sup> weeks of gestation 25–50 micrograms vaginal every 4 hours, or 50–100 micrograms oral every 2 hours [Grade C].
- There is insufficient evidence available to recommend a specific regimen of misoprostol for use at more than 28<sup>+0</sup> weeks of gestation in women who have had a previous caesarean birth or transmural uterine scar [Grade D].
- Women with more than two lower segment caesarean births or atypical scars should be advised that the safety of induction of labour is unknown [Grade D].
- Staff should be educated in discussing mode of birth with bereaved parents. Vaginal birth is recommended for most women, but caesarean birth will need to be considered for some [Grade D].
- A detailed informed discussion should be undertaken with parents of both physical and psychological aspects of a vaginal birth versus a caesarean birth [Grade C].
- Parents should be cared for in an environment that provides adequate safety according to individual clinical circumstance, while meeting their needs to grieve and feel supported in doing so (GPP).
- Clinical and laboratory tests should be recommended to assess maternal well-being (including coagulopathy) and to determine the cause of fetal death, the chance of recurrence and possible means of avoiding future pregnancy complications [Grade D].
- Parents should be advised that with full investigation (including postmortem and placental histology) a possible or probable cause can be found in up to three-quarters of late intrauterine fetal deaths [Grade B].
- All parents should be offered cytogenetic testing of their baby, which should be performed after written consent is given (GPP).
- Parents should be advised that postmortem examination can provide information that can sometimes be crucial to the management of future pregnancy [Grade B].

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#### PURPOSE AND SCOPE

- To identify evidence-based options for parents and their families who have a late intrauterine fetal death (IUFD) after 24<sup>+0</sup> completed weeks of pregnancy of a singleton
- To incorporate information on general care before, during and after birth, and care in future pregnancies.

The guideline is primarily intended for obstetricians and midwives but also for women and their families, general practitioners and commissioners of health care. This guideline does not include the management of pregnancies at the current limit of viability (22<sup>+0</sup>-23<sup>+6</sup> weeks), multiple pregnancies with a surviving fetus, fetal death following late feticide, late birth of fetus papyraceous or the management of specific medical conditions associated with increased risk of late IUFD, although many of the principles may be extrapolated to these clinical situations. Recommendations about the psychological aspects of late IUFD are focused on the main principles of care to provide a framework of practice for maternity clinicians. The section on postmortem examination covers clinical aspects required for obstetricians and midwives caring for women who have suffered a late IUFD.

This guideline is for healthcare professionals who care for women, non-binary and trans people. Within this document we use the terms woman and women's health. However, it is important to acknowledge that it is not only women for whom it is necessary to access women's health and reproductive services in order to maintain their gynaecological health and reproductive wellbeing. Gynaecological and obstetric services and delivery of care must therefore be appropriate, inclusive and sensitive to the needs of those individuals whose gender identity does not align with the sex they were assigned at birth.

### INTRODUCTION AND BACKGROUND EPIDEMIOLOGY

In the UK, stillbirth is legally defined as 'a baby delivered with no signs of life known to have died after 24<sup>+0</sup> completed weeks of pregnancy'. Late intrauterine fetal death refers to babies with no signs of life in utero after 24<sup>+0</sup> completed weeks of pregnancy. Late IUFD occurs in approximately 1 in 250 babies; this compares with 1 sudden infant death per 10 000 live births. In the MBRRACE-UK national perinatal mortality surveillance report, extended perinatal mortality reduced by 18% over 6 years, from 6.04 per 1000 total births in 2013 to 4.96 per 1000 total births in 2019, equivalent to approximately 770 fewer deaths in 2019. Perinatal mortality rates increased across the UK in 2021 after 7 years of yearon-year reduction.

Stillbirth rates have reduced by just over 20% from 4.20 per 1000 total births in 2013 to 3.35 per 1000 total births

in 2019, representing approximately 610 fewer stillbirths in 2019. The overall reduction in the stillbirth rate was mainly due to a reduction in the rate of term stillbirths by one-fifth (19%), from 1.45 per 1000 total births in 2015 to 1.17 in 2019. However, stillbirth rates per 1000 total births in 2021 for the UK were 3.54 and varied between the devolved nations; 3.52 (England); 3.27 (Scotland); 3.88 (Wales); and 4.09 (Northern Ireland). Babies born to women living in the most deprived areas are twice as likely to be stillborn.<sup>2</sup> Mortality rates remain exceptionally high for fetuses of Black and Black British ethnicity: stillbirth rates are over twice those for fetuses of white ethnicity.

There has been a substantial reduction in stillbirths recorded as having an intrapartum cause in the Causes of Death and Associated Conditions (CODAC) classification from 189 (5.8%) late IUFDs in 2014 to 51 (1.8%) late IUFDs in 2017. Using CODAC, the proportion of stillbirths with unknown cause of death has fallen from around a half (46.0%) in 2014 to around one-third (34.6%) in 2017.

The national perinatal mortality surveillance system (MBRRACE-UK) reviewed a representative UK sample of unexpected stillbirth at term in whom the postmortem did not identify a cause. The review revealed that failure to screen for gestational diabetes mellitus (GDM) both universally or in the high risk population was one of the most significant risk factors that could have prevented stillbirth in this group. Additional risk factors for stillbirth are detailed in the table below (Table 1).<sup>3-14</sup>

In addition to any physical effects, it is important to acknowledge that stillbirth often has profound emotional, psychological and social effects on parents, their families and friends. Stillbirth is a potential trigger to major economical and psychological consequences for women, families, healthcare providers and communities.

### **IDENTIFICATION AND** ASSESSMENT OF EVIDENCE

This guideline was developed using standard methodology for developing RCOG Green-top Guidelines. 15 The Cochrane Library (including the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effects [DARE] and the Cochrane Central Register of Controlled Trials [CENTRAL]), EMBASE, MEDLINE and Trip were searched for relevant papers. The search was inclusive of all relevant articles published from 2011 until June 2021. The databases were searched using the relevant Medical Subject Headings (MeSH) terms, including all subheadings and synonyms, and this was combined with a keyword search. Search terms included 'stillbirth', 'stillborn', 'fetal death' or 'foetal death', 'intrauterine death' or 'iufd'. The search was limited to studies on humans. Relevant guidelines were also searched for using the same criteria in the National Guideline Clearinghouse and the National Institute for Health and Care Excellence (NICE) Evidence Search.



#### TABLE 1 Risk factors for late IUFD

TABLE 1    Risk factors for late IUFD.
Non-modifiable
Nulliparity
Maternal age above 35
Maternal age below 20
Black, Asian and other non-white women
Previous stillbirth
Previous adverse pregnancy outcomes (preterm birth, pre-eclampsia, fetal growth restriction [FGR])
Multiple pregnancy
Advanced gestational age > 41 <sup>+0</sup> weeks
FGR and/or SGA < 10 <sup>th</sup> centile
Low educational attainment
Reduced fetal movements
Thyroid disease
Thrombophilia
Malaria infection
COVID -19 infection
Cholestasis
Systemic lupus erythematous/antiphospholipid syndrome (APS)

#### Potentially modifiable

Pre-existing hypertension

Obesity/overweight/weight gain

Smoking more than 10 cigarettes/day

Alcohol use

Renal disease

Illicit drug use

Going to sleep supine

Living in areas of most deprivation

Where possible, recommendations are based on available evidence. <sup>16</sup> Areas lacking evidence are highlighted and annotated as 'good practice points'. Further information about the assessment of evidence and the grading of recommendations may be found in Appendix I.

### 4 | DIAGNOSIS

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

Recommendation	Evidence quality	Strength	Rationale for the recommendation
Ultrasonography is essential for the accurate diagnosis of late IUFD and should be available at all times.	3	D	Evidence extrapolated from series where cases were missed with auscultation alone.

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Recommendation	Evidence quality	Strength	Rationale for the recommendation
A second opinion should be obtained for the diagnosis.	4	GPP	This is recommended to minimise the chance of diagnostic error.
Auscultation and cardiotocography should not be used to diagnose late IUFD.	3	D	Evidence extrapolated from series where cases were missed with auscultation alone.
Women should be prepared for the possibility of passive fetal movement. If a woman reports fetal movement after the scan to diagnose late IUFD, a repeat scan should be offered.	4	GPP	Case reports have described women have the perceptions of fetal movements after late IUFD.

Auscultation of the fetal heart by Pinard stethoscope or Doppler ultrasound is not sufficiently accurate for diagnosis of late IUFD and should be avoided. In a series of 70 late pregnancies in which fetal heart sounds were inaudible on auscultation, 22 were found to have viable fetuses. [Evidence level 2+]

Real-time ultrasound allows direct visualisation of the fetal heart. Imaging can be technically difficult, particularly in the presence of maternal BMI over 30 kg/m<sup>2</sup>, abdominal scars and oligohydramnios, but views can often be augmented with colour Doppler of the fetal heart and umbilical cord.

In addition to the absence of fetal cardiac activity, other secondary features might be seen: collapse of the fetal skull with overlapping bones, <sup>18</sup> hydrops, or maceration [meaning to soften in liquid] resulting in unrecognisable fetal mass. Intrafetal gas (within the heart, blood vessels and joints) is another feature associated with late IUFD that might limit the quality of real-time images. <sup>19,20</sup> [Evidence level 3]

Discussion of the ultrasound findings of severe skin and body changes (maceration and gross skin oedema) should be offered to the parents in anticipation of the appearance of baby at birth and to sensitively explain the estimated time of fetal death. Skin and body changes observed either after birth or on ultrasonography examination is an important change to recognise in the fetus (see Appendix II). The process is gradual and progressive, allowing a rough estimation of time of fetal death in relation to birth. <sup>18,20</sup>

Evidence of occult placental abruption might also be identified, however, the sensitivity to diagnose this by ultrasonography can be as low as 15%. Even large abruptions can be missed with ultrasound alone. [19] [Evidence level 3]

After the diagnosis of late IUFD, women sometimes continue to experience (passive) fetal movement.<sup>21</sup>

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

### 4.2.1 | Diagnosis

Recommendation	Evidence quality	Strength	Rationale for the recommendation
If a women is unaccompanied, an immediate offer should be made to call their partner, family or friends.	4	GPP	This is recommended as good practice.
An appropriate place for the discussions should be found.	4	D	Qualitative research on parents' perceptions have highlighted the importance of having discussions in a place with appropriate privacy.
Clear language with no euphemisms or jargon should be used. If an interpreter is required, a professional one is preferable to the use of family or friends. Other formats of conveying information to those with learning difficulties should be considered.	4	D	Qualitative research on parents' perceptions has highlighted the importance of clear language and the importance of adequate communication.
The woman and her family should be given time to absorb any news, and the clinician should answer any questions they are capable of within their scope of practice.	4	GPP	This is recommended as good practice.
Discussions should aim to support maternal/ parental choice.	3	D	Evidence from qualitative research studies have highlighted the need for discussions to support parents' thoughts and wishes.
The woman and her family should be given written information to supplement discussions, which should include information about ongoing care and the contact details of a named healthcare professional.	4	GPP	It is good practice to ensure clear ongoing information and a key contact. Clear easily understandable and structured information given sensitively at appropriate times can help the woman and their family through the experience.

Many strategies have been described for discussing bad news. Late IUFD can be sudden and unexpected, although in 70% of cases women present to maternity services with concerns for their baby's wellbeing.<sup>22</sup> A crucial component is to determine the feelings and emotional needs of the women and their companions.<sup>23</sup> This empathetic approach seeks to identify and understand parents' thoughts and wishes

but without trying to shape them. Women with a late IUFD and their partners value acceptance and recognition of their emotions. <sup>24,25</sup> [Evidence level 3]

Empathetic techniques, can be learned and retained as a skill<sup>25-28</sup> and can be helpful in this context (National Bereavement Care Pathway [NBCP] el [elearning] programmes www.e-lfh.org.uk/programmes/national-bereavement-carepathway/ and the Sands, stillbirth and neonatal death society, training training.sands.org.uk/).<sup>29</sup> [Evidence level 4]

It is important to provide written information, such as the RCOG patient information *When your baby dies before birth* and to consider alternative formats where this would help communication and understanding.<sup>28</sup>

Sands has led the development of the NBCP project, in collaboration with other charities and with the support of the Department of Health and Social Care and the All Party Parliamentary Group on Baby Loss. The project has aimed to ensure bereaved parents are offered equal, high quality, individualised, safe and sensitive care in any experience of pregnancy or baby loss. They have developed a care pathway and good practice recommendations for optimal care of bereaved parents after an IUFD, including at the time of diagnosis.<sup>29</sup>

### 4.2.2 | Care following diagnosis

Recommendation	Evidence quality	Strength	Rationale for the recommendation
The woman and her family should be given as much privacy and time alone as they wish.	3	D	Research has shown that parents need a dedicated space for privacy, but do not want to perceive that they have been abandoned.
Staff should support women and their family to express any concerns.	4	GPP	This is recommended as good practice.
Details of the birth plan should be discussed, including mode of birth, pain relief, timings and memory-making opportunities. If an interpreter is required, a professional interpreter should always be offered, rather than using friends and family. Other formats of conveying information to those with learning difficulties should be considered.	4	GPP	This is recommended as good practice to ensure parents have all the information to make a birth plan.
All staff caring for a woman and her family during labour and birth should be made aware of the baby's death.	4	GPP	This is recommended as good practice.



Recommendation	Evidence quality	Strength	Rationale for the recommendation
Staff should be sensitive to sounds that may be upsetting for bereaved parents and their family to hear and, where safely possible, cared for away from the labour ward environment.	4	GPP	This is recommended as good practice.
Continuity of caregiver should be ensured where possible.	3	D	This has been highlighted in qualitative research as important for parents.

Evidence (INSIGHT study) has shown that parents perceived staff focused on the woman's needs, however, the parents' priorities were still with their baby. It was also shown that partners may have different needs to the woman and that they want to be involved in decision making. Furthermore, staff need to be aware of the importance of keeping parents informed of what is happening and provide information at an appropriate pace, along with written information (RCOG patient information *When your baby dies before birth*) and expressions of empathy. Continuity of caregiver and supplementary written information are valued by women experiencing adverse pregnancy events.

