Management of Preterm Labour

Classification:	Guideline		
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Guideline to be followed by (target staff): All obstetric, midwifery and neonatal staff working in Women's Health who come into contact with women in threatened pre-term labour with intact membranes.			
To be read in conjunction with the following documents: None			
Are there any eCARE implications?			
CQC Fundamental standards: Regulation 9 – person centered care Regulation 10 – dignity and respect Regulation 11 – Need for consent Regulation 12 – Safe care and treatment Regulation 13 – Safeguarding service users from abuse and improper treatment Regulation 14 – Meeting nutritional and hydration needs Regulation 15 – Premises and equipment Regulation 16 – Receiving and acting on complaints Regulation 17 – Good governance Regulation 18 – Staffing Regulation 19 – Fit and proper			

Disclaimer

Since every patient's history is different, and even the most exhaustive sources of information cannot cover every possible eventuality, you should be aware that all information is provided in this document on the basis that the healthcare professionals responsible for patient care will retain full and sole responsibility for decisions relating to patient care; the document is intended to supplement, not substitute for, the expertise and judgment of physicians, pharmacists or other healthcare professionals and should not be taken as an indication of suitability of a particular treatment for a particular individual.

The ultimate responsibility for the use of the guideline, dosage of drugs and correct following of instructions as well as the interpretation of the published material **lies solely with you** as the medical practitioner.

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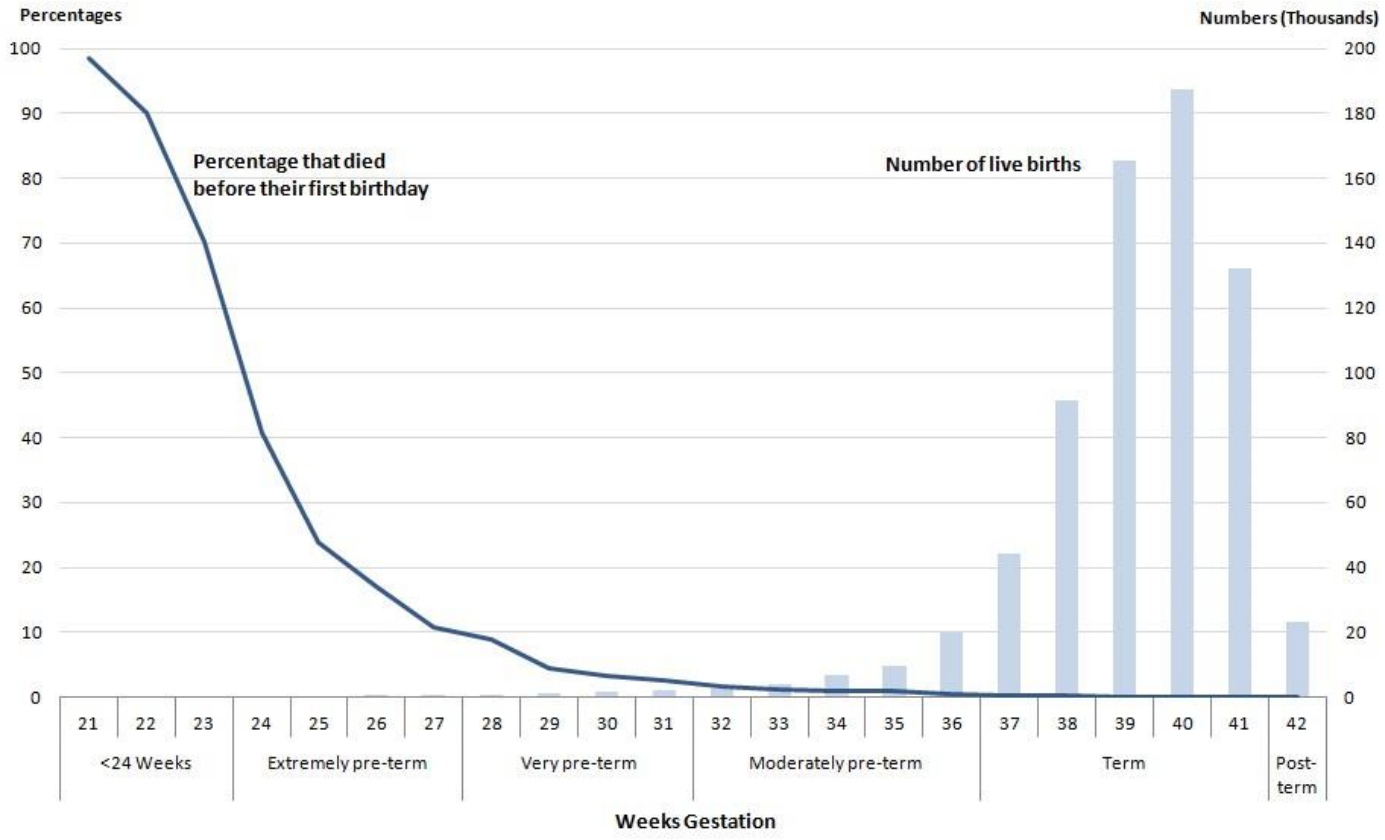
Guideline Statement

To enable staff to care for women with threatened pre-term labour.

Executive Summary

Preterm birth (PTB), defined as delivery at less than 37+0 week's gestation, is a common complication of pregnancy, comprising around 8% of births in England and Wales. 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. (Saving Babies Lives Version 2)

Percentage of infant deaths and number of live births by week gestation 2013
(Office for National Statistics, (2013). Pregnancy and ethnic factors influencing births and infant mortality. London: Office for National Statistics)



Prevention of preterm birth is now a national priority, and all maternity services should ensure that measures are in place to realise this ambition.

The Department of Health has set an ambition to reduce the national rate of pre-term births from 8% to 6% in order to achieve the national Maternity Safety Ambition (to halve the rates of stillbirths, neonatal and brain injuries that occur during or soon after birth by 2030 .

The British Association of Perinatal Medicine (BAPM) 2019 Framework has been developed by a multidisciplinary working group in the light of evidence of improving outcomes for babies born before 27 completed weeks of gestation and evolving national and international changes in the approach to their care.

The BAPM reports that whilst overall outcomes are improving, the prognosis remains guarded for extremely premature babies: 7 out of 10 babies who are born alive at 22 weeks will die whereas the outcome for babies born alive at 26 weeks is much better: 8 in 10 babies will survive with active stabilisation at birth.

The BAPM framework 2019 states that management of labour, birth and the immediate neonatal period should reflect the wishes and values of the mother and her partner, informed and supported by consultation and in partnership with obstetric and neonatal professionals.

Saving Babies Lives Care Bundle Version 2 has introduced an element that aims to reduce preterm birth from 8% to 6 % by focussing on prediction and prevention of preterm birth and ensuring better preparation when preterm birth is unavoidable. Prediction and prevention of preterm birth is addressed by the **preterm surveillance clinic SOP**. This guideline will focus on diagnosis and management and preparation when preterm delivery is likely (in women that require admission to hospital, administration of antenatal steroids, magnesium sulphate and tocolysis).

Pre-term labour and birth is thought to be a syndrome of multiple mechanisms, including infection, uteroplacental ischaemia or haemorrhage, uterine over distention and other immunological processes. **However, the majority of premature births occur without any obvious cause or known risk factors**.

Correctly diagnosing pre-term labour is difficult. Fewer than 50% of women presenting with suspected pre-term labour will deliver during the current episode. Administration of antenatal steroids to the mother reduces the rate of respiratory distress syndrome, intraventricular haemorrhage and death in the neonate. Repeated courses of antenatal steroids, however, may be associated with harm to the neonate and should be avoided.
Obstetric care therefore aims to correctly diagnose those women likely to deliver preterm, and who require admission to hospital and antenatal steroids.

We must time steroids appropriately - Steroids are beneficial to babies if delivery occurs between 1-7 days after administration (less respiratory distress syndrome and intraventricular haemorrhage). Even just one course, after 7 days, does harm (lower birth weight, head circumference and weight).

Foetal fibronectin is a glycoprotein and biochemical marker which can be detected in a woman's cervicovaginal secretions throughout pregnancy. In normal pregnancy fFN is present in the vagina up to the fusion of the chorionic membrane with the maternal decidua at approximately 20 – 22 weeks of gestation. After this time the level of fFN then falls to below 50ng/ml. After 22 weeks of gestation, a level above 30ng/ml is thought to result from inflammatory or mechanical insult to either the placenta or the foetal membranes indicating separation of the chorion and the deciduas, and imminent delivery.

