

Dr Laura Goodfellow - Written evidence (PRT0013)

Background information regarding expertise

I am an NIHR Academic Clinical Lecturer at the University of Liverpool, with over 8 years experience in preterm birth research and clinical practice in spontaneous preterm birth (sPTB) prevention services in the North West of England. I am co-lead author of the largest prospective observational study into Preterm Prelabour Rupture of Membranes (PPROM) under 23 weeks' gestation, published March 2024, and linked commentary.^{1,2} I am a member of the UK Preterm Birth National Clinical Network and co-lead organiser of the UK PTB conference held in Liverpool in 2024. These opinions are my own.

Background information regarding the condition

I am focusing this submission on Preterm Prelabour Rupture of Membranes, abbreviated to PPRM, and the women for whom this occurs very early in pregnancy, under 23 weeks' gestational age. This describes the situation when the protective membranes surrounding the baby rupture, resulting in leaking amniotic fluid before the onset of labour. The baby remains alive, but at risk of labour commencing at a gestation when the baby is either too immature to survive or just on the cusp of when survival is possible (extremely preterm birth).

To improve the chance of the baby surviving, the pregnancy needs to continue. During this time the baby and mother are at risk of serious complications including extremely preterm birth, cord prolapse, placental abruption, infection, and potentially sepsis and death.

The outlook for the babies after PPRM under 23 weeks' gestation is often judged to be so poor that termination is offered, and in many cases advised. We cannot understate the gravitas of the decision to end a wanted pregnancy for women and their families. In this vulnerable

position, they rely heavily on doctors' advice and require evidence to help support their decision making. My colleague, Dr Angharad Care, and I have worked closely with Miss Ciara Curran, founder of the patient support and advocacy group, Little Heartbeats,³ and Professor Marian Knight, chair of the UK Obstetric Surveillance System (UKOSS)⁴ to perform the largest prospective observational study into this condition. This study included all women who experienced PPRM between 16⁺⁰ and 22⁺⁶ weeks' gestation from September 2019 to March 2021 in the UK.

Issues I wish to highlight:

1. PPRM under 23 weeks' gestation is a rare complication of pregnancy (affecting about 1 in 1000 pregnant women⁵) but an important cause of maternal sepsis and mortality. Early PPRM has contributed to at least 6 maternal deaths in the UK since 2013 according to national maternal mortality reports.⁶⁻⁹ Two women (out of 364, 0.5%, 95%CI 0.15-1.98%) with early PPRM died from sepsis within our prospective observational cohort study.¹ This risk of death is comparable to the risk of death of pregnant women admitted to hospital with Covid-19 during 2020-21.¹⁰
2. Historical UK practice was to recommend termination of pregnancy for medical reasons (TFMR) in cases of PPRM under 23 weeks' gestation, and over 30 years ago this was normal practice. This was largely due to the perceived poor outlook for the babies along with concerns about maternal infection.¹¹ Neonatal care has improved over time, and survival of babies born extremely preterm is now possible.¹² Alongside this societal attitudes to termination have changed, and in 2019-21 two thirds of women with PPRM under 23 weeks' gestation chose to continue their pregnancies. This means we need to understand how to best care for women in this situation, on a background of little historical data because most pregnancies would have previously ended with TFMR.

3. There are currently no national or international guidelines about how to best manage women with PPRM under 23 weeks' gestation.
4. There is very little evidence on which to base guidelines for management of this condition. The RCOG Green Top guideline on PPRM specifically focuses on PPRM over 24 weeks' gestation.¹³
5. Women and families who experience early PPRM describe severe psychological distress associated with the condition. The prolonged period of uncertainty and inconsistent information contribute to this.¹⁴
6. A substantial minority of babies now survive early PPRM; 26% of women with expectantly managed singleton pregnancies had babies that survived to hospital discharge within our cohort.¹ This similar to the survival rate in the only other prospective cohort study to our knowledge, based in the Netherlands.¹⁵ There is numerical uncertainty within the infant survival figures owing to 32% of women having a termination for medical reasons (TFMR). To account for this, a minimum-maximum range is given assuming that all women with TFMR had poor or good outcomes, respectively. This range is 17-53% for survival to discharge of singleton babies. To fully understand the prognosis it is important to communicate this uncertainty to the women and families, but the optimal way of doing that has yet to be determined.
7. Over half of the surviving babies within our prospective observational study of PPRM under 23 weeks' gestation did not appear to have severe morbidity at discharge,¹ however this information is limited by the disconnect between maternity and neonatal medical records. Documentation of PPRM within maternity records is appropriate, but within neonatal records is inconsistently reported; local audit showed it was recorded in under half of eligible cases. This limits the clinician's ability to give parents the long-term prognosis information that is so desperately wanted.

8. Maternity services are currently ill-suited to the needs of women with early PPROM, who cross the gestational age threshold between gynaecology/emergency departments (differently organised in each hospital but commonly up to 20 weeks' gestation) and obstetrics (typically over 20 weeks' gestation). Women require intensive input from obstetricians, neonatologists, midwives, bereavement support and psychological support, potentially over a long time period as the pregnancy can potentially progress for 4-5 months after the membranes have ruptured. I believe an obstetrician with an interest in PPROM/preterm birth is ideally placed to co-ordinate this care and provide continuity to the woman and family, but currently there are no clinics/referral pathways/funding streams to facilitate ongoing care of women with early PPROM.
9. Recommending immediate termination of pregnancy for medical reasons is unlikely to avoid all maternal sepsis. Within our study 10% (6/62) of women who had opted for termination of pregnancy for medical reasons after their initial consultation with a doctor after PPROM still developed sepsis, compared to 13% (33/264) of women who initially chose to continue their pregnancies. Therefore service improvements need to include women opting for termination too.
10. The optimal gestation for birth after early PPROM is currently unknown. A planned early preterm birth by induction of labour or caesarean section might avoid complications such as cord prolapse, placental abruption, infection, and potentially sepsis and death. However earlier birth increases the risk of neonatal death or severe disability due to complications of prematurity.¹²
11. Further research is urgently needed in this area. I believe this should be conducted in two ways, in parallel. One component should focus how to optimise current care for women with early PPROM, and the other component should focus on novel interventions for the diagnosis and management of this condition.

