Humber, Coast and Vale
Local Maternity System

Guideline for the Management of women at risk of preterm birth or in preterm labour between 22 weeks and 36 weeks and 6 days pregnant

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1 Introduction

Preterm birth, defined as delivery at less than 37^{+0} week's gestation, is a common complication of pregnancy, affecting around 8% of births in England and Wales.[1] It is the most important single determinant of adverse infant outcome with regards to survival and quality of life. Babies born preterm have high rates of early, late, and post-neonatal mortality and morbidity. PTB is estimated to cost health services in England and Wales £3.4bn per year.

1.1 Purpose of the Guideline

- To provide strategies to identify women at risk of spontaneous preterm birth (sPTB), screening/preventive options for these women, and management of suspected preterm labour, preterm prelabour rupture of membranes (PPROM) and imminent preterm birth (PTB).
- To improve the diagnosis and management of women in preterm labour between 22 weeks and 36 weeks + 6 days of pregnancy.

1.2 Scope and Exclusions

This guideline applies to all pregnant women booked for maternity care within HCV LMS. It also includes women presenting with suspected preterm labour or who are unbooked or booked elsewhere who contact a maternity unit within HCV.

1.3 Definitions

- A **Senior Obstetrician** refers to a Registrar ST6/7 or Consultant in Obstetrics and Gynaecology (O&G).
- An **Obstetrician** refers to a speciality Registrar (ST3 and above) or Trust Grade O&G Doctor.
- A **Doctor** refers to a qualified Doctor working within Obstetrics and Gynaecology – these include Foundation Year Doctors and GP VTS Trainees

Instructions and/or information in orange box may vary slightly between Trusts within the HCV Local Maternity System

1.4 Roles and Responsibilities

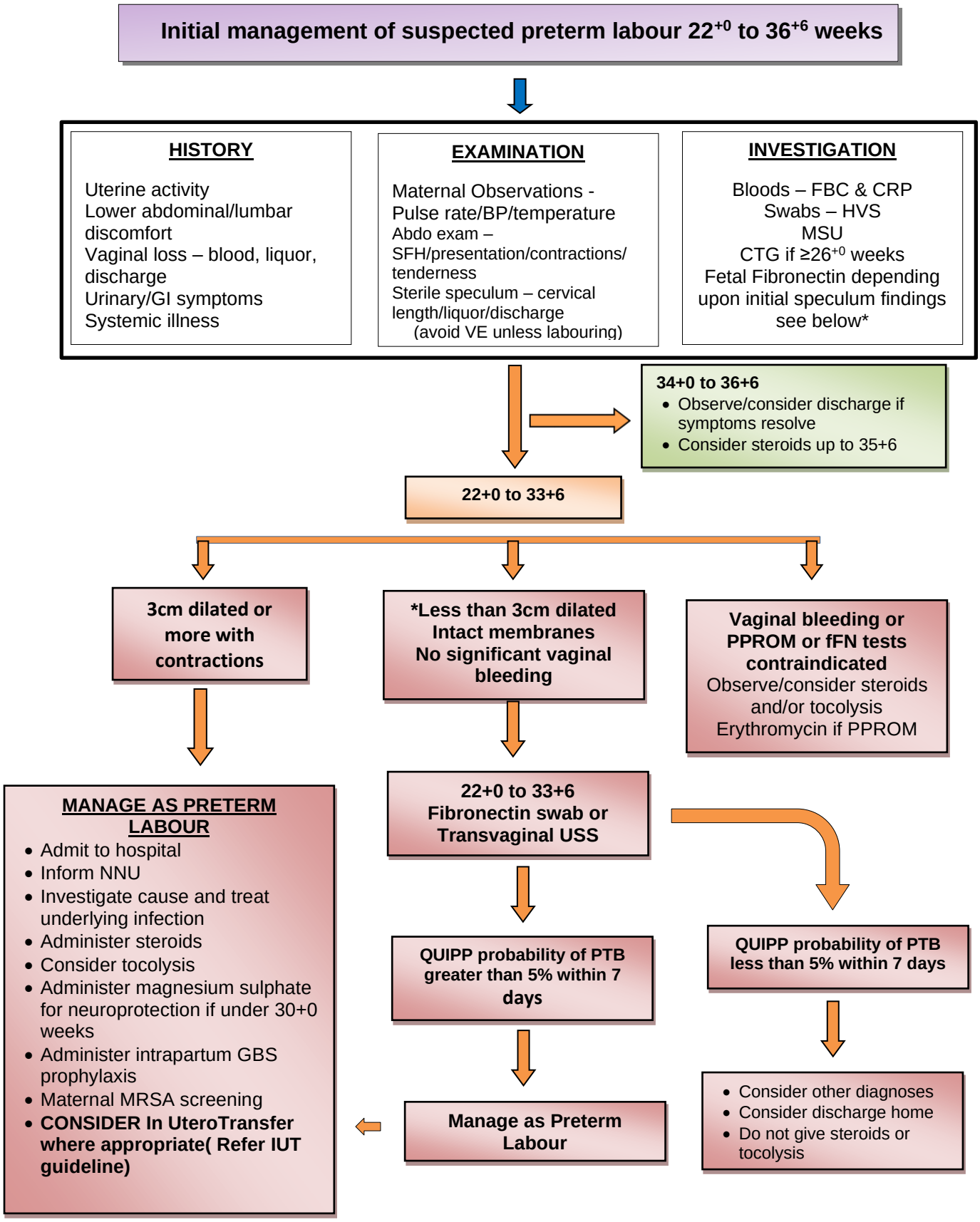
It is the responsibility of all HCV LMS healthcare professionals providing care to pregnant women to be aware of the content of this guideline.

1.5 Trust Sign-up

TRUST	SIGNATURE OF LOCAL GOVERNANCE LEAD	DATE
HUTH		
NLaG		
YSTHFT		

2 Summary Flow Charts

2.1 Initial management of suspected preterm labour 22^{+0} to 36^{+6} weeks



3 Guideline

3.1 Risk factors for preterm birth

The following conditions are associated with sPTB and therefore history and examination should be performed to identify or rule out any of these conditions.