Concentrations ≥50ng/ml during 23 – 35 weeks of gestation have been shown to indicate a greater risk of preterm delivery. Meta-analysis suggests that foetal fibronectin has a sensitivity of 77% and a specificity of 87% in predicting delivery within 7 days in symptomatic women.
When the fFN measurement is combined with a cervical length measurement and a woman's risk factors in **the QUiPP app** (https://quipp.org/) a woman's risk of preterm birth can be calculated which can be helpful when discussing interventions with women. QUIPP app can be used even in the absence of cervical length measurement in symptomatic women.

For women with suspected preterm labour under 30 weeks' gestation, NICE recommends a 'treat all' strategy, without reference to either fFN or CL tests. Using **the QUiPP App**, it has been found that 89% of hospital admissions may be safely avoided if a ***threshold of 5% risk of delivery within the 7 days*** is used to guide clinical practice, allowing outpatient management in the vast majority of cases.

Definitions

ADAU- Antenatal Day Assessment Unit
BAPM- British Association of Perinatal Medicine
CTG- Cardiotocograph
FFN- Fetal fibronectin
HVS- High vaginal swab
IV- Intravenous
IUT- In utero transfer
LVS- Low vaginal swab
LW- Labour Ward
MgSO4- Magnesium sulphate
NICE- National Institute of Clinical Excellence
NNU- Neonatal Unit
OAHSN-Oxford Academic Health Science Network
PReCePT- Preventing Cerebral Palsy in Preterm labour
PTB- Preterm Birth
SOP- Standard Operating Procedure
SROM- Spontaneous Rupture of Membranes

1.0 Roles and Responsibilities

Obstetricians: Assessment of all women presenting with preterm labour, requesting relevant Investigations and prescription of medication including steroids, Atosiban or Nifedipine and Magnesium Sulphate if eligible.

Midwives: Initial assessment, sending investigations, monitoring of foetal wellbeing and administering medication including Magnesium Sulphate as per protocol.

It is the responsibility of both midwives and obstetrician to liaise with neonatal team and make arrangements such as in utero transfer if needed.

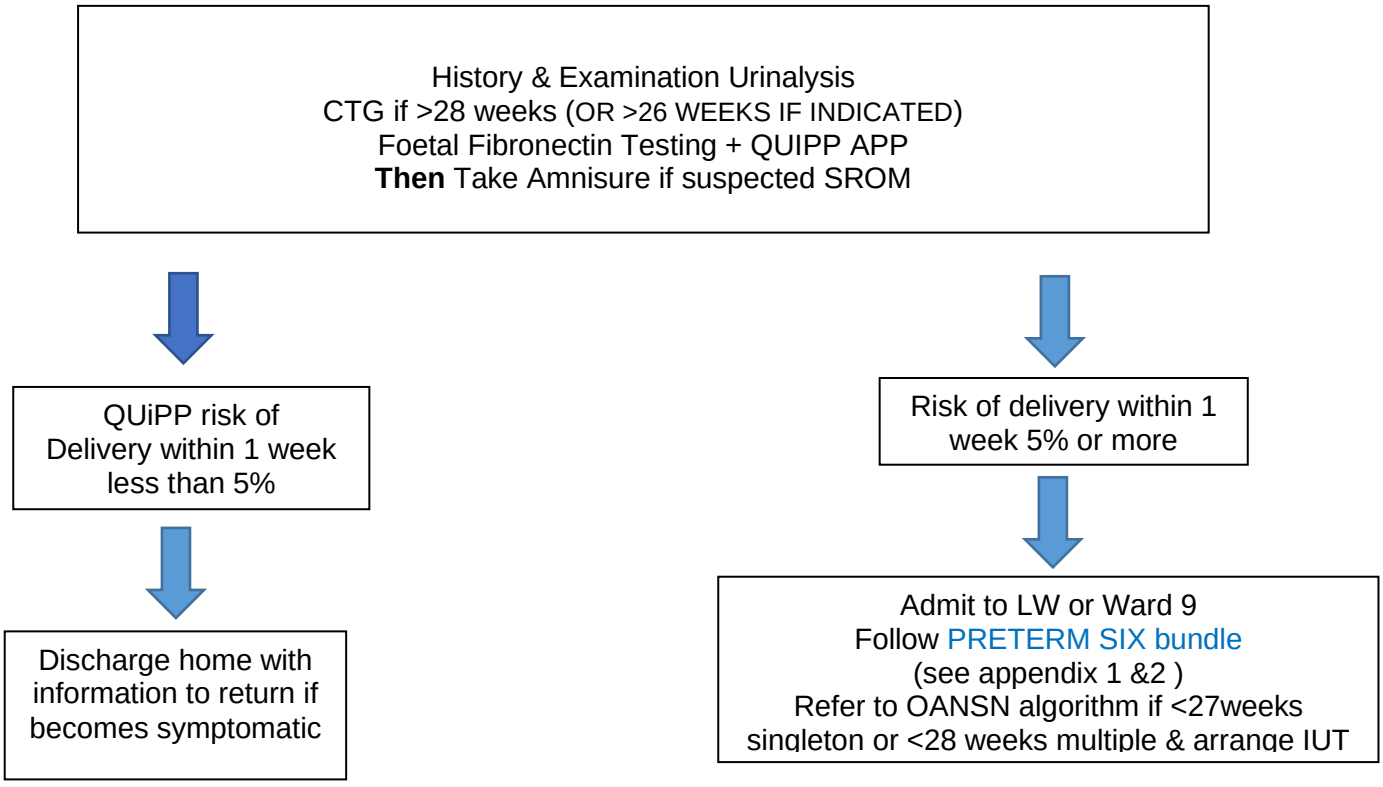
2.0 Implementation and dissemination of document

This Guideline has followed the Guideline review process and is accessible via the Trust Intranet.

3.0 Processes and procedures

3.1 Initial assessment

Flow Chart for the Management of Threatened and Confirmed Preterm Labour



Consider initial assesssment on ADAU if mild abdominal pain (as per RAG rating assessment) . In the presence of moderate to severe abdominal pain, women should be transferred to labour ward for initial assessment .

If following initial assessment, diagnosis of preterm labour is confirmed, arrange transfer to labour ward.

Following initial assessment and an established diagnosis of preterm labour, **PRETERM SIX BUNDLE** should be initiated (see appendix 1 & 2).

A full history should be taken, including details on:

- previous obstetric history
- previous medical history
- history of present pregnancy to date including gestational age from agreed EDD
- the start and timing of contractions
- any vaginal loss of blood or fluid
- urinary and bowel symptoms
- symptoms of systemic illness
- history of recent sexual intercourse

Obstetric examination should include:

- abdominal palpation to determine the lie and presentation of the fetus
- symphysial-fundal height
- abdominal ultrasound examination *by a trained operator* to assess foetal viability, presentation, estimate foetal weight, measure the liquor volume and placental site
- any evidence of uterine, suprapubic or renal angle tenderness • any palpable uterine contractions
- maternal pulse, BP, temperature and respiratory rate

Speculum examination should then be performed:

- Pass a sterile speculum
- look for a pool of liquor, significant vaginal blood and/or cervical dilatation
- if appropriate a fibronectin swab should then be taken (see below) .This should be taken **prior** to taking other vaginal swabs.
- Take swabs from the vaginal fornix (HVS), low vagina (LVS) and endocervical canal (Chlamydia) for infection screen .
- If unable to visualise the cervix or advanced dilatation is suspected, a gentle sterile digital examination can be performed to assess cervical effacement and dilation OR Transvaginal ultrasound for cervical length if skilled operator available
- Digital examination should be avoided if premature rupture of membranes is suspected
- Digital examination should be avoided if cervix is clearly visible

Investigations:

- CTG if gestation >= 28 weeks or at earlier gestation (from 26 weeks) if clinically indicated. Urine dipstick and MSU
- Blood for FBC, CRP, G&S .
- Follow sepsis pathway if any clinical triggers of infection.

3.2 Foetal Fibronectin (fFN) Analysis

The Foetal Fibronectin Test is an *in vitro* diagnostic test that uses single-use, disposable cassettes called Rapid fFN 10Q Cassettes. Analysis to measure the fFN concentration in a swab taken of the cervicovaginal secretions is done using the automated *PeriLynx System.* The machine gives a result within 10 minutes of the swab being tested. The test will give a quantitative result.

