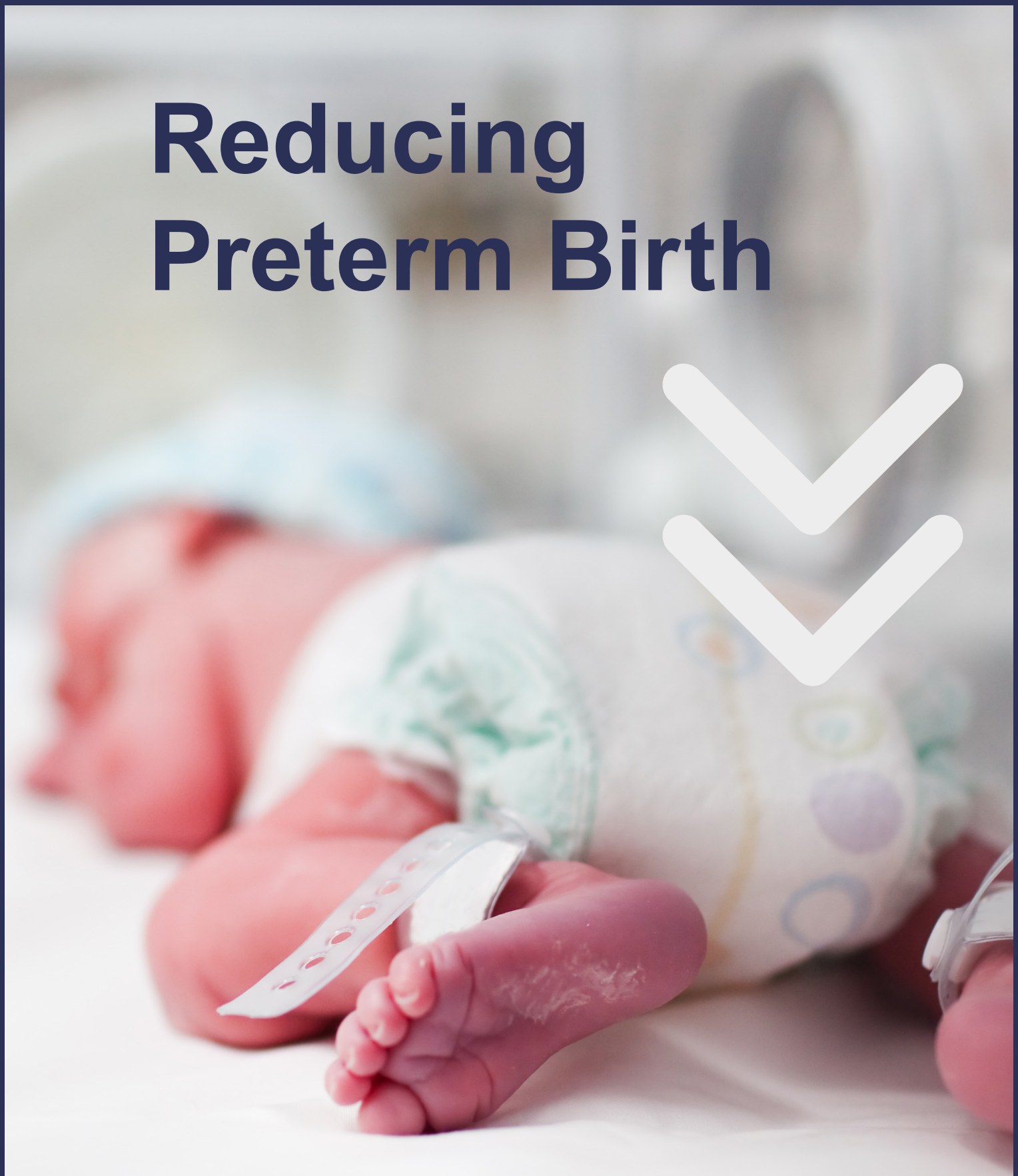
Reducing Preterm Birth



Guidelines for Commissioners and Providers

UK Preterm Clinical Network

2019

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Definitions and Abbreviations

CL	cervical length
Extremely preterm	birth prior to 28 weeks gestation
Late miscarriage	pregnancy loss between 16+0 and 23+6 weeks gestation
MDT	multidisciplinary team
Moderate preterm	birth between 32+0 and 36+6 weeks gestation
NICE	National Institute for Health and Care Excellence
PPROM	preterm prelabour rupture of membranes
Preterm birth	birth prior to 37+0 weeks gestation
PTB	preterm birth
qfFN	quantitative fetal fibronectin
Very preterm	birth between 28+0 and 31+6 weeks gestation
WHO	World Health Organisation

Scope

Reducing preterm birth is a priority for Maternity and Children's services. In the recent DH publication *Safer Maternity Care* the Secretary of State for Health made it clear that 'we will not achieve the national Maternity Safety Ambition [to halve the rates of stillbirths, neonatal … and brain injuries that occur during or soon after birth by 2025] unless the rate of preterm births is reduced' and he set an additional ambition to reduce the national rate of preterm births from 8% to 6%. He suggested 'specialist pre-term birth clinics across the country…can provide a mechanism around which change can be focussed and delivered'[1].

In order to do this, best practice pathways and agreed models of care to reduce variation in care should be deployed nationally.