Parents need a dedicated space for privacy, but do not want to perceive that they have been abandoned.<sup>27</sup> [Evidence level 3]

Healthcare professionals should neither persuade parents nor make assumptions that would limit parental choice. <sup>26-31</sup> Parents should be given detailed options about their care and the time to consider them. There is some evidence that an integrated care pathway combining the psychological and medical components of care can improve the delivery of care for women and their families after a diagnosis of late IUFD has been made. <sup>32</sup> [Evidence level 3]

#### 5 | LABOUR AND BIRTH

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

Recommendation	Evidence quality	Strength	Rationale for the recommendation
The mode of birth should be an informed decision between the parents and an appropriately experienced obstetrician. Vaginal birth is recommended for most women, but caesarean birth will need to be considered for some.	3	D	Qualitative research has shown staff should be considerate of parents' wishes and beliefs when discussing mode of birth.

	-7	Obstet	rics and Gynaecology
Recommendation	Evidence quality	Strength	Rationale for the recommendation
A detailed informed discussion should be undertaken with parents of both physical and psychological aspects of a vaginal birth versus a caesarean birth.	2++	С	This recommendation is based on evidence that shows known risks and benefits of both vaginal birth versus a caesarean birth should be discussed.
Late IUFD is not a contraindication to pool birth in suitable circumstances.	3	D	Case reports/case series have demonstrated the use of pool birth after late IUFD, therefore limited evidence indicates this could be considered. Qualitative studies highlight the importance of retaining parent choice.
Recommendations about labour and birth should consider the woman's choices, as well as her medical condition and previous intrapartum history.	3	D	Qualitative research studies have highlighted the need to explore parents' beliefs and choices when planning birth as well as taking into account her medical condition.
Women who are severely unwell or at high risk of deterioration should be strongly advised to take immediate steps towards birth, for example if there is sepsis, pre-eclampsia, placental abruption or membrane rupture. A more flexible approach can be discussed if this is not the case.	3	D	Limited evidence is available to guide optimal time interval from diagnosis to birth, but there is some evidence to suggest this should be expedited for some obstetric conditions and sepsis.
Women who are physically well with intact membranes and no laboratory evidence of disseminated intravascular coagulation (DIC) should be advised that they are unlikely to come to physical harm if they delay labour for a short period (48 hours), but they may develop severe medical complications and suffer greater anxiety with prolonged delays. Women who delay labour for periods longer than 48 hours should be advised to have testing for DIC (Table 2).	3	D	Limited evidence has shown that an increased interval between diagnosis and birth can increase the risk of anxiety and of developing DIC.

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Recommendation	Evidence quality	Strength	Rationale for the recommendation
If the woman returns home before labour, they should be given a 24-hour contact number for information and support this should include what signs/ symptoms to be aware of that should prompt action/ return to hospital.	4	GPP	A key contact after discharge from hospital is recommended as good practice.
Women contemplating prolonged expectant management should be advised that the diagnostic value of postmortem may be reduced, and the appearance of the baby may deteriorate.	3	D	Limited evidence has shown that the diagnostic value of the postmortem will be reduced in women with prolonged expectant management. It is recommended good practice that women are counselled about the appearance of the baby in cases of prolonged expectant management.

Options for birth after diagnosis of late IUFD include spontaneous vaginal birth, immediate induction, delayed induction, caesarean birth or expectant management. Methods of induction include misoprostol (with or without mifepristone), oxytocin infusion and mechanical methods.

Regarding time interval to birth, there is no good evidence to guide the optimal time, as birth is often expedited by induction or a caesarean birth. However, evidence has shown the degree of maceration does not correlate with disseminated intravascular coagulation (DIC) and other factors like abruption are more indicative. 33 There is a 10% chance of maternal DIC within 4 weeks from the date of fetal death and an increasing chance thereafter. <sup>33,34</sup> [Evidence level 3]

A Swedish study of 380 women with late IUFD and 379 controls with a live healthy baby showed that an interval of 24 hours or more from the diagnosis of death in utero to the start of labour was associated with an increased risk of moderately severe anxiety or worse (OR 4.8, 95% CI 1.5–15.9).35 [Evidence level 2+]

Evidence has shown that vaginal birth can occur within 24 hours of induction of labour for late IUFD in about 90% of women.<sup>36</sup> [Evidence level 2+]

Vaginal birth is recommended for most women with intent to optimise future pregnancy outcomes, but caesarean birth will need to be considered for some. Vaginal birth carries the potential advantages of both quicker physical recovery and return to home, but with the risks of vaginal/ perineal trauma and the need for forceps/ventouse or an emergency caesarean.<sup>37</sup>

A systematic review has concluded that when compared with vaginal birth, caesarean birth is associated with a reduced rate of perineal trauma, urinary incontinence and pelvic organ prolapse, but this should be weighed against

surgical morbidity and the association with increased risks for fertility, and risks in future pregnancies.<sup>38</sup>

Caesarean birth is occasionally recommended because of the clinical context or maternal condition.

Qualitative research reported that for some parents, in the context of late IUFD, a caesarean birth might be requested for reasons not anticipated by staff.<sup>27</sup> Vaginal birth was described as emotionally distressing by 47% of 314 women with a late IUFD compared with just 7% of 322 matched controls who had a live birth. <sup>39</sup> [Evidence level 2+]

Providers of maternity care should be alert to the rate of maternal medical complications associated with labour and birth with late IUFD. 40,41 A review in the USA has demonstrated high rates of shoulder dystocia, clinical chorioamnionitis, postpartum haemorrhage and retained placenta in women with late IUFDs. 41 Similarly, a cohort study of over 25 000 women in the USA who had experienced a late IUFD found a four-fold increase in severe maternal morbidity compared with live births using the International Classification of Diseases, 9th Revision, Clinical Modification (18 diagnostic codes including blood transfusion, disseminated intravascular transfusion, acute renal failure, adult respiratory distress syndrome, sepsis, shock and hysterectomy). 42 All this information necessitates a careful and sensitive discussion with women, and their families, to inform their decision, including the implications of caesarean birth for future pregnancies. [Evidence level 2+]

Evidence has shown that with no medical contraindications, the use of a birthing pool for the birth of a stillborn baby could be considered. 43 [Evidence level 4]

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

Recommendation	Evidence quality	Strength	Rationale for the recommendation
A combination of mifepristone and a prostaglandin preparation should usually be recommended as the first-line intervention for induction of labour.	1+	В	Good evidence from randomised controlled trials [RCTs] has shown the superior effectiveness of a combination of mifepristone and a prostaglandin preparation compared with the medications used alone.
Misoprostol can be used in preference to prostaglandin E2 because of equivalent safety and efficacy with lower cost but at doses lower than those currently marketed in the UK.	1+	В	Extrapolated evidence from RCTs has demonstrated that lower dose misoprostol is more cost effective with equal efficacy and safety than prostaglandin E2 so can be used for induction of birth.



Recommendation	Evidence quality	Strength	Rationale for the recommendation
Women should be advised that vaginal misoprostol is as effective as oral therapy but associated with fewer adverse effects.	1+	В	Extrapolated evidence from RCTs demonstrates that vaginal misoprostol has fewer adverse effects than oral therapy but is as effective.
A single 200 milligram dose of mifepristone is appropriate for this indication, followed by: 24 <sup>+0</sup> -24 <sup>+6</sup> weeks gestation - 400 micrograms misoprostol every 3 hours; 25 <sup>+0</sup> -27 <sup>+6</sup> weeks of gestation - 200 micrograms misoprostol every 4 hours; from 28 <sup>+0</sup> weeks of gestation - 25-50 micrograms vaginal misoprostol every 4 hours, or 50-100 micrograms oral misoprostol every 2 hours.	4	C	There is limited evidence to guide doses used for this indication.  There is insufficient evidence overall of superiority of one dose or schedule of misoprostol over another for use in pregnancies at or over 13 weeks of gestation. These recommendations have been taken from FIGO guidance where the aim was to have the highest overall effectiveness with the lowest adverse effects, but it is acknowledged that a range of doses could be effective and safe.

Previous studies have evaluated various combinations of mifepristone, misoprostol and oxytocin, however most research evidence on the induction of labour and late IUFD has been extrapolated from data on the termination of pregnancy in the second trimester.<sup>44</sup>

### 5.2.1 | Mifepristone use

In a small prospective study of 40 women with a late IUFD, conducted by Sharma et al., there was significantly shorter time to birth for women who received mifepristone and misoprostol  $(6.72 \pm 3.34 \text{ hours})$  when compared with the group who received misoprostol alone  $(11.81 \pm 6.33 \text{ hours})$ . [Evidence level 2]

Two further randomised trials have been undertaken. Chaudhuri et al. undertook an RCT of 110 women who had experienced fetal death later than 20 weeks of gestation, and demonstrated that mifepristone prior to misoprostol increased the chance of a vaginal birth from 71.2% to 92.5%. The mean induction-birth interval was also shorter when using mifepristone plus misoprostol than using misoprostol alone (9.8 hours [SD 4.4] compared with 16.3 hours [SD 5.7], respectively; P < 0.001). Fevidence level 1+1

Agrawal et al. undertook a further RCT of 100 women to assess using misoprostol with or without mifepristone after late IUFD. The number of misoprostol doses needed in the combination group was less than the misoprostol alone group and women in the combination group had an earlier onset of labour. However, total induction to birth interval was not different. In the combination group, 85.7% gave

birth within 24 hours of the first dose of misoprostol and in the group who received misoprostol alone, 70% gave birth within 24 hours (P = 0.07). 47

### 5.2.2 | Misoprostol dose

A systematic review was conducted in 2009 to assess the benefits and risks associated with the administration of misoprostol, which found in 14 studies that vaginal and oral misoprostol had up to 100% effectiveness of achieving birth at 48 hours. 44

In 2023 FIGO recommended a new dosing regimen for the use of misoprostol. 48 There is still currently insufficient evidence overall of superiority of one dose or schedule of misoprostol over another for use in pregnancies at or over 13 weeks of gestation. In making recommendations, FIGO acknowledged that providers might be keen to identify lowest possible doses because of reduced adverse effect, but that it was also important to consider success rates and time to birth: low doses have been shown to be associated with a longer induction-to-birth interval and lower overall effectiveness and in many studies "higher" doses have been used without evidence of harm. Recommendations were compiled with this in mind, while also acknowledging that it is possible that a range of dosages could be effective and safe. 48

FIGO have recommended that a single 200 mg dose of mifepristone is appropriate for late IUFD, followed by:

- 24<sup>+0</sup>-24<sup>+6</sup> weeks of gestation 400 micrograms buccal/ sublingual/vaginal/oral of misoprostol every 3 hours;
- 25<sup>+0</sup>–27<sup>+6</sup> weeks of gestation 200 micrograms buccal/sublingual/vaginal/oral of misoprostol every 4 hours;
- from 28<sup>+0</sup> weeks of gestation 25–50 micrograms vaginal every 4 hours, or 50–100 micrograms oral every 2 hours.

NICE has also reinforced the view that there is no robust evidence to guide optimum dosage of misoprostol, <sup>49</sup> especially in terms of safety and assessing rare outcomes such as uterine rupture.

Misoprostol use for induction of labour following a still-birth is off-label in the UK.<sup>50</sup> The 200 microgram tablet can dissolved in water and administered in measured aliquots, or divided with a tablet cutter, both of which hospital pharmacies could be asked to prepare to reduce variation in dose.<sup>51</sup> A 25 microgram tablet is now available in the UK but is not licensed for induction in these circumstances.

A systematic review and network meta-analysis of trials to assess the effectiveness and safety of prostaglandins used for labour induction in women with a live fetus, showed that vaginal misoprostol (50 microgram or more) had the highest probability of achieving a vaginal birth within 24 hours. The trials were inconsistent with regards to risk of hyperstimulation. 52-53 [Evidence level 1+ extrapolated]

There is no evidence available to make recommendations on maximum doses of misoprostol so local protocols should be followed.  $^{48}$ 

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 TABLE 2
 A summary of the investigations for late IUFD and their indications 136,143-171.

Test	Reason(s) for test	Evidence level	Additional comments	Timing
Maternal standard haematology and biochemistry including CRP and bile salts <sup>143</sup>	Pre-eclampsia and its complications Multiorgan failure in sepsis or haemorrhage Obstetric cholestasis	<i>r</i> 0	Platelet count to test for occult DIC     If abnormally low, discuss with haematologist     and suggest repeating, according to advice	As soon as possible after fetal death.  Repeat platelets as required based on the clinical picture
Maternal coagulation times and plasma fibrinogen	DIC	<i>c</i> ,	Not a test for cause of late IUFD     Maternal sepsis, placental abruption and preclampsia increase probability of DIC     Especially important for regional anaesthesia use or if there has been an interval of more than 48 hours since IUFD until birth	As soon as possible after diagnosis of sepsis, abruption, pre-eclampsia, or other pre-disposing condition(s); before regional anaesthesia
Kleihauer <sup>144</sup>	Lethal fetomaternal haemorrhage (FMH) Decide level of requirement for anti-Rh(D) gammaglobulin	2	<ul> <li>FMH is a cause of late IUFD</li> <li>Kleihauer should be recommended for all, not simply those who are Rh(D) negative (ensure laboratory aware if Rh(D) positive)</li> <li>Tests should be undertaken before birth as red cells might clear quickly from maternal circulation</li> <li>In Rh(D) negative women, a second Kleihauer test also determines whether sufficient anti-Rh(D) has been given</li> </ul>	As soon as possible after diagnosis of fetal death, or latest within 3 hours from birth
Maternal bacteriology 145-148 - Blood cultures - Midstream urine - Vaginal swabs - Cervical swabs	Suspected infection including <i>Listeria</i> monocytogenes and <i>Chlamydia spp</i>	<u>+</u>	Indicated in the presence of:  • Maternal fever  • Flu-like symptoms  • Abnormal liquor (purulent appearance/ offensive odour)  Prolonged ruptured membranes before late IUFD Abnormal bacteriology is of doubtful significance in the absence of clinical or histological evidence of chorioamnionitis (Evidence level 3) Also used to direct maternal antibiotic therapy	As soon as possible after diagnosis of fetal death
Maternal serology: - Viral screen - Tropical infections	Undiagnosed maternal-fetal infection	+	Stored serum from booking tests can provide baseline serology     Hydrops not necessarily feature of Parvovirus-related late IUFD     Treponemal serology – usually known already     Others – if presentation suggestive, e.g. travel to endemic areas	Before discharge

