

INTRODUCTION

It has been suggested that commencing vaginal progesterone (VP) at 16 weeks' gestation in women with a previous history of sPTB or PPROM <34 weeks is an effective treatment modality for reducing sPTB in subsequent pregnancies, even with a normal cervical length (>25mm) (1).

However, there is paucity of evidence for whether targeted therapy following an USS-confirmed diagnosis of a short cervix (<25mm) is a more effective treatment pathway than with empirical VP for all (2,3).

At Liverpool Women's Hospital PTB Prevention Clinic, a policy of empirical VP to this cohort of high-risk women was introduced in 2018, whereby serial cervical length scans are performed until 26 weeks' gestation, and second line therapy is offered where cervical shortening, or 'progesterone failure' (PF) is identified.

OBJECTIVES

- To calculate respective sPTB rates <34 and <28 weeks between women treated with empirical VP at 16 weeks' and those managed with USS-surveillance targeted therapy, with further analysis of PTB rates within subgroups requiring additional treatment.
- To define what measurement thresholds clinicians are using 'triggering' the need for second line therapy - or 'progesterone failure'.

METHODOLOGY

This is a retrospective cohort study of 772 women with singleton pregnancies and a previous history of sPTB or PPROM <34 weeks attending PTB prevention clinic. Data was collected via the PCN database and an in-house service evaluation database between February 2014 - June 2023 and 2 groups were identified:

- Empirical VP from 16 weeks' group
- USS-surveillance group

Following application of inclusion and exclusion criteria, final numbers were concluded and calculation of sPTB rates within each group was undertaken.

The cervical length trends for all patients included were evaluated, and in those patients who required further treatment (VP Group = 2nd line therapy; USS Only Group = 1st line therapy) the absolute number reduction (in mm) and % reduction difference in length between 2 measurements at the 'trigger point' of clinician decision to treat was plotted.

This was performed to assess any significant average difference between those already on VP vs those not on any treatment (USS-surveillance only).

REFERENCES

- Lancet: IPD meta-analysis: EPPPIC study. Stewart, LA. et al. (2021)
BMJ: Network systematic review and meta-analysis. Care, A. et al. (2022)
JAMA: systematic review and meta-analysis. Conde-Agudelo, A. et al. (2022)

CONCLUSION

- From our data, empirical VP from 16 weeks' confers a lower PTB rate <34 and <28 weeks when compared to USS-surveillance targeted therapy in women with a singleton pregnancy and a previous history of sPTB or PPROM <34 weeks.
- Our data suggests that there is a 47% reduction of risk of sPTB <28 weeks when using empirical VP from 16 weeks' compared to USS-indicated therapy (2.8% vs 4.8%).
- At present, a 37% reduction in CxL is what clinicians are willing to accept as a cut-off 'triggering' 1st line or additional treatment, which equates to -13mm.

Figure 1. Visualisation of study methodology and analysis of preterm birth rates by group