The aim of this document is to provide evidence-based recommendations for commissioning groups and providing organisations to implement services and pathways which will reduce the incidence of preterm birth, and reduce the burden of this outcome for babies and their families.

The key areas outline provision of care designed to:

- **predict** women at risk of PTB
- implement strategies to **prevent** PTB
- **prepare** the mother and baby when PTB is inevitable
- where PTB has taken place before 34 weeks, the importance of **post-pregnancy** consultation with parents is also discussed

Sources of funding and ways of evaluating performance are also outlined. This document was initially drafted by a working group within the Preterm Clinical Network (Dr Lisa Story, Professor Anna David, Professor Andrew Shennan, Mr Nigel Simpson) which received substantial advice and input from preterm prevention specialists and other high risk obstetricians, in addition to charities and support groups representing women and their families likely to be affected by the proposed recommendations.

The guidance is designed to complement and expand upon recommendations contained within other national guidance issuing from NICE and the RCOG, but is most closely linked with those outlined in NHSE's *Saving Babies' Lives Care Bundle*.

Background

Preterm birth (PTB)

Preterm birth (PTB), defined as birth less than 37+0 weeks gestation, is a common complication of pregnancy, comprising around 8% of births in England and Wales[2]. It is the most important single determinant of adverse infant outcome with regards to survival and quality of life[3].

- babies born preterm have high rates of early late and post neonatal mortality
- morbidity is inversely correlated to gestational age
- the most significant adverse outcomes are associated with very PTB defined as occurring less than 32+0 weeks gestation
- PTB is estimated to cost health services in England and Wales £3.4bn per year[2]

Short-term complications

These involve multiple organ systems including:

- the central nervous system, (intraventricular haemorrhage, periventricular leukomalacia and hydrocephalus)
- the gastrointestinal tract (necrotising enterocolitis)
- the respiratory system (respiratory distress syndrome, chronic lung disease)
- other complications such as retinopathy of prematurity[4]

Longer-term complications

Longer-term complications associated with preterm birth include adverse neurodevelopmental outcomes involving motor (cerebral palsy), cognitive, and behavioural/socialisation disorders (such as autism spectrum)[5].

Moderate complications

Even moderate PTB (32+0–36+6 weeks gestation), whilst not necessarily associated with significant inpatient care and mortality, is linked with increased need for educational support (through Education, Health and Care Plans) in childhood[6].

Incidence of PTB

There has been no decline in the incidence of PTB in England and Wales. Advances in neonatal care mean increasing numbers of individuals born extremely preterm (under 28 weeks) are surviving (from 40% in 1995 to 53% in 2006) with similar rates of disability. The prevalence of bronchopulmonary dysplasia, major cerebral scan abnormality, and weight and/or head circumference less than two standard deviations remain static at 68%, 13% and 44% and 23% respectively. There has also

been an increase in the proportion of babies treated for retinopathy of prematurity from 13% to 22%[7]. The consequences of preterm birth are therefore significant for individuals, their families and health services.

This consultation guideline has been developed in collaboration with clinical experts in preterm birth, the UK Preterm Clinical Network, charities and support groups engaged in preterm birth prevention and advocacy, and aims to provide recommendations to ensure optimal, standardised care for women at high risk of preterm birth and thereby reduce the incidence of PTB.

- consideration has been given to the 2015 National Institute for Health and Care Excellence (NICE) clinical guideline on preterm labour and birth[2]
- multifactorial difficulties related to improving outcomes in preterm birth are acknowledged
- adequate input with regards to financial assistance for training and development of care pathways is imperative, and may be identified within existing maternity tariffs for Intermediate Care

Definition of Preterm Birth

Preterm birth is defined by World Health Organisation (WHO) as referring to all births before 37 completed weeks of gestation or fewer than 259 days since the first day of a woman's last menstrual period[8]. Further subdivision can occur:

- extremely preterm (<28+0 weeks)
- very preterm (28+0 – <31+6 weeks)
- moderate preterm (32+0 – <36+6 weeks)

The majority of prematurity-related adverse outcomes relate to births at earlier gestations; for example, mortality increases from 2% for infants born at 32 weeks gestation to >75% of those born at 23 weeks gestation. However, even defining 37 weeks as a 'safe' gestation is somewhat arbitrary as it has been shown that the incidence of short and long term complications continues to fall up to 40 weeks gestation[9].