As soon as possible after diagnosis of hydrops or

endomyocardial fibroelastosis

As soon as possible after diagnosis of fetal

intracranial haemorrhage

• If fetal intracranial haemorrhage found on

thrombocytopenia

Alloimmune

Maternal alloimmune antiplatelet antibodies 162

postmortem

• Evidence of hydrops, endomyocardial fibroelastosis, or AV node calcification at

postmortem Indicated if:

postmortem

Indicated if:

autoimmune disease

Occult maternal

Maternal anti-Ro and anti-La antibodies  $^{161}$ 

Test	Reason(s) for test	Evidence level	Additional comments	Timing
Maternal random blood glucose <sup>149,152</sup>	Undiagnosed maternal diabetes mellitus	ъ	Rarely a woman will have incidental, undiagnosed pre-existing diabetes mellitus. The presence of severe ketoacidosis and other symptoms should alert clinicians to the need for glucose testing. Women with gestational diabetes mellitus (GDM) return to euglycaemia within few hours after late IUFD has occurred	As soon as possible after diagnosis
Maternal HbA1c <sup>149-153</sup>	Undiagnosed maternal pre- existing diabetes mellitus or GDM	2+	<ul> <li>Excludes occult type 1 or type 2 diabetes mellitus</li> <li>Can be indicative of GDM if HbA1c &gt;41</li> </ul>	Before discharge
Maternal thyroid function <sup>154</sup>	Undiagnosed maternal thyroid disease	3	• TSH, FT4 & FT3	Before discharge
Maternal thrombophilia screen 98,99,155-157	Maternal thrombophilia	±	Indicated to screen for APS especially if:  • Evidence of FGR or placental disease Antiphospholipid screen to be repeated if abnormal Advised to include antibodies against beta 2-glycoprotein I, lupus anticoagulant and anticardiolipin antibodies in antiphospholipid screen Inherited thrombophilia screen is not routinely indicated.	Screen – 6 weeks after birth not reliable in pregnancy
Anti-red cell antibody serology <sup>158-160</sup>	Immune haemolytic disease	3	Indicated if:  • Fetal hydrops evident clinically or on	As soon as possible after the diagnosis of hydrops

(Continued)

TABLE 2

(Continues)

		Evidence		
Test	Reason(s) for test	level	Additional comments	Timing

(Continued)

TABLE 2

Test	Reason(s) for test	Evidence level	Additional comments	Timing
Parental blood for karyotype <sup>163-165</sup>	Parental balanced translocation Parental mosaicism	г.	Indicated if:  • Fetal unbalanced translocation • Recommended by geneticist • Fetal genetic testing fails and history suggestive of aneuploidy (fetal anomaly on postmortem, previous unexplained IUFD, recurrent miscarriage)	As soon as possible after diagnosis of fetal genetic anomaly or suspicion of genetic anomaly
Maternal toxicology <sup>166</sup>	Occult drug use	<u>‡</u>	<ul> <li>With consent, if history and/or presentation are suggestive</li> <li>Urine is efficient and effective; nails and hair can be used</li> <li>Meconium toxicology may become widely available</li> </ul>	As soon as possible after diagnosis of fetal death
Fetal and placental microbiology - Fetal blood - Fetal swabs - Placental swabs	Fetal infections	3 <del>+</del> 8	<ul> <li>More informative than maternal serology for detecting viral infections</li> <li>Cord sample if possible, in lithium heparin</li> <li>Written consent advisable if cardiac bloods – cardiac blood can be taken by the histopathologist and used for bacterial culture and/or genetic testing if there is no cord blood.</li> <li>Need to be obtained using clean technique</li> </ul>	As soon as possible after birth
Fetal and placental tissues for cytogenetics (and possible single gene testing) <sup>167-171</sup> - Fetal cord - Placenta	Aneuploidy Single gene disorders See section 5.4 on sexing Suspected genetic anomaly	+ + 5	<ul> <li>Send several specimens – cell cultures might fail</li> <li>Cultures bottles must be kept on labour ward in a refrigerator – stored separately from formalin preservation bottles</li> <li>Genetic material should be stored if a singlegene syndrome is suspected</li> <li>Absolutely contraindicated</li> <li>if:</li> <li>Parents do not wish (written consent essential)</li> </ul>	As soon as possible after birth and after parents' consent
Postmortem examination 136,172  - External  - Autopsy  - Microscopy  - X-ray  - Placenta and cord  - Ultrasound scan/magnetic resonance imaging	See section 7.6	т	External examination should include weight and length measurements     FGR is a significant association for late IUFD     Perinatal pathologist or neonatologist can examine for dysmorphic features if parents do not want autopsy  Absolutely contraindicated if:     Parents do not wish (written consent essential)	As soon as possible after birth and after parents' consent
COVID-19 PCR test	See section 7.2	1		As soon as possible after diagnosis



### 5.2.3 | Misoprostol versus other methods of induction

An RCT comparing intravenous oxytocin with intravaginal misoprostol for induction of labour in women with a late IUFD showed that misoprostol was more effective.<sup>54</sup> [Evidence level 1+]

Two further RCTs comparing prostaglandin E2 with low-dose misoprostol for women with a live fetus found misoprostol to be more efficacious in cervical ripening and labour induction. The studies demonstrated a similar maternal safety profile for both groups. 55-56 [Evidence level 1+ extrapolated]

For third- (and second-) trimester termination of pregnancy, a systematic review found that vaginal misoprostol for induction of labour appears equally effective as gemeprost but is much cheaper, but information about maternal safety was limited.<sup>57</sup> [Evidence level 1+]

# 5.3 | What is best practice for induction of labour for a woman with a history of lower segment caesarean birth?

Recommendation	Evidence quality	Strength	Rationale for the recommendation
A discussion of the potential benefits and harms of induction of labour should be undertaken by an appropriately experienced obstetrician.	4	GPP	It is good practice to have an informed discussion with parents about induction of labour for women with a history of lower segment caesarean birth.
Women undergoing vaginal birth after caesarean birth (VBAC) should be closely monitored for features of scar rupture.	4	D	Maternal clinical features could alert to signs of scar rupture so should be monitored for during induction and labour.
Oxytocin augmentation can be used for VBAC, but the decision should be made following discussion with a consultant or obstetrician with equivalent training.	4	GPP	This is recommended as there is lack of evidence to guide the decision.
Misoprostol can be used for women with previous caesarean birth or other transmural uterine scar between 13 <sup>+0</sup> and 27 <sup>+6</sup> weeks of gestation -24 <sup>+0</sup> -24 <sup>+6</sup> weeks of gestation - 400 micrograms buccal/ sublingual/vaginal/oral of misoprostol every 3 hours; -25 <sup>+0</sup> -27 <sup>+6</sup> weeks of gestation - 200 micrograms buccal/ sublingual/vaginal/oral of misoprostol every 4 hours	4	D	A Cochrane meta-analysis has concluded there are insufficient data to assess the occurrence of uterine rupture with IUFD and a previous caesarean scar. The use of misoprostol is considered justified on the basis of FIGO recommendations, and extrapolation of data from midtrimester termination of pregnancy.

Recommendation	Evidence quality	Strength	Rationale for the recommendation
There is insufficient evidence available to recommend a specific regimen of misoprostol for use at more than 27 <sup>+6</sup> weeks of gestation in women who have had a previous caesarean birth or transmural uterine scar.	4	D	There is insufficient evidence to guide a recommendation for more than 27 <sup>+6</sup> weeks of gestation.
Women with more than two lower segment caesarean births or atypical scars should be advised that the safety of induction of labour is unknown.	4	D	There is insufficient evidence to guide a recommendation for this indication.

Overall, RCT evidence on methods of induction of labour for women with a prior caesarean birth is inadequate, and studies are underpowered to detect clinically relevant differences for many outcomes.

FIGO have concluded that misoprostol can be used for women with a history of caesarean birth or other transmural uterine scar between 13<sup>+0</sup> and 27<sup>+6</sup> weeks of gestation. They state that there is insufficient evidence available to recommend a regimen of misoprostol for use at more than 28 weeks of gestation in women who have had a previous caesarean birth or transmural uterine scar. Therefore, without evidence to support a safe regimen, the recommendation is to follow local protocol for women with uterine scars. Therefore,

### 5.3.1 One previous caesarean birth

RCOG Green-top Guideline No. 45 states that women should be informed of the two- to three-times increase in the risk of uterine rupture and around 1.5-times increase in the risk of caesarean birth in induced and/or augmented labour compared with spontaneous VBAC labour. 58 In a population-based case-control study of 611 late IUFDs, induction of labour resulted in vaginal birth for 91% (41 of 45) of women with a history of caesarean birth with two cases of uterine rupture. 59

### 5.3.2 Two or more previous caesarean births

No studies looking into the safety of induction of labour in women with two or more caesarean births and late IUFD were found. VBAC is not ordinarily recommended for women with three previous caesarean births, previous uterine rupture or upper segment incisions. <sup>58-60</sup> [Evidence level 4]

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### Uterine rupture

Fetal heart rate anomaly, the most common early sign of scar dehiscence, does not apply to late IUFD. Other clinical features include maternal tachycardia, atypical pain, vaginal bleeding, high head on examination, shoulder tip pain, haematuria on catheter specimen and maternal collapse.<sup>58</sup>

After 28 weeks of gestation with a previous caesarean, cervical ripening with a transcervical Foley catheter has been associated with uterine rupture rates comparable to spontaneous labour so could be helpful, especially in women with an unfavourable cervical examination. 61

### What are considered suitable facilities for labour?

Recommendation	Evidence quality	Strength	Rationale for the
During labour, women should be cared for in an environment that provides appropriate facilities for obstetric emergency care according to their individual circumstances.	4	GPP	This is recommended, as individual circumstances will vary.
Maternity units should aim to develop a special labour ward room for women who are physically well with an otherwise uncomplicated late IUFD that pays special heed to emotional and practical needs without compromising safety. This can include a bed for her partner or other companion to share, away from the sounds of other women and babies. Busy units should consider provision of a second room.	4	GPP	This is recommended as good practice.
Care in labour should be given by an experienced midwife with an accessible experienced obstetrician.	4	GPP	This is recommended as good practice.

In development of special labour ward rooms, maternity units should balance the location of the room with the need for parents and families to have their loss recognised and not feel shut away and isolated. 62-63 This element of isolation may be addressed and mitigated via appropriate communication with the parent and family by the medical and midwifery team. Studies both in the UK and elsewhere have shown that formal education and training of healthcare professionals in bereavement care is important. However, this needs to be supplemented by mentoring of midwives through the process of caring for bereaved women and families. 62,63 [Evidence level 3]

The National Bereavement Care Pathway highlights the need to be always open and honest about the situation and to ensure introduction of any new members of staff throughout the labour process. It reinforces the importance of enabling the birthing parent to have a partner or support person(s) with them at all times and, with the woman's consent, keep the partner or support person(s) informed. Providing the partner or support person with emotional support is also vital.<sup>2</sup>

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

Recommendation	Evidence quality	Strength	Rationale for the recommendation
Women with sepsis should be treated with intravenous broad-spectrum antibiotic therapy (including antichlamydial agents).	2-	С	No studies were found on the routine use of antibiotics for late IUFD so women should only be treated in cases of sepsis.
Routine antibiotic prophylaxis should not be used.	3	С	No studies were found on the routine use of antibiotics for late IUFD, so women should only be treated in cases of sepsis.
Intrapartum antibiotic prophylaxis for women colonised with group B streptococcus is not indicated.	4	GPP	The use of antibiotics for women colonised with group B streptococcus is not indicated as its use is for prevention of neonatal infection and there is no evidence to guide use in these circumstances.

A cross-sectional study reported that chorioamnionitis can occur in up to 26% of late IUFDs. 41 This relatively common complication can lead to the development of severe sepsis from a wide range of bacteria, including severe systemic chlamydial infection.<sup>64</sup> Regardless of the primary cause of death, the fetus can act as a focus for severe secondary sepsis, including gas-forming clostridial species, which can result in severe DIC. 65-66 [Evidence level 2]

Artificial rupture of membranes may facilitate ascending infection, but no studies exist to support this association in the context of late IUFD. No studies were found on the use of antibiotics for the prevention of maternal infection in pregnant people with a late IUFD.

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

Recommendation	Evidence quality	Strength	Rationale for the recommendation
All usual modalities of intrapartum pain relief should be made available to women with late IUFD, unless there are specific contraindications.	2+	D	As evidence overall is limited, it is reasonable to offer all modalities of pain relief.

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Analgesia was more frequently used during labour for late IUFD,<sup>67</sup> [Evidence level 3] however choice of analgesia can be influenced by different factors.<sup>67</sup> [Evidence level 2 extrapolated]

All usual modalities of pain relief should be made available, including regional analgesia, patient-controlled analgesia and water birth if there are no clinical contraindications. In a non-IUFD population a study of pethidine compared with diamorphine for intramuscular injections showed that diamorphine provided better pain relief. However, when using diamorphine, the duration of labour is longer and women therefore experience more pain overall. Overall, findings from the 2019 Cochrane review indicated that parenteral opioids provided some pain relief and moderate satisfaction with analgesia in labour, but there was not enough evidence to assess which opioid drug provided the best pain relief with the least adverse effects. Evidence level 3 extrapolated

A retrospective case–control study has indicated that there is no increased risk of perinatal laceration with neuraxial labour analgesia following a stillbirth.<sup>70</sup>

Regional anaesthesia is contraindicated in the presence of DIC. $^{71}$ 

#### 6 | PUERPERIUM

professional.

### 6.1 | What care should women receive before returning home?

Recommendation	Evidence quality	Strength	Rationale for the recommendation
Women should be cared for in an environment that provides adequate safety according to individual clinical circumstance, while meeting their needs to grieve and feel supported in doing so.	4	GPP	This is recommended as good practice.
Lactation, milk donation and milk suppression should be discussed with the woman.	4	GPP	This is recommended as good practice, as for some women lactation not being suppressed could be distressing.
Women should be advised which ongoing physical symptoms, such as bleeding and pain, can be expected and when to contact a healthcare	4	GPP	This is recommended as good practice.

Recommendation	Evidence quality	Strength	Rationale for the recommendation
Women should have continuity of care specialist/ bereavement midwife if one is employed by the hospital.	4	GPP	This is recommended as good practice, including having a key contact after leaving hospital.
A discussion on contraception should take place prior to discharge home.	4	GPP	This is recommended as good practice.