3.1.1 Previous preterm birth

Previous preterm birth is the most significant risk factor.[2] This association is modified by three risk factors:

- the number of prior preterm births
- the gestational age at which the previous birth(s) occurred, and
- the order in which the prior preterm birth(s) occurred

For example, the risk with one previous preterm birth is 15-20%, after two preterm births is 35-40% and with one preterm and a subsequent term birth is 10-15%.[2]

3.1.2 Abnormal vaginal flora

The imbalance of microbial subpopulations seen in bacterial vaginosis (BV; predominance of anaerobes and deficiency of lactobacilli) is associated with an increased risk of preterm birth;[3] pathogenic organisms such as *Neisseria gonorrhoeae* and *Chlamydia trachomatis* may also trigger an inappropriate inflammatory response leading to labour. Early screening and treatment (before 20 weeks) can be considered.[4] Group B streptococcal colonisation is normally seen in up to 25% of inner-city populations and is not an indication for antepartum treatment unless accompanied by symptomatic discharge or bacteriuria.[5]

3.1.3 Urinary tract infection (UTI)

UTI including asymptomatic bacteriuria, cystitis, and pyelonephritis is associated with PTB.[6]

3.1.4 Systemic bacteraemia

Both acute (e.g. pyelonephritis, appendicitis, pneumonia and dental abscesses) and chronic bacteraemias are associated with preterm birth. This is presumed to be either due to direct blood-borne spread of infection to the uterine cavity or indirectly due to chemical triggers such as accompanying endotoxins or cytokines.[7,8]

3.1.5 Cervical compromise

Cervical compromise (to length or strength) may arise following large loop excision of the transformation zone –LLETZ (particularly >10mm depth of excision in X1 previous LLETZ,, more than one LLETZ procedure), Knife cone biopsy, multiple dilatations of the cervix, including hysteroscopic procedures where the cervix has been

dilated up to or beyond Hegar 10, or in conjunction with Mullerian variants (alterations in uterine size/shape such as unicornuate or bicornuate uteri). [9-11] Late first stage and second stage caesarean sections may also inadvertently damage the internal so increasing the risk of sPTB or midtrimester loss in subsequent pregnancies.[12]

3.1.6 Uterine capacity

Conditions that increase uterine distension or interfere with uterine capacity such as polyhydramnios, multiple pregnancy, or seen because of Mullerian variants are risk factors for PTB.[11]

3.1.7 Placentation

Antepartum haemorrhage and/or persisting extrachorionic haemorrhage due to abnormal placentation, with chronic and repeated bleeding, is also a recognised risk factor for PTB.[13]

3.2 Identification and care of women at risk of preterm birth

Prevention of preterm birth involves the screening of all women to identify and initiate intervention tailored to specific risk factors.

The following risk factors should be identified at the booking visit.

3.2.1 Smoking

This doubles the risk of preterm birth. All women should be asked about smoking, and cessation advice and/or referral should be provided. Women who have experienced a previous preterm birth who stopped smoking early in the pregnancy (<15 weeks gestation) modify their risk back to that of a non-smoker. If smoking cessation is delayed until the third trimester this modifiable benefit is lost. The importance of promoting smoking cessation is therefore one of the most important prevention strategies to implement.

3.2.2 Maternal age

Young women (<18 years) have an increased risk of preterm birth. Appropriate referral to the Teenage Pregnancy team should be offered to provide adequate support and advice throughout the pregnancy.

3.2.3 Domestic violence

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

3.2.4 Urinary tract infection (UTI):

A midstream urine sample (MSU) should be taken and sent for culture and sensitivity in all pregnant women at booking. Culture-positive samples should be repeated and if the same bacterial species is present this should be treated even in symptom-free women (asymptomatic bacteriuria). Following any positive culture and

treatment, a repeat MSU to confirm clearance is recommended. Those who have a recurrent episode require review in secondary care.

3.2.5 Vaginal infection:

Pathogens such as *Neisseria gonorrhoeae* and *Chlamydia trachomatis* are associated with PTB, and screening should be offered to at-risk women. In particular, the booking midwife should inform each pregnant woman under the age of 25 years about the high prevalence of chlamydial infection in their age group and offer screening.

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 in an asymptomatic woman is not an indication to treat until in labour unless also isolated from a midstream urine specimen.

3.2.6 Risk factors requiring referral to the preterm prevention clinic:

A further set of questions should be used to ascertain risk factors associated with preterm birth at this appointment. This will appropriately identify at-risk women who may benefit from preventive strategies and/or further assessment and more intensive monitoring within the hospital setting. They can then be offered higher risk care as outlined below:

Risk factor	Referral pathway
Previous use of cervical cerclage	Referral to be seen at the Preterm Prevention clinic **by 10 weeks**
History of trachelectomy (for cervical cancer)	Referral to be seen at the Preterm Prevention clinic **by 10 weeks**
Previous preterm birth, midtrimester loss, and/or PPROM between 16 and 30 weeks' gestation	Referral to be seen at the Preterm Prevention clinic **at 12 weeks-14weeks**
Previous preterm birth, and/or PPROM between 30 and 34 weeks' gestation	Referral to be seen at the Preterm Prevention clinic **at 16 weeks**
Known or suspected uterine variant (i.e. unicornuate, bicornuate uterus or uterine septum)	Referral to be seen at the Preterm Prevention clinic **at 16 weeks**
Intrauterine adhesions (Ashermann's syndrome)	Referral to be seen at the Preterm Prevention clinic **at 16 weeks**
History of significant cervical excisional event: • any LLETZ where greater than 10mm depth removed* • more than one LLETZ procedure • any knife cone biopsy	Referral to be seen at the Preterm Prevention clinic **at 16 weeks**
Previous delivery by caesarean section at full dilatation (or documented extensions to lower segment incision at operation)	Referral to be seen at the Preterm Prevention clinic **at 16 weeks**

** this can be found from the histopathology report documenting the size of the specimen excised (by convention the third measurement recorded); if uncertain refer to a general antenatal clinic for speculum and onward referral if cervix appears flush with the vaginal vault.*

3.3 Prevention of preterm birth in high risk women

Transvaginal sonography is used to assess cervical length and the appearance of the internal so between 16 and 26 weeks. In low-risk women, cervical length is a normally distributed variable with a mean of 35-40mm from 14 to 30 weeks. The lower 10th percentile is 25mm.[14] Cervical length is a good predictor of PTB for high risk women, with sensitivity of 60-80% and PPV of 70% when cervical length is less than 25mm between 16-18 weeks.[15,16] After 30 weeks of gestation, the cervix progressively shortens physiologically in preparation for labour and thus it is not usual to rely on cervical length measurement at this gestation and beyond for the prediction of spontaneous preterm birth in asymptomatic women.

After assessment within the preterm birth prevention clinic, based on history and/or additional screening, women may be offered treatment to prevent second trimester miscarriage and preterm birth.

Several interventions have been assessed for women at high risk of preterm birth: cervical cerclage, progesterone and Arabin pessaries. Cervical cerclage is an established procedure, progesterone is recommended in certain situations by NICE, and there are randomised trials suggesting benefit in the use of Arabin pessaries in at-risk women.

At present the evidence base cannot determine precisely in which women, and in what circumstances, each intervention will be most effective. Care must, therefore, always be individualised, taking into account the women's wishes, and following a discussion with a clinician able to discuss the potential risks and benefits of each intervention.

The following options will usually be discussed at the preterm prevention clinic:

3.3.1 Women with a history of spontaneous preterm birth or late miscarriage (16-34 weeks):

- transvaginal ultrasound surveillance of the cervix within the second trimester or a history-indicated (planned, prophylactic, elective) cervical cerclage
- history-indicated cerclage will usually be placed by the end of the first trimester where possible, typically after the dating scan and aneuploidy screening has been performed
- for women having ultrasound surveillance, intervention will be discussed when the closed length of cervix is <25mm: either cervical cerclage, Arabin pessary or prophylactic progesterone* (vaginal or intramuscular).