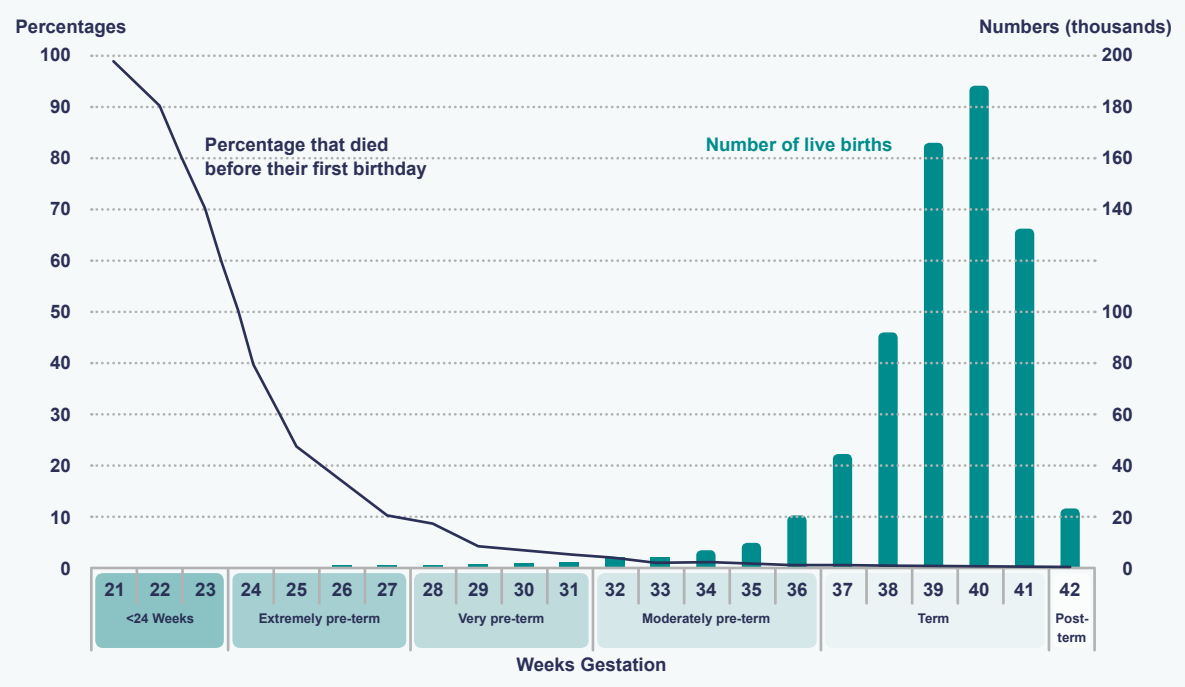
National Context

Around 8% (around 60,000) babies are born prematurely each year in the UK[10]. Morbidity is inversely correlated to gestational age, and the most significant adverse outcomes are associated with very preterm birth, defined as occurring less than 32+0 weeks gestation. These births account for 1.4% of all deliveries in the United Kingdom[11], affecting 13,500 individuals every year.

In 2013 in England and Wales, 0.1% of live births occurred at less than 24 weeks. The infant mortality rate for these babies was 877.2 deaths per 1000 live births. The majority of these deaths (93%) occurred during the early neonatal period[10].

The financial implications associated with preterm birth are significant. A recent economic analysis has concluded that delaying preterm birth by a single week across all gestational categories would see a fall in the total public sector cost due to preterm birth (excluding any intervention costs) from £2.946 billion to £1.952 billion, an annual saving of £994 million.[44]

Percentage of infant deaths and number of live births by week gestation 2013[10]



The NHS Outcome Framework

The NHS Outcome Framework noted that the '…primary purpose of the NHS is to improve the outcomes of healthcare for all'. The 2015/16 Outcomes Framework outlined objectives to:

- reduce deaths in babies and young children
- improve the safety of maternity services (admission of full-term babies to neonatal care)

This has been further developed in *Safer Maternity Care* where the Secretary of State for Health made it clear that 'we will not achieve the national Maternity Safety Ambition [to halve the rates of stillbirths, neonatal … and brain injuries that occur during or soon after birth by 2025] unless the rate of preterm births is reduced' and set an additional ambition to reduce the national rate of preterm births from 8% to 6%[1].

> **National maternity safety ambition to reduce the national rate of preterm births from 8% to 6%**

Patient Perspective

Preterm birth can have significant consequences for families. Preterm birth is the biggest cause of neonatal death and families are impacted long term by this event, including time off work, greater need for primary health services including mental health services. Parents who have lost a baby have significantly altered needs in subsequent pregnancies, needing greater reassurance and monitoring even if a subsequent pregnancy is low risk.

Parents whose preterm babies survive sometimes spend significant time visiting their baby in NICUs with the associated disruption on the entire family, especially siblings.

Preterm birth is associated with a range of disabilities from cerebral palsy, deafness, blindness, poor infant and child health, learning and behavioural difficulties and managing these issues can place a lifelong burden on parents including major changes to how a family manages for instance resulting in one parent being unable to work and the subsequent financial hardship. Preterm babies add significant long-term costs to local services including primary health care, social care and education. Some babies require long-term health care in specialist paediatric services.

It is imperative that service users are fully involved in all aspects of decision-making, including choosing the most appropriate care pathway for the women and her baby. Capturing regular feedback from service users can also be used to benchmark individual units and ensure that the quality of care provided is of high quality and continually improving.

The involvement and support of patient groups relating to preterm birth is a powerful force, providing a support network for affected individuals, increasing awareness of the issues related to preterm delivery and providing insight to the challenges faced. Their input is essential in the implementation of local guidelines regarding the management issues associated with PTB.

This document is written with input from and the support of Tommy's, Incompetent Cervix UK, Bliss, Cerebra, Little Heartbeats, TAMBA and the Harris-Wellbeing Preterm Birth Centre.

Tommy's
Funding research
Saving babies' lives

Incompetent Cervix UK

Bliss
for babies born premature or sick

CEREBRA
Working wonders for children with brain conditions

Little heartbeats

Tamba
TWINS & MULTIPLE BIRTHS ASSOCIATION

HARRIS-WELLBEING PRETERM BIRTH CENTRE
WELLBEING OF WOMEN

Risk factors for Preterm Birth

Preterm birth may be sub-divided into two categories: spontaneous (70%) or indicated (30%), where delivery is expedited for maternal or fetal indications. Conditions that may necessitate medically-indicated delivery of a preterm baby include maternal pre-eclampsia or fetal growth restriction, however, spontaneous preterm birth will be the focus of this guidance document.