Some women have acute medical problems after birth (e.g. sepsis, pre-eclampsia etc.) with possible critical care needs. Women without acute medical issues who do not want to return home immediately and/or wish to be with their baby might wish to receive care within the hospital but away from the maternity unit (if such a facility is available). Postnatal care should include GP follow up to assess any ongoing physical or mental health issues and a discussion on contraception should take place prior to discharge home (FSRH Clinical Guideline *Contraception After Pregnancy*, available online: www.fsrh.org/standards-and-guidance/documents/contraception-after-pregnancy-guideline-january-2017/).<sup>72</sup>

Some parents may choose to donate their milk to a breast milk bank. While discussing milk donation may be difficult, staff should sensitively give parents information about donating milk (further information can be found on page 28 of the National Bereavement Care Pathway).<sup>29</sup>

To improve the information on lactation following a perinatal bereavement, a helpful 25-point framework has been developed to support healthcare professionals and organisations.<sup>73</sup> This framework categorises information based on acknowledgment of human milk and lactation; breast changes commonly associated with milk production; advice on alleviation of symptoms of discomfort and engorgement; and descriptions of on the full range of suppression, sustained expression and milk donation options.<sup>73</sup>

### 6.2 | What are the options for suppression of lactation?

Recommendation	Evidence quality	Strength	Rationale for the recommendation
Women should be advised that almost one-third of those who choose non- pharmacological measures to suppress lactation experience	1+	A	Clear evidence from RCTs shows the benefit of pharmacological measures for lactation suppression.

Lactation suppression is frequently not discussed with women; with about half of women experiencing a late IUFD in qualitative studies not receiving information. Despite the use of simple measures, such as a support bra, ice packs and analgesics, up to one-third of women experience severe breast pain. It is therefore important to provide women with adequate postnatal information about lactation suppression. Evidence level 2

A single double-blind RCT of 272 women requesting lactation suppression compared a single dose of cabergoline (1 mg) with bromocriptine (2.5 mg twice daily) for 14 days. The two regimens had very similar effectiveness, but cabergoline was reported to be simpler to use and had significantly lower rates of rebound breast activity and adverse events.<sup>79</sup> [Evidence level 1+]

Dopamine agonists are cautioned for use in women with hypertension or pre-eclampsia. 80 as they can increase blood pressure and have been associated with intracerebral haemorrhage. 81-82 However, in a study of 85 women with late IUFD and hypertensive disorders, no adverse maternal effects were shown with their use. 83 After discussing simple physical measures, risks versus benefits of dopamine agonists should be discussed in women with hypertension or pre-eclampsia. Women commencing bromocriptine should have blood pressure monitoring especially during the first days of treatment. 84

A 2012 Cochrane review of treatments for lactation suppression included 62 trials (6428 women). The trials were generally small and of limited quality. Seven trials involving estrogen preparations (diethylstilbestrol, quinestrol, chlorotrianisene, hexestrol) suggested that they significantly reduced the proportion of lactating women compared with no treatment at, or within, 7 days postpartum (RR 0.40, 95% CI 0.29–0.56). No trials comparing non-pharmacologic methods with no treatment were found. Trials comparing bromocriptine with other pharmacologic agents such as metergoline, prostaglandins, pyridoxine, cabergoline, diethylstilbestrol and cyclofenil suggested similar effectiveness. At day 14 postpartum, bromocriptine had similar risks of treatment failure compared with cabergoline (two trials included, 308 women;

RR 1.38, 95% CI 0.93–2.05)<sup>85</sup> Adverse effects were poorly reported in the trials and no case of thromboembolism was recorded in the four trials that reported it as an outcome.<sup>85</sup>

### 6.3 What are the criteria for thromboprophylaxis?

Recommendation	Evidence quality	Strength	Rationale for the recommendation
Women should be routinely assessed for thromboprophylaxis, noting that late IUFD in the current pregnancy is an independent risk factor for venous thromboembolism (VTE).	2+	В	Evidence has shown that late IUFD increases the risk of VTE up to six times so risk assessment for thromboprophylaxis is vital.
Heparin thromboprophylaxis should be discussed with a haematologist if the woman has DIC.	4	GPP	This is recommended as good practice, as DIC necessitates specialist haematology input and multidisciplinary care.

Late IUFD in a current pregnancy increases the risk of postpartum VTE up to six times compared with a live birth, with a rate of 2444 (109–5440) per 1000 person years. RCOG Green-top Guideline No. 37a Reducing the Risk of Venous Thromboembolism during Pregnancy and the Puerperium indicates that late IUFD in a current pregnancy should be considered as a risk factor for VTE. Revidence level 2+1

### 6.4 | Who should be informed of the late IUFD?

Recommendation	Evidence quality	Strength	Rationale for the recommendation
All key staff responsible for the care of the woman during pregnancy and afterwards should be informed of events.	4	GPP	This is recommended as good practice.
All existing antenatal appointments should be cancelled - maternity units should keep a list of likely specialties that need to be contacted and should also notify other healthcare providers involved in care.	4	GPP	This is recommended as good practice.
Primary care healthcare professionals should be informed where the woman will be staying when they leave the hospital.	4	GPP	This is recommended as good practice.

All key staff groups must be informed to ensure cancellation of existing antenatal appointments and continuity of follow-up. This includes the community midwives, health visitor, antenatal class coordinator and general practitioner. In the event of a woman who has been transferred between localities, extra care must be taken to ensure relevant parties have been informed.

Other existing healthcare professionals, such as psychiatrists, secondary care specialists and drug workers, should also be contacted. Voluntary groups who distribute free items to new parents should also be contacted, but specific details should not be released to maintain confidentiality. Appointments for antenatal clinics (hospital and community), ultrasound scans and preoperative assessment should be cancelled.

### 7 | INVESTIGATIONS OF THE CAUSE OF LATE IUFD

### 7.1 | What are the general principles of investigations?

Recommendation	Evidence quality	Strength	Rationale for the recommendation
Detailed history taking is a vital first step that will guide subsequent investigations into the cause of death of the baby.	3	D	Verbal autopsy tool enables a structure for history taking.
Clinical and laboratory tests should be recommended to assess maternal wellbeing (including coagulopathy) and to determine the cause of fetal death, the chance of recurrence and possible means of avoiding further pregnancy complications.	2++	D	Evidence has shown an important purpose of investigation is to assess maternal wellbeing and that performing laboratory assessments, placental pathology and postmortem all play an important role in finding a probable cause of death.
Parents should be advised that with full investigation (including postmortem and placental histology) a possible or probable cause can be found in up to three-quarters of late IUFDs, and they should be kept updated throughout the process	2++	В	Recommendation from large population- based studies suggest that full investigations have a high rate of finding a probable cause for late IUFDs.
Parents should be advised that when a cause is found it can potentially influence care in a future pregnancy.	4	GPP	This is recommended as good practice when counselling parents regarding investigations.

		_	
Recommendation	Evidence quality	Strength	Rationale for the recommendation
Healthcare professionals should be aware that an abnormal test result is not necessarily related to the late IUFD; correlation between tests and postmortem examination should be sought. Further tests might be indicated following the results of the postmortem examination.	4	GPP	This is recommended as good practice when counselling parents regarding investigations.
Systems that take into account fetal birthweight centile and capture multiple contributing factors should be used to categorize late IUFDs.	2++	В	Evidence has shown that the proportion of unclassified late IUFDs can be significantly reduced with use of the definition of FGR in late IUFD. <sup>75</sup>

History, including family history, <sup>89</sup> and tests aim to identify the cause of late IUFD and so provide the answer to the parents' question 'Why?' In a study of 314 women, 95% stated that it was important emotionally to have an explanation of their baby's death. However, parents are sometimes reluctant to proceed with investigations, in particular a perinatal postmortem examination. This can be for a variety of reasons, including a perception that their baby's body will be unavailable for burial. Studies have shown that following late IUFD, parents realise the importance of decisions they make around the time of diagnosis and birth of their baby. The information parents receive and the understanding that postmortem is respectful and useful is valuable in informing their decision making. <sup>27</sup> [Evidence level 3]

A Cochrane systematic review<sup>90</sup> of interventions for investigating and identifying the causes of stillbirth found no RCTs comparing stillbirth investigation strategies.

A review of stillbirth investigation guidelines in four high income countries found agreed recommendations including medical history evaluation, postmortem examination (including minimally invasive techniques), placental pathological examination, genetic analysis, microbiology of fetal and placental tissues, and a Kleihauer test.<sup>91</sup>

Taking a thorough clinical history, performing laboratory assessments, placental pathology and postmortem all play an important role in finding a probable cause of death.

Another important purpose of investigation is to assess maternal wellbeing and ensure prompt management of maternal disease.

It is important to recognise that there is a distinction between the underlying cause of death (the disease process), the mode of death (for example asphyxia) and the classification of the death (for example growth restriction). Conventional diagnostic systems fail to identify a specific cause in about half of IUFDs. The proportion of unclassified late IUFDs can be significantly reduced with systems that use

customised weight for gestational age charts, <sup>92,93</sup> such as the relevant condition at death (ReCoDe) system, <sup>94</sup> or systems that capture multiple and/or sequential contributing factors, such as Tulip, Initial Causes of Fetal Death Evaluation (INCODE), Perinatal Society of Australia and New Zealand – Perinatal Death Classification (PSANZ-PDC), Wisconsin Stillbirth Service Programme (WiSSP), Causes of Death and Associated Conditions (CODAC). <sup>95</sup> [Evidence level 2++]

A Delphi consensus method has aimed to define growth restriction in late IUFD. <sup>96</sup> Further research is required to determine the optimal classification method and tools. <sup>96</sup>

Comprehensive investigation can be important, even though one cause in particular may be suspected. With a very clear cause such as massive abruption, non-lethal fetal malformations might be identified at postmortem that would only have been revealed had the baby lived.

### 7.2 | What tests should be recommended to identify the cause of late IUFD?

Recommendation	Evidence quality	Strength	Rationale for the recommendation
All women with a late IUFD should be offered a postmortem, genetic testing and placental pathology. See Table 2 for more detail on investigations.	2+	В	Evidence has shown that these are the most useful tests for investigating late IUFD.

A secondary analysis of 512 stillbirths enrolled in the Stillbirth Collaborative Research Network from 2006–08 was performed to determine the usefulness of each test for diagnosing late IUFD. The usefulness of each test was as follows: placental pathology 64.6% (95% CI 57.9–72.0), postmortem 42.4% (95% CI 36.9–48.4), genetic testing 11.9% (95% CI 9.1–15.3), testing for antiphospholipid antibodies 11.1% (95% CI 8.4–14.4), FMH 6.4% (95% CI 4.4–9.1), glucose screen 1.6% (95% CI 0.7–3.1), parvovirus 0.4% (95% CI 0.0–1.4) and syphilis 0.2% (95% CI 0.0–1.1). They concluded the most useful tests were placental pathology and fetal postmortem followed by genetic testing and testing for antiphospholipid antibodies. <sup>97</sup> [Evidence level 2+]

A number of mostly retrospective cohort studies have found weak associations between heritable thrombophilia and late IUFD, however the published literature is inconsistent. Acquired thrombophilia does appear to be associated with placenta-mediated pregnancy complications, specifically antiphospholipid antibodies and late IUFD. Furthermore, late IUFD and miscarriage were shown to be more common in women with APS who had had a previous thrombosis compared with women with APS who had not. Poorer outcome was also associated with triple positive antibodies. The 2022 British Society for Haematology guidance has therefore recommended against heritable thrombophilia screening for adverse pregnancy outcomes but that screening

for antiphospholipid antibodies should be considered. *[Evidence level 2+]* 

Transplacental infections associated with IUFD include: cytomegalovirus [Evidence level 2+]; syphilis<sup>100</sup> [Evidence level 1+]; parvovirus<sup>101</sup> [Evidence level 2+]; listeria<sup>100,102,103</sup> [Evidence level 2+]; rubella<sup>104</sup> [Evidence level 3]; toxoplasmosis<sup>100</sup> [Evidence level 2+]; herpes simplex<sup>105</sup> [Evidence level 2+]; coxsackievirus; leptospira; Q fever; and Lyme disease.<sup>106</sup> Malaria parasitaemia has also been associated with IUFD (OR 2.3, 95% CI 1.3–4.1).<sup>107</sup> [Evidence level 2++]

Ascending infection, with or without membrane rupture, with *Escherichia coli*, Klebsiella pneumoniae, Group B Streptococcus, Enterococcus, Mycoplasma/Ureaplasma, *Haemophilius influenzae*, and chlamydia are the more common infectious causes in developed countries. 100,108,109 [Evidence level 2+]

British Association for Sexual Health and HIV (BASHH) provide guidance on treatment for syphilis (www.bashhguidelines.org/current-guidelines/genital-ulceration/syphilis-2015/).

An increased rate of stillbirth among women who were not vaccinated and acquired a COVID-19 infection during pregnancy was described across different studies and countries. Higher rates of stillbirth were associated with the delta variant of COVID-19, 110-113 however, other variants, such as omicron, had a lower associated stillbirth risk. 114

# 7.3 | What special actions should be recommended for women with rhesus D negative blood group?

Recommendation	Evidence quality	Strength	Rationale for the recommendation
Women who are rhesus D (RhD) negative should be offered a Kleihauer test undertaken urgently to detect large FMH that might have preceded late IUFD. Anti RhD should be administered as soon as possible after presentation.	2+	С	FMH is a silent cause of late IUFD.
If there has been a large FMH, the dose of anti- RhD should be adjusted and the Kleihauer test should be repeated at 48 hours to ensure the fetal red cells have cleared.	2+	С	Evidence suggests doses of anti- RhD should be increased with large FMH.
Anti-RhD immunoglobulin should be given within 72 hours of FMH but has beneficial effects up to 10 days.	2+	С	Evidence has shown benefit of anti- RhD up to 10 days post sensitising event although should be given within 72 hours.



Recommendation	Evidence quality	Strength	Rationale for the recommendation
Fetal blood group should be determined by cell free fetal DNA testing of maternal blood when required.	2	D	Evidence shows fetal blood group can be determined by free fetal DNA testing of maternal blood.

Anti-RhD immunoglobulin has beneficial effects up to 10 days after a sensitising event, but its effect is reduced when given beyond 72 hours. [115-120] [Evidence level 2+]

Women who have had a late IUFD and who are RhD-negative, could potentially have had a sensitising bleed days prior to diagnosis compromising the window for optimal administration of anti-RhD immunoglobulin (72 hours). 118

Persistent Kleihauer positivity usually occurs because the baby's blood group is also RhD-negative but can also occur with very large RhD-positive FMH. It is important to distinguish between the two; the baby's blood type can be typed using conventional serology on cord blood. If a fetal blood sample is not available or obtainable, typing with free fetal DNA from maternal blood is now widely available and in antenatal setting is highly accurate in predicting the RhD type of the fetus. <sup>119,120</sup> This is routinely performed for RhD-negative women in many units in the first trimester. [Evidence level 2–]

### 7.4 | What precautions should be taken when determining the fetal sex?

Recommendation	Evidence quality	Strength	Rationale for the recommendation
Parents should be advised before the birth about the potential difficulty in sexing the baby.	4	GPP	This is recommended as good practice when counselling parents.
Two experienced healthcare practitioners (midwives, obstetricians, neonatologists, pathologists) should examine the external genitalia of babies born extremely preterm, severely macerated or with hydrops.	4	GPP	This is recommended as good practice to aid in determining the fetal sex.
If there is any difficulty or doubt, rapid genetic testing could be offered.	2++	В	Sexing can also be performed rapidly and reliably by fluorescence in situ hybridisation (FISH).