3.3.2 Women with a previous failed transvaginal suture:

- referral to Leeds Teaching Hospital Preterm Prevention Team should be considered leedsth-tr.preterm@nhs.net

- The circumstances of the failed suture and other clinical factors will be considered prior to placement, and a Shirodkar (high vaginal) or transabdominal cerclage may be considered.
- Transabdominal placement during pregnancy needs to be undertaken prior to 14 weeks

3.3.3 Women with no history of spontaneous preterm birth or midtrimester loss in whom a transvaginal cervix scan has been carried out between 16+0 and 26+0 weeks of pregnancy and the cervix is less than 25mm:

- care for these women should be individualised; counselling should include options of continued surveillance or intervention which should include cervical cerclage, pessary and progesterone* as appropriate.

Women with an intervention (cerclage, pessary or progesterone*) will usually remain under the care of the preterm prevention clinic until delivery.

Women undergoing transvaginal cervix scan screening usually continue this until 22-26 weeks; if no intervention is recommended, women may be transferred to routine pathways of care. Midwifery-led care is appropriate if no other additional risk factors are identified.

3.3.4 * Dose for progesterone:

400mg progesterone pessaries PV nocte from 16-36 weeks

or

250mg 17 alpha hydroxyprogestrone caproate IM weekly from 16-36 weeks
<u>If this is available locally</u>

3.4 Management of suspected preterm labour and/or preterm, prelabour rupture of the membranes (PPROM)

3.4.1 History

A full history should be taken with specific reference to:

- uterine activity
- lower abdominal or lumbar discomfort suggestive of cervical shortening
- vaginal loss – blood, liquor and/or discharge
- urinary/renal symptoms, gastrointestinal symptoms
- other symptoms of systemic illness

The management of women in suspected preterm labour at extremes of viability is difficult and should always be discussed with a senior obstetrician. The BAPM framework for management of preterm birth before 27 weeks is recommended for further guidance specific to this group.[17] Accurate information about the current pregnancy, including assessment of both fetal and maternal health should be used to refine gestation-based risk of absolute survival and survival without severe impairment. A range of factors are associated with increased or decreased risk: fetal factors, clinical conditions, therapeutic strategies and clinical settings, see appendix A.

3.4.2 Examination

General examination: A full medical examination including pulse, temperature, blood pressure, documented on a MOEWS chart.

Abdominal examination should record fundal height, fetal lie, presentation and engagement of the presenting part. If there is uncertainty regarding presentation an ultrasound scan should be performed. The presence of uterine activity/irritability should be noted.

A ***sterile speculum examination*** should be performed to assess the state of the cervix, recording cervical length and dilatation and the presence/absence of vaginal loss or rupture of membranes. A high vaginal swab should be obtained regardless of whether the membranes have ruptured. Digital examination is best avoided unless there is strong suspicion that the woman may be in labour.

The diagnosis of ruptured membranes relies on

- evidence from the woman's pad and/or
- visible loss of liquor between the labia on vulval inspection and/or
- the visualisation of liquor pooling in the posterior fornix or within the speculum

There are no reliable screening tests that have been fully evaluated (i.e. with subsequent assessment of management strategies) to assist the diagnosis of PPROM, and at present we are not recommending *routine* use of any in clinical practice. The diagnosis of PPROM can be uncertain therefore the woman should be advised to return if concerns of further PV loss despite an initially inconclusive speculum examination.

3.4.3 Investigations

TEST	**REASONING**
Blood Tests: *FBC and CRP*	Blood should be taken for a **full blood count** (FBC) and a **C-reactive protein** (CRP). In cases of PPROM these are repeated daily (whilst an inpatient) then weekly (through the antenatal day unit).
Low vaginal swab (LVS)	This should be taken and sent at the time of the first speculum examination.
Quantitative fetal fibronectin (fFN)	fFN for prediction of preterm birth helps because only 3-5% of women with symptoms will deliver within 7 days.[18-20] Correct assessment avoids unnecessary use of tocolytics and steroids, and aids decision making for *in utero* transfer. NICE guidance (NG25) suggests treating all women who clinically appear to be in preterm labour less than 29+6 weeks. However, newer studies[21] demonstrate it is reasonable to use fibronectin swabs and rely on the results of the tests in conjunction with the QUIPP app rather than initiating unnecessary treatment.
QUIPP app	This may help quantify the likelihood of diagnosis, plan care with parents, and avoid unnecessary intervention. A risk of greater than 5% of giving birth within 7 days may be used as a threshold for further care as per the EQUiPP and QUIDS studies.[21] The app can be downloaded on to smartphones or found at https://quipp.org
MSU	This should be sent, even with a negative urine dipstick.
Cardiotocography (CTG)	CTG should be performed to assess fetal wellbeing if the gestation is beyond 26+0 weeks. This should ideally be a computerised CTG with Dawes-Redman criteria analysis; however, if uterine activity is present this should be a non-computerised CTG. For gestations less than 26 weeks, intermittent auscultation is preferred.
Transabdominal (TA) ultrasound (USS)	TA USS should be performed to confirm presentation in MAC. A formal ultrasound scan should be arranged following diagnosis of PPROM to assess fetal growth and wellbeing.
Transvaginal (TV) ultrasound (USS)	Where available TV USS examination for funnelling or shortening of cervix may be considered. A closed cervical length of less than 15mm is suggestive of preterm labour.

3.5 Management of bulging membranes before 24 weeks

Second trimester miscarriage and very early preterm birth results in significant risks of morbidity and mortality to babies. Cervical weakness is one important cause of midtrimester birth. An established treatment for cervical insufficiency is vaginal cervical cerclage.

In a situation where the cervix has opened and the fetal membranes are exposed, an emergency cervical cerclage (ECC) may be considered. This procedure aims to halt further cervical dilatation and prolong pregnancy, preventing miscarriage or PTB, and thus potentially improving neonatal outcome. However, ECC has not been fully evaluated for clinical and cost effectiveness and carries risks to both the mother and baby. These risks include cervical trauma, severe infection/sepsis and iatrogenic rupture of membranes during the procedure leading to fetal loss.

There remains uncertainty about both the immediate benefit and long-term development of babies born following ECC. Specifically, *in utero* infection may result in worsening neurodevelopmental outcome.

If a woman at 16-24 weeks gestation presents with bulging membranes ECC may be considered.

Contraindications to a cerclage would be where pain, contractions, heavy bleeding, ruptured membranes, chorioamnionitis were present, or where fetal parts were no longer in the uterus.