Women transferred to Milton Keynes Hospital via *in utero* transfer should have an fFN swab performed if they fulfil the criteria for testing and provided, they have not had an fFN swab performed at their referral hospital. NOTE: If the woman has had a digital vaginal examination in the last 24 hours at the referring hospital, the fFN test may show a false positive result and be invalid. Testing for fFN should be delayed until 24 hours after the digital vaginal examination.

Criteria for testing:

- Women with signs and symptoms of pre-term labour between 22 & 34 weeks of gestation
- **WITH Intact membranes** AND
- Minimal Cervical dilatation (<=3cm)

Specimens should be collected prior to:

- Digital cervical exam
- Collection of culture specimens
- Vaginal probe ultrasound exams

Contraindications:

The test is not valid in the presence of:

- Ruptured membranes

- Placenta praevia
- Placental abruption
- Moderate or gross vaginal bleeding*
- Within 24 hours of sexual intercourse*
- Within 24 hours of manipulation of the cervix e.g. digital examination of the vagina or vaginal probe ultrasound exams

- Cervical cerclage (especially within 4 weeks of cerclage placement)

**If the test is <10ng/ml under either of these two testing conditions it can be interpreted as a valid result*

Avoid contaminating the cervicovaginal secretions with lubricants, soap, disinfectants, creams or jelly.

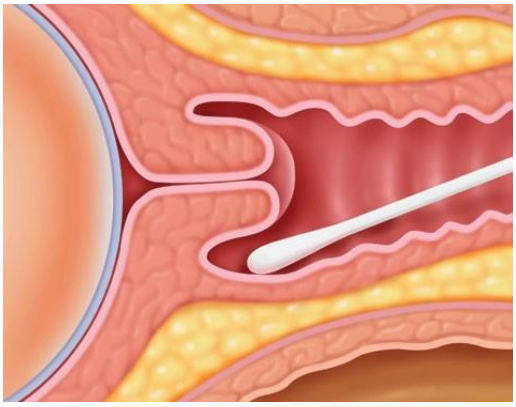
Use water to lubricate the speculum

Taking a fFN swab

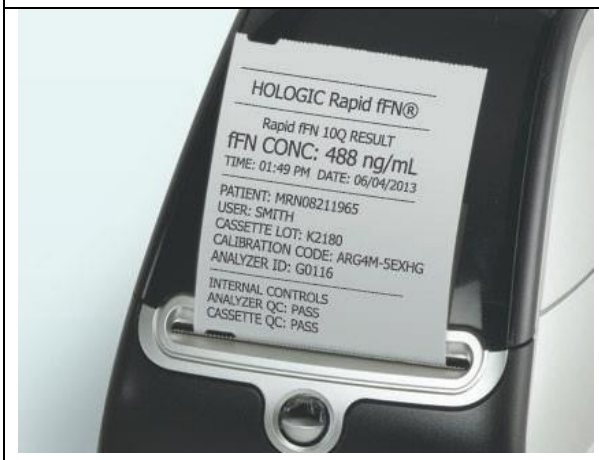
The sample should be collected **before** digital examination is carried out. You will need:

- Sterile speculum
- Fibronectin swab
- Buffer solution
- PeriLynx System with Rapid fFN 10Q Cassette

Only use water to lubricate the sterile speculum (no cream or lubrication jelly)

	STEP 1 During speculum examination, lightly rotate the supplied swab across the posterior fornix of the vagina for 10 seconds to absorb cervicovaginal secretions

	STEP 2 Remove swab and immerse tip in buffer. Gently mix the swab in the buffer solution and remove if the test is to be performed immediately ***Note:*** *Refer to transportation and storage notes overleaf if test is to be performed at a later time.*
	STEP 3 Enter User ID, Press 'NEXT' Enter Rapid fFN 10Q Cassette lot number and press 'NEXT' Enter Patient ID and press 'NEXT' Insert the Rapid fFN 10Q Cassette and press 'NEXT'

	STEP 4 Pipette **0.2mL (200µl)** from the sample collected in the buffer solution into the well of a Rapid fFN 10Q Cassette and press 'START TEST'
	STEP 5 Internal Quality Control results can be found on the print out • The fFN concentration will be displayed and printed in 10 minutes • A permanent record is now available for patient notes ***Note:*** *Press Print to obtain a second copy of the printout.*

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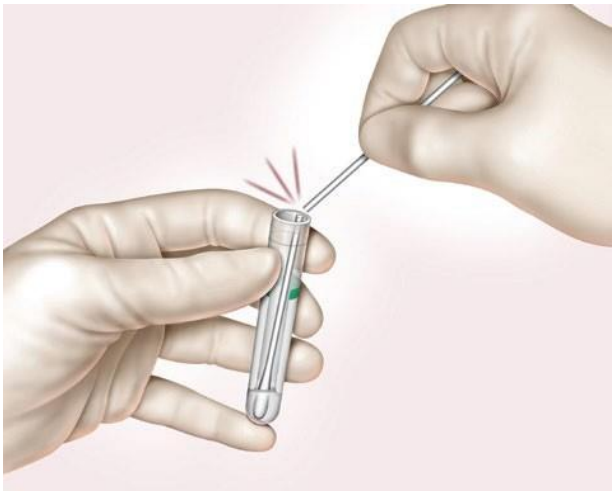
Transportation of Collected Sample (In instances where a patient sample is not processed immediately)

- Transport samples at 2-25°C, or frozen
- Samples are stable for up to 8 hours at room temperature
- Samples not tested within 8 hours of collection must be stored refrigerated at 2-8°C and tested within 3 days of collection, or frozen and tested within 3 months to avoid degradation of the analyte.

	Break the shaft (at the score) even with the top of the tube
	Align the shaft with the hole inside the tube cap and push down tightly over the shaft, sealing the tube for transfer ***Warning:*** *The shaft must be aligned to avoid leakage*
	Send fFN sample to a Rapid fFN PeriLynx Analyser near you

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Negative fFN result (concentration < 50ng/ml)

If fFN testing is negative (concentration 50 ng/ml or less) **or QUIPP APP risk is less than 5%,** explain to the woman that it is unlikely that she is in preterm labour and think about alternative diagnoses. Discuss with her the benefits and risks of going home compared with continued monitoring and treatment in hospital. Advise her that if she does decide to go home, she should return if symptoms suggestive of preterm labour persist or recur. A negative foetal fibronectin (fFN) is associated with a 99.5%negative predictive value for preterm birth within 7 days and 99.2% in the next 14 days.

Positive fFN result (concentration >=50ng/ml)

If fFN testing is positive (concentration more than 50 ng/ml), use the QUIPP app to calculate the % risk for preterm birth. **If the QUIPP APP risk is above 5% risk of delivery within 1 week, admit and follow the PRETERM SIX BUNDLE. If fFN positive but QUiPP <5% risk of delivery within 1 week** consider differential diagnosis and home.

Explain that there is an increased risk of preterm birth within 7 days. For Guidance on use of the QUIPP APP, see appendix 4

- offer antenatal corticosteroids according to protocol below
- offer tocolysis according to protocol below
- Inform NNU and neonatal sister in charge for all gestations 22 weeks or more. The neonatal registrar or consultant should counsel the woman and partner appropriately.
- If there is no NNU cot available, then in-utero-transfer should be considered. This should be discussed with the consultant on call.

3.3 Implementation

Training: Healthcare professionals performing the Fibronectin test and analysis should be trained in its use. Appropriate training will be performed at induction of junior doctors and midwives, and at regular intervals on the Labour Ward for midwifery and consultant staff. Only those individuals who have received adequate training will be able to perform the Fibronectin test and analysis.

Audit of use: The machine log book will be examined on a weekly basis for 3 months and then monthly thereafter to ensure tests are being performed on the appropriate women, being logged correctly and the test results are clearly documented.

An audit of outcomes of women tested by Fibronectin test will be performed 3 and 6 months after implementation and then yearly thereafter. The results of the audit will be communicated to all those involved in antenatal patient care.

