

## EBM - Verdict

### Placental growth factor testing to assess women with suspected pre-eclampsia

*Pre-eclampsia diagnosis is currently made based on clinical signs including blood pressure and proteinuria measurements. A recent trial analysed the use of placental growth factor to assess women with suspected pre-eclampsia.*

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*EBM Verdict on: Placental growth factor testing to assess women with suspected pre-eclampsia: a multicentre, pragmatic, stepped-wedge cluster-randomised controlled trial. Lancet. 2019 May 4;393(10183):1807-1818. doi: 10.1016/S0140-6736(18)33212-4.*

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Pre-eclampsia occurs in 2 to 8% of pregnancies, and is a significant contributor to maternal morbidity and mortality, however the exact causes are unclear [1]. Current diagnosis is based on clinical features including hypertension and proteinuria, requiring regular monitoring [2]. Low circulating concentration of placental growth factor (PIGF), an angiogenic factor, has been shown to have a high sensitivity and negative predictive value for pre-eclampsia, suggesting PIGF could be a useful test in women with suspected preeclampsia [3].

The stepped-wedge cluster-randomised controlled trial aimed to determine whether knowledge of the circulating concentration of placental growth factor (PIGF), integrated with a clinical management algorithm, decreased the time for clinicians to make a diagnosis in suspected pre-eclampsia, and whether this approach reduced subsequent maternal or perinatal adverse outcomes.

The trial was performed in 11 UK maternity units and included 1,023 women aged 18 years and older with singleton pregnancy presenting with suspected pre-eclampsia at 20 to 36 weeks gestation [4]. At the start of the trial all participants had PIGF measurements, which were concealed from clinicians and women. PIGF measurements were revealed at the initiation time of the intervention for each successive block and used alongside usual care, which consisted of a clinical management algorithm based on the National Institute for Health and Care Excellence (NICE) guidelines [5]. In the comparator group PIGF tests were concealed. The primary outcome was time from presentation with suspected pre-eclampsia to documented pre-eclampsia.

The median time to pre-eclampsia diagnosis was ~2 days shorter in the revealed testing group compared with concealed testing (1.9 days [IQR 0.5–9.2] vs. 4.1 days [IQR 0.8–14.7]) respectively. Use of PIGF testing was also associated with fewer maternal severe adverse outcomes, defined as maternal mortality or one or more serious CNS, cardiorespiratory, hepatic, renal, or haematological morbidity (22 [4%] vs 24 [5%] events; adjusted odds ratio 0.32, 95% CI 0.11–0.96; p=0.043). There were five serious events (two eclamptic fits, two strokes, and one cardiac arrest in four women, all of whom had low PIGF concentrations) in the concealed testing group, with no similarly serious events in the revealed testing group. A higher proportion of women in the concealed testing group than the revealed testing group received transfusion of blood products (14 [3%] vs 9 [2%]).

Of the several secondary outcomes assessed no differences were observed in gestational age at delivery, perinatal adverse outcomes, prevalence of spontaneous vaginal delivery or the use of caesarean sections. However, more women in the intervention group received a scan (77% vs 69%).

The use of a step-wedge cluster randomisation in blocks and intention to treat analysis strengthens the analysis, although due to the nature of the intervention it was not masked to clinicians. The step-wedge design may have introduced some selection bias due to lower recruitment in the early months relative to later months [6].

Trials to assess the effects of diagnostic tests on clinical care and patient outcomes are uncommon and as a consequence many tests are implemented in practice without robust evidence [7]. Assessing the test in a real-world setting and assessing the effect on the clinical pathway and health outcomes strengthens the generalisability of the results. Based on this research placental growth factor blood tests for pre-eclampsia are to be made more widely available in the UK [8]. It should, however, be noted that the trial did not include women with multiple foetuses nor those presenting with late-onset pre-eclampsia. The study was conducted in a high resource setting and findings may not be applicable to other settings.

**EBM Verdict:** Placental growth factor measurement improves pre-eclampsia diagnosis and management, reducing time-to-diagnosis and improving maternal outcomes.

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### Declaration of interests

AP reports grants from NIHR, grants from NIHR School of Primary Care Research, and occasionally receives expenses for teaching Evidence-Based Medicine.

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