On identification of a woman with bulging membranes at 16-24 weeks:

- Admit
- bloods – FBC and CRP
- HVS&MSU(even if recently Normal results)
- TED stockings
- Inform on call consultant / or Preterm Clinic Consultant
- If labour appears to be progressing, then there should be consideration of steroids and magnesium sulphate for gestations above 22 weeks
- There is no evidence of benefit for a head-down tilt, total bed rest or urinary catheter insertion and so these should be avoided.
- Senior input & Consideration of an ECC and careful counselling.

3.6 Management of women following Preterm Prelabour Rupture of Membranes PPROM

Many of these women will deliver within 48 hours. Treat as follows:

- Antenatal corticosteroids: betamethasone or dexamethasone 12mg for two doses 12 hours apart
- erythromycin: 250mg qds for ten days (for women who cannot tolerate erythromycin consider oral amoxicillin 250mg qds for a maximum of 10 days)[22]
- portable presentation scan

- admit to the antenatal ward: 6hrly MEOWS, departmental growth scan

Outpatient care may be considered after a period of 48 hours of inpatient observation. A senior obstetrician should be involved in the decision.

If a *malpresentation* is present which is likely to be associated with cord presentation and subsequent prolapse in early labour (for example in transverse lie), careful discussion with the woman is required; continued inpatient care may be preferred given the need for swift intervention if cord prolapse occurs. Decision-making may also be influenced by other factors such as gestational age, and consultant involvement in these situations is to be preferred.

Women may take their temperature at home once or twice a day. They should be advised of the symptoms associated with infection such as palpitations, temperature rise, or change in the nature of discharge.

Women should be reviewed in the Antenatal Day Unit for weekly FBC/CRP and CTG.

The PPROMT trial was a multicentre RCT performed to establish the optimum management of birth after PPROM. Women were randomised to immediate delivery or expectant management between 34 and 36+6 weeks. There was no difference in neonatal sepsis or neonatal morbidity or mortality between expectant management or immediate birth. However, neonates born to mothers in the immediate delivery group had increased rates of respiratory distress, mechanical ventilation and more time in intensive care. Women in the expectant group had a slightly increased risk of antepartum haemorrhage and fever requiring antibiotics but a lower risk of caesarean section.

Therefore, in the absence of overt signs of infection, fetal compromise, or known carriage of Group B Streptococcus, a policy of expectant management with appropriate surveillance of maternal and fetal wellbeing may be recommended to women who present with ruptured membranes close to term. It would be reasonable to consider delivery at 37 weeks.[23] However, if clinical picture changes from 34 weeks onwards, there should be a low threshold to expedite delivery.

3.7 Care following diagnosis of preterm labour

Treatment is aimed at:

- addressing the precipitating cause
- improving fetal outcome with the use of steroids and magnesium sulphate
- prevention of chorioamnionitis
- delaying delivery to enable corticosteroids to act or permit *in utero* transfer

3.7.1 Corticosteroids

Women between 23+6 and 33+6 weeks of gestation, in whom active management of the baby is anticipated, should be given betamethasone 12mg by intramuscular injection, two doses, 12 hours apart.[24] Steroids can be considered from 34+0 to 35+6

if there is a high likelihood of delivery in the next 48 hours. If betamethasone is unavailable, then dexamethasone is a suitable alternative (same dosage/administration).

The decision to administer corticosteroids at gestations between 22 and 23^{+6} weeks of gestation, in whom active management of the baby is anticipated, should be made by a senior obstetrician taking all clinical aspects into consideration and after consultation with the MDT (including neonates and parents).

If given to women with pre-existing or poorly controlled gestational diabetes, a sliding scale of insulin should be discussed with a consultant. Unnecessary steroids should be avoided, especially in diabetic women.

The period of maximal effectiveness of steroids is from 24 hours to 7 days after first injection for respiratory distress syndrome. However, the benefit for reduction of IVH and perinatal death is greatly reduced to within 3 days of administration.[24,25] A steroid-to-delivery interval of greater than seven days should be avoided if possible.

Do not routinely offer repeat courses of maternal corticosteroids, but take into account:

- the interval since the end of last course
- gestational age
- the likelihood of birth within 48 hours.[26]

Further courses or single rescue doses should be discussed with a consultant.

3.7.2 Antibiotics

Preterm or low birthweight babies are particularly vulnerable to Group B Streptococcal sepsis so women in ***confirmed*** preterm labour should be given intrapartum antibiotic prophylaxis as below. However, if a woman is showing clinical evidence of sepsis antibiotic treatment should be modified appropriately to be directed towards treating the source of her infection.

Procedure	Standard Prophylaxis	Penicillin allergy	If previous high vaginal swab shows GBS with resistance to benzylpenicillin & clindamycin
Preterm Labour	Insert Trust specific antibiotic regimen here*	Insert Trust specific antibiotic regimen here*	Insert Trust specific antibiotic regimen here*

Please *insert local Antibiotic Prophylaxis Guideline link here

3.7.3 Tocolysis

Tocolytics may be used to delay delivery and so enable the effect of steroids in at-risk women under 34 weeks' gestation.

In randomised trials there was no decrease in perinatal mortality or morbidity associated with tocolytic use and it should be remembered that prolongation of the pregnancy is not always beneficial for the baby.[27] Its use is mainly to allow time for steroids to be effective or to enable an *in utero* transfer.

Indications for tocolysis

Uterine contractions of at least 30 seconds duration and QUIPP probability of birth >5% within 7 days

OR

Cervical dilatation of 1-3cm and effacement of at least 50% and QUIPP probability of birth >5% within 7 days

Relative contraindications to tocolysis

- less than 24+0 or more than 34+0 weeks gestation
- antepartum haemorrhage
- chorioamnionitis
- known hypersensitivity to the active substance or any of the excipients (the carrier vehicle for the active drug)
- any other conditions in the mother or fetus in which continuation of the pregnancy would be hazardous

3.7.3.1 Nifedipine

Nifedipine should be used as the first-line tocolytic. The decision to start nifedipine should be taken by a senior obstetrician with the aim of delaying delivery long enough to administer steroids. There is good evidence that the calcium channel blocker nifedipine is effective in treating preterm labour, does not cause a significant fall in blood pressure in normotensive women, and has no significant fetal/neonatal side effects but may in fact have some positive benefits in terms of reduced neonatal complications (when compared with β-sympathomimetics).

Nifedipine is contraindicated in women with cardiac disease.

Nifedipine should be used with caution in women with diabetes or multiple pregnancy due to the risk of pulmonary oedema.

3.7.3.2 Nifedipine regime

Loading dose

Immediate release nifedipine orally, 10mg every 15 minutes until contractions stop (maximum dose 40mg)

Maintenance therapy

Modified release (MR) orally, 20mg 6 hourly for a maximum of 48 hours

Monitoring

- Blood pressure and pulse every 15mins for the first 2 hours.
- Continuous EFM if >26 weeks gestation for the first 2 hours which can be discontinued if contractions settle

If Nifedipine is contraindicated then Atosiban should be used as a first-line tocolytic

3.7.3.3 Atosiban Regime (for 24+0 to 34+0 weeks gestation)

The decision to start atosiban should be taken by a senior obstetrician with the aim of delaying delivery long enough to administer steroids.