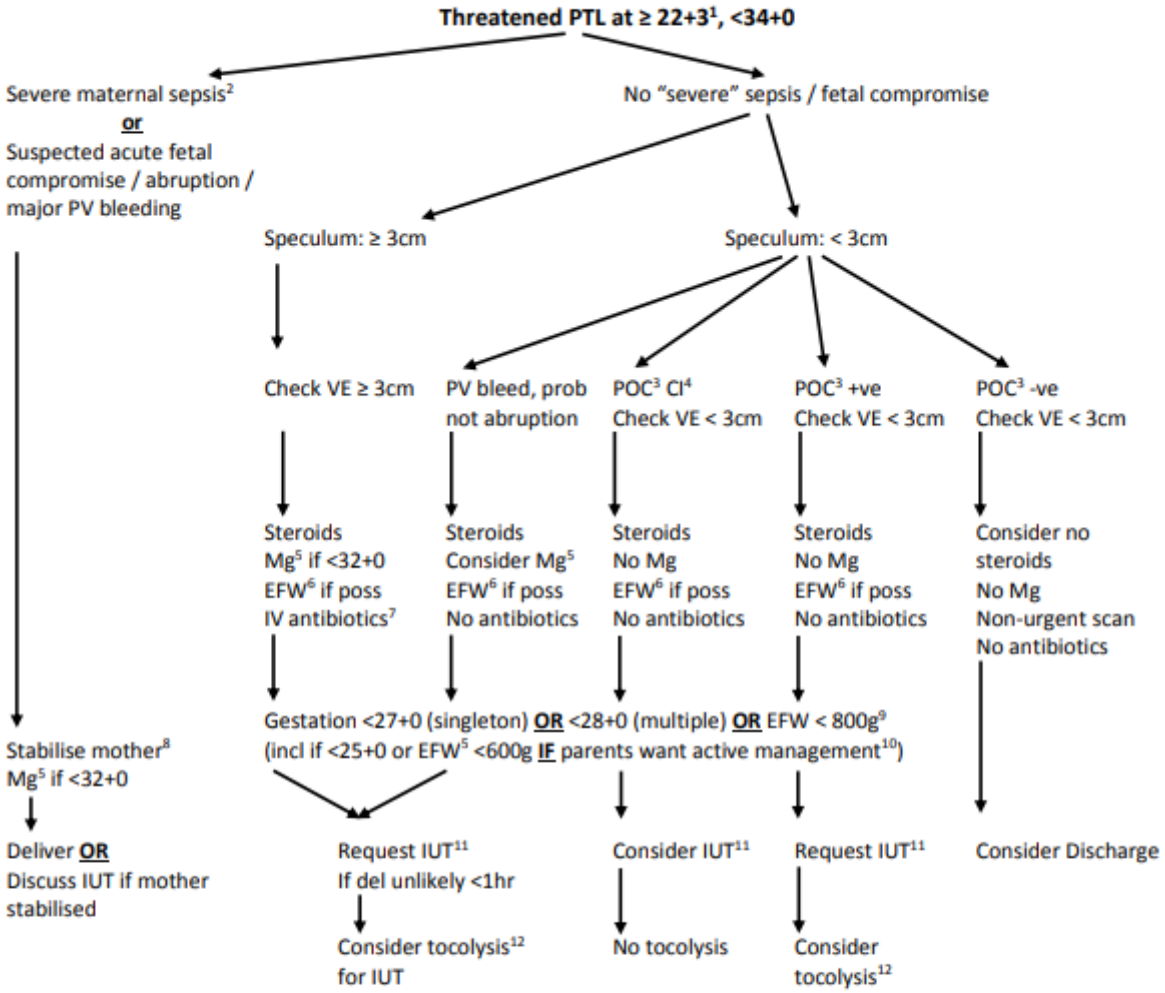
An audit of the machine is regularly performed by the point of care coordinator

3.4 Management of pregnant women presenting with Threatened Extreme Preterm Labour- Please refer to Oxford AHSN algorithm below

Oxford Academic Health Science Network MATERNITY

Oxford AHSN Regional Maternity Guideline

Algorithm for Management of Threatened Extreme Preterm Labour and IUT (updated Jan2020)



Footnotes:

Dates according to CRL excl in IVF pregnancies. Note this gestation has been modified following new BAPM Guidelines. Active resuscitation for neonates <23+0 will be offered if there are good prognostic (eg >/+22+3, had steroids, delivery in Level 3). If there is uncertainty about the circumstances or the dates, call obstetric consultant at OUH.

Women potentially suitable for emergency cerclage (i.e. >16 weeks, no sepsis and with painless cervical opening) should be discussed with Level 3 FMU consultant.

1. Sepsis meeting criteria for local severe sepsis bundle
2. POC: Point of care test (e.g. fibronectin or equivalent) to assess likelihood of preterm delivery more accurately than history and examination
3. CI: contraindicated/ not recommended. Consider fFN usage if postcoital as false negatives unlikely
4. Mg: Magnesium bolus 4g (16mmol) Magnesium Sulphate as 20mls of 20% magnesium sulphate IV over 5 – 10 minutes if <32+0 weeks. Note PReCePT suggests 30 but clinical benefit up to 32 weeks.
5. EFW: estimated fetal weight +/-15% if possible
6. IV antibiotics. Follow unit antibiotic guideline; avoid co-amoxiclav. Prophylactic antibiotics only to be used in labour.
7. Stabilisation of acutely unwell mother beyond scope of this document
8. Criteria for delivery in Level 3 Neonatal Unit. If criteria not met, manage as per local preterm labour guideline
9. If time, offer discussion with paediatrician. Document any discussion regarding IUT with parents. Consider providing Thames Valley Neonatal Network patient information leaflets if available.
10. For IUT: try OUH first. 8-5pm call Delivery Suite (01865 221988/7), and specifically request to speak to the consultant obstetrician on Delivery Suite. From 5pm to 8am, hospital switchboard (01865 741166), with the request to speak to the obstetric consultant on call. DO NOT call neonatal unit or delivery ward manager first.
11. Tocolysis. Follow unit tocolysis guideline. Do not use nifedipine if magnesium has been given or is to be given

IUT Threatened Extreme Preterm Labour V3 updated Jan 2020 Author: Mr Lawrence Impey, Clinical Lead Oxford AHSN Maternity

If there is evidence of ruptured membranes, follow the **Preterm Premature Rupture of Membranes Guideline** available on intranet**.**

If there is no NNU cot available, then in-utero-transfer should be considered.

3.5 Antenatal Corticosteroids

Offer steroids to all women with preterm labour between 22+3 weeks to 34 weeks. NICE guidance on ***Preterm labour & birth*** advises to also **consider** maternal corticosteroids for women between 34^{+0} and 35^{+6} weeks of pregnancy who are in suspected, diagnosed or established preterm labour, are having a planned preterm birth or have P-PROM.

Neonatal stabilisation may be considered for babies born from 22+0 weeks of gestation following assessment of risk and multiprofessional discussion with parents. It is not appropriate to attempt to resuscitate babies born before 22+0 weeks of gestation. Therefore, fo**r pregnancies at 22 weeks and above, neonatal teams at MKUH should be informed**.

The effect of treatment is optimal if the baby is delivered more than 24 hours after administration of corticosteroids and less than 7 days after the start of treatment.

Corticosteroids:

Contraindications:

- Active tuberculosis

Caution:

- Systemic maternal sepsis. In the presence of definite evidence of chorioamnionitis, the administration of betamethasone should first be discussed with the on-call consultant and its relative merits and potential adverse effects discussed.
- In Gestational diabetes or type1/2 diabetes steroids can exacerbate hyperglycaemia and the course of steroids may need to be given in conjunction with extra doses of insulin (see MKH guidelines on gestational diabetes).

The most extensively studied regimens of corticosteroid treatment for the prevention of RDS are two doses of betamethasone 12 mg given intramuscularly (IM) 24 hours apart or four doses of dexamethasone 6 mg given intramuscularly 12 hours apart.

However, as long as 24 mg of either drug is given within a 24–48-hour period, any dosing regimen can be used.

At Milton Keynes university hospital, steroids regime should be prescribed as follows:

Betamethasone 12 mg IM as 2 doses 12 to 24 hours apart

(Refer to the following trust guideline for further information: Antenatal corticosteroids to reduce neonatal morbidity and mortality)

Repeat courses of corticosteroids

If repeat courses of corticosteroids are being considered, consultant opinion must be sought. There is some evidence to support a significant benefit with repeat corticosteroids if the first course is given very early in pregnancy (less than 26^{+0}weeks of gestation). There is, however, mounting evidence that repeated courses can be harmful, associated with decreased birth weight and head size, sepsis and neonatal death.

