

Thank you for taking the time to read this information leaflet.

As a staff member involved in the care of women with preterm prelabour rupture of membranes (PPROM), we would like you to be familiar with the PPRMT trial and its aims. Women with PPROM between 34 and 36⁺⁶ weeks may be eligible for PPRMT and will be invited to consider participation in this trial. We would like you to be able to offer PPRMT to eligible women, obtain consent and initiate recruitment into the trial.

This leaflet aims to provide you with some important information about PPRMT. Further details can be obtained from the clinical collaborators at your hospital and the PPRMT research assistant.

INFORMATION ABOUT PPRMT

BACKGROUND

Preterm prelabour rupture of membranes complicates up to 2% of all pregnancies and is the cause of 40% of all preterm births¹.

Clinical decision-making requires consideration of the potential risks and benefits of induction of labour against expectant management until term or complications such as chorioamnionitis intervene necessitating delivery. The aim of such management is to maximise the benefits of fetal maturity while avoiding the potential harms of remaining in utero. At gestations between 34 and 37 weeks, whilst the neonate is potentially at increased risk of respiratory distress, difficulty with thermoregulation and difficulty with breast-feeding, these risks need to be balanced against the increased incidence of chorioamnionitis associated with expectant management in women with PPROM². Histological evidence of chorioamnionitis is present in up to 50% of women who give birth preterm and is often not associated with clinical symptoms or signs³. Chorioamnionitis is a known significant risk factor for the neonate for the development of cerebral palsy^{3,4}. It is possible that there are increased risks of long term adverse neurological outcomes in those infants whose mothers are

managed expectantly with PPROM by increasing their duration of exposure to subclinical chorioamnionitis.

A systematic review⁵ to assess immediate delivery compared with expectant care in women with ruptured membranes included 3 trials in the meta-analysis⁶⁻⁸.

Outcome	No. Trials	No. Women	Immediate Delivery	Expectant Care	RR (CI)
Caesarean Section	2	140	8/72 (11.1%)	6/68 (8.8%)	1.21 (0.45-3.28)
Chorio-amnionitis	3	260	8/129 (6.2%)	31/131 (23.6%)	0.25 ** (0.12-0.53)
Neonatal sepsis	3	257	9/128 (7.0%)	8/129 (6.2%)	1.00 (0.41-2.45)
RDS	3	257	5/128 (3.9%)	3/129 (2.3%)	1.56 (0.41-5.97)
Perinatal Mortality	3	260	2/129 (1.6%)	2/131 (1.5%)	1.24 (0.19-8.06)

** p<0.05

This meta-analysis showed that immediate delivery was associated with a significant decrease in chorioamnionitis compared with those pregnancies that are managed expectantly. There were insufficient data to show differences in respiratory distress, neonatal sepsis or caesarean section.

There is insufficient evidence on the benefits and harms of immediate delivery compared with expectant care for women with ruptured membranes between 34 and 36⁺⁶ weeks to make recommendations for clinical practice. Thus, this trial will provide guidance for the management of women with PPROM near term.

PRIMARY HYPOTHESES

Early planned delivery of women with PPROM close to term is associated with:

- 1. Less neonatal and maternal morbidity compared with expectant management**
- 2. Fewer economic costs compared with expectant management**

ENTRY CRITERIA

1. Women with a singleton pregnancy
2. Gestation of 34 to 36⁶ weeks
3. Rupture of membranes determined clinically and/or confirmed by positive amniocentesis swab

EXCLUSION CRITERIA

Women in established labour
Indications for *immediate* delivery such as:
Clinical evidence of chorioamnionitis
Meconium stained liquor
Antepartum haemorrhage

TREATMENT ALLOCATION

Consenting women will be allocated via a central randomisation service to either **early planned birth** or **expectant management**. Women randomised to early planned birth will be scheduled for delivery as soon as possible and preferably within 24 hours of randomisation. The mode of birth will be determined by the usual obstetric indications. In women randomised to expectant management, birth will occur after spontaneous labour, at term or when the clinician feels that birth is indicated according to usual care.

The care of women will otherwise be managed by the obstetric team with care of the infant by the attending neonatologist.

PRIMARY STUDY ENDPOINTS

The primary study endpoint will be the incidence of neonatal sepsis, classified as either definite or probable by an adjudication committee blinded to treatment allocation.

SECONDARY STUDY ENDPOINTS

Secondary maternal endpoints include outcomes such as chorioamnionitis, endometritis requiring antibiotics, post partum fever, placental abruption, induction of labour, caesarean section, assisted vaginal delivery, maternal satisfaction, views of care, duration of antenatal and postnatal hospitalisation, time to fully establish breast-feeding and maternal emotional wellbeing.

Secondary infant endpoints include respiratory distress, perinatal mortality, duration of stay in special care unit, duration of stay in hospital, birthweight, Apgar scores at 5 minutes, any assisted ventilation and early infant development as measured by questionnaires at four months post-partum.

If it is established that long-term maternal and child outcomes are likely to be equivalent between the treatment groups, a cost analysis will be conducted in line with methods previously described.

SAMPLE SIZE

A trial of 1812 women will have an 80% probability of detecting a statistically significant difference at an alpha level of 0.05 of reducing the risk of proven and probable neonatal sepsis from 5% in those managed expectantly to 2.5% in those managed with immediate delivery. Such a trial will have adequate power to detect an increase in the need for ventilatory support from 4% in the expectant arm to 7% in the immediate delivery arm.

HOW CAN I ASSIST RECRUITMENT TO PPRMOT?

For all women under your care who fulfil the trial entry criteria, please discuss the alternative modes of care for women with PPRMOT and the uncertainty about the care that is best for mother and baby. Patient Information Sheets are available in the blue PPRMOT folder in the antenatal and labour wards. Please let the women know that they will be approached by a member of the PPRMOT study team. Please also contact the trial coordinator at your centre when you identify a woman who is eligible for the trial.

HOW CAN I OBTAIN CONSENT FOR PPRMOT FROM ELIGIBLE WOMEN?

Women who give consent to take part in PPRMOT need to sign the PPRMOT consent form, copies of which are in the blue folder in the antenatal and labour ward.

HOW CAN I INITIATE RECRUITMENT IN PPRMOT?

This can be achieved by the following steps:

1. Record entry details on the pink trial entry form (copy in the PPRMOT study folder).
2. Telephone the PPRMOT central telephone randomisation service on 08 8161 7661. Be prepared to provide the randomisation code of your centre and information from the trial entry form that checks eligibility provides characteristics of the women and enables stratification.
3. A Study Number and Treatment Group allocation will be given once all entry details are given and eligibility confirmed. Record these numbers on the trial entry form.
4. Ask the woman to complete the blue Study Entry Questionnaire (Form is in the PPRMOT study folder).

WE LOOK FORWARD TO THE CONTRIBUTION YOU WILL BE ABLE TO MAKE TO PPRMOT AT YOUR CENTRE

For further information please contact Prof Jonathan Morris, or clinical trial coordinator, Kate Levett, Dept of Obstetrics & Gynaecology, Royal North Shore Hospital, St Leonards NSW 2065.

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PPROMT

**PRETERM PRE-LABOUR RUPTURE OF MEMBRANES
CLOSE TO TERM TRIAL**



Health Professional

Information Sheet