STEP 1 Initial bolus dose (6.75milligrams) over one minute.	Draw up 0.9mL from 5mL ampoule of atosiban 7.5mg/mL concentrate for intravenous infusion and give over one minute
STEP 2 Immediately followed by a continuous high dose infusion (300micrograms/min) of Atosiban over three hours	Withdraw 18.1mL from a 100mL bag of 0.9% sodium chloride Add to the remaining sodium chloride (81.9mL), a total of 9.1mL of atosiban 7.5mg/mL (the 4.1mL from the first 5mL ampoule. and a second 5mL ampoule of the same concentrate) The resulting solution (0.75mg/mL) should be infused at 24mL/hour (300micrograms/min) over three hours This solution will last nearly four hours
STEP 3 Followed by a lower dose of atosiban infusing at 100micrograms/min for up to 45 hours or a total treatment length of 48 hours	Withdraw 10mL from a 100mL bag of 0.9% sodium chloride Add two 5mL ampoules of atosiban 7.5mg/mL concentrate for solution for infusion. The resulting solution (0.75mg/mL) should be infused at 8mL/hour (100micrograms/min)

Step	Regime	Injection/infusion rate	Atosiban dose	Length
1	0.9mL IV bolus	Over 1 minute	6.75mg	1 minute
2	3 hours IV loading infusion	24mL/hour	18mg/hour (300mcg/min)	3 hours
3	Subsequent IV infusions	8mL/hour	6mg/hour (100mcg/min)	Up to 45 hours

If the uterus remains quiescent, discontinue infusion.

Response to atosiban should be judged by uterine activity and not by repeated vaginal examinations.

Monitoring

- Maternal pulse and BP every 15 minutes for first hour then hourly
- Continuous electronic fetal monitoring (greater than 26 weeks) until contractions stop after which intermittent auscultation should be carried out every 4 hours and a CTG twice daily until the atosiban infusion is completed. Continuous electronic fetal monitoring (greater than 26 weeks) should be restarted if contractions recommence.

If labour progresses, discontinue atosiban

3.7.4 Preparations for delivery if preterm birth imminent

The neonatal team and neonatal unit need to be informed of the management proposed by the obstetric team regarding time, place and mode of delivery.

There needs to be joint parental counselling with the neonatal team regarding resuscitation in cases of compromise (growth restriction, infection, prolonged oligohydramnios) or extreme prematurity (below 27 weeks). The BAPM Framework provides further useful information.[17]

In cases of non-availability of a neonatal cot, a decision has to be made about *in utero* transfer. Transfer is not usually advisable if cervical dilatation is more than 3cm with uterine contractions and *ex utero* transfer may have to be considered in conjunction with the neonatal team. The use of the QUIPP app may be valuable in aiding the decision to transfer, as a probability less than 5% of delivering within 7 days would suggest that delivery is not imminent and therefore would avoid unnecessary transfer.

If delivery appears likely then administration of magnesium sulphate for neonatal neuroprotection should be offered in gestations at 30 weeks or less (and can be considered up to 33+6 weeks) following discussion with a senior obstetrician. In meta-analyses use of magnesium sulphate reduced the likelihood of cerebral palsy from 10

to 7% in babies born at less than 30 weeks.[28] It is likely that benefit is conferred even after the loading dose has been given so administration to mothers should be considered even if delivery appears imminent, and should also be given to mothers undergoing delivery as a planned event e.g. for fetal growth restriction.

3.7.4.1 Magnesium Sulphate Regime

Loading dose – intravenous (IV)

4g Magnesium sulphate - 20mLs of 20% Magnesium Sulphate IV over 20 minutes

Maintenance therapy – intravenous (IV)

1g/hr Magnesium Sulphate - 20% Magnesium Sulphate IV run at 5mls/hr via syringe pump to be continued whilst in active labour until delivery

Important Monitoring when giving IV Magnesium Sulphate

- Urine output should be >100ml in the previous 4 hrs. 97% of magnesium is excreted in the urine; presence of oliguria can lead to toxic levels. Consider an indwelling urinary catheter and fluid balance chart, alternatively measure and record each void accurately.
- Hourly respiratory rate – should be >12 breaths/min
- Four Hourly maternal deep tendon reflexes checks should be performed i.e. biceps

Side Effects / Concerns

- If a woman has or develops oliguria or other signs of renal failure monitor more frequently for magnesium toxicity or think about reducing/stopping the infusion.
- Discontinue the magnesium sulphate if there is:-
  - Motor Paralysis
  - Respiratory Depression
  - Absent tendon reflexes
  - Cardiac Arrhythmia

If side effects occur, get a senior Obstetric or Anaesthetic Medical review and consider 10ml 10% calcium gluconate IV

Optimal cord management and temperature regulation should be recommended to improve neonatal outcomes. Babies at less than 32 weeks gestation should be placed directly into a plastic bag immediately after birth.

3.7.5 Mode of delivery

Extreme preterm babies (less than 26 weeks) are usually delivered vaginally. Caesarean section carries significant maternal morbidity with risk of classical caesarean section and implications for future pregnancies.

In preterm labour after 26 weeks, a decision on mode of delivery will be governed by obstetric factors as per term delivery. There is no clear evidence to suggest benefit from caesarean section for preterm breech presentation; the risk of head entrapment (up to 10%) is a feature of all breech births under 37 weeks, regardless of route.[28]

The available evidence does not support the use of 'prophylactic' outlet forceps or elective episiotomy for vaginal delivery. Ventouse delivery and fetal scalp electrodes must be avoided below 34 weeks gestation and used with caution thereafter.

The use of epidural anaesthesia is not contraindicated and is frequently advocated. Postulated benefits include avoiding expulsive efforts before full dilatation or a precipitate delivery, a relaxed pelvic floor and perineum and the ability to proceed quickly to abdominal delivery. Other types of analgesia are also safe and choice should be guided by maternal wishes in conjunction with the usual clinical indicators such as progress of labour.

4 Training

Training should be undertaken and competency assessed in relation to the following:

- Symphysis-fundal height measurement
- Performing CTG
- Antenatal/Non-labour CTG interpretation.

5 Patient Involvement

The LMS Maternity Voice Partnership group will review and advise on the content of this guideline. The guideline will be available for public access on the LMS website.