Errors in fetal sexing can result in severe emotional harm for parents.<sup>121</sup> Extreme prematurity, maceration and hydrops can all make the diagnosis difficult. Where possible, the difficulties should be discussed with the parents before birth and consideration given to the genetic sex being tested rapidly on skin or placental tissue, even of macerated babies.<sup>121</sup> [Evidence level 3]

QF-PCR with additional Y chromosome markers can provide a highly accurate result within 2 working days in more than 99.9% of samples. <sup>122</sup> Sexing can also be performed rapidly and reliably by FISH. If these techniques fail, sex can be determined on cell culture or at postmortem, but these methods can take longer. [Evidence level 2++ extrapolated]

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

### 7.5 | What is the best practice guidance for cytogenetic analysis of the baby?

Recommendation	Evidence quality	Strength	Rationale for the recommendation
All women should be offered cytogenetic testing of their baby and given information both verbally and in writing and only performed if consent is given.	4	GPP	This is recommended as good practice when counselling parents regarding investigations.
The chance of informative results should be increased by using multiple cytogenetic techniques and samples from multiple fetal tissues.	4	D	Increased use of varied cytogenetic techniques and different tissues can increase the information provided in results.

Cytogenetic testing is an important element of the investigation as 6–13% of stillborn babies will have a cytogenetic anomaly. Some anomalies may be recurrent and could be tested for in future pregnancies. If cytogenetic testing is abnormal, advise referral to clinical geneticists.

Karyotyping, microarray analysis and QF-PCR can all be used to screen for and identify anomalies. Karyotyping is useful for detecting mosaicism, however it can underestimate the contribution of genetic anomalies to late IUFD because in up to 50% of karyotype attempts cell culture is unsuccessful. Microarray analysis provides more results than karyotyping as it not only detects aneuploidy but also detects copy number variants (smaller deletion and duplications) not detectable by karyotype, but has the disadvantage that it identifies variations of unknown clinical significance. QF-PCR can be performed on directly extracted DNA. Certain postmortem findings usually trigger specific requests for microarray analysis.

There is no recommendation for pre-birth amniocentesis. Placentas should not be placed in formalin before the biopsy is taken. A placental biopsy approximately 1 cm diameter should be taken from the fetal surface close to the cord

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insertion to avoid tissue of maternal origin. Cord biopsy can be undertaken and should be about 0.5 cm in length. Place specimens in a sterile tissue culture medium of lactated Ringer's solution. [Evidence level 4]

# 7.6 | What information should be discussed with women and their families regarding perinatal postmortem?

Recommendation	Evidence quality	Strength	Rationale for the recommendation
Parents should be offered full postmortem examination to help explain the cause of a late IUFD.	4	GPP	This is recommended as good practice when counselling parents regarding the postmortem.
Ample time should be allowed for this discussion, and ensure the discussion takes place in a quiet, private place.	4	GPP	This is recommended as good practice.
Parents should be advised that postmortem examination can provide information that can sometimes be crucial to the management of future pregnancy.	2+	В	Recommendation from large observational studies have demonstrated the benefit of postmortem in providing information on causation of late IUFD.
Consent must be given for any invasive procedure on the baby, and prior discussion should be with a senior obstetrician or midwife with appropriate knowledge given the nature and specifics of perinatal postmortem.	4	GPP	This is recommended as good practice when counselling parents regarding the postmortem, to support parents to make informed decisions.
Pathological examination of the cord, membranes and placenta should always be recommended.	4	С	Evidence has highlighted the usefulness of the examination of the placenta and cord in providing information on causation of late IUFD and should be therefore always recommended.
The examination should be undertaken by a specialist perinatal pathologist.	4	D	This is recommended under published national standards.
Parents who decline full postmortem might be offered a limited examination (sparing certain organs), but this should be discussed with a perinatal pathologist before being offered.	4	GPP	Parents should be counselled about the options of a limited examination after discussion with a perinatal pathologist.

Recommendation	Evidence quality	Strength	Rationale for the recommendation
Non-invasive, minimally invasive, and limited postmortem examination methods should be offered, where expertise and facilities are available, to parents who decline a full postmortem examination after discussion of their advantages and disadvantages.	3	С	Parents should be counselled on the current evidence for non-invasive, minimally invasive and limited postmortems, if a full postmortem is declined and facilities are available.
Ultrasound and magnetic resonance imaging (MRI) can be offered as a substitute for conventional postmortem, depending on local expertise and availability of resources.	3	С	Postmortem ultrasound and MRI have high sensitivity and specificity compared with standard postmortem.
If imaging is the only option, ultrasound scan (USS) and MRI remain the first line imaging non-invasive investigations for perinatal autopsy.	3	С	The time interval has been reported to be the most significant factor in acquiring a diagnostic quality postmortem ultrasound study owing to the tissue breakdown and laxity of skull sutures. It would be preferential when there is suspicion of an underlying cardiac anomaly or if the time interval time is more than 24 hours between death and birth to consider an MRI.

In a population-based study in the USA including IUFDs from 20 weeks in 59 centres, 500 women consented to postmortem. In 60.9% (95% CI, 56.5%–65.2%) a probable cause was found, and a possible or probable case found in 76.2% (95% CI, 72.2%–79.8%). [28 [Evidence level 2++]

In a cohort study in the USA, clinical findings led to a probable cause in 24.3% of cases, adding placental pathology increased this to 61.1%. A subsequent postmortem led to 74.3% having a probable cause of death. Performing placental pathology alone can lead to identifying a probable cause of death in 11.2–64.9% of cases, therefore gross and microscopic examination of the placenta, umbilical cord and fetal membranes by a trained pathologist is the single most useful aspect of the evaluation of late IUFD. [Evidence level 2+]

A systematic review of placental pathology reported in association with late IUFD showed that 65% had placental anomaly identified. Furthermore, a retrospective study (n = 1064) showed that 32% of late IUFDs had the cause of death assigned to placental anomalies. *[Evidence level 1++]* 

Independent of full postmortems, placental pathology therefore should be offered even if a postmortem examination of a baby is declined.

The National Bereavement Care pathway recommends that a minimum of 1 hour should be dedicated for the discussion regarding the postmortem, in a quiet private place. The pathway highlights the need to tell the parents if the postmortem examination will take place at a different hospital and explain where and why. Furthermore, they state that attempts to persuade parents to choose postmortem must be avoided; individual, cultural and religious beliefs must be respected. Parents should be offered a description of what happens during the procedure and the likely appearance of their baby afterwards. This should include information on how their baby is treated with dignity and any arrangements for transport, and that all discussions should be supplemented by the offer of written information.<sup>29</sup> [Evidence level 3]

It is essential to offer conventional postmortem examination to all parents. It is recommended that all practitioners who discuss postmortems with parents have a responsibility to understand the process so that consent is fully informed. It is also recommended that the consent form should include sections on the purpose of the postmortem; the extent of the examination; possible organ/tissue retention and purpose; what should happen to tissues/organ after postmortem; and research and education. <sup>29,132</sup>[Evidence level 2+]

All consent takers should be trained and specifically approved to take informed consent and decision making for a post mortem examination and should have observed a postmortem examination of a baby. If possible see Code of Practice A: Guiding principles and the fundamental principle of consent. 133

Postmortem examination might reveal the cause(s) and time of death, inform discussions of relevance to risk of recurrence and provide information for any medicolegal proceedings. <sup>134,135</sup> [Evidence level 3]

In terms of information for subsequent pregnancies, in a study of late IUFDs, abnormal findings were found in 51.1% of postmortems which is in keeping with a study which demonstrated that postmortem alone provided a classification of death in 45.9% of cases. When combined with other diagnostic tests, it offered information relevant to recurrence risk in 40.1% of cases and to management of next pregnancy in 51%. Important information that affected management of next pregnancy was elicited in 10% of stillborn babies with no recognisable cause of death from other clinical or laboratory investigations. [Evidence level 3]

There are published standards for the conduct of perinatal postmortems. <sup>136</sup> [Evidence level 4]

Alternatives to a standard postmortem include less invasive alternatives such as using only postmortem imaging – X-ray, USS or MRI (non-invasive postmortem) – or the addition of image guided organ biopsies (minimally invasive autopsy). Different imaging modalities have different advantages and disadvantages according to the clinical scenario

and gestational age. Local expertise and availability should be confirmed before they are offered, and their advantages and disadvantages discussed in the light of available evidence. <sup>137</sup>[Evidence level 2]

In the largest prospective paediatric postmortem study to date (the MARIAS study, including 400 children of whom 277 (69%) were perinatal losses) there was more than 90 concordance of MRI for overall diagnoses compared with standard postmortem (sensitivity of 89.7%, specificity of 95%) particularly for anomalies of the heart, brain and musculoskeletal system. <sup>138</sup>

When the imaging is of diagnostic quality, ultrasound has been reported to have similar accuracy to both 1.5T and 3T MRI with an estimated overall sensitivity of 73% and specificity 97%. The highest sensitivity was found for brain imaging (84%) and the lowest for cardiothoracic anomalies (51%). The time interval has been reported to be the most significant factor in acquiring a diagnostic quality postmortem ultrasound study because of the tissue breakdown and laxity of skull sutures. It would be preferential when there is suspicion of an underlying cardiac anomaly or if the time interval time is more than 24 hours between death and birth to consider an MRI over USS. [Evidence level 1]

Use of X-rays has been repeatedly shown to have minimal yield in routine use, and should be reserved for targeted use only when there is a suspected skeletal anomaly. [Evidence level 3]

Minimally invasive postmortem with laparoscopically assisted sampling has the potential to increase the diagnostic yield of less invasive postmortem by improving the quality and quantity of tissue samples obtained, while permitting visualisation, extraction and examination of internal organs through a small incision, but will also depend on local skill and expertise. [Evidence level 3]

A mixed methods study demonstrated that less invasive perinatal postmortem methods are viable and acceptable (except for unexplained deaths), and likely to potentially increase uptake.  $^{142}$ 

### 8 | PHYSICAL, PSYCHOLOGICAL AND SOCIAL ASPECTS OF CARE

# 8.1 | What physical, psychological and social problems can follow late IUFD and what is best practice for the use of interventions that might aid psychological recovery?

Recommendation	Evidence quality	Strength	Rationale for the recommendation
Healthcare professionals should be aware of, and responsive to, possible variations in individual and cultural approaches to death.	4	GPP	This is recommended as good practice.

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Recommendation	Evidence quality	Strength	Rationale for the recommendation
Appropriate counselling should be offered to all women and their partners although clinicians should be aware that evidence on the effectiveness of counselling is limited.	4	D	There is limited evidence to guide this recommendation. Best practice is for all bereaved parents to be informed about and, if requested, referred for emotional support and for specialist mental health support when needed.
Other family members, especially existing children and grandparents, should also be considered for counselling.	4	D	This is recommended as good practice, as late IUFD has been known to have deleterious impact on the wider family.
Parents should be advised about support groups.	4	GPP	This is recommended as good practice.

Experiencing the birth of a stillborn child is a lifechanging event. The focus of the consequences may vary with parent, gender and culture. Late IUFD can have devastating psychological, physical and social costs, with ongoing effects on interpersonal relationships and subsequently born children. [Evidence level 1+]

Healthcare professionals must be alert to the fact that women, partners, children and grandparents are all at risk of prolonged severe psychological reactions, including posttraumatic stress disorder (PTSD), but that their reactions might be very different. [Evidence level 3]

Parents who experience perinatal death are at increased risk of hospital admission owing to postnatal depression and suicide. 175,176 A nested case-control study has shown that the risk of completed suicide was higher in women who experienced a late IUFD [adjusted odds ratio (aOR) 5.2; 95% CI 1.77-15.32] than in those who had a live birth. [Evidence level 2]

Unresolved grief responses can evolve into PTSD. 175,176 Parents with poor social support are particularly vulnerable.<sup>176</sup> [Evidence level 3]

Partners of women with a late IUFD can also experience severe grief responses, but the prevalence of such psychological disorders in partners is not precisely known, and they can also develop PTSD.<sup>175</sup> Discordant grief reactions between partners are more common after IUFD than after neonatal death and this is a risk factor for developing a prolonged grief disorder. [Evidence level 3]

An online survey of LGBTQ+, mostly lesbian people from the UK, USA, Canada and Australia demonstrated that the experience of loss was amplified due to contextual factors and the investment respondents made into impending motherhood. [Evidence level 3]

A review of qualitative studies of the psychosocial impact of IUFD has shown that recurrent themes ranged from negative psychological symptoms post bereavement and in subsequent pregnancies, to disenfranchised grief, and incongruent grief. There was also impact on siblings and on the wider family. They included mixed-feelings about decisions made when the baby died, avoidance of memories, anxiety over other children, chronic pain and fatigue and a different approach to the use of healthcare services. Grief suppression, employment difficulties, financial debt and substance use were particularly prominent in fathers. These included motivation for engagement in healthcare improvement and changed approaches to life and death, self-esteem, and own identity. 173,174 [Evidence level 1+]

A study in 2011 has shown that bereaved parents who experience late IUFD or infant death have markedly increased mortality compared with non-bereaved parents, up to 25 years after the death of their child. 178 Furthermore, parental relationships have a 40% higher risk of dissolving after late IUFD compared with live birth. [Evidence level 2]

A systematic review in 2017 failed to identify evidence of sufficient quality on which to base recommendations of interventions to reduce the psychosocial impact after late IUFD.<sup>180</sup> [Evidence level 1+]