General demographic

The aetiology of spontaneous preterm birth is complex and multifactorial. General demographic correlations exist between preterm birth and social deprivation, extremes of maternal age, domestic violence, smoking in pregnancy, low body mass index and teenage pregnancy[12].

Previous history of preterm birth

A previous history of preterm birth is the single most important risk factor for subsequent preterm birth, with the risk increasing the earlier the previous birth occurred, or with multiple incidences of preterm birth[13].

First-time mothers

Despite it being the strongest risk factor, and therefore one way of identifying those at risk of PTB, around 50% of preterm births occur in first-time mothers. General strategies to reduce the chance of PTB in these women, such as smoking cessation and continuity of carer, are therefore highly relevant.

Additional risk factors

Additional risk factors include a history of previous late miscarriage (16–24 weeks gestation), preterm prelabour rupture of membranes (PPROM)[12], and cervical surgery[14].

Excisional cervical surgery may be performed by a cone biopsy or a large loop excision of the transformation zone (LLETZ) following discovery of cervical dysplasia. Several population-based cohort studies have found the incidence of preterm birth to be significantly increased after cervical excisional procedures of any kind. However, there is evidence that knife cone biopsy or multiple LLETZs increase the risk of PTB more than a single LLETZ. This is primarily due to the increased amount of tissue excised, which correlates to an increased risk of PTB[14]. Recent evidence also indicates that emergency (and particularly full dilatation) caesarean sections are also a significant risk factor in subsequent preterm birth. This may be due to an inadvertently low incision at the time of delivery through cervicoisthmic tissue which may lead to a weakened cervix[15].

Variations in uterine size and shape

The presence of variations in uterine size and shape in expectant mothers is associated with a two to five-fold increase in the risk of spontaneous preterm birth compared to those with normal uterine anatomy[16]. The most common variations include a uterine septum, a unicornuate, bicornuate, or didelphys uterus. These are often unrecognised pre-pregnancy but may be suspected on early pregnancy scans, and are also linked with growth restriction and malpresentation later in pregnancy[17]. Women who have had surgery for uterine anomalies such as septum resection may still face an increased risk of preterm birth.

Infection

Infection, both local (urinary tract and abnormal vaginal flora) and systemic (pyelonephritis, appendicitis, cystic fibrosis) have been consistently linked to an increased incidence of PTB[12].

Multiple pregnancies

Multiple pregnancy carries a substantial risk of preterm delivery and despite only accounting for 2–3% of infants results in 15–20% of all preterm births[12]. Uterine overdistension resulting in premature uterine activity contractions and PPROM is believed to be one causative mechanism[18].

Management of multiple pregnancy has not been specifically addressed in this document but twins and higher order multiple pregnancies are at significantly higher risk of preterm birth and so strategies aimed at reducing risk should be discussed within each maternity unit in conjunction with the local specialist clinic. General guidance is available in the NICE Clinical Guideline ‘Multiple pregnancy: antenatal care for twin and triplet pregnancies[19], due to be updated later in 2018. A recent report from TAMBA has highlighted improved outcomes in units adopting these pathways of care[20].

Many strategies for preterm birth prevention in singletons are not effective in multiple pregnancy – so units are encouraged to discuss ongoing studies within the NIHR’s Clinical Research Network Portfolio specifically addressing twin pregnancy and preterm birth, such as STOPPIT2[21].

Principles of Care

By creating a standardised approach to the management of women at high risk of spontaneous preterm birth, alongside measurement of common outputs, each maternity unit will benefit from information sharing and benchmarking. Outcome 'dashboard' measures, for example the overall number and proportion of singleton deliveries occurring between 16 and 37 weeks' gestation, can then be compared across regions to ensure standardisation of care across the country.

Multidisciplinary team (MDT) working is needed to provide both physical and psychological care to mothers at risk of, or who have experienced preterm birth (and in many cases, subsequent perinatal loss).

Preterm prevention strategies should:

- provide standard care pathways for women deemed at high risk of spontaneous preterm birth before, during, and after pregnancy
- provide access to specialised care in acute units that is available 52 weeks a year
- facilitate the establishment of a preterm birth network and database to encourage multicentre trials and large datasets of patient information (with patient consent) to improve management and treatment of women at high risk of preterm birth and reduce associated morbidity and mortality.
- ensure women are given adequate evidence-based information and can actively participate in decisions regarding their management

> **Correct identification of women at high risk of preterm birth, both asymptomatic and symptomatic, will give windows of opportunity to administer interventions which have been shown to be beneficial either in prolongation of the pregnancy or in reducing subsequent neonatal morbidity and mortality**

All acute maternity units should offer basic measures to identify and manage women at high risk of preterm birth, with more specialised care provided by more experienced practitioners within or adjacent to each Local Maternity System who can provide additional services such as high vaginal or transabdominal cerclage. Once specialised preterm prevention clinics have been established these extra measures should be achievable within existing tariffs.

Prediction

A coordinated approach to identify women at high risk of preterm birth involves both community and hospital-based care settings. Identification should occur early in pregnancy to maximise the treatment options and opportunities available to women.