6 Evidence Base

References

1. Beck, S., et al., The worldwide incidence of preterm birth: a systematic review of maternal mortality and morbidity. Bull World Health Organ. 88(1): p. 31-8
2. McManemy J, Cooke E, Amon E, Leet T. Recurrence risk for preterm delivery. Am J Obstet Gynecol. 2007 Jun; 196(6):576.e1-6
3. Meis, P.J. et al. The preterm prediction study: significance of vaginal infections. National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. Am J Obstet Gynecl. 1995, 173(4), pp.1231-5.
4. Lamont, R.F. et al. Treatment of abnormal vaginal flora in early pregnancy with clindamycin for the prevention of spontaneous preterm birth: a systematic review and metaanalysis. Am J Obstet Gynecol. 2011, 205(3), pp.177-90.
5. Easmon CS. The carrier state: group B streptococcus. *JAntimicrob Chemother* 1986;18 Suppl A:59–65.
6. Smaill, F. and Vazquez, J.C. Antibiotics for asymptomatic bacteriuria in pregnancy. Cochrane Database Syst Rev. 2007, (2), pCD000490.
7. Wren, B.G. Subclinical renal infection and prematurity. Med J Aust. 1969, 2(12), pp.596-600.
8. Offenbacher, S. et al. Progressive periodontal disease and risk of very preterm delivery. Obstet Gynecol. 2006, 107(1), pp.29-36.
9. Poon, L.C. et al. Large loop excision of transfornation zone and cervical length in the prediction of spontaneous preterm delivery. BJOG. 2012, 119(6), pp. 692-8.

10. Shah, P.S. et al. Induced termination of pregnancy and low birthweight and preterm birth: a systematic review and meta-analyses. BJOG. 2009, 116(11), pp.1425-42.
11. Hua, M. et al. Congenital uterine anomalies and adverse pregnancy outcomes. Am J Obstet Gynecol. 2011, 205(6), pp. 558 e1-5.
12. Glazewska-Hallin A, Story L, Suff N, Shennan A (2019) Late-stage Caesarean section causes recurrent early preterm birth: how to tackle this problem? Ultrasound Obstet Gynecol 54: 293–296
13. Arias, F. et al. Maternal placental vasculopathy and infection: two distinct subgroups among patients with preterm labour and preterm ruptured membranes. Am J Obstet Gynecol. 1993, 168(2), pp.585-91.
14. Iams, J.D. et al. The length of the cervix and in the risk of spontaneous premature delivery. National Institute of Child health and Human Development Maternal-Fetal Medicine Unit Network. N Eng J Med. 1996, 334(9), pp.567-72.
15. Owen, J. et al. Mid-trimester endovaginal sonography in women at high risk for spontaneous preterm birth. JAMA. 2001, 286(11), pp.1340-8.
16. Berghella, V. et al. Cervical ultrasonography compared with manual examination as a predictor of preterm delivery. Am J Obstet Gynecol. 1997, 177(4), pp.723-30.
17. https://www.bapm.org/resources/80-perinatal-management-of-extreme-preterm-birth-before-27-weeks-of-gestation-2019
18. Honest H, Bachmann LM, Gupta JK, Kleijnen J, Khan KS. Accuracy of cervicovaginal fetal fibronectin test in predicting risk of spontaneous preterm birth: systematic review. BMJ. 2002;325(7359):301.
19. Abbott DS, Radford SK, Seed PT, Tribe RM, Shennan AH. Evaluation of a quantitative fetal fibronectin test for spontaneous preterm birth in symptomatic women. Am J Obstet Gynecol. 2013;208(2):122-e1.
20. Peaceman AM, Andrews WW, Thorp JM, Cliver SP, Lukes A, Iams JD, et al. Fetal fibronectin as a predictor of preterm birth in patients with symptoms: A multicenter trial. Am J Obstet Gynecol. 1997;177(1):13–8.
21. https://www.bapm.org/pages/187-quipp-app
22. Kenyon S, Taylor D, Tarnow-Mordi W, for the ORACLE Collaborative Group. Broad-spectrum antibiotics for preterm, prelabour rupture of fetal membranes: the ORACLE 1 randomised trial. Lancet 2001; 357: 979-88.
23. Morris, J.M. et al. Immediate delivery compared with expectant management after preterm pre-labour rupture of the membranes close to term (PPROMT trial): a randomised controlled trial. Lancet 2016; 387: 444–452.
24. Royal College of Obstetricians and Gynaecologists Antenatal corticosteroids to prevent respiratory distress syndrome. RCOG Guideline No 7 October 2010
25. Roberts D, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev 2006;(3):CD004454. DOI:0.1002/14651858.CD004454.pub2.
26. McKinlay, C.J., et al., Repeat antenatal glucocorticoids for women at risk of preterm birth: a Cochrane Systematic Review. Am J Obstet Gynecol, 2012. 206(3):187-94
27. Gyetvai, K et al. Tocolytics for preterm labor: a systematic review. Obstet Gynecol. 1999 Nov;94(5 Pt 2):869-77.
28. Conde-Agudelo A, Romero R. Antenatal magnesium sulfate for the prevention of cerebral palsy in preterm infants less than 34 weeks' gestation: a systematic review and metaanalysis. Am J Obstet Gynecol. 2009;200(6):595–609.
29. Robertson PA, Foran CM, Croughan–Minihane MS, Kilpatrick SJ. Head entrapment and neonatal outcome by mode of delivery in breech deliveries from 28 to 36 weeks of gestation. Am J Obstet Gynecol 1996; 174:1742–7.

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8 Monitoring Compliance and Effectiveness (Quality & Safety)

Compliance with the guideline will be monitored through incident reporting and audit according to the table below.

Where monitoring identifies recommendations, an action plan will be developed and reported to the appropriate group. The identified group will monitor the implementation of the action plan.

Process indicators

- Percentage of singleton live births (less than 34+0 weeks) receiving a full course of antenatal corticosteroids, within seven days of birth.
- Percentage of singleton live births (less than 34+0 weeks) occurring more than seven days after completion of their first course of antenatal corticosteroids.
- Percentage of singleton live births (less than 30+0 weeks) receiving magnesium sulphate within 24 hours prior to birth.
- Percentage 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)

Audit results should be presented in line with each Trust's current governance procedures.

9 Document Control

Version Control

Version number	Revision date	Changes made by	Summary of changes	Approved by
1	September 2024	PTB sub group	1st version produced	LMS Clinical Leads

9.1 Review process

The guideline will be reviewed initially after 1 year then as a minimum every 3 years. When relevant national guidance is published, the guideline will be reviewed and updated accordingly.

9.2 Consultation process

Consultation will include all HCV provider organisations and representatives from midwifery, obstetric and ultrasonography professions.