3.6 Tocolytics

Tocolysis aims to:

- delay delivery
- allow steroid administration
- allow time for transfer to another unit when NNU has no available cots

Contraindications

- Gestation is over 34 weeks
- Placental abruption
- Antepartum haemorrhage associated with placenta previa
- Evidence or strong suspicion of chorioamnionitis[7]
- Abnormal CTG
- After delivery of first preterm twin
- Atosiban is not licensed for use in women under 18 years of age
- Any situation where delaying delivery would be harmful to the mother

Tocolysis can be considered in preterm premature rupture of the membranes to buy time for maternal corticosteroids to have maximum benefit or to allow *in utero* transfer to another hospital. However, care should be taken when there is evidence or suspicion of chorioamnionitis.

If the decision is made to use a tocolytic drug, Nifedipine and Atosiban appear to have comparable effectiveness in delaying delivery, with fewer maternal adverse effects and less risk of rare serious adverse events than alternatives such as Ritodrine or Indomethacin. Ritodrine and Atosiban are licensed in the UK for the treatment of threatened preterm labour. Although the use of Nifedipine for preterm labour is an unlicensed indication, it has the advantages of oral administration and a low purchase price. The available evidence should be discussed with the woman and her partner and their preferences taken into account in determining her care.

Although Nifedipine is not licensed in the UK (and thus the responsibility lies with the prescribing doctor), there is considerable experience with its use in this clinical situation and is also recommended by the Royal College of Obstetricians and gynaecologists (2011). Nifedipine also has the advantage as it can be given orally. **Nifedipine should therefore be used first line** unless there are any contraindications.

Evidence shows that Nifedipine and Atosiban have comparable effectiveness at delaying birth for up to 7 days (RCOG green top guideline 1b). It is as effective as ß agonists such as Ritodrine, but it has fewer side effects. **Atosiban is therefore the second line** choice for tocolytic when Nifedipine is contraindicated.

Nifedipine:

Contraindication:

- Allergy to Nifedipine
- Cardiac disease
- Severe hypotension
- Concurrent use of IV salbutamol, transdermal nitrates (GTN), or antihypertensive agents.

Use with caution:

- Diabetes
- Multiple pregnancy due to risk of pulmonary oedema
- Impaired liver function, dose reduction may be required in severe impairment.
- Concurrent use of IV magnesium sulfate due to risk of hypotension

Dose:

The suggested dose of Nifedipine is an initial oral dose of 20 mg followed by 10–20 mg three to four times daily, adjusted according to uterine activity for up to 48 hours. A total dose above 60 mg appears to be associated with a three- to four-fold increase in adverse events such as headache and hypotension.

Side effects:

- Hypotension – if significant hypotension occurs treatment should be discontinued.
- Tachycardia, palpitations
- Flushing, headaches, dizziness and nausea
- Hyperglycaemia (Rarely)

Atosiban:

Contraindications:

- Eclampsia and severe pre-eclampsia
- Intra-uterine infection
- Intra-uterine foetal death
- Antepartum haemorrhage (requiring immediate delivery)
- Placenta praevia
- Abruptio placenta
- Intrauterine growth restriction with abnormal foetal heart rate
- Premature rupture of membranes after 30 weeks gestation.

Dose and Administration:

Step	Regimen	Infusion rate	Atosiban dose
1	Initial bolus	Over 1 minute	6.75 mg
2	3-hour high dose Intravenous infusion	24ml / hr	18mg / hr
3	low dose Intravenous Infusions for up to 45 hours	8ml / hr	6mg / hr

Step 1

IV bolus of 6.75mg over 1 minute:

- The vial comes ready prepared as a 0.9ml IV injection containing 6.75mg.
- Draw up the 0.9ml (6.75mg) and dilute with 10ml of sodium chloride 0.9%.
- Inject via IV bolus over 1 minute.

Step 2

3-hour continuous high dose IV infusion:

- Remove and discard 10ml from a 100ml bag of sodium chloride 0.9%
- Add the contents of two 5ml Atosiban 7.5mg/ml vials in to the bag.
- The resulting solution will contain 75mg of Atosiban (0.75mg/ml)
- Give by IV infusion at a rate of **24ml/hour** (i.e.18mg/hour) for **3 hours**

Step 3

Continuous low dose infusion:

- Once the high dose infusion has completed (after 3 hours)
- Reduce the infusion rate to **8ml/hour** (i.e. 6mg/hour) for up to **45 hours**

Maximum duration of treatment with Atosiban must not exceed 48hours.

Use a Baxter infusion pump for setting the infusion rates

Observations:

- BP and pulse hourly
- Continuous CTG, monitor contractions
- Temperature 4 hourly • No need for routine BM's

Side effects:

- Nausea, vomiting
- Tachycardia
- Hypotension
- Headache
- Dizziness
- Hot flushes
- Hyperglycaemia
- NB: The most common side effect is nausea; therefore, antiemetics may be required.

There is insufficient evidence for any firm conclusions about whether or not maintenance tocolytic therapy following threatened preterm labour is worthwhile. Thus, maintenance therapy is not recommended

3.7 Magnesium Sulfate for neuroprotection

PReCePT (The preventing cerebral palsy in preterm labour) & NICE guideline on *Preterm labour & Birth* suggest offering MagSO4 for neuroprotection of the baby before 30 weeks but clinical benefit is seen up to 32 weeks *(New Meta-Analysis: Crowther et al, Assessing the neuroprotective benefits for babies of antenatal magnesium sulphate: An individual participant data meta-analysis, 2017, PLoS Medicine)*

Oxford AHSN guideline therefore advises to offer Magnesium sulphate for neuroprotection to women from 22+3 weeks to *under 32 weeks* at high risk of imminent preterm delivery within 12 hours. (see oxford AHSN flowchart).

NICE Guidance on *Preterm labour & Birth* advises to *consider* intravenous magnesium sulfate for neuroprotection of the baby for women between 30^{+0} and 33^{+6} weeks of pregnancy who are in established preterm labour or having a planned preterm birth within 24 hours.

3.7.1 Evidence

The Cochrane review by Doyle et al concluded that antenatal magnesium sulphate therapy given to women at risk of preterm birth substantially reduced the risk of cerebral palsy in their children with a relative risk (RR) of 0.68 (95%CI 0.54–0.87). There was also a significant reduction in the rate of substantial gross motor dysfunction (RR 0.61; 95% CI 0.44–0.85)

The RCOG Specialist Advisory Committee Opinion paper (29) concluded that Magnesium Sulfate given to mothers shortly before delivery reduces the risk of cerebral palsy and protects gross motor function in those infants born preterm.

National recommendations are that both a bolus and an infusion are used.
Magnesium infusions require intensive monitoring and therefore increase workload. Adverse events have also been reported.
The most recent meta-analysis by Crowther et al (2017) concludes that a bolus plus infusion regime is ***not superior*** to a bolus only regime and that some benefit is gained up to at least 32 weeks. It is therefore suggested a ***bolus only regime*** is used and that Mg is used up to 32+0 weeks.

3.7.2 Eligibility

At Milton Keynes University hospital, Mg SO4 should be offered to mothers from 22+3 weeks to under 32 weeks (consider upto 33+6 weeks) who are at high risk of delivery within 12 hours i.e.

1. Planned CS at time of preparation of anaesthetic.
2. Confirmed preterm labour, especially if Cervix > 4cm dilated

For those women suitable for IUT, please discuss with Obstetric on call team at OUH /tertiary centre whether to give MAGSO4 prior to transfer.

3.7.3 Preparation & administration

Bolus: Take one 20 ml syringe and fill with the contents of two 10ml ampoules of 20% Magnesium Sulphate. This contains 4g (16mmol) of Magnesium Sulphate.
Give the 4g (16mmol) Magnesium Sulphate by slow IV bolus, over 5-10 minutes.

3.7.4 Timing and Repeat doses of neuroprotective dosage

Magnesium Sulphate can be given just prior to birth and is effective within minutes.
If birth is imminent >12 hrs after a bolus has been given, ***the loading dose can be repeated.***
The 4g bolus is sufficient because of lack of evidence for better outcomes with infusions, in conjunction with manpower /risk issues with prolonged infusions.