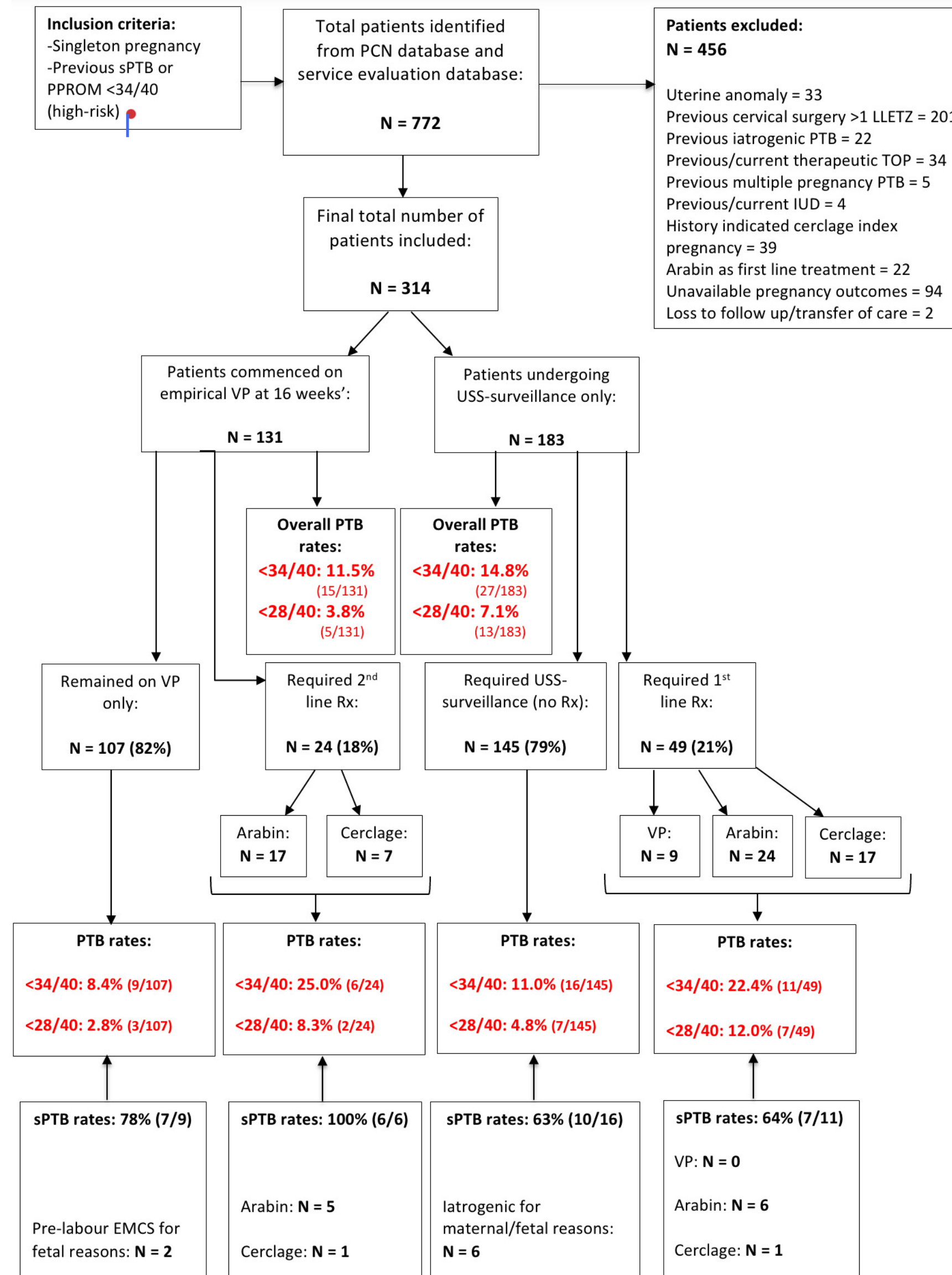


Figure 2. Number of patients offered Rx (VP + additional; USS-only + 1st line) by CxL reduction ie. the 'trigger' threshold, with corresponding averages and ranges of reduction

CxL measurement 'triggering' decision to treat with additional or 1st line Rx.	VP Group (N = 20)*	USS-surveillance Group (N = 49)
<10mm	2	4
11 - 14mm	5	11
15 - 19mm	1	9
20 - 24mm	7	19
>25mm	5	5
Mean reduction in CxL in mm and corresponding ranges	-12.95mm (+1 - -33mm)	-13.7mm (-4 - -42mm)
Mean reduction in CxL % and corresponding ranges	-36% (4% - -80%)	-38.8% (-13% - -86%)

*4 patients removed from original 24 patients in VP group as additional therapy was required at the 1st appointment in PTB prevention clinic for a short cervix <25mm

DISCUSSION

We have evaluated a specific group of pregnant women at high risk with singleton pregnancy where there remains clinical equipoise about current preventative treatments and understanding of the optimal timing to treat.

Principal findings relating to the objectives:

- In our data, when compared to USS-surveillance targeted therapy, empirical VP confers an overall lower preterm birth rate at both <34 weeks (11.5% vs 14.8%) and <28 weeks' (by 3.8% vs 7.1%) respectively.
- For women receiving VP the overall sPTB <28 weeks was 2.8% compared to 4.8% in women receiving USS-surveillance only (a comparative reduction of 47%).
- The average reduction in cervical length 'triggering' clinicians to offer medical treatment is -13mm, which was similar between both groups - with the most common overall length being between 20-24mm, with the choice of cervical cerclage being 2nd line treatment the preferred choice with a much shorter cervical length.

In 2017, a policy of commencing omega-3 supplementation in the above cohort of women was introduced, approximately 80% of the patients in the VP group were taking omega-3 from the data available in the PCN database.

This study informs the need for further research, namely in the form of an RCT to explore our findings of the effect of VP compared to USS-surveillance protocols, factoring in the potential contribution of omega-3 combination therapy, as conclusions cannot be drawn from this study.