A further systematic review in 2023 identified only four research studies evaluating counselling as an intervention following late IUFD. 181 Simpson et al. assessed grief, anxiety and depression following bereavement counselling and found that symptoms had significantly reduced following the intervention, although it was noted that grief in the control group had also declined within the study period. 182 Rogers et al. evaluated a specialised bereavement counselling service in the UK using the CORE (Clinical Outcomes in Routine Evaluation) to assess the severity of subjective wellbeing, symptoms or problems, function, and risk to self and others. It was noted that the severity of psychological problems had decreased following bereavement counselling. 183 Navidian et al. measured PTSD severity following psychological grief counselling and found that symptoms had reduced. 184 Cacciatore et al. evaluated whether or not counselling was 'helpful' for parents and found that the majority of respondents thought that counselling was either 'very helpful' or 'helpful'. [Evidence level 4]

A randomised trial explored the feasibility and acceptability of a 12-week, home-based, online-streamed yoga intervention, among women after a late IUFD. The results demonstrated the intervention was acceptable and feasible and preliminary efficacy was shown; there were significant decreases in PTSD and depression, and improvements in selfrated health. They concluded a larger RCT was warranted. 186

Guilt is a common emotion after late IUFD but is not necessarily voiced. 187

A 10-year study of 843 parents who experienced a late IUFD, newborn death or sudden unexpected death in infancy included extended family members, primarily grandparents. The most common response of grandparents was a profound need to protect their own child. The study found that grandparents need information on how they can help their children recover from their loss, how long grief lasts and the differences between men's and women's grief responses.<sup>188</sup> [Evidence level 3]



Child-parent relationships can be affected and some parents wish to have guidance on how to explain the death to siblings and how to help them mourn. [189] [Evidence level 2+]

Support groups, such as Sands, have been developed to offer help to both partners. In an observational study of 23 women who attended pregnancy loss groups, interviews showed that the primary focus for women was the need to seek recognition and acceptance of their grief. The introduction of bereavement support officers has been shown to improve the care for those who have experienced perinatal loss. <sup>190</sup> Support services or charities (such as PETALS, the baby loss counselling charity) are available to provide specialised counselling services for individuals or couples who experience trauma or loss during pregnancy or birth. <sup>191</sup> [Evidence level 3]

### 8.2 | What is the evidence for seeing, holding, naming and mementos?

	Evidence		Rationale for the
Recommendation	quality	Strength	recommendation
The opportunity to spend time with a baby, and to make memories with a baby should be actively supported and offered.	1+	A	Recommendation from systematic review which showed benefit of memory making.
It is reasonable to offer parents a chance to see their baby more than once, and they should be informed that they can change their mind at any point, but once this decision has been made it should be respected.	1+	A	A systematic review assessing outcomes after stillbirth suggested positive outcomes for parents who saw or held their baby, but this option may not be beneficial for all.
Some parents who choose not to see their baby may find it helpful for healthcare professionals to describe the appearance as an alternative. It is, however, an informed choice and parents' views should be respected. An 'options form' can be a useful way to help make this decision (e.g. 'Creating memories – offering choices' is available from www.nbcpa thway.org.uk)	4	D	This is considered good clinical practice.
Artefacts of remembrance should be offered to parents to keep.	3	С	Recommendation from qualitative studies showed this to be of benefit.
Maternity units should have the facilities for producing good-quality photographs, palm and footprints and locks of hair with presentation	3	С	Recommendation from survey and qualitative studies showed this to be of benefit so this should be offered.

frames.

Recommendation	Evidence quality	Strength	Rationale for the recommendation
Consent should be sought from the parents and information governance regulations should be complied with for clinical photography.	4	GPP	Information governance regulations should be followed.
It should be explained that clothes on a macerated baby might become stained.	4	GPP	This is recommended as good practice.

Give parents time to react and decide what they want. Refer to NBCP www.nbcpathway.org.uk/pathways/stillbirth -bereavement-care-pathway. Consider the condition of the baby when offering memory-making options. Discuss with parents:

- · Washing and dressing the baby
- Photographs
- Hand and footprints
- Certificate of birth (a template certificate is available from www.nbcpathway.org.uk)
- Taking the baby out of the hospital environment (a template form is available from www.nbcpathway.org.uk)
- Memory box
- Other memorials.

At present there is a mixed body of evidence surrounding seeing and holding the baby after birth. Some studies have described beneficial effects of memory making, such as facilitating grief, 74,192 as opposed to others which have documented more adverse outcomes such as depression and PTSD.<sup>26</sup> In 2013, a Cochrane review concluded that the evidence of the effect of seeing and holding the baby remains inconclusive<sup>193</sup>. A subsequent systematic review (2014) found that the evidence of the impact of holding a stillborn baby on mental health and wellbeing is sparse and poor quality.<sup>194</sup> The studies included within the systematic review were too heterogeneous in their outcome measurements and the authors were unable to quantitatively synthesise the results to form a meaningful conclusion. 194 A secondary analysis of survey data from a postal survey in 2016 of 468 women who had experienced a stillbirth, found that women who had seen and held their baby had higher self-reported anxiety levels, PTSD and relationship difficulties. 195 However, there should be caution in interpreting these data, as the survey had a low response rate (30.2%) and used an unvalidated self-reported symptoms checklist. 195 Conversely, another systematic review suggested that parents seeing and holding their baby could be beneficial to their future wellbeing. 196 In summary, due to the mixed body of research, parents should continue to be offered to hold their stillborn baby. It is essential that when parents express a desire to see and hold their baby that this is supported by experienced staff. [Evidence level 1+]

An online survey of bereaved parents' experiences concluded that women who have given birth to stillborn babies

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felt more natural, good, comfortable and less frightened if the staff supported assumptive bonding by simply offering the baby to the woman. [Evidence level 3]

Some parents may wish to name their baby, but others may decide not to do so. Either option is allowable in law, but once the stillbirth has been registered, names cannot be added or changed (Births and Deaths Registration Act 1953; amended by the Still-Birth (Definition) Act 1992). 198

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

Recommendation	Evidence quality	Strength	Rationale for the recommendation
Parents should be provided with the medical certificate certifying late IUFD.	4	GPP	This should follow legal requirements.
Parents should have a discussion and be provided with written information about the registration process, including where and how to register. Inform parents that a baby must be registered within 42 days.	4	GPP	This is recommended as good practice to ensure parents have clear information.
It should be ensured that parents have any other information they will need for medical certification of stillbirth.	4	GPP	This is recommended as good practice.
Obstetricians and midwives should be aware of the law related to late IUFD.	4	GPP	This is recommended as good practice.

The following practice guidance is derived from statute and code of practice (for further detail see Appendix III):

- Stillbirth must be medically certified by a fully registered doctor or midwife; the doctor or midwife must have been present at the birth or examined the baby after birth. (Statute)
- HM Coroner must be contacted if there is doubt about the status of a birth. (Statute) Babies born later than 24<sup>+0</sup> weeks who are known to have died before 24<sup>+0</sup> weeks do not have to be certified or registered. (Code of Practice)
- The baby can be registered as indeterminate sex awaiting further tests. (Code of Practice)
- The parents are responsible in law for registering the birth but can delegate the task to a healthcare professional. (Statute)

Evidence suggests that medical certificates of stillbirth contain a number of inaccuracies with a large amount of stillbirths incorrectly classified as "unexplained". FGR is particularly overlooked as the cause of stillbirth. Practitioners should complete medical certificates of stillbirth considering all potential causes. [Evidence level 3]

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

Recommendation	Evidence quality	Strength	Rationale for the recommendation
Maternity units should have arrangements with all common faiths and non-religious spiritual organisations as a source of guidance and support for parents.	4	GPP	This is recommended as good practice.
The legal responsibility for the child's body rests with the parents but can be delegated to hospital services.	4	GPP	This is recommended as good practice.
Maternity units should provide a book of remembrance for parents, relatives and friends.	4	GPP	This is recommended as good practice.
Healthcare professionals should offer parents the option of leaving toys, pictures and messages in the coffin.	4	GPP	This is recommended as good practice.

Parents might wish to seek guidance from a spiritual leader or religious elder. Funeral options including burial and cremation should be discussed with parents, taking into account religious and cultural considerations.<sup>200</sup>

Practical issues should be discussed with the parents, at a time and to an extent that suits them.

An observational study found that most parents appreciate rapid arrangements for the funeral or cremation. <sup>201</sup>[Evidence level 3]

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

If the parents request cremation they have to complete Cremation Form 3 (CF3) (application for cremation of remains of a stillborn child). Together with a copy of the Stillbirth Certificate (known also as Cremation Form 9), they submit CF3 to the Medical Referee, who issues Cremation Form 10 (authorisation to cremate a stillborn child). Cremation Form 2 is the equivalent of CF3 for retained body parts of a stillborn child when the body has already been cremated. The systems and procedures vary in Scotland<sup>202</sup> and Northern Ireland,<sup>203</sup> however the following guidance is adhered to (www.cremation.org.uk/cremationcodes-of-practice).<sup>204</sup>



### 8.5 | What advice should be given about fertility?

Recommendation	Evidence quality	Strength	Rationale for the recommendation
With regards to inter-pregnancy intervals, it is important to balance physical and psychological considerations.	1+	A	Evidence suggests a higher rate of adverse events with shorter inter-pregnancy intervals, although the absolute risks are low and other evidence has found no increased risk. Some parents may feel disinclined to delay before attempting to conceive again.

An international study including a cohort from Finland, Norway and Western Australia found the median interpregnancy interval after stillbirth was 9 months (interquartile range 4–19 months) and 63% of women conceived within 12 months of the stillbirth. This large international cohort study found that conception within 6–12 months of a stillbirth was not associated with increased risk of the majority of adverse outcomes in the subsequent pregnancy. Evidence level 2

A 2006 meta-analysis<sup>206</sup> of the general maternity population suggested that there is a higher rate of adverse events with shorter inter-pregnancy intervals, but the absolute risk remained low. Inter-pregnancy intervals shorter than 6 months were associated with increased risks of preterm birth, low birthweight and small-for-gestational-age (SGA) babies (aOR [95% CI] 1.40 [1.24–1.58], 1.61 [1.39–1.86] and 1.26 [1.18–1.33], respectively).<sup>206</sup> [Evidence level 1+]

A further systematic review in 2012 found that short inter-pregnancy intervals were associated with stillbirth (aOR 1.35, 95% Cl 1.07–1.71) and early neonatal death (aOR 1.29, 95% Cl 1.02–1.64). [Evidence level 1+]

# 8.6 | How should healthcare professionals caring for women who experience a stillbirth be supported?

Recommendation	Evidence quality	Strength	Rationale for the recommendation
Healthcare professionals should be offered training and support when caring for parents who experience a late IUFD.	1++	A	This is recommended from evidence from a systematic review.

In a qualitative study of obstetricians' experiences of caring for women with a late IUFD it was found that late IUFD was identified as being among the most difficult experiences for consultants. Two superordinate themes emerged: the human response to late IUFD and the weight of responsibility. The human response to late IUFD was characterised by the personal impact for consultants and, in turn, how this shapes the care they provide. [Evidence level 3]

Furthermore, a systematic review has highlighted the need for targeted training and support for healthcare professionals who have cared for parents experiencing perinatal loss. <sup>209</sup>

Examples include training by Sands (training.sands.org. uk) or the SUPPORT perinatal bereavement care course which has demonstrated pre- and post-course improvement in attendees' confidence in communication, providing bereavement care and understanding parent's experiences, as well as improved accuracy with clinical knowledge assessments.<sup>210</sup>

### 9 | FOLLOW-UP

for example sent by post or email if a follow-up

meeting is declined.

# 9.1 | What are the options for the perinatal mortality review process and follow-up meetings?

O			
Recommendation	Evidence quality	Strength	Rationale for the recommendation
The wishes of the woman, and of those who she wishes to be involved, should be considered when arranging follow-up.	4	GPP	This is recommended as good practice.
Before the visit, it is essential to ensure that all results are available, and if results are delayed, an interim visit offered.	4	GPP	This is recommended as good practice.
Parents should be informed about the review process(es) in place for reviewing their baby's death before they leave hospital.	3	С	A national consensus group advise all parents should be informed about any and all review processes prior to leaving hospital.
Parents should be given the opportunity to engage in the review process(es).	3	С	A national consensus group and qualitative study advise all parents should be given the opportunity to be engaged in the review process after the death of their baby.  Engaging bereaved parents in the review process, does not mean having the parents present at the review, it means talking to them and asking them for their views and any questions so that these can be taken into account in the review.
A plain English summary of the review process(es) findings should be given and discussed with parents at the follow-up meeting or offered to be communicated to them,	3	С	A national consensus group and qualitative study advise all parents should be given the findings of the review process after the death of their baby.

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Recommendation	Evidence quality	Strength	Rationale for the recommendation
Families should be fully informed of the likely timescales to review and follow up, any unexpected delays should be clearly communicated to avoid further distress.	4	GPP	This is recommended as good practice including having a key contact after leaving hospital.

A collaboration led by MBRRACE-UK has established a national standardised Perinatal Mortality Review Tool (PMRT) building on the work of the Department of Health and Social Care/Sands Perinatal Mortality Review 'Task and Finish Group' (see Appendix IV). The PMRT aims to support objective, robust and standardised reviews of deaths of babies (up to 28 days post birth) to provide answers for bereaved parents about why their baby died, other local and national review process may be also undertaken depending on the circumstances of the late IUFD.

The PARENTS 2 study led by the University of Bristol has developed, piloted and evaluated parental engagement in the perinatal review process. They have recommended that parents should be informed that a review process will occur to review the death of their baby and they should be given the option to contribute comments and questions to the meeting. <sup>211,212</sup> Furthermore, a plain English summary of the meeting should be produced for parents after the review meeting. <sup>211,212</sup> Parent engagement materials have been developed in conjunction with the PMRT group [www.npeu.ox.ac.uk/pmrt/parent-engagement-materials; www.sands.org.uk/professionals/fewer-baby-deaths/reviewing-every-baby-death]. <sup>213</sup> [Evidence level 3]

It is recognised that some parents find it very distressing to return to the unit where their baby was stillborn.<sup>29</sup> The option of home visits or virtual appointments should be offered to parents. Six to twelve weeks is common practice for the timing of the appointment, when the placental and the postmortem histology results usually become available, but this can vary across the UK and a flexible approach is appropriate according to the needs of the parents and the range of tests and reviews performed. The outcome of the review process should be communicated to parents.

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

Recommendation	Evidence quality	Strength	Rationale for the recommendation
Parents should be advised about the cause of late IUFD, chance of recurrence and any specific means of preventing further loss.	4	GPP	This is recommended as good practice to fully inform parents on the results of any investigations.
Parents should be offered general pre-pregnancy advice, including support for smoking cessation.	4	GPP	This is recommended as good practice, to optimise health for any future pregnancies.

