



## ORIGINAL RESEARCH ARTICLE

# Comparing the results from a Swedish pregnancy cohort using data from three automated placental growth factor immunoassay platforms intended for first-trimester preeclampsia prediction

Ylva Carlsson<sup>1,2</sup>  | Anna Sandström<sup>3,4</sup>  | Lina Bergman<sup>1,5</sup> | Peter Conner<sup>4,6</sup> | Stefan Hansson<sup>7</sup> | Marius Kublicka<sup>8</sup> | Uzay Görmüş<sup>9</sup> | Peter Lindgren<sup>8</sup> | Göran Oleröd<sup>10</sup> | Anna-Karin Wikström<sup>11</sup> | Anders Larsson<sup>12</sup>

<sup>1</sup>Department of Obstetrics and Gynecology, Region Västra Götaland, Sahlgrenska University Hospital, Gothenburg, Sweden

<sup>2</sup>Center of Perinatal Medicine and Health, Institute of Clinical Sciences, University of Gothenburg, Gothenburg, Sweden

<sup>3</sup>Clinical Epidemiology Division, Department of Medicine, Solna, Karolinska Institute, Stockholm, Sweden

<sup>4</sup>Department of Women's Health, Division of Obstetrics, Karolinska University Hospital, Stockholm, Sweden

<sup>5</sup>Department of Obstetrics and Gynecology, Institute of Clinical Sciences, University of Gothenburg, Gothenburg, Sweden

<sup>6</sup>Department of Women's and Children's Health, Karolinska Institute and Center for Fetal Medicine, Karolinska University Hospital, Stockholm, Sweden

<sup>7</sup>Department of Clinical Sciences Lund, Obstetrics and Gynecology, Lund University and Skåne University Hospital, Lund/Malmö, Sweden

<sup>8</sup>Department of Clinical Science, Intervention and Technology – CLINTEC, Karolinska Institutet and Center for Fetal Medicine, Karolinska University Hospital, Stockholm, Sweden

<sup>9</sup>PerkinElmer Genomics, Stockholm, Sweden

<sup>10</sup>Department of Clinical Chemistry, Sahlgrenska University Hospital, Gothenburg, Sweden

<sup>11</sup>Department of Women's and Children's Health, Uppsala University, Uppsala, Sweden

<sup>12</sup>Department of Medical Sciences, Clinical Chemistry, Uppsala University, Uppsala, Sweden

## Correspondence

Ylva Carlsson, Department of Obstetrics, Östra/Sahlgrenska University Hospital, Diagnosvägen 14, 416 85 Gothenburg, Sweden.

Email: [ylva.carlsson.2@obgyn.gu.se](mailto:ylva.carlsson.2@obgyn.gu.se)

## Funding information

Frimurarfonden Barnhusdirektionen Foundation, Grant/Award Number: YC GLS 7000991; Region Skåne Research funds, Grant/Award Number: SH 2020-0281; Regional research funds Uppsala/Örebro region, Grant/Award Number: LB AK RFR-839171 930161; Stiftelsen Handlanden Hjalmar Svenssons, Grant/Award Number: YC 2021; Stiftelsen Mary von Sydows, född Wijk, donationsfond: YC; Stiftelserna Wilhelm och Martina

## Abstract

**Introduction:** Risk evaluation for preeclampsia in early pregnancy allows identification of women at high risk. Prediction models for preeclampsia often include circulating concentrations of placental growth factor (PIGF); however, the models are usually limited to a specific PIGF method of analysis. The aim of this study was to compare three different PIGF methods of analysis in a Swedish cohort to assess their convergent validity and appropriateness for use in preeclampsia risk prediction models in the first trimester of pregnancy.

**Material and methods:** First-trimester blood samples were collected in gestational week 11<sup>+0</sup> to 13<sup>+6</sup> from 150 pregnant women at Uppsala University Hospital during November 2018 until November 2020. These samples were analyzed using the

**Abbreviations:** PIGF, placental growth factor; sFlt-1, soluble fms-like tyrosine kinase-1; VEGF, vascular endothelial growth factor; VEGF R1, VEGF receptor 1.

This is an open access article under the terms of the [Creative Commons Attribution-NonCommercial-NoDerivs](https://creativecommons.org/licenses/by-nc-nd/4.0/) License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2023 The Authors. *Acta Obstetrica et Gynecologica Scandinavica* published by John Wiley & Sons Ltd on behalf of Nordic Federation of Societies of Obstetrics and Gynecology (NFOG).

Lundgrens, Grant/Award Number: YC 2018-2094; Swedish state under the agreement between the Swedish government and the county councils, the ALF agreement, Grant/Award Number: YCALFGBG-77860, ALFGBG-75710 and ASALFStockholm-590448; The Gothenburg Society of Medicine, Grant/Award Number: YC GLS-973367; The Healthcare Board, Region Västra Götaland, Grant/Award Number: YC 931960, YC 968567 and YC 979810; The Swedish Medical Society, Grant/Award Number: YC 2022

different PIGF methods from Perkin Elmer, Roche Diagnostics, and Thermo Fisher Scientific.