9.3 Approval process

Approval will be in line with the LMS Guidelines Group approval process

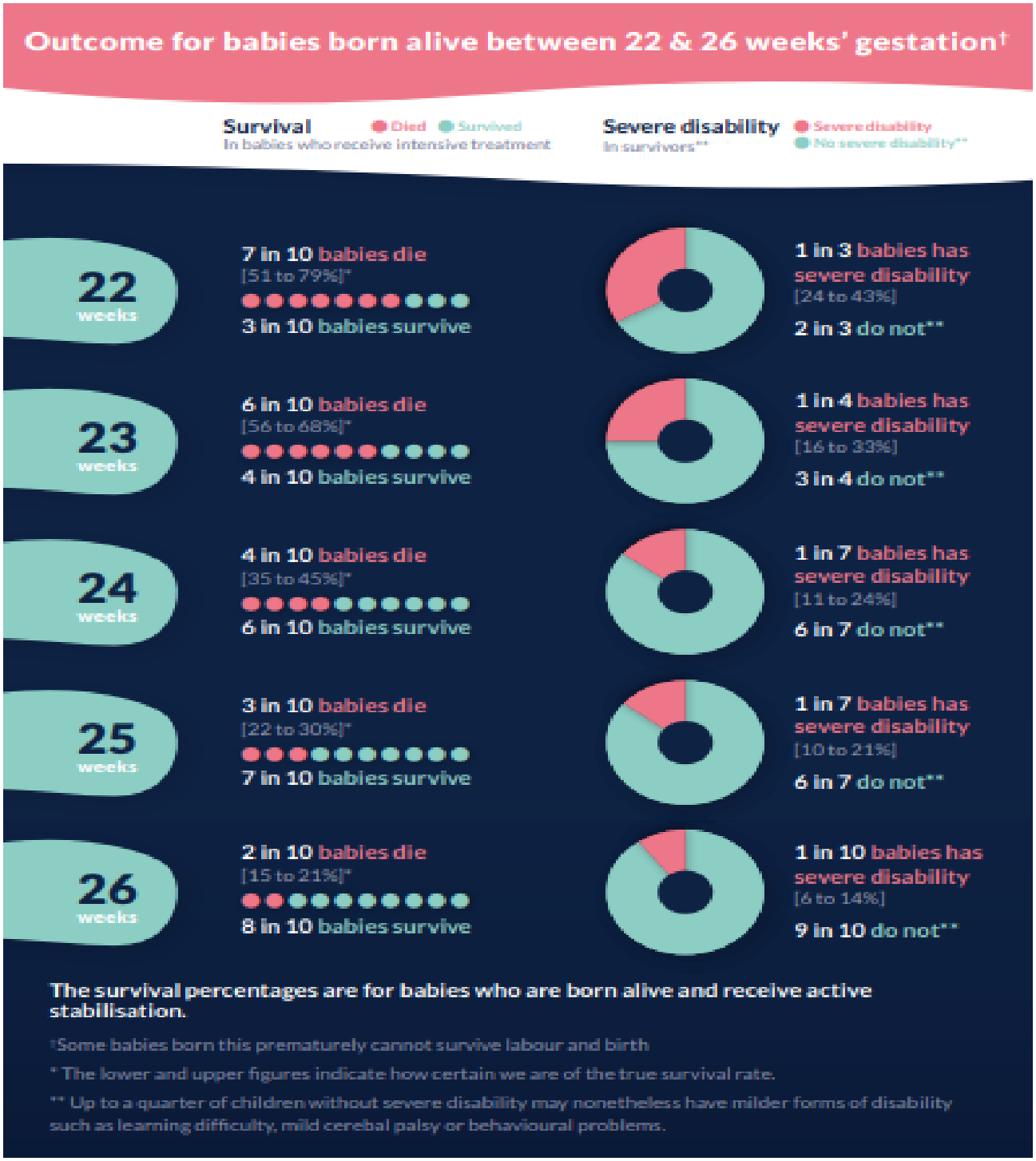
9.4 Publication and dissemination

Following approval, the guideline will be launched to all HCV Trusts by email.

Trusts will be responsible for removing and electronically archiving previous versions.

At Trust level, all relevant staff groups will be informed of the new publication.

10 Appendix A: British Association of Perinatal Medicine (BAPM) infographic for outcomes in extremely preterm babies



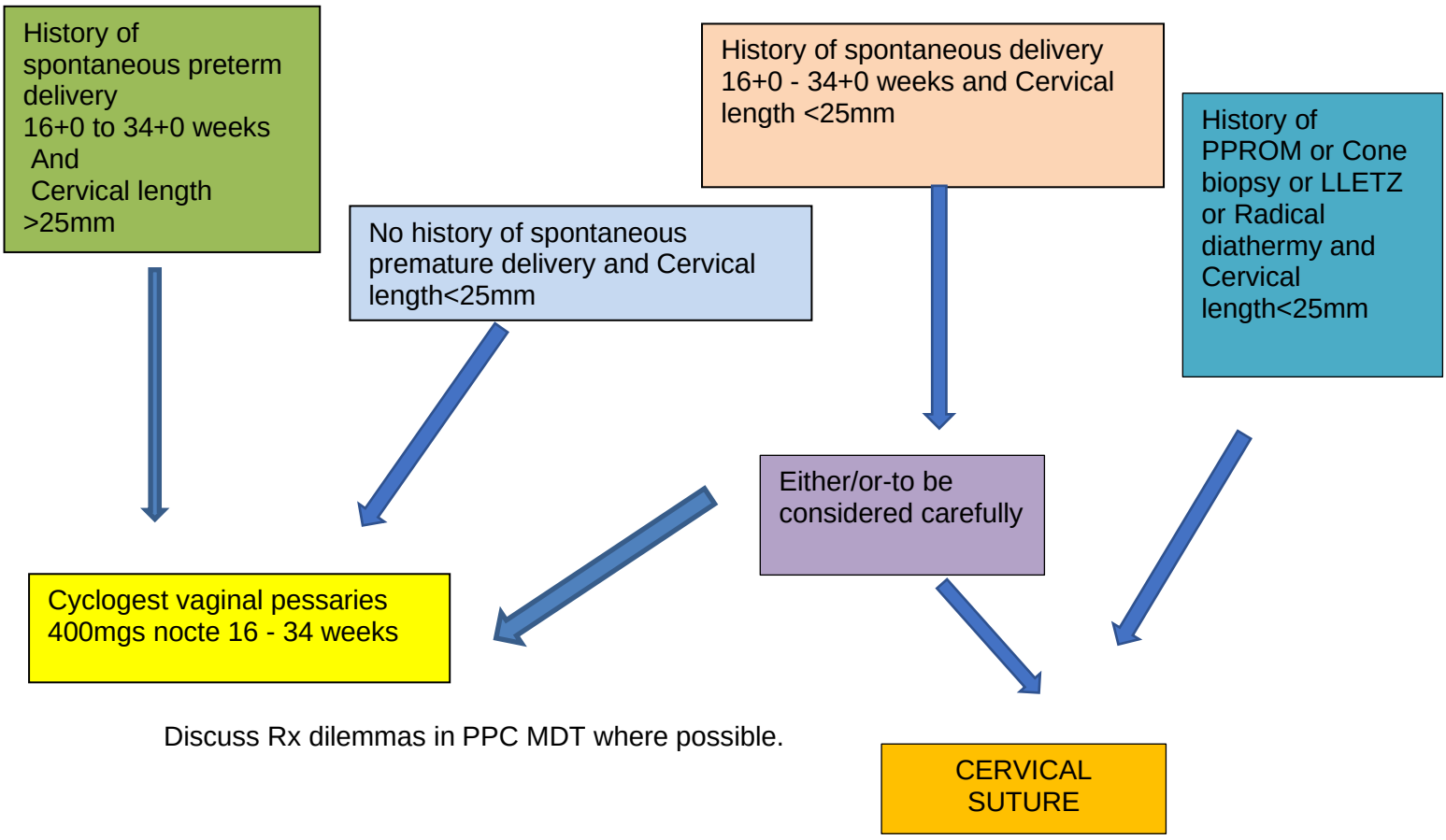
Taken from https://www.bapm.org/resources/80-perinatal-management-of-extreme-preterm-birth-before-27-weeks-of-gestation-2019