3.7.5 The Antidote for Magnesium Sulfate Is Calcium Gluconate

The dose is 1g calcium gluconate IV. This pack contains a 10ml ampoule of 10% calcium gluconate, which should be administered IV over 10 minutes. Calcium gluconate should only be given under Consultant/Registrar supervision.

3.8 "Rescue" cervical cerclage

The decision for emergency or 'rescue' cerclage insertion is based on the clinical presentation. Emergency cervical cerclage implies cervical dilatation and therefore bulging membranes into the vagina, seen on speculum examination.

Nice Guidance 2019 advises not to offer 'rescue' cervical cerclage to women with:

- signs of infection **or**
- active vaginal bleeding **or**
- uterine contractions

Nice guidance 2019 advises to Consider 'rescue' cervical cerclage for women between 16^{+0} and 27^{+6} weeks of pregnancy with a dilated cervix and exposed, unruptured foetal membranes:

- take into account gestational age (being aware that the benefits are likely to be greater for earlier gestations) and the extent of cervical dilatation
- discuss with a consultant obstetrician and consultant paediatrician.

Explain to women for whom 'rescue' cervical cerclage is being considered (and their family members or carers as appropriate):

- about the risks of the procedure
- that it aims to delay the birth, and so increase the likelihood of the baby surviving and of reducing serious neonatal morbidity

If "rescue" cervical cerclage is used, ensure that a plan is in place for removal of the suture which will usually be offered at 37 weeks

3.9 Intrapartum antibiotics

- Consider intrapartum antibiotic prophylaxis using intravenous benzylpenicillin to prevent early onset neonatal infection for women in preterm labour if there is prelabour rupture of membranes of any duration.
- Consider intrapartum antibiotic prophylaxis using intravenous benzylpenicillin to prevent early onset neonatal infection for women in preterm labour if there is suspected or confirmed intrapartum rupture of membranes lasting more than 18 hours.
- Offer benzylpenicillin as the first choice for intrapartum antibiotic prophylaxis. If the woman is allergic to penicillin, offer clindamycin unless individual group B streptococcus sensitivity results or local microbiological surveillance data indicate a different antibiotic.

3.10 Fetal monitoring

Discuss with women in suspected, diagnosed or established preterm labour (and their family members or carers as appropriate):

- the purpose of foetal monitoring and what it involves
- the clinical decisions it informs at different gestational ages
- if appropriate, the option not to monitor the foetal heart rate (for example, at the threshold of viability).

Involve a senior obstetrician in discussions about whether and how to monitor the foetal heart rate for women who are between 23^{+0} and 25^{+6} weeks pregnant.

Explain the different foetal monitoring options to the woman (and her family members or carers as appropriate), being aware that:

- there is limited evidence about the usefulness of specific features to suggest hypoxia or acidosis in preterm babies
- the available evidence is broadly consistent with that for babies born at term (see monitoring during labour in the NICE guideline on intrapartum care)
- a normal cardiotocography trace is reassuring and indicates that the baby is coping well with labour, but an abnormal trace does not necessarily indicate that foetal hypoxia or acidosis is present.

Explain to the woman (and her family members or carers as appropriate) that there is an absence of evidence that using cardiotocography improves the outcomes of preterm labour for the woman or the baby compared with intermittent auscultation.

Offer women in established preterm labour but with no other risk factors (see monitoring during labour in the NICE guideline on intrapartum care) a choice of foetal heart rate monitoring using either:

- cardiotocography using external ultrasound **or**
- intermittent auscultation.

3.11 Fetal scalp electrode

Do not use a foetal scalp electrode for foetal heart rate monitoring if the woman is less than 34^{+0} weeks pregnant unless all of the following apply:

- it is not possible to monitor the foetal heart rate using either external cardiotocography or intermittent auscultation
- it has been discussed with a senior obstetrician
- the benefits are likely to outweigh the potential risks
- the alternatives (immediate birth, intermittent ultrasound and no monitoring) have been discussed with the woman and are unacceptable to her.
-

Discuss with the woman (and her family members or carers as appropriate) the possible use of a foetal scalp electrode between 34^{+0} and 36^{+6} weeks of pregnancy if it is not possible to monitor the foetal heart rate using either external cardiotocography or intermittent auscultation.

3.12 Fetal blood sampling

Do not carry out foetal blood sampling if the woman is less than 34^{+0} weeks pregnant.

Discuss with the woman the possible use of foetal blood sampling between 34^{+0} and 36^{+6} weeks of pregnancy if the benefits are likely to outweigh the potential risks.

When offering foetal blood sampling, discuss this with the woman and advise her that if a blood sample cannot be obtained a caesarean section is likely.

3.13 Mode of birth

Discuss the general benefits and risks of caesarean section and vaginal birth with women in suspected, diagnosed or established preterm labour and women with P-PROM (and their family members or carers as appropriate).

Explain to women in suspected, diagnosed or established preterm labour and women with P-PROM about the benefits and risks of caesarean section that are specific to gestational age. In particular, highlight the difficulties associated with performing a caesarean section for a preterm birth, especially the increased likelihood of a vertical uterine incision and the implications of this for future pregnancies.
Explain to women in suspected, diagnosed or established preterm labour that there are no known benefits or harms for the baby from caesarean section, but the evidence is very limited.
Consider caesarean section for women presenting in suspected, diagnosed or established preterm labour between 26^{+0} and 36^{+6} weeks of pregnancy with breech presentation.

3.14 Timing of cord clamping for preterm babies (born vaginally or by caesarean section)

Consider delayed cord clamping for 1 minute if the baby is stable. Optimal Cord Management reduces death in preterm babies by nearly a third.

Position the baby at or below the level of the placenta before clamping the cord.

Contraindications:
The need for maternal resuscitation in the face of massive, acute haemorrhage would be a rare, justifiable reason to proceed with early clamping of the cord.

A ruptured vasa praevia, snapped cord or other trauma to the cord vessels which will result in haemorrhage from the baby are also reasons for early cord clamping.

BAPM recommends that units should only reserve umbilical cord milking for those rare situations such as maternal collapse requiring resuscitation where cord clamping is required to be expedited for maternal safety. In these cases, the reason must be documented. Do not perform cord milking if baby is <28 weeks

4.0 Statement of evidence/references

References:

BAPM Perinatal Management of Extreme Preterm Birth Before 27 weeks of Gestation (2019 Framework of Practice https://hubble-live-assets.s3.amazonaws.com/bapm/attachment/file/182/Extreme_Preterm_28-11-19_FINAL.pdf

Optimal Cord Management Toolkit | British Association of Perinatal Medicine (bapm.org)

Saving Babies' Lives Version Two: A care bundle for reducing perinatal mortality, July 2019 https://www.england.nhs.uk/wp-content/uploads/2019/07/saving-babies-lives-care-bundle-version-two-v5.pdf

Oxford AHSN Maternity Network Guideline-Threatened extreme preterm labour V3 updated Jan 2020

Oxford Academic Health Science Network (2019) *Guideline for Magnesium Sulphate use:*
loading dose for severe pre-eclampsia/ eclampsia and neuroprotective dose for severe preterm birth V2. [Online]. Available from: https://www.patientsafetyoxford.org/wp-content/uploads/2019/07/MgSO4-bolus-guideline-V2.pdf

Crowther, C.A., et al. (2017) Assessing the neuroprotective benefits for babies of antenatal magnesium sulphate: An individual participant data meta-analysis. *PLoS Medicine* [Online] **14**(10): e1002398. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5627896/ [Accessed 10 October 2019]

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Saigal S, Doyle LW (2008). *An overview of mortality and sequelae of preterm birth from infancy to adulthood*. Lancet: 371(9608): 261-9. Available from: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(08)60136-1/fulltext [Accessed on]

5.0 Governance

5.1 Document review history

Version number	Review date	Reviewed by	Changes made
9.3	02/02/2022	Mis F Nizami	Use of **QUIPP app** to risk assess women presenting with symptoms of preterm labour **OAHSN** preterm flowchart 2020 updated Section 3.14 Timing of cord clamping for preterm babies