Community Care

> **The role and action of midwives at the booking appointment is fundamental towards identifying women at high risk of PTB.**

At the booking visit, factors known to have an association with preterm birth can be ascertained and directly addressed:

Smoking

This doubles the risk of preterm delivery[22]. NICE produced guidance regarding smoking cessation in 2010, however implementation has not been consistent or comprehensive across the country[23]. A recent study has shown that women, who had experienced a previous preterm birth, who stopped smoking early in the first two trimesters of pregnancy, modified their risk back to that of a non-smoker, however, when cessation was delayed until the third trimester this effect was lost[24]. The importance of promoting smoking cessation support is therefore of vital importance in modifying the risk of preterm birth both pre-pregnancy and in early pregnancy. Counselling interventions have been shown to be effective in promoting smoking cessation and reducing preterm birth rates and it has been suggested that peer support and incentive-based approaches are likely to provide additional benefit[25].

Maternal age

Young women (<18yrs) have an increased risk of preterm birth. Appropriate referral to specialist teenage pregnancy teams should be offered to provide adequate support and advice throughout the pregnancy. Women above the age of 40yrs may have coexisting risk factors increasing risk of PTB, indicating specific preventive strategies such as the use of low-dose aspirin.

Domestic violence

Women experiencing domestic violence and/or other social pressure should be directly counselled and referred for specific support through local pathways.

Urinary tract infection

While asymptomatic bacteriuria in non-pregnant women is usually benign, the accompanying obstruction to flow in pregnancy may increase the likelihood of pyelonephritis, which is in turn associated with a 20–50% incidence of preterm birth[26]. As indicated in NICE guidance, midstream urine samples should be taken and sent for culture and sensitivity in all pregnant women at booking. Culture positive samples, even in symptom-free women (asymptomatic bacteriuria), should be promptly treated[27]. Those who have a recurrent episode require review in secondary care.

Vaginal infection

The carriage of pathogens such as *Neisseria gonorrhoeae* and *Chlamydia trachomatis* is associated with preterm birth, and screening should be offered to at-risk women. Healthcare professionals should inform pregnant women under the age of 25 years about the high prevalence of chlamydial infection in their age group, and give details of their local National Chlamydia Screening Programme.

The role of organisms found in bacterial vaginosis (BV) remains controversial; the presence of BV is linked with preterm birth, but the varying methods used to ascertain its presence, and the timing and means of treatment in several studies have meant that no consensus currently exists as to its screening and treatment in at-risk women. The presence of Group B Streptococci in a vaginal swab is not an indication to treat until in labour unless also isolated from a midstream urine specimen[28].

Identifying women at risk

A further set of questions should be used to ascertain risk factors associated with preterm birth at this appointment to appropriately identify women at risk who may benefit from preventive strategies and/or further assessment and more intensive monitoring within the hospital setting. Women can be then be offered intermediate or high risk care as outlined on the following page.

Table 1: Risk factors associated with preterm birth and recommended referral pathways for preterm prevention surveillance

Risk Factor	Care
High risk • Previous preterm birth or mid-trimester loss (16 to 34 weeks gestation) • Previous preterm prelabour rupture of membranes <34/40 • Previous use of cervical cerclage • Known uterine variant (i.e. unicornuate, bicornuate uterus or uterine septum) • Intrauterine adhesions (Ashermann's syndrome) • History of trachelectomy (for cervical cancer)	**Surveillance** • Referral to local or tertiary Preterm Prevention (PP) clinic by 12 weeks • Further risk assessment based on history +/- examination as appropriate in secondary care with identification of women needing referral to tertiary services • All women to be offered transvaginal cervix scanning as a secondary screening test to more accurately quantify risk every 2–4 weeks between 16 and 24 weeks • Additional use of quantitative fetal fibronectin in asymptomatic women may be considered where centres have this expertise **Management** • Interventions should be offered to women as appropriate, based on either history or additional screening tests by clinicians able to discuss the relevant risks and benefits according to up to date evidence and relevant guidance, for example PCN guidance and NICE73 guidance. These interventions should include cervical cerclage, pessary and progesterone as appropriate.
Intermediate risk • Previous delivery by caesarean section at full dilatation • History of significant cervical excisional event i.e. LLETZ where >10mm depth removed, or >1 LLETZ procedure carried out or cone biopsy (knife or laser, typically carried out under general anaesthetic)	**Surveillance** • Refer to preterm birth prevention clinic by 12 weeks • Further risk assessment based on history +/- examination as appropriate in secondary care with discussion of option of additional screening tests, including: A single transvaginal cervix scan between 18–22 weeks as a minimum Additional use of quantitative fetal fibronectin in asymptomatic women can be considered where centres have this expertise **Management** • Interventions should be discussed with women as appropriate based on either history or additional screening tests by clinicians able to discuss the relevant risks and benefits according to up to date evidence and relevant guidance. These interventions should include cervical cerclage, pessary and progesterone as appropriate. • Women at intermediate risk should be reassessed at 24 weeks for consideration of transfer back to a low risk pathway

Women at risk of PTB can access further information, support, and guidance from sites such as those provided by charities and support groups such as Tommy's[29] (www.tommys.org) which can help them adopt healthier lifestyles and recognise signs of impending PTB.