11 Appendix B: Flow chart for Surveillance in PTB Clinic

<table>
<tr><td></td><td colspan="6">High Risk</td><td colspan="3">Intermediate risk</td></tr>
<tr><td>History</td><td colspan="2">History of trachelectomy (for cervical cancer)
Previous Failed cervical cerclage</td><td>Previous use of cervical cerclage</td><td>Previous preterm birth, midtrimester loss, and/or PPROM between 16 and 30 weeks gestation</td><td>Known uterine variant (i.e. unicornuate, bicornuate uterus or uterine septum).</td><td>Intrauterine adhesions (Ashermann’s syndrome)</td><td>Previous preterm birth, midtrimester loss, and/or PPROM between 31 and 34 weeks gestation</td><td>Previous delivery by caesarean section at full dilatation</td><td>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 generalanaesthetic).</td></tr>
<tr><td>10week</td><td colspan="2">Review history; booking MSU, Referred to tertiary services(Leeds Teaching Hospital Preterm Prevention Team should be considered leedsth-tr.preterm@nhs.net)</td><td>Review history; booking MSU; Low vaginal swab(LVS) If high risk/request high cerclage. Consider referral to Leeds</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>12-14 weeks</td><td colspan="2" rowspan="7">Follow advice from tertiary unit if returns to care for local surveillance as previous use of cervical cerclage</td><td colspan="4">Review history and booking MSU, LVS; Trans vaginal Scan</td><td colspan="3">Review history and booking MSU; LVS</td></tr>
<tr><td>16weeks</td><td colspan="4">Trans vaginal Scan,MSU,LVS</td><td colspan="3">TVS in clinic Review MSU ,LVS,repeat tests,
Treatment plan pending scan Results</td></tr>
<tr><td>18weeks</td><td colspan="2">Trans vaginal Scan,MSU,LVS</td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>20weeks</td><td colspan="4">Urinalysis +/-MSU; LVS; Trans vaginal Scan</td><td colspan="3">Urinalysis +/-MSU; LVS; Trans vaginal Scan for cervical length in PPC /@ 20 werek USS with sonographers</td></tr>
<tr><td>22weeks</td><td colspan="2">Trans vaginal Scan,MSU,LVS</td><td></td><td></td><td colspan="3" rowspan="3">Back to midwife lead care if no other risk factors identified</td></tr>
<tr><td>24weeks</td><td colspan="4">Trans vaginal Scan,MSU,LVS</td></tr>
<tr><td>28-30 weeks</td><td colspan="4">Trans vaginal Scan ; Back to midwife lead care if no other risk factors identified</td></tr>
<tr><td>34 weeks</td><td colspan="2"></td><td colspan="4"></td><td colspan="3"></td></tr>
</table>

***Speculum assessment should be carried out at first consultation in PTBC and if cervical cerclage is being considered**

12 Appendix C: Recommended treatment options in_Premature Birth Prevention Clinic



Discuss Rx dilemmas in PPC MDT where possible.

Consider Treating Amniotic sludge noted on USS with Clindamycin 300mgs qds and Cephalexin 250mgs qds for 7 days

Resolution of acute cervical insufficiency after antibiotics in a case with amniotic fluid sludge; The journal of maternal-fetal & neonatal medicine- https://doi.org/10.1080/14767058.2021.1881477

Clinical significance of the presence of amniotic fluid 'sludge' in asymptomatic patients at high risk for spontaneous preterm delivery J. P. Kusanovic† et al,Ultrasound Obstet Gynecol 2007; 30: 706–714DOI: 10.1002/uog.4081

13 Appendix D: Pre-term prevention clinic -Booking Risk Assessment

Patient ID **Name** **DOB**

Date completed **Name of Referrer**

Risk factors	Tick as appropriate
Smoking (CO, Referral, cessation advice, GAP scans per protocol)	
Maternal age<18(referral)	
Domestic violence (EHASH referral)	
Suspected UTI (Send MSU)	

Risk factors requiring referral to the preterm prevention clinic:

A further set of questions should be used to ascertain risk factors associated with preterm birth at this appointment. This will appropriately identify at-risk women who may benefit from preventive strategies and/or further assessment and more intensive monitoring within the hospital setting. They can be then be offered high-risk care:

Please send this form via email to (HCV LMS units use local email) **for HUTH-**

hyp-tr.pretermclinichull@nhs.net

Risk factor	Referral pathway	Pls TICK
Previous use of cervical suture **(urgent referral)**	Referral to be seen at the Preterm Prevention clinic **by 10 weeks**	
History of trachelectomy-removal of cervix for cervical cancer **(urgent referral)**	Referral to be seen at the Preterm Prevention clinic **by 10 weeks**	
Previous preterm birth, midtrimester loss, and/or PPROM between 16 and 30 weeks' gestation (**urgent referral**)	Referral to be seen at the Preterm Prevention clinic **at 12 weeks-14weeks**	
Known or suspected uterine variant (i.e. unicornuate, bicornuate uterus or uterine septum)	Referral to be seen at the Preterm Prevention clinic **at 16 weeks**	
Intrauterine adhesions (Ashermann's syndrome)	Referral to be seen at the Preterm Prevention clinic **at 16 weeks**	
Previous preterm birth, and/or PPROM between 30 and 34 weeks' gestation	Referral to be seen at the Preterm Prevention clinic **at 16 weeks**	
History of significant cervical excisional event: • **ANY PREVIOUS LLETZ** where greater than 10mm depth removed* • **>1 LLETZ procedure** • any knife cone biopsy	Referral to be seen at the Preterm Prevention clinic **at 16 weeks**	
Previous delivery by caesarean section at full dilatation (or documented extensions to lower segment incision at operation)	Referral to be seen at the Preterm Prevention clinic **at 16 weeks**	

**** This can be found from the histopathology report***

Please note if any of the above criteria are not met, this patient is not eligible for an appointment in a PPC clinic. (Exclusion criteria for preterm prevention clinic (Iatrogenic preterm delivery e.g. Induction of labour/ emergency section due to IUGR, preeclampsia /Current multiple pregnancy /Previous loss of a twin),When patients don't meet criteria for PPC clinic triage for consultant/midwifery led as appropriate)

Please send MSU & LVS at time of this referral.