12. Now that we have prospectively collected data about pregnancy outcomes of pregnancies complicated by PPRM under 23 weeks' gestation in the UK I believe and hope that this information can be used to provide appropriate counselling for this difficult complication, and is the first step to optimising management.

Summary

Preterm prelabour rupture of membranes (PPROM) before 23 weeks' gestation is a serious complication of pregnancy with high rates of morbidity for mothers and babies. Contemporary UK-based data is now available to describe the outcomes of such pregnancies. I urge the Preterm Birth Committee to consider this data in two ways. Firstly, by recognising the serious nature of the condition and facilitating a re-organisation of services to ensure these women and babies are not lost in the system. Secondly, by supporting research into the complex pathologies, including sepsis, of pregnancies affected by early PPRM.

References

1. Goodfellow L, Care A, Curran C, Roberts D, Turner MA, Knight M, et al. Preterm Prelabour Rupture Of Membranes (PPROM) before 23 weeks gestation: A prospective observational study. *BMJ Med.* 2024 Mar 1;3:e000729.
2. Goodfellow L, Curran C, Care A, Goodfellow L, Curran C, Care A. Early PPRM: women and babies who should not be lost in the system. *BMJ.* 2024;384(March):q690.
3. Little Heartbeats. What to expect- in hospital [Internet]. 2023 [cited 2023 Jan 9]. Available from: <https://www.little-heartbeats.org.uk/what-to-expect-c10zs>

4. NPEU. UK Obstetric Surveillance System (UKOSS) [Internet]. [cited 2023 Apr 28]. Available from: <https://www.npeu.ox.ac.uk/ukoss>
5. Linehan LA, Walsh J, Morris A, Kenny L, O'Donoghue K, Dempsey E, et al. Neonatal and maternal outcomes following midtrimester preterm premature rupture of the membranes: a retrospective cohort study. *BMC Pregnancy Childbirth*. 2016 Jan;16:25.
6. Knight M, Bunch K, Felker A, Patel R, Kotnis R, Kenyon S, et al. *Saving Lives, Improving Mothers' Care Saving Lives, Improving Mothers' Care Lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity State of the Nation Surveillance Report 2019-21*. University of Oxford. 2023.
7. Knight M, Nair M, Tuffnell D, Shakespeare JM, Kenyon S, Kurinczuk JJ. *Saving Lives, Improving Mothers' Care - Lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2013-15*. Oxford; 2017.
8. Knight M, Bunch K, Tuffnell D, Patel R, Shakespeare J, Kotnis R, et al. *Saving Lives, Improving Mothers' Care - Lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2017-19*. Oxford; 2021.
9. Knight M, Bunch K, Tuffnell D, Shakespeare JM, Kotnis R, Kenyon S, et al. *Saving Lives, Improving Mothers' Care - Lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2016-18*. Oxford; 2020.
10. Engjom HM, Ramakrishnan R, Vousden N, Bunch K, Morris E, Simpson NAB, et al. Severity of maternal SARS-CoV-2 infection and perinatal outcomes of women admitted to hospital during the omicron variant dominant period using UK Obstetric Surveillance System data: prospective, national cohort study. *BMJ Med*. 2022;1(1):e000190.

11. Waters TP, Mercer BM. The management of preterm premature rupture of the membranes near the limit of fetal viability. *Am J Obstet Gynecol* [Internet]. 2009;201(3):230–40. Available from: <http://dx.doi.org/10.1016/j.ajog.2009.06.049>
12. Costeloe KL, Hennessy EM, Haider S, Stacey F, Marlow N, Draper ES. Short term outcomes after extreme preterm birth in England: Comparison of two birth cohorts in 1995 and 2006 (the EPICure studies). *BMJ* [Internet]. 2012 Dec 4 [cited 2019 Mar 11];345(7886):e7976. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/23212881>
13. Thomson AJ. Care of Women Presenting with Suspected Preterm Prelabour Rupture of Membranes from 24+0 Weeks of Gestation: Green-top Guideline No. 73. *BJOG An Int J Obstet Gynaecol*. 2019;126(9):e152–66.
14. Challacombe F, Suchomelova Z, Avena- Zampieri C, Hall M, Curran C, Shennan A, et al. Preterm Premature Rupture of the Membranes (PPROM): a study of patient experiences and support needs. *J Reprod Infant Psychol*. 2024;
15. Simons NE, de Ruigh AA, van der Windt LI, Kazemier BM, van Wassenaer-Leemhuis AG, van Teeffelen AS, et al. Maternal, perinatal and childhood outcomes of the PPROMEXIL-III cohort: Pregnancies complicated by previable prelabor rupture of membranes. *Eur J Obstet Gynecol Reprod Biol* [Internet]. 2021;265:44–53. Available from: <https://doi.org/10.1016/j.ejogrb.2021.08.007>

23 March 2024