5.2 Consultation History

Stakeholders Name/Board	Area of Expertise	Date Sent	Date Received	Comments	Endorsed Yes/No
Dr Indranil Misra	Neonatal consultant	24/11/2021	24/11/2021	Delayed cord clamping for 1 minute if baby is stable Cord milking not advisable if <28 weeks	Yes
Emma Mitchener	Deputy HOM	24/11/2021		No comments	yes
Miss Anya Bibby	Consultant O&G	14/12/2021		Regarding Steroids in introduction: I think a line needs to be added regarding the poorer outcome of babies born at term who have been exposed to pre-term steroids due to inappropriate steroid administration. There is a line which says that steroids should be used in the right woman and the right time (ie 24hr – 7 days pre-preterm birth). Regarding QUIPP app - can still be	Yes

				helpful in symptomatic women even without a recent CL. My understanding was that if there is SROM – that FFN is NOT used as it will be very high. FFN should also be delayed by 24 hours after a TVUSS - is written in one place and not in another. Is there any way in the Oxford AHSN maternity guide flowchart that POC can be replaced by fFN?	
Miss Joyce Elliot	Consultant O&G	14/12/2021		Is there ever a scenario of +ve FFn and QUIPP less than 5%? If so, what is the advice	Yes
Natalie Lucas	Midwife	16/12/2021		There seems to be a variety of font sizes used throughout the document	Yes
Lauren Mitchell	Consultant Midwife	24/12/2021		insert references ,remove appendix 1 of PRETERM six Do we have Baxter infusion pumps these at MKUH Is this in accordance with our fetal monitoring guideline : (Offer women in established preterm labour but with no other risk factors (see monitoring during labour in the NICE guideline on intrapartum care) a choice of fetal heart	Yes

				rate monitoring using either: cardiotocography using external ultrasound **or** intermittent auscultation.	
Melissa Coles	ADAU lead midwife			I cannot see an abbreviation list in first box can we change to history of or suspected SROM rather than 'if SROM' Would flow better if the flow chart was here in initial assessment. Could we include 'consider initial assesssment on ADAU if mild abdo pain (as per RAG rating assessment) If mod/severe abdo pain for assessment on LW. If following initial assessment and established diagnosis of preterm labour to transfer to LW Also think flow chart needs to say fFN + Quipp (not +/-) as all women should have it used to advise management shouldnt they? could this procedure go in the appendix? If with fFN of more than 50 but Quipp app risk is less than 5% , consider alternative diagnosis and they go home?	Yes

5.3 Audit and monitoring

Audit/Monitoring Criteria	Tool	Audit Lead	Frequency of Audit	Responsible Committee/Board
Was test performed with any contraindications present?	eCare	Audit Midwife	annually	Labour Ward Forum, Audit meetings
The proportion of babies delivered before 34/40 who received antenatal corticosteroid	eCare	Audit Midwife	annually	Labour Ward Forum, Audit meetings
The proportion of babies delivered between 22+3 weeks & 32 weeks who received magnesium sulphate	eCare	Audit Midwife	annually	Labour Ward Forum, Audit meetings
The proportion of babies delivered before 37/40 who received GBS prophylaxis in labour	eCare	Audit Midwife	annually	Labour Ward Forum, Audit meetings

5.4 Equality Impact Assessment

As part of its development, this Guideline and its impact on equality has been reviewed. The purpose of the assessment is to minimise and if possible remove any disproportionate impact on the grounds of race, gender, disability, age, sexual orientation, religion or belief, pregnancy and maternity, gender reassignment or marriage and civil partnership. No detriment was identified. Equality Impact assessments will show any future actions required to overcome any identified barriers or discriminatory practice.

Equality Impact Assessment			
Division	Women's and Children's Health	Department	Maternity
Person completing the EqIA	Miss Faryal Nizami	Contact No.	On Email
Others involved:		Date of assessment:	17/09/2019
Existing policy/service	Yes	New policy/service	No

Will patients, carers, the public or staff be affected by the policy/service?	Yes
If staff, how many/which groups will be affected?	

Protected characteristic	Any impact?	Comments
Age	NO	Positive impact as the policy aims to recognise diversity, promote inclusion and fair treatment for patients and staff
Disability	NO	
Gender reassignment	NO	
Marriage and civil partnership	NO	
Pregnancy and maternity	NO	
Race	NO	
Religion or belief	NO	
Sex	NO	
Sexual orientation	NO	

What consultation method(s) have you carried out?
Obstetric consultants, registrar's, midwives, pharmacy and the library
How are the changes/amendments to the policies/services communicated?
These will be communicated via newsletters, email and unit teaching
What future actions need to be taken to overcome any barriers or discrimination?

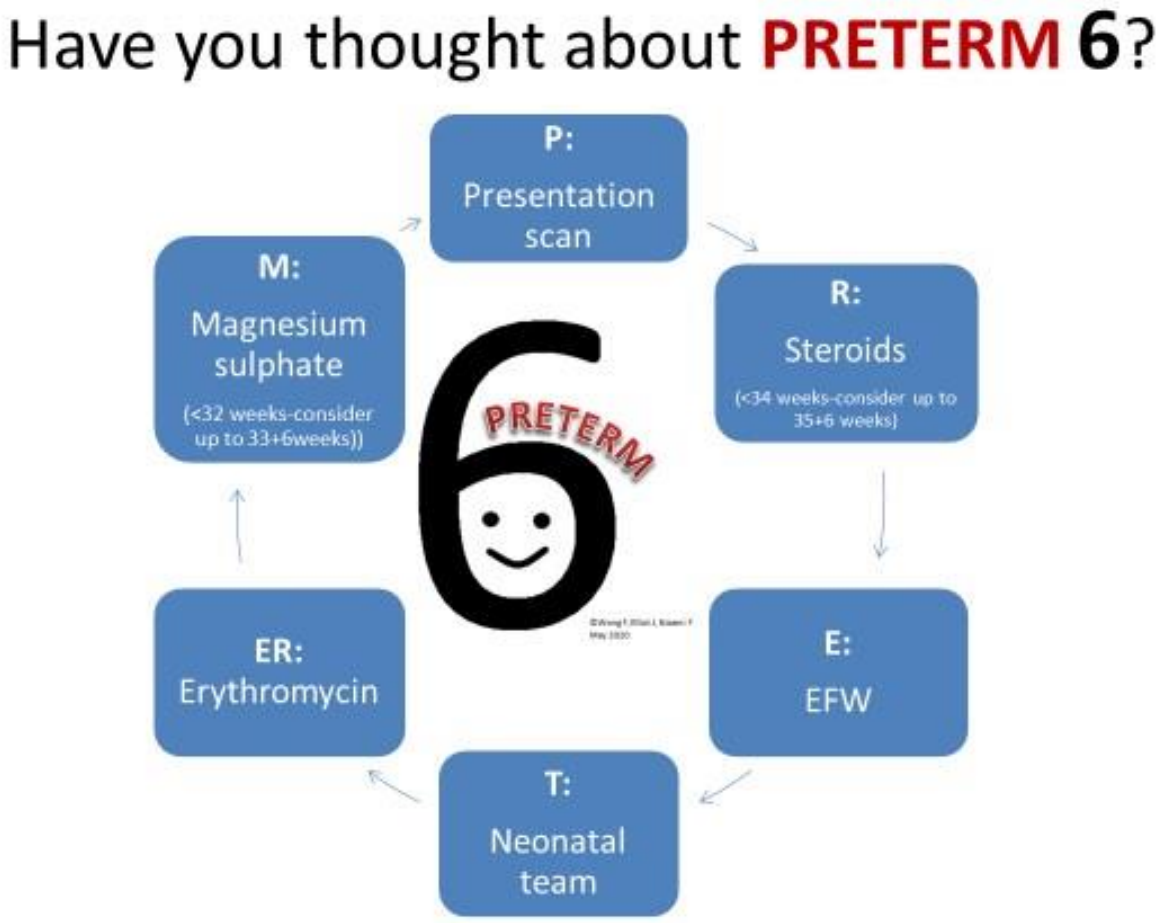
What?	Who will lead this?	Date of completion	Resources needed
Review date of EqIA			

Appendix 1: Preterm 6 Checklist

PRETERM 6 Checklist

- ❑ P – Presentation scan: _____
- ❑ R – Respiratory: Steroids
  - ❑ 1st dose betamethasone 12mg IM (date: time:)
  - ❑ 2nd dose betamethasone 12mg IM (date: time:)
- ❑ E – EFW: _____ (last scan dated: _____)
- ❑ T – Team: Neonatal unit informed
- ❑ ER – Erythromycin/ antibiotics started
- ❑ M – Magnesium sulphate 4g IV bolus

