



OBJECTIVES

Pregnancy of unknown location (PUL) affects 5–42% of women presenting to early pregnancy units. The M6 model uses serial hCG and progesterone to stratify PUL into low- and high-risk categories for ectopic pregnancy (EP). As progesterone is not universally available, this study compared the performance of M6 with progesterone (M6P) versus without progesterone (M6NP).



METHODS

A retrospective cohort of 651 women with PUL and adequate follow-up data was analysed. Both M6P and M6NP algorithms were applied using established EP risk thresholds. Sensitivity, specificity, overall accuracy, and AUC were calculated and ROC curves constructed to determine optimal thresholds.



RESULTS

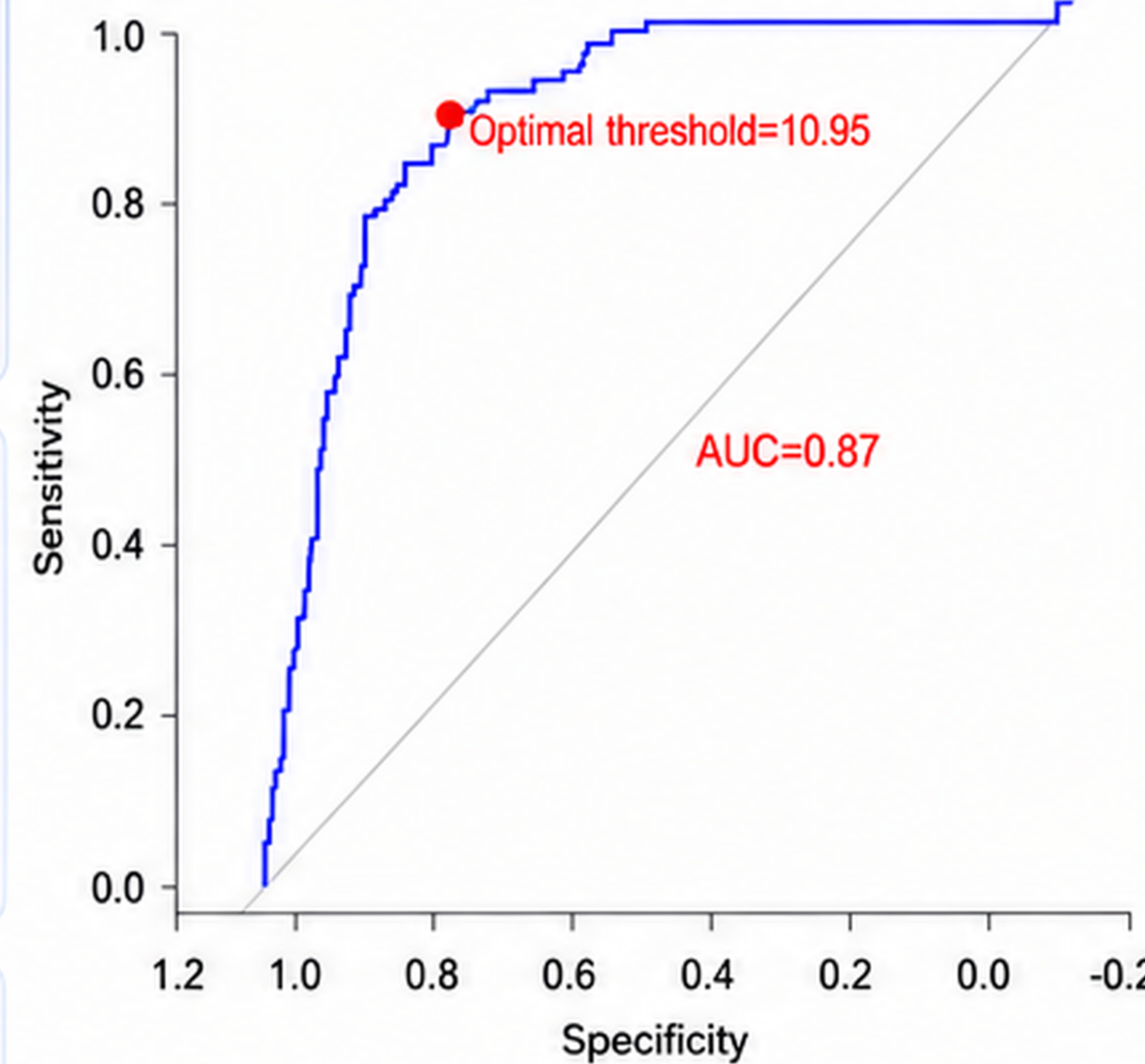
- M6P demonstrated superior overall accuracy compared to M6NP (80.49% vs 61.75%, $p < 0.0001$).
- At the clinically relevant 5% threshold, both models achieved identical sensitivity (88.61%), with M6P showing marginally superior specificity (68.18% vs 63.81%).
- At optimal thresholds, M6P achieved 86.08% sensitivity and 77.27% specificity (AUC 87%), whilst M6NP achieved 75.95% sensitivity and 83.22% specificity (AUC 85%, $p = 0.29$).