Hospital-Based Care

There should be provision for designated preterm prevention specialists (PPS) in every maternity unit, together with appropriate support to provide an outpatient service within their antenatal clinic for women referred for screening. This should provide coordination for:

- tests to accurately quantify risk such as transvaginal ultrasound for cervical length and/or quantitative fibronectin (qfFN) for asymptomatic high risk women

  and

- timely interventions for preterm birth prevention (cerclage, progesterone, pessary)

Preterm prevention clinics in more experienced units (ideally at least one within each Local Maternity System, but if not present, identified and accessed elsewhere) should be contacted to assess women with complex obstetric and medical histories, and have the facilities to provide high vaginal (Shirodkar) and transabdominal cerclage where appropriate.

Cervical length (CL) screening should be performed as a minimum at both 16 and 22 weeks in women identified at high risk, and outside of this window and/or more frequently where clinically indicated. Those at intermediate risk should have at least one CL assessment between 18 and 22 weeks, with referral to the local PPS team if the CL is less than 25mm. If the CL is equal or greater to 25mm they may return to a low-risk pathway. In asymptomatic women there is usually no need to routinely carry out CL assessments beyond 26 weeks.

Cervicovaginal quantitative fetal fibronectin may be used in high risk asymptomatic women from 18 weeks gestation[30]. Preterm surveillance clinics have been shown to have significant benefit in appropriately triaging women at high risk of preterm delivery. Women who are seen in a preterm surveillance clinic and managed using sonographic cervical length and qfFN who are not admitted have been shown to have a low incidence of preterm birth and a lack of neonatal complications[31].

Prevention

Several interventions have been assessed for women at high risk of preterm birth: cervical cerclage, progesterone and pessaries. Cervical cerclage is an established procedure, progesterone is recommended in certain situations by NICE, and there are randomised trials suggesting benefit from the use of Arabin pessaries in at-risk women. Precisely in which women, and in what circumstances, each is most helpful is not clear. A pilot three-way comparison trial of these three modalities has been conducted (ReCAP)[21] and a randomised control trial of these three interventions is currently ongoing (SUPPORT)[21].

Cervical Cerclage

> **Women with a history of recurrent spontaneous preterm birth or late miscarriage (16 – 34 weeks) may be offered a history-indicated (planned, elective) cervical cerclage, but use of transvaginal scan surveillance of cervical length within the second trimester is recommended for most women who have had a single episode**

Cerclage, whereby a braided or monofilament suture is placed around the cervix, provides mechanical support to the cervix and enables preservation of the mucus plug within the cervical canal, discouraging ascent of colonising bacteria from the vagina and descent of the fetal membranes from the lower pole of the uterus.

A meta-analysis has indicated in women who have previously given birth between 16 and 34 weeks' gestation, that ultrasound surveillance is an effective alternative strategy to the elective placement of a prophylactic suture. Cervical length screening, together with cerclage for a short cervix (i.e. where the cervical length was less than 25mm), was associated with a similar incidence of preterm birth before 37 weeks (31% compared with 32%) and perinatal mortality compared with a history-indicated placement. In the transvaginal ultrasound cervical length screening group 42% developed a short cervical length and received cerclage[32].

History-indicated cerclages should be placed by the end of the first trimester where possible, however often it may be prudent to wait until after the dating scan and aneuploidy screening has been performed, so that significant fetal malformations can be excluded.

In women who have had a failed transvaginal suture, a transabdominal cerclage may be considered based on the findings of the MAVRIC trial. The circumstances of the placement and other clinical factors should be considered prior to placement, and appropriately- experienced clinicians should be involved in the decision-making and surgery. Placement during pregnancy should be undertaken prior to 14 weeks. Guidelines regarding laparoscopic placement have previously been published by NICE[33].

All Trusts should identify two or three clinicians to specialise in transvaginal cervical cerclage to enable sufficient capacity for 52 week cover.

Local and national audit/research findings (such as the CSTICH trial) will update the network standard for the use of cerclage and the best method to use.

Progesterone

The mechanism(s) by which progesterone reduces the risk of preterm birth remains uncertain. It probably increases the tenacity of the cervical mucus plug, may reduce myometrial contractility, and dampens the pro-inflammatory immune response of maternal/fetal tissues to colonising bacteria.

As an alternative to prophylactic cervical cerclage, women who have had a history of spontaneous preterm birth or mid-trimester loss between 16+0 and 34+0 weeks of pregnancy and in whom a transvaginal scan reveals a cervix of less than 25mm may be offered prophylactic progesterone[2] (vaginal or intramuscular).

Where a short cervix is found in women with no history of spontaneous preterm birth or midtrimester loss in whom a transvaginal scan has been carried out between 16+0 and 26+0 weeks of pregnancy and the cervix is less than 25mm, progesterone may also be offered[2].

Pessary

The use of pessaries, placed around the vaginal portion of the cervix, has been used for over fifty years. More recently the use of the Arabin silicon pessary has been evaluated, and several randomised controlled trials in at-risk populations have shown benefit in its use.

As an alternative to prophylactic cervical cerclage or progesterone, women who have had a history of spontaneous preterm birth or mid-trimester loss between 16+0 and 34+0 weeks of pregnancy and in whom a transvaginal scan reveals a cervix of less than 25mm may be offered placement of an Arabin pessary.

This obviates the need for regional anaesthesia (cerclage) or ongoing administration (progesterone), and is easy to remove at 36 weeks or if labour supervenes. As with the other preventive modalities ongoing studies will help define which women will most benefit from pessary use.