**Results:** There were strong correlations between the PIGF results obtained with the three methods, but the slopes of the correlations clearly differed from 1.0:  $\text{PIGF}_{\text{PerkinElmer}} = 0.553$  (95% confidence interval [CI] 0.518–0.588) \*  $\text{PIGF}_{\text{Roche}} - 1.112$  (95% CI -2.773 to 0.550);  $r = 0.966$ , mean difference -24.6 (95% CI -26.4 to -22.8).  $\text{PIGF}_{\text{PerkinElmer}} = 0.673$  (95% CI 0.618–0.729) \*  $\text{PIGF}_{\text{ThermoFisher}} - 0.199$  (95% CI -2.292 to 1.894);  $r = 0.945$ , mean difference -13.8 (95% CI -15.1 to -12.6).  $\text{PIGF}_{\text{Roche}} = 1.809$  (95% CI 1.694–1.923) \*  $\text{PIGF}_{\text{PerkinElmer}} + 2.010$  (95% CI -0.877 to 4.897);  $r = 0.966$ , mean difference 24.6 (95% CI 22.8–26.4).  $\text{PIGF}_{\text{Roche}} = 1.237$  (95% CI 1.113–1.361) \*  $\text{PIGF}_{\text{ThermoFisher}} + 0.840$  (95% CI -3.684 to 5.363);  $r = 0.937$ , mean difference 10.8 (95% CI 9.4–12.1).  $\text{PIGF}_{\text{ThermoFisher}} = 1.485$  (95% CI 1.363–1.607) \*  $\text{PIGF}_{\text{PerkinElmer}} + 0.296$  (95% CI -2.784 to 3.375);  $r = 0.945$ , mean difference 13.8 (95% CI 12.6–15.1).  $\text{PIGF}_{\text{ThermoFisher}} = 0.808$  (95% CI 0.726–0.891) \*  $\text{PIGF}_{\text{Roche}} - 0.679$  (95% CI -4.456 to 3.099);  $r = 0.937$ , mean difference -10.8 (95% CI -12.1 to -9.4).

**Conclusion:** The three PIGF methods have different calibrations. This is most likely due to the lack of an internationally accepted reference material for PIGF. Despite different calibrations, the Deming regression analysis indicated good agreement between the three methods, which suggests that results from one method may be converted to the others and hence used in first-trimester prediction models for preeclampsia.

#### KEYWORDS

first-trimester screening, method comparison, method correlation, preeclampsia, PIGF, placental growth factor, screening, ultrasound

## 1 | INTRODUCTION

Preeclampsia occurs in 3%–5% of all pregnancies in western high-income countries,<sup>1</sup> and is one of the main causes of maternal and perinatal morbidity and mortality.<sup>2,3</sup> Identification of women at risk is important since early detection of preeclampsia has been shown to benefit the mother and the unborn child.<sup>4</sup> In addition, prophylactic aspirin treatment initiated in early pregnancy to high-risk pregnancies decreases the incidence of preeclampsia up to 40%.<sup>5</sup> Different multivariable preeclampsia prediction models have been developed using a combination of maternal characteristics, medical history, biophysical examinations and blood-based biomarkers.<sup>6</sup>

One important blood-based biomarker for preeclampsia prediction is placental growth factor (PIGF). PIGF is mainly expressed in the human placenta and umbilical cord during normal pregnancy conditions.<sup>7,8</sup> PIGF belongs to the vascular endothelial growth factor (VEGF) family involved in angiogenesis as well as the development and maintenance of the vascular and lymphatic endothelia. PIGF consists of 149 amino acids and binds to both membrane-bound and soluble VEGF receptor 1 (VEGF R1), also called soluble fms-like tyrosine kinase-1 (sFlt-1). In a non-preeclamptic pregnancy, there is a clear increase in circulating PIGF levels from gestational week 14, reaching peak values at gestational weeks 27–30. After gestational

#### Key message

Placental growth factor (PIGF) is often used in algorithms for first-trimester prediction of preeclampsia. PIGF methods have different calibrations but there is good consistency between the three methods, allowing conversion of results from one method to another.

week 30, the PIGF values starts to decline.<sup>9</sup> Circulating concentrations of PIGF are decreased in the first trimester in women who later in pregnancy develop preeclampsia<sup>10</sup> and intrauterine growth restriction.<sup>11</sup>

Placental growth factor is currently included in several different prediction models for preeclampsia.<sup>12–14</sup> There is no internationally accepted calibrator for PIGF, leading to variable test results obtained from different laboratory platforms. The introduction of international reference standards is intended to reduce, if not eliminate, the calibration differences between different manufacturers.

Today, the main manufacturers of immune-based PIGF analysis for clinical use are PerkinElmer, Roche Diagnostics and Thermo Fisher Scientific.

The objective of this study was to compare assay results obtained with the existing analytic platforms for determining circulating PIGF concentrations and to develop equations for converting PIGF results obtained with the different methods.

## 2 | MATERIAL AND METHODS

This is an observational study comparing three different methods used to analyze PIGF from maternal serum of 150 pregnant women. Women were recruited within the IMPACT study<sup>15</sup> in gestational weeks 11<sup>+0</sup> to 13<sup>+6</sup> at Uppsala University Hospital's ultrasound department between November 2018 and November 2020. In Uppsala County, all obstetric ultrasound scans are performed at Uppsala University Hospital, and all pregnant women are offered a first-trimester combined ultrasound and biochemical scan with an 80% acceptance rate. The women were included in the study after receiving written and oral information. Women who did not speak Swedish or were under 18 years of age were excluded from the study.

Serum samples were randomly chosen from the larger IMPACT study cohort and frozen at  $-80^{\circ}\text{C}$ . For analysis of PIGF, samples were thawed, mixed, and centrifuged at 2400g for 10min before they were divided into three aliquots and subsequently frozen for shipment. The samples were sent to Stockholm, Uppsala, and Gothenburg to be analyzed by the platforms provided by Perkin Elmer, Roche Diagnostics, and Thermo Fisher, respectively. The time to assay was less than 2 months from shipment.

Delfia Express® Model: 6000-0010 (PerkinElmer, Turku, Finland) was used in Stockholm, Roche Diagnostics cobas e 601 analyzer (Roche Diagnostics GmbH, Mannheim, Germany) was used in Uppsala while BRAHMS PIGF plus KRYPTOR (Thermo Fisher Scientific, Hennigsdorf, Germany