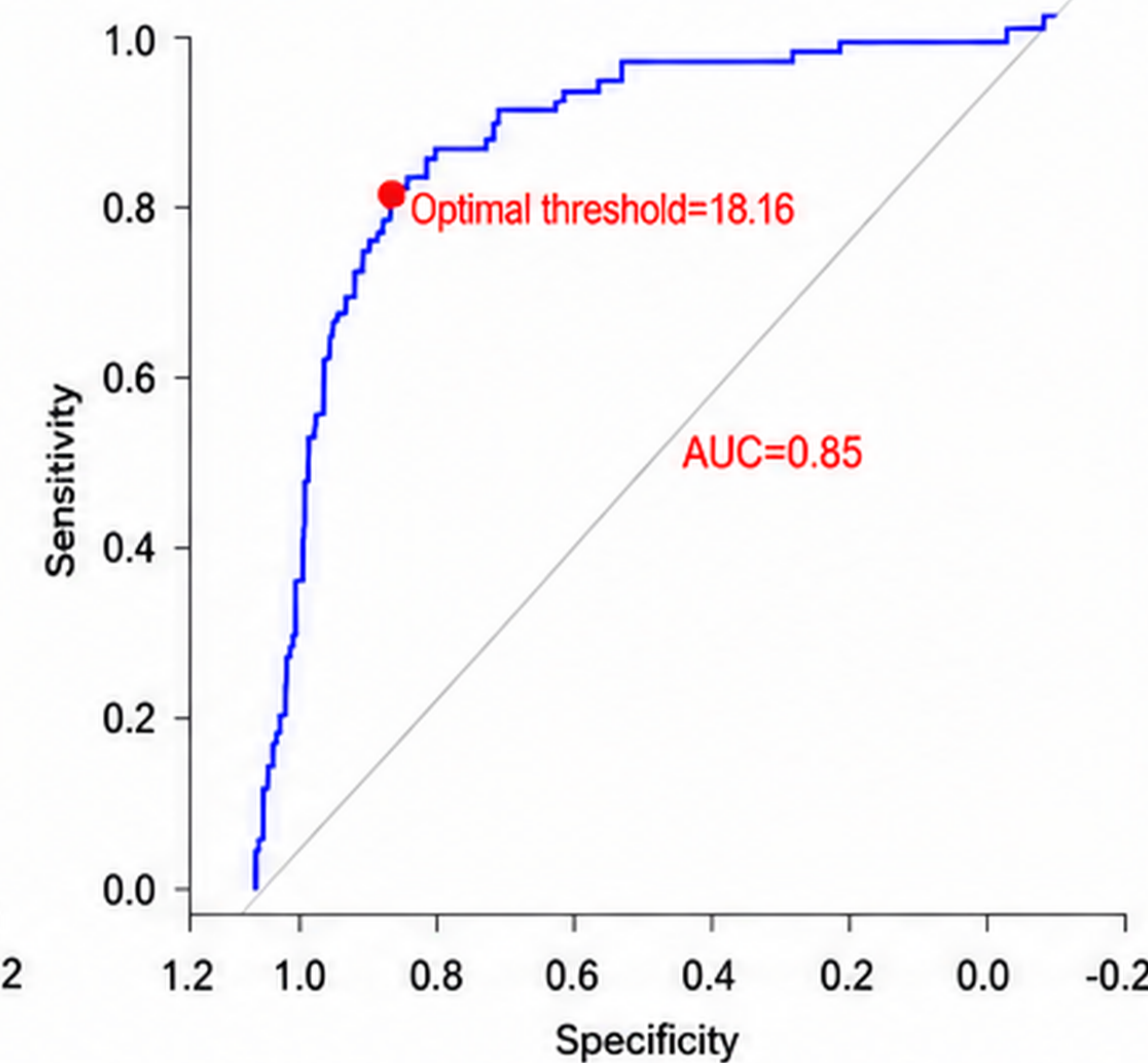
CONCLUSIONS

M6P and M6NP demonstrate equivalent EP detection sensitivity at the 5% threshold, confirming M6NP as a safe alternative when progesterone is unavailable. Given equivalent safety profiles and potential cost savings, M6NP merits consideration as standard practice for sustainable PUL management.

ROC curve with optimal threshold for EP with PRG



ROC curve with optimal threshold for EP without PRG



KEY TAKEAWAYS



At the clinically relevant 5% threshold, both models achieved identical sensitivity (88.61%).



M6P showed marginally superior specificity (68.18% vs 63.81%).



M6NP offers a safe, cost-effective alternative when progesterone is unavailable.

M6 MODEL PERFORMANCE COMPARISON

Metric	M6 with Progesterone (M6P)		M6 without Progesterone (M6NP)		p-value
	At 5% Threshold (Clinical)	At Optimal Threshold (Model-Derived)	At 5% Threshold (Clinical)	At Optimal Threshold (Model-Derived)	
Sensitivity (%)	88.61	86.08	88.61	75.95	0.29
Specificity (%)	68.18	77.27	63.81	83.22	0.29
Overall Accuracy (%)	80.49		61.75		<0.0001
AUC	0.87 (87%)		0.85 (85%)		0.29

PUL = Pregnancy of unknown location; EP = Ectopic pregnancy; hCG = Human chorionic gonadotrophin; PRG = Progesterone; AUC = Area under the curve; M6P = M6 model with progesterone; M6NP = M6 model without progesterone.