Preparation

When women present with symptoms of preterm labour, it is important to identify those at risk of imminent delivery so as to exclude those at low risk in order to appropriately implement interventions to reduce neonatal morbidity and mortality.

Predictive tests can may be used. In accordance with NICE guidance[2], where the woman is suspected to be in preterm labour and is over 30 weeks gestation, ultrasound measurement of cervical length may be used as a diagnostic test. Where the cervical length is less than 15mm she is deemed to be at high risk of preterm birth.

Fetal fibronectin can also be used as a diagnostic test in symptomatic women to determine the likelihood of delivery within 48 hours for women who are 30+0 weeks where ultrasound assessment is not available. The use of quantitative fibronectin estimation (other than at levels +/- 50 ng/ml) and other near-patient tests such as placental alpha macroglobulin-1 (PAMG-1, PartoSure) and insulin-like growth factor binding protein-1 (IGFBP-1, Actim Partus) is not currently recommended by NICE to diagnose preterm labour[34].

The approach to women at or under 30 weeks gestation remains controversial. NICE guidelines recommend treating all symptomatic women on the basis that this is both cost-effective, avoids the risk of missing women with false-negative tests, and may reduce the number of early neonatal transfers. In practice, this has not been easy to implement. Women and clinicians are concerned about the implications of a 'treat-all' approach as over half of all women clinically diagnosed do not actually deliver within the following week (or indeed preterm), and treatment is not without risk (hospital admission, tocolysis, steroids, magnesium sulphate).

Each of these tests have very high negative predictive values, indicating that delivery is unlikely to ensue within the following two weeks, and intervention is not required.

The predictive value of 'positive' tests is lower, however, but sufficient to implement intervention. The role of quantitative testing and its use in clinical care (in conjunction with the use of algorithms deployed in the QUIPP app[35]) remain encouraging and may assist individualised consultation with parents.

Further guidance regarding the role of near-patient tests may be available following the conclusion of current studies evaluating their use such as QUIDS, EQUIPP, and PETRA.

Following confirmation of at-risk status, the following interventions are recommended:

Corticosteroids

Corticosteroids should be considered from 23+0 to 35+6 weeks (and offered between 26+0 and 33+6) where a planned preterm delivery is occurring, PPROM has occurred, or women are who are in suspected, diagnosed or established preterm labour[2].

Repeat courses of steroids may be considered when the first dose has been given early in gestation and there is clinical concern regarding the likelihood of imminent delivery. Care should be individualised.

Steroids have significant benefit in reducing the incidence of perinatal death, intraventricular haemorrhage, necrotising enterocolitis and respiratory distress syndrome need for mechanical ventilation and sepsis in the first 48 hours of life when administered 7 days prior to delivery[36].

The importance of timing and appropriate administration has been highlighted by a recent Cochrane review where even single steroid doses were associated with a reduction in birthweight in those infants who delivered between 1 and 7 days (mean difference -105.92 grams, 95% CI -212.52 to 0.68g) compared with placebo or non-treatment, and in those who delivered more than 7 days after the first dose (mean difference -147.01grams, 95% CI -291.97 to -2.05g)[37].

Repeated doses of steroids may be considered where the first dose has been given early in gestation and delivery has not occurred, as it does result in a reduction in respiratory distress syndrome compared with placebo (RR 0.83, 95% CI 0.75 to 0.91). No difference was observed in fetal or neonatal mortality, a reduction in composite serious infant outcome was noted, but again the benefit was at the expense of a slight reduction in mean birthweight although there was no change in the proportion of small for gestational age infants[37].

Avoiding unnecessary administration is the most important target to aim for. The use of ‘prophylactic’ steroids, in women at risk of preterm birth but not imminent or symptomatic, is not evidence-based and should be discouraged.

Magnesium Sulphate

Magnesium sulphate should be offered between 24 and 29+6 weeks of pregnancy who are in established labour or are having a planned preterm birth within 24 hours[2]. Its use should be considered between 30 and 33+6 weeks[2]. A 4g intravenous bolus should be given over 15 minutes followed by an infusion of 1g per hour until the birth or for 24 hours (whichever is sooner)[2].

In randomised trials magnesium sulphate is a proven intervention to decrease the risk of cerebral palsy when administered to mothers at risk of imminent preterm birth at <34 weeks[38]. The PReCePT initiative is an AHSN-driven strategy from the West of England which has demonstrated clinical benefit in reducing cerebral palsy and is recommended in units seeking to adopt best practice in this regard[39].

Tocolysis

The use of tocolysis is not recommended for women at risk of imminent preterm birth to improve neonatal outcomes although the evidence is of low quality[8].

Therefore, acute tocolysis may be used when short term delay is desirable i.e. *in utero* transfer, and probably to ensure adequate antenatal exposure to corticosteroid/magnesium sulphate (ie no longer than 48hrs).

There is no evidence that maintenance tocolysis is beneficial.

When compared with no tocolytic treatment, oxytocin anatagonists and calcium channel blockers appear effective in delaying birth for more than 48 hours. In the absence of any contraindications nifedipine is the preferred agent for tocolysis[2].

This may provide a window for *in utero* transfer to an appropriate birth setting, however there is no direct evidence to support this.