Recommendation	Evidence quality	Strength	Rationale for the recommendation
Women should be advised on healthy weight management. This should be discussed and approached sensitively.	2++	В	Evidence has shown that BMI of over 30 kg/m <sup>2</sup> is a risk factor for late IUFD.
Healthcare professionals should be aware that wishes relevant to conception timing tend to be individual.	4	GPP	This is recommended as good practice.
The meeting should be documented for the parents in a letter that includes an agreed outline plan for future pregnancy. This should be in clear non-medicalised language, using the name of the baby and sent directly to the woman and a copy sent to their general practitioner.	4	GPP	This is recommended as good practice.
Clinicians can use a proforma to aid preparation discussions during the meeting.	4	GPP	This is recommended as good practice.

For the meeting, women and those who the woman wishes to be involved might wish to keep a written log of questions and comments. As well as an opportunity to ask about the physical and emotional wellbeing of the pregnant person and those who the pregnant person has chosen to be involved, the meeting allows parents time to discuss the results of tests and the likely cause of late IUFD. The meeting can also focus on the prognosis and options for future pregnancies. The discussion should cover general preparation for pregnancy: lifestyle, smoking status, folic acid supplementation and rubella vaccination. There should be an open, honest discussion with an opportunity to make comments and the chance to raise any concerns they might have. If any investigation reveals incidences of poor care leading to harm, clinicians have a duty of candour (under GMC Good Clinical Practice Regulation 20) to disclose this and advise parents of the investigatory process to ensure review and that appropriate lessons are learned.

A suggested summary checklist for postnatal consultations is included in Appendix V of this guideline.

### 10 | PREGNANCY FOLLOWING STILLBIRTH

# 10.1 | What recommendations should be made for subsequent antenatal care following late IUFD?

Recommendation	Evidence quality	Strength	Rationale for the recommendation
Parents with a previous unexplained IUFD should be recommended to have obstetrician-led antenatal care with continuity of	4	GPP	This is recommended as good practice.

Recommendation	Evidence quality	Strength	Rationale for the recommendation
The single most important risk factor for recurrent late IUFD is the history of previous late IUFD. A woman's recurrence risk should be stratified based on the investigations following index late IUFD and other known maternal risk factors.	1+	A	Systematic review and meta-analysis showed that previous late IUFD is associated with a 4.8-fold increased risk of late IUFD. Recommendations from high quality observational studies have reinforced the importance of the risk in the next pregnancy being based on previous history and risk factors; therefore, highlighting the importance in establishing these in subsequent pregnancies to plan the antenatal care.
Women in a subsequent pregnancy after late IUFD either associated with placental dysfunction or in unexplained cases should be offered fetal biometry and amniotic fluid measurement with additional Doppler flow velocimetry of the umbilical artery where appropriate (at a minimum of every 3-4 weeks from 26-28 weeks of gestation).	2	В	SGA infants are found approximately 2–3 times more frequently in women who had a late IUFD than live births; therefore, assessment of fetal growth is recommended in subsequent pregnancies.
Given that those with a previous IUFD may be at risk of placental insufficiency, low dose aspirin (150 mg) may be offered to all women with a previous IUFD either associated with placental dysfunction or in unexplained cases.	1++	В	Evidence from high quality systematic reviews and RCTs has shown the efficacy of low dose aspirin in reducing placental disorders, because of the association of placental disorders with late IUFD and low risk of harm with low dose aspirin this should be recommended in all subsequent pregnancies following late IUFD with previous evidence of placental insufficiency or pre-eclampsia, and unexplained.

		-
2	С	Women with previous late IUFD have a higher risk of GDM in a subsequent pregnancy and further evidence has shown women not screened for GDM have a 44% higher risk for late IUFD so consideration should be given to test women and pregnant people for GDM in a subsequent
		pregnancy.

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Recommendation	Evidence quality	Strength	Rationale for the recommendation
Women in subsequent pregnancies after late IUFD should not routinely be offered low-molecular-weight heparin (LMWH) throughout pregnancy unless there are other medical considerations, thrombophilias or APS present.	3	D	There is currently no evidence for routine use of LMWH.
Women and families who have experienced prior late IUFD may need emotional support and should be provided with support during pregnancy.	1+	A	A meta-synthesis demonstrated that women and their partners have additional psychological needs in subsequent pregnancies.
Women in subsequent pregnancies after late IUFD should be offered induction of labour or birth by 39 <sup>+0</sup> weeks of gestation.	2+	C	At 39 weeks of gestation and beyond, evidence suggests induction of labour is not associated with an increase in caesarean birth, assisted vaginal birth, fetal morbidity or admission to the neonatal intensive care unit. This discussion and decision should however also be balanced against the specific medical and emotional considerations around timing of birth in women and pregnant people with a history of IUFD (including an increased risk of recurrence secondary to a placental cause).

Future reproductive choices and management decisions made in subsequent pregnancies can be altered after a late IUFD occurs. Care in the subsequent pregnancy varies among providers as demonstrated by large national and multinational surveys, <sup>214,215</sup> and a Cochrane review has demonstrated that evidence to guide such care is sparse. <sup>216</sup>[Evidence level 1+]

Parents and families who have experienced prior late IUFD need emotional support and should be provided with support during pregnancy.<sup>217</sup> [Evidence level 1+]

There is an international consensus statement to provide guidance on care for women in pregnancies after late IUFD, which should be used as a basis for care. There is evidence that routine "high-risk" antenatal care does not address women's needs in pregnancy/ies after late IUFD and some evidence from specialist services, such as pregnancy after loss clinics, demonstrates improved psychological outcomes for women. <sup>219</sup>

Late IUFD due to placental causes or preterm birth are the most likely to recur. Causes like antiphospholipid antibody syndrome may benefit from treatment and can lead to more favourable outcomes in the future pregnancy if identified. Women with known risk factors, such as smoking, a BMI above 30 kg/m², and poorly controlled pre-gestational diabetes, can benefit from modification and optimisation of health prior to a subsequent pregnancy. These risk factors must be addressed sensitively. [Evidence level 2]

When the cause of late IUFD has not been found, treatment for a likely placental cause may improve outcomes in the subsequent pregnancy. <sup>226</sup> [Evidence level 2]

With respect to mode of birth in pregnancy subsequent to late IUFD, there is an absence of data from studies to inform the role of a caesarean birth for non-medical reasons in women with a history of late IUFD in reducing perinatal mortality or morbidity, or maternal psychological morbidity. Therefore, as with all other choices related to timing and mode of birth in women who have had a late IUFD, a planned caesarean birth needs to be part of an informed decision-making process. This decision may be greatly influenced by the timing of the previous late IUFD. Families report the wish to have the option of flexible and additional appointments for additional monitoring that is above standard care. They also report a wish for increased emotional support and to provide a compassionate and understanding response to anxiety. [Evidence level 3]

### 10.1.1 | Gestational Diabetes Mellitus (GDM)

Evidence has shown that history of previous GDM is a risk factor for late IUFD. <sup>227</sup> A case–control study reported that women 'at risk' of GDM, but not screened, experienced 44% greater risk of late stillbirth than those not 'at risk' (aOR 1.44, 95% CI 1.01–2.06), therefore a test for GDM in a pregnancy subsequent to stillbirth should be offered, as well as vigilance for signs and symptoms; especially if the previous late IUFD was unexplained <sup>227</sup> and/or if there were signs of macrosomia or placental findings consistent with glucose dysmetabolism, such as delayed villous maturity or fetal vascular malperfusion. <sup>228</sup>

### 10.1.2 | Ultrasonography

Impaired fetal growth secondary to placental dysfunction is considered to be one of the main reasons for perinatal morbidity and mortality. Fetuses under the 10th centile are found approximately 2–3 times more frequently among late IUFDs than live births. <sup>229,230</sup> Furthermore, a systematic review found that women with a history of a late IUFD have an increased risk of birth of a SGA baby (OR 1.39, 95% CI 1.10–1.76). <sup>231</sup> Consequently, additional ultrasound examinations are among the most frequently offered tests of fetal wellbeing in pregnancies after late IUFD. <sup>232,233</sup> [Evidence level 2+]

However, this strategy is undermined by data demonstrating that the relationship between fetal size and adverse outcome weakens significantly with advancing gestation

such that near term, the majority of late IUFDs occur in normally sized fetuses.  $^{234}$ 

The key evidence-based measurement in performing scans in high-risk pregnancies is Doppler flow velocimetry of the umbilical artery. Uterine artery Doppler anomalies may help identify women at risk in their subsequent pregnancy after late IUFD. Low cerebroplacental ratio (CPR) values in the third trimester of pregnancy have been shown to be an independent predictor of late IUFD and perinatal mortality. Studies looking at first and second trimester uterine artery Doppler anomalies have suggested a correlation with late IUFD, however these models have not yet proven applicable to the subsequent pregnancy after late IUFD population. Studies [Evidence level 2 extrapolated]

The evidence for using fetal growth velocity to predict adverse perinatal outcomes is inconclusive. Studies of fetal growth velocity have reported inconsistent results, with lack of consensus of what constitutes a suboptimal fetal growth velocity, whether this varies with gestational age and the relationship of growth velocity to adverse pregnancy outcome. <sup>236,237</sup>

In view of the association of SGA with late IUFD, in a subsequent pregnancy after late IUFD serial fetal biometry and amniotic fluid measurements with Doppler flow should be considered. There are no data to determine the optimal frequency for ultrasound assessment of fetal growth in pregnancy after late IUFD. Women's perceptions as to the ideal frequency of ultrasound monitoring should be taken into consideration when formulating a pregnancy plan. Care providers should be aware that some parent's anxiety may increase before ultrasound scans, because of the association with the confirmation of death of their previous stillborn baby. <sup>238</sup>[Evidence level 3]

#### 10.1.3 | Induction of labour

The ARRIVE trial<sup>239</sup> showed that induction of labour at 39 weeks reduces caesarean birth rate significantly. In the trial, perinatal death and other adverse events were 4.4% in the induction of labour group and 5.4% in the expectant management group (RR 0.81, 95% CI 0.64–1.01; *P*=0.06). Epidemiological evidence showed that universal induction at 39 weeks would reduce overall rates of late IUFD.<sup>240</sup> At 37–38 weeks, induction has been associated with increased risks of perinatal morbidity, whereas perinatal outcomes after induction are optimal at 39–41 weeks.<sup>240</sup> The 35/39 trial showed that for women over 35 years old, routine induction at 39 weeks might prevent stillbirths without increasing caesarean birth rates.<sup>241</sup>[Evidence level 1 extrapolated]

There is no evidence for the value of an unindicated birth prior to 37 weeks with no risk factors other than prior stillbirth. Overall, there is enough evidence to consider and discuss induction of labour or birth by 39 weeks of gestation in women and pregnant people in a subsequent pregnancy after late IUFD. Earlier birth might be considered for women and pregnant people with an earlier IUFD, cholestasis, pre-eclampsia, insulindependent diabetes and other maternal conditions, including

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psychological considerations, and the decision is always a risk/ benefit balance with prematurity of the fetus.

A study of 306 women with a previous IUFD found that 161 had a clear indication for earlier intervention. Of the remaining 145 women, 42 of the remaining participants (with no known previous medical problems) developed complications during their pregnancy necessitating earlier (before 39 weeks) birth. Of the remaining 92 women 47 (51%) went into spontaneous labour before their induction date; all 92 pregnant people gave birth without major complications. 242

It is vital to carefully consider maternal wellbeing and emotional state throughout the pregnancy and to provide ongoing psychosocial support. It may be helpful to outline the possible pathway early in pregnancy such as birth at 39 weeks of gestation as a clear goal from the beginning, and it may help alleviate anxiety.

### 10.1.4 | Low dose aspirin

Low-dose aspirin may reduce the risk of perinatal death in women at risk for placental insufficiency, and women with a history of stillbirth may fall into this category.

Low-dose aspirin (60–150 mg) has been widely evaluated as a method for preventing placental-related complications in pregnancy, and in particular pre-eclampsia. Early studies showed that women who took low dose aspirin as prophylaxis during pregnancy were less likely to develop pre-eclampsia than women who had not taken aspirin. Aspirin prophylaxis in pregnancies at risk of pre-eclampsia resulted in a reduction in the rate of FGR (RR 0.44, 95% CI 0.30–0.65) and fetal or neonatal death (RR 0.86, 95% CI 0.76–0.98).

The 2013 systematic review of RCTs showed reduced preeclampsia, perinatal death, and FGR among individuals at high risk commenced on aspirin before 16 weeks.  $^{245}$  A further systematic review of 45 RCTs identified increased benefits with more than 100 mg aspirin daily, without increasing adverse effects.  $^{246}$ 

There is limited evidence assessing low dose aspirin use in pregnancy that are powered to detect stillbirth risk reduction. The ASPRE trial<sup>247</sup> randomly assigned 2971 participants at high risk of pre-eclampsia to 150 mg aspirin or placebo; they reported a possible lower rate of stillbirth and neonatal death among those receiving low dose aspirin versus placebo (8 [1.0%] of 798 versus 14 [1.7%] of 822, OR 0.59 [95% CI 0.19–1.85]).

Studies have shown that the effectiveness of low dose aspirin on pre-eclampsia reduced with decreasing compliance.  $^{248,249}$ 

The Saving Babies Lives Care Bundle version 3 (SBLCBv3) recommends low dose aspirin as prophylaxis for a number of indications related to placental disorders in order to reduce the number of stillbirths. <sup>250</sup> Therefore, aspirin should be considered for woman at risk of late IUFD starting from 12 weeks of gestation to 36 weeks of gestation. [Evidence level 1++]

### 10.1.5 | Low-molecular-weight heparin (LMWH)

LMWH use should only be used to prevent maternal VTE and further research is required before its use is recommended for the primary aim of preventing adverse fetal outcomes, unless there are other medical considerations, thrombophilias or APS present.<sup>251</sup>

### 11 | CLINICAL GOVERNANCE

### 11.1 | What are the risk management standards for IUFD?

Recommendation	Evidence quality	Strength	Rationale for the recommendation
Maternity units should ensure they are tracking their outcomes and benchmarking against other organisations using the national indicators dashboard.	4	GPP	This is recommended as good practice.

The Maternity Action Plan<sup>252</sup> and SBLCBv3<sup>250</sup> both aim to reduce stillbirths by 50% by 2025 and provide relevant auditable standards.

