Title

Extending the scope of individual patient data meta-analyses: merging algorithms for biomarker measurements from heterogeneous laboratory platforms. The CoLAB Preeclampsia Angiogenic Factor Study.

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Abstract

Objectives: Circulating placental growth factor (PlGF) is a potential biomarker for preeclampsia. Prior studies show its limited precision in predicting or diagnosing preeclampsia, underscoring a common problem in biomarker data analyses in general - that large studies are needed to overcome clinical heterogeneity and to provide sufficient statistical power. Attaining such sample sizes often requires aggregation of cohorts. Different studies may use disparate platforms for laboratory analyses, complicating data merging. Here, we assessed whether PlGF concentrations could be merged across studies using inter-platform standardization.

Methods: Of 16516 pregnancies from 23 cohorts, 12804 had at least one PlGF concentration (gestational age >20 weeks), analysed using one of four platforms: R&D Systems, Alere-Triage, Roche-Elecsys or Abbott-Architect. Two merging algorithms, using Z-Score or Multiple of Median (MOM) transformations, were applied. A single Best Reference Curve (BRC), based on merged non-case PlGF concentrations, was constructed. Case-identification performance of the BRC for PlGF was compared to platform-specific curves.

Results: PlGF concentrations from different analytical platforms were merged (Z-scores marginally better than MOMs) and, overall, BRC case-identification rates out-performed platform-specific curves.

Conclusion: Laboratory measurements from different platforms can be standardised and merged to give reference curves from aggregated PlGF datasets. This method allows for analysis of PlGF as a diagnostic marker for preeclampsia and is generalisable to other medical questions, thereby extending the scope of individual studies to answer a variety of important medical questions.