In utero transfer

Transfer of a mother with her baby *in utero* ensures that she is in the right facility to receive the appropriate obstetric and neonatal care for her and her baby. *In utero* transfer is associated with reduced neonatal morbidity and mortality - there is a reduced incidence of IVH in very low birthweight babies when transfer is *in utero* along with lower neonatal mortality and allied costs compared to postnatal transport [40,41].

More widely, evidence indicates that lower neonatal mortality rates for babies born extremely premature (under 27 weeks) are found when birth takes place in a setting with a Level 3 NICU[42]. It is now a priority NHS England recommendation for LMS to take action to ensure that all women <27 weeks are delivered in centres with a neonatal intensive care unit (NICU), and that LMS and corresponding Operational Delivery Networks (ODN) have clear guidelines for antenatal transfer in the event of impending delivery <27 weeks[43].

Post Pregnancy Care

Follow up pathways are imperative for all women who have undergone a preterm birth. All women who have delivered prior to 34 weeks should be offered a postnatal consultation by the local obstetric team, and if repeated or more complex, by a more experienced preterm prevention specialist. This facilitates debriefing and provides information regarding the delivery. It should also lead to a plan of care prior to and during any future pregnancy.

Placental histology should be routine for all deliveries prior to 34 weeks gestation and these examinations should be undertaken by a specialist perinatal pathologist to assess for signs of infection/inflammation and ischaemia/infarction. In addition psychological support should be available where required.

Women with a history of extreme preterm birth (<28 weeks) despite the placement of a transvaginal cervical cerclage should be counselled about the option of placing an abdominal cervical cerclage either before the next pregnancy (laparoscopic or open) or during the next pregnancy (open), to reduce the risk of preterm birth.

Funding Considerations

The financial implications associated with preterm birth are significant. A recent economic analysis has concluded that delaying preterm birth by a single week across all gestational categories would see a fall in the total public sector cost due to preterm birth (excluding any intervention costs) from £2.946 billion to £1.952 billion, an annual saving of £994 million.[44]

Funding for specialist pathways can be identified within existing tariffs. Women deemed to be at risk of preterm birth and requiring specialist care (early preterm birth <34 weeks, uterine surgery, fetal loss) access the intermediate-rate tariff, £700 above the standard tariff.

In a typical setting of a unit overseeing 5000 deliveries each year, around 400 women are likely to be identified as being at-risk, and funds of between £25–30k thereby available to provide the necessary medical, midwifery, and ultrasound staffing costs to deliver local staffing and costs encountered with progesterone and pessary usage.

Day case or overnight surgical procedures for cerclage insertion can be covered under early pregnancy/gynaecology tariffs.

Service Evaluation

The following guidance is recommended for individual maternity providers.

Continuous learning

Maternity care providers must examine their outcomes in relation to the interventions where trends and themes arising their own incident reporting involving prematurity and/or optimisation of the preterm infant was felt to be a contributory factor.

Individual Trusts must examine their outcomes in relation to neighbouring Trusts within their own LMS to understand variation and inform potential improvements.

Maternity providers are encouraged to focus improvement in the following areas:

- appropriate risk stratification for primiparous women for risk factors for preterm labour by the correct gestation
- appropriate screening of women at high risk of preterm birth, including appropriate cervical length surveillance and use of cervical cerclage
- appropriate optimisation of women with suspected preterm labour, including effective use of antenatal corticosteroids and magnesium sulphate
- appropriate place of birth for women at risk of preterm delivery, both in relation to their own population and neighbouring Trusts

Process indicators

- the proportion of singleton livebirths (less than 34 weeks) receiving a full course of antenatal corticosteroids prior to birth, within seven days prior to birth
- the proportion of singleton livebirths (less than 30 weeks) receiving a full course of magnesium sulphate within 48 hours prior to birth
- the proportion of women who give birth in an appropriate care setting for gestation (in accordance with local ODN guidance)

Outcome indicators

The incidence of women with a singleton pregnancy giving birth (liveborn and stillborn) as a % of all singleton births:

- in the late second trimester (from 16+0 to 23+6 weeks)
- preterm (from 24+0 to 36+6 weeks)

Conclusions and Recommendations

- a national guideline should be introduced standardising care for women at high risk of preterm birth incorporating and broadening the advice contained within NICE guidance[2].
- the establishment of a preterm birth care pathway should facilitate early identification of risk factors and appropriate referral to a preterm prevention specialist or clinic.
- women at risk of preterm birth should be identified by midwives at the booking appointment and prompt referral to specialist services should occur when appropriate.
- other healthcare providers (GPs, A&E staff) need to be aware of signs and symptoms in women presenting with suspected preterm labour, and local referral pathways.
- all Trusts should be able to offer high quality care to women at high risk of preterm birth, with further provision within or adjacent to Local Maternity Systems for more experienced care which may result in net cost savings.
- post-pregnancy follow up should be available for all women who deliver between 16 and 34 weeks' gestation, with access to specialised placental histopathology, the opportunity to review the pregnancy and delivery and provide recommendations for future pregnancies.
- continuous improvement of services via annual peer group support meetings and incorporation of service user feedback is recommended.
- participation in ongoing peer-reviewed research endorsed and supported by the NIHR Clinical Research Network is recommended; women should be given the opportunity to consider and, as appropriate, take part in studies designed to optimise their care
- local and national involvement of service users and patient support groups are central to service planning within each Local Maternity System.

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