### 11.2 | What are the standards for documentation?

Recommendation	Evidence quality	Strength	Rationale for the recommendation
Standardised checklists can be used to ensure that all appropriate care options are offered and the response to each is recorded.	3	D	A retrospective study of an integrated care pathway for stillbirth improved delivery of care for women who experienced a stillbirth.
Consent for perinatal postmortem examination should be documented using the nationally recommended form.	4	GPP	This is recommended as good practice.
All stillbirths should be reviewed in a multi-professional meeting using the standardised PMRT to ensure lessons are learned from each IUFD and shared widely. Results of the discussion should be recorded in the woman's case record and discussed with the parents.	4	GPP	This is recommended as good practice.

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Recommendation	Evidence quality	Strength	Rationale for the recommendation
All stillbirths should be reported to:  MBRRACE-UK,  National Maternity and Perinatal Audit,  PMRT database.  Maternity and Newborn Safety Investigations (MNSI) (if intrapartum)  All research studies in bereavement care or evaluations of breavement service for stillbirth should consider the use the developed core outcome set for stillbirth care (iCHOOSE study) to assess effectiveness.	4	GPP	This is recommended as good practice.

An international core outcome set to evaluate the effectiveness of stillbirth care was developed in 2022 (iCHOOSE Study).<sup>253</sup> This was developed using a mixed-methods research methodology including a systematic review, qualitative interviews with bereaved families, an international Delphi survey and consensus meetings with key stakeholders, including 542 bereaved families, stillbirth researchers, healthcare professionals and stillbirth advocates from 29 different countries. The core outcome set for stillbirth care includes:

Mandatory outcomes in all circumstances: life-threatening complications and death, parents' experience of respectful and supportive care, grief, mental health and emotional wellbeing, isolation, stigma, impact on work, impact on relationship with immediate family.

**Mandatory outcomes in investigation of stillbirth studies**: cause of death identified and parents' understanding of cause of death.

Mandatory subsequent pregnancy care outcomes: antenatal complications for women, antenatal complications for baby, survival of baby, neonatal outcomes and attachment to baby.

Mandatory outcomes for when a baby dies in a twin or multiple pregnancy: Survival of baby/ies, preterm birth, pregnancy complications for baby and neonatal outcomes.

### 12 | RECOMMENDATIONS FOR FUTURE RESEARCH

- Effectiveness of stillbirth care guidelines and the bereavement care pathway on core outcomes (core outcome set for stillbirth care)
- Feasibility and utility of non-invasive and minimally invasive postmortem examination of the baby.
- Impact of models of care in subsequent pregnancies after late IUFD.
- Induction of labour to prevent adverse outcome in subsequent pregnancies after late IUFD.
- Association between microbiome and pregnancy loss including late IUFD.
- Effectiveness of bereavement counselling or other interventions post late IUFD.

- Optimal methods of induction for women with late IUFD.
- Validation and clinical evaluation of risk prediction models for late IUFD.

### 13 | AUDITABLE TOPICS

- Proportion of women who were offered postmortem after late IUFD. (100% target)
- Proportion of women who had placental histopathology after late IUFD. (100% target)
- Proportion of women who had cytogenetic analysis after late IUFD. (100% target)
- Patient experience following late IUFD (using established validated tools).
- Proportion of women who were involved in the PMRT process after a late IUFD. (> 95% target)
- Proportion of women who had a postnatal visit after a late IUFD. (100% target)
- Proportion of women who had access to postnatal counselling after a late IUFD. (100% target)
- Percentage of staff who have had bereavement care training. (> 95% target)

### 14 | USEFUL LINKS AND SUPPORT GROUPS

Sands www.sands.org.uk/support-you

PETALS www.petalscharity.org

RCOG Patient information When your baby dies before birth www.rcog.org.uk/for-the-public/browse-our-patient-information/when-your-baby-dies-before-birth/

#### **FUNDING INFORMATION**

All those involved in the development of the Green-top Guidelines, including the Guidelines Committee, Guidelines Committee co-chairs, guideline developers, peer reviewers and other reviewers, are unpaid volunteers and receive no direct funding for their work in producing the guideline. The exception to this are the RCOG staff involved who are salaried employees of the College and Guidelines Committee members who receive reimbursement for expenses for attending Guidelines Committee meetings. Please see more information on travel expense rules on the RCOG website.

#### CONFLICTS OF INTEREST STATEMENT

CB has received a National Institute of Health and Research (NIHR) Research for Patient Benefit award for the RECOGNISE study (Reference: NIHR203182), NHSX Award ID: AI\_AWARD02591 and Clinical Decision Tool to Reduce Placental Disorders in Pregnancy - a multi-centre cluster RCT. AH is the director of the Tommy's Maternal and Fetal Health Research Centre and has received centre funding to the University of Manchester; he has also received a grant to the University of Manchester for the Evaluation of MNSI and PMRT reviews after perinatal

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deaths as part of the NIHR Research Policy Programme and received a grant to Manchester University NHS Foundation Trust for MiNESS20-28 study (to find antenatal risk factors for stillbirth between 20 and 28 weeks' gestation) as part of the NIHR Research for Patient Benefit. He has received consulting fees from Norgine Ltd for a video on induction of labour, payment from Canon Ultrasound for a lecture on the Evaluation of NHS England Saving Babies Lives Care Bundle, as well as medicolegal expert witness work relating to stillbirth. He has also acted as medical advisor for Count the Kicks and the Star Legacy Foundation. DB has received an award from the NIHR (Award ID: DRF-2017-10-130) and is a Trainee Scientific Editor at BJOG. DS has received grants from Welcome LEAP for Near Infrared Spectroscopy and Stillbirth, MRC for MRI to predict birth outcome and NIHR for rotational birth and provides medicolegal reports on stillbirth. He is also chair of the DMC of the PANDA stillbirth trial, chair of the DMC of the CRAFT RCT and is on the advisory board of Sands. He is the former chair of the ISA Bereavement and Clinical Care Group. AM has received the NIHR Advanced Fellowship about birth Options, has participated in the PARTNER Trial and is the BMFMS Labour and Delivery Representative.

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### APPENDIX I: Explanation of guidelines and evidence levels

#### Classification of evidence levels

1++	High-quality meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a very low risk of bias		
1+	Well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias		
1-	Meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a high risk of bias		
2++	High-quality systematic reviews of case–control or cohort studies or high-quality case–control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal		
2+	Well-conducted case-control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal		
2–	Case-control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal		
3	Non-analytical studies, e.g. case reports, case series		
4	Expert opinion		

#### **Grades of Recommendation**

Α	At least one meta-analysis, systematic reviews or RCT rated as 1++, and directly applicable to the target population; or a systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population and demonstrating overall consistency of results
В	A body of evidence including studies rated as 2++ directly applicable to the target population, and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 1++ or 1+

A body of evidence including studies rated as 2+ directly applicable to the target population, and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 2++

Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+

#### **Good Practice Points**



D

Recommended best practice based on the clinical experience of the guideline development group.\*

\*on the occasion when the guideline development group find there is an important practical point that they wish to emphasise but for which there is not, nor is there likely to be any research evidence. This will typically be where some aspect of treatment is regarded as such sound clinical practice that nobody is likely to question it. These are marked in the guideline, and are indicated by  $\checkmark$ . It must be emphasised that these are NOT an alternative to evidence-based recommendations, and should only be used where there is no alternative means of highlighting the issue.

#### APPENDIX II: Timing of maceration after late IUFD

#### **Maceration timing**

0–6 hours	Little change, clear corneas
6 hours – 1 day	Skin peeling on peripheries, bony prominences.
1–2 days	More widespread skin peeling, with bullae (fluid blisters in epidermis), developing discoloration of abdomen.
2–3 days	Hemolytic changes in cord, serosanguinous nasal fluid, fluid in body cavities, uniform pink tissues.
4–7 days	Skull bone starting to become more separated. Eyes beginning to become sunken. Mandible suture more mobile. Periosteum and dura lifts from skull bones.
7 days and OVER	Brown discoloration.
10-12 days	Increased loss of fluid and eventually after many weeks a fetus papyraceous.



#### APPENDIX III

#### Stillbirth registration

The current law on stillbirth registration is set out in the Births and Deaths Registration Act 1953 (amended by the Still-Birth (Definition) Act 1992). The legal definition of stillbirth is "any child expelled or issued forth from its mother after the 24th week of pregnancy that did not breathe or show any other signs of life". Legal advisors for the Department of Health and Social Care and the Office for National Statistics have agreed that a fetus that is expelled after 24 weeks of pregnancy, provided it was no longer alive at the 24th week of pregnancy (this fact being either known or provable from the stage of development reached by the dead fetus), does not fall within the category of births to be registered as a stillbirth under the above Acts. This interpretation is also accepted by the General Register Office for Scotland and the General Register Office for Northern Ireland. When the gestational age is not known before the birth, with unbooked pregnancies for example, the decision about the status (if defined as stillbirth) of the birth should be made on the basis of the stage of development of the baby on examination. The doctor or midwife attending the stillbirth is required to issue a Medical Certificate of Stillbirth that enables the birth to be registered. The cause and sequence of medical events leading to the IUFD should be given in as much detail as possible. Nonspecific terms such as anoxia, prematurity and so on should be avoided. Certification should not be delayed for the results of the postmortem.

The mother (or either parent if they are married or in a civil partnership at the time of birth) is responsible for registering the stillbirth, normally within 42 days (21 days in Scotland and Northern Ireland 1 year) but with a final limit of 3 months for exceptional circumstances. This responsibility can be delegated to healthcare professionals, including a midwife or doctor present at the birth or a bereavement support officer. The person registering the birth has to be able to provide the following:

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

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

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

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

If information about the father is not recorded initially, it is possible for the birth to be re-registered to include his details later. Most local authorities have websites on the registering of stillbirth. There are no fees for registration, but additional certificates do carry a charge. HM Coroner does not normally have jurisdiction over stillbirth, even if the cause of death is not known, but contact should be made for an apparently fresh stillbirth not attended by a healthcare professional. HM Coroner also has discretion to be involved if the death followed a criminal act such as common assault and can then request for any postmortem to be expedited. Twenty-one stillbirths were referred to HM Coroner Services for England and Wales in 2007 and 13 in 2008. Following the RCOG best practice guidance for healthcare professionals, there is no legal obligation to contact the police following an abortion, pregnancy loss or unattended birth.

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### APPENDIX IV: - Perinatal Mortality Review Tool (PMRT)

The PMRT has been designed with user and parent involvement to support high quality standardised perinatal reviews on the principle of 'review once, review well'. The aim of the PMRT programme [www.npeu.ox.ac.uk/pmrt/programme] is to introduce the PMRT to support standardised perinatal mortality reviews across NHS maternity and neonatal units in England, Scotland and Wales. The tool supports:

 Systematic, multidisciplinary, high quality reviews of the circumstances and care leading up to and surrounding each stillbirth and neonatal death, and the deaths of babies who die in the post-neonatal period having received neonatal care.

- Active communication with parents to ensure they are told that a review of their care and that of their baby will be carried out and how they can contribute to the process.
- A structured process of review, learning, reporting and actions to improve future care.
- Coming to a clear understanding of why each baby died, accepting that this may not always be possible even when full clinical investigations have been undertaken; this will involve a grading of the care provided.
- Production of a report for parents which includes a meaningful, plain English explanation of why their baby died and whether, with different actions, the death of their baby might have been prevented.
- Other reports from the tool which will enable organisations providing and commissioning care to identify

- emerging themes across a number of deaths to support learning and changes in the delivery and commissioning of care to improve future care and prevent avoidable future deaths.
- Production of national reports of the themes and trends associated with perinatal deaths to enable national lessons to be learned from the nationwide system of reviews.

Parents whose baby has died have the greatest interest of all in the review of their baby's death. Alongside the national annual reports a lay summary of the main technical report will be written specifically for families and the wider public. This will help local NHS services and baby loss charities to help parents engage with the local review process and improvements in care.



#### APPENDIX V: Stillbirth Follow-up Consultation Checklist

### STILLBIRTH FOLLOW-UP CONSULTATION CHECKLIST **Patient Name and Identifier: Consultant Obstetrician:** Date of Meeting: Name of the baby (if appropriate – check with parents): Pre-meeting review: Summary of Case: Date of diagnosis: Medical history: BMI at booking: Allergies / Asthma (aspirin contraindicated?): **Obstetric History: Antenatal Course:** GTT at weeks: Y/N - result BMI at 36 weeks: Results back **Tests** Taken FBC/Biochemistry/clotting LFTs/TBAs **TFTs** HbA1c Thrombophilia screen Microbiology Cytogenetics Post mortem Parental engagement perinatal mortality review process Outcome from perinatal mortality review process Taken Results back Tests Labour/Birth Summary Date: Birthweight: Postnatal Course (including any postpartum physical complications): **Current physical wellbeing:** Current mental and emotional wellbeing: Discussion on coping with grief: Discussion on support and relationship with immediate family (including children if applicable): Counselling, support groups or support information sources discussed and offered: Discussion about planning future pregnancy including contraception\* if appropriate:

GTT, glucose tolerance test; FBC, full blood count; LFTs, liver function tests; TBAs, total bile acids; TFTs, thyroid function tests; HbA1c, glycated haemoglobin (A1c).



### APPENDIX VI

### **GLOSSARY**

Stillbirth	legally defined as 'a baby delivered with no signs of life known to have died after $24^{+0}$ completed weeks of pregnancy
Late intrauterine fetal death (IUFD)	babies with no signs of life in utero after $24^{-10}$ completed weeks of pregnancy.
Feticide	act of killing a fetus or causing a miscarriage
Disseminated intravascular coagulation (DIC)	a rare but serious condition that causes abnormal blood clotting throughout the body's blood vessels
Sudden infant death	sudden and unexpected death of a baby less than 1 year old in which the cause was not obvious before the investigation
Perinatal mortality	stillbirths and death of an infant less than 7 days
Extended perinatal mortality	stillbirths and neonatal deaths (a baby born at any time during pregnancy who lives but dies within 4 weeks of being born)
Hydrops fetalis	a life threatening condition in which abnormal amounts of fluid accumulate in two or more body areas of an unborn baby
Perinatal Mortality Review Tool (PMRT)	standardised perinatal mortality reviews across NHS maternity and neonatal units in England, Scotland and Wales
Small-for-gestational-age (SGA)	infant born with a birthweight less than the 10th centile.

The review process will commence in 2027, unless otherwise indicated.



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

The review process will commence in 2027, unless otherwise indicated.

#### **DISCLAIMER**

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

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