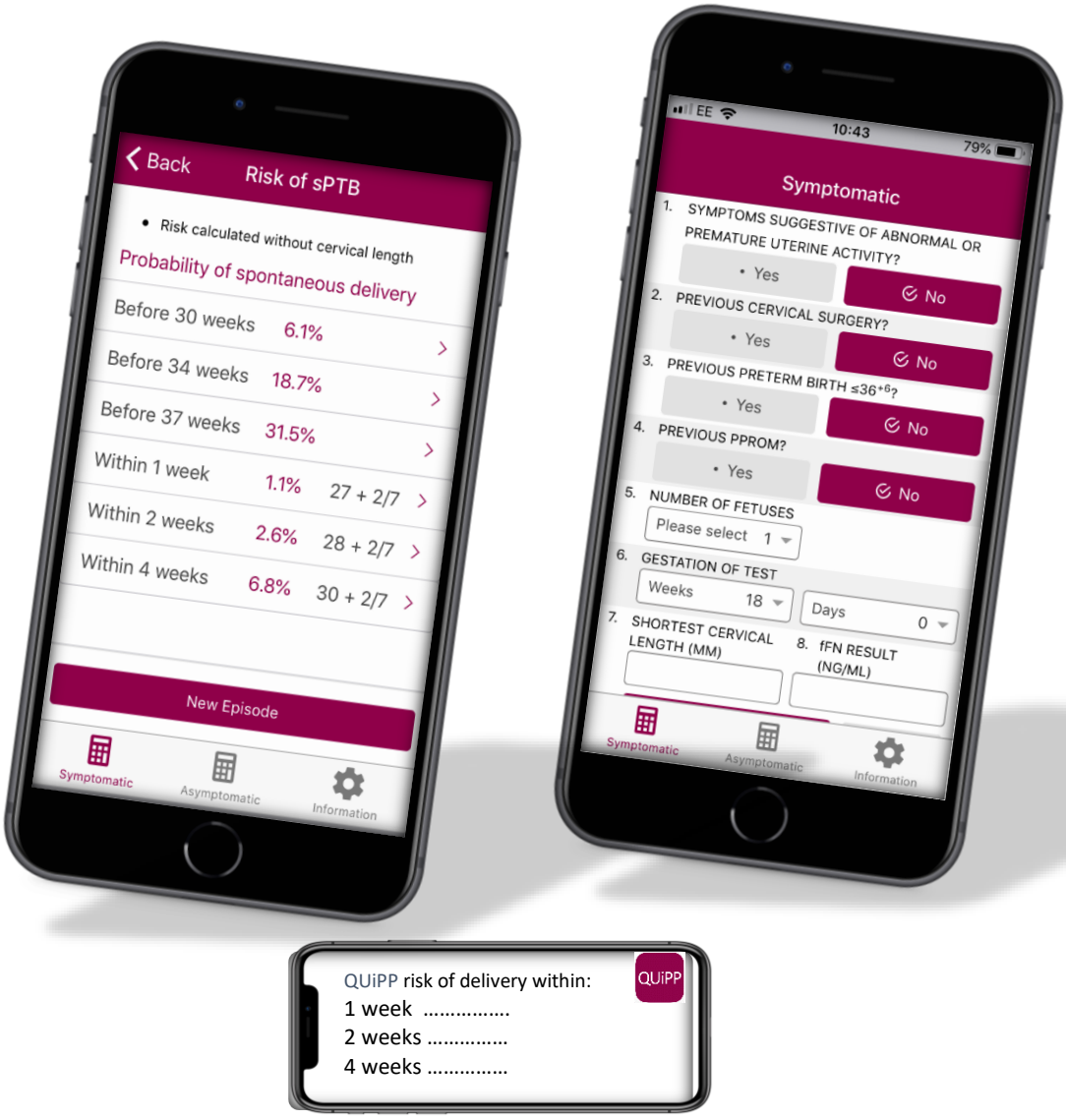
Appendix 2: Preterm 6 Poster



Appendix 3: The QUIPP® App

The QUIPP app

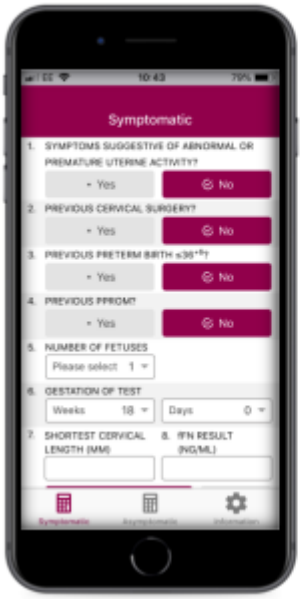
- Free to download on Apple and Android– search 'QUiPP'
- Website version available at: www.quipp.org
- Gives individualised scores for risk of having a spontaneous preterm delivery
- Uses medical history, her quantitative Fetal Fibronectin result and/or cervical length
- 3 separate algorithms [a) fFN only, b) cx length only, c) fFN and cx length combined]
- We use the actual concentration of fFN in the app (no cut off)
- Decision-support tool



Appendix 4

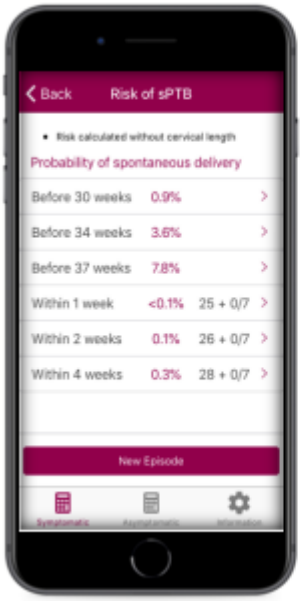
How to use QUIPP APP

The App interface looks like this for symptomatic women:



1. This should be yes because she has arrived at your unit with symptoms
2. Cervical surgery includes large loop excision of transformation zone, laser treatments or cone biopsy
3. This refers to a spontaneous preterm birth at 36+6 or less
4. This refers to a spontaneous premature rupture of membranes in a previous pregnancy
5. The app can be used in twins or singletons
6. The current gestation of the woman
7. Her cervical length via transvaginal scan (within the last 24 hours only). If you do not have a result for this please leave this section blank
8. The woman's quantitative Fetal Fibronectin result

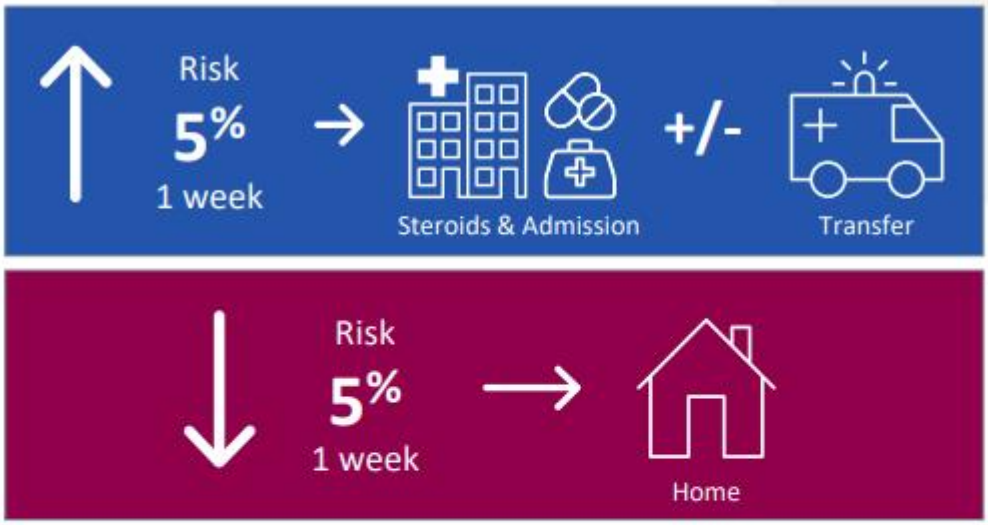
Press calculate!



This woman has a risk of less than 0.1% of delivering within the next week.

If this was more than 5% you may consider admitting her, giving her steroids and/or transferring to another unit.

You can use the longer term predictions to decide when to see her again.



If you click on any of the result scores you get a donut illustration of the woman's risk score. You can use this to explain the results to the woman, and to aid shared decision-making.

If you require more information, look at the other resources in the toolkit such as the FAQ section.

You can also look at the information section on the App, or contact us at quippapp@gmail.com