

The M6 risk prediction model and two-step strategy to characterize pregnancies of unknown location: a multicentre external validation study

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Abstract

Objective. To externally validate the M6 risk model and the two-step triage strategy (2ST) to triage pregnancies of unknown location (PUL), and compare performance with the M4 model and beta human chorionic gonadotropin (BhCG) ratio cut-offs. **Design.** Model validation study. **Setting.** Eight UK hospitals with early pregnancy assessment units. **Population.** Women presenting with a PUL and BhCG >25 IU/L. **Methods.** Women were managed using the 2ST protocol: step 1 classifies PUL as low risk of ectopic pregnancy (EP) if presenting progesterone ≥ 2 nmol/L, M6 is used as step 2 in the remaining cases. We validated 2ST and M6 alone (with and without progesterone as a predictor: M6P and M6NP). M6 and M4 require the BhCG ratio over two days. Based on these models, we classified PUL as high risk for EP when the risk was $\geq 5\%$. We meta-analysed centre-specific results. **Main outcome measures.** Discrimination, calibration and clinical utility (decision curve analysis) for predicting EP. **Results.** Of 2899 eligible women, the main analysis excluded 297 (10%) women that were lost to follow-up. 16% (95% confidence interval 12-20) of women had presenting progesterone ≥ 2 nmol/L. The area under the ROC curve for EP was 0.88 (0.86-0.90) for 2ST and 0.89 (0.86-0.91) for M6P. Sensitivity for EP was 94% (89%-97%) for 2ST and 96% (91%-98%) for M6P. Both approaches had good overall calibration, with modest variability between centres. M4 and BhCG ratio cut-offs had inferior performance and lower clinical utility. **Conclusions.** The 2ST and M6P alone are the best approaches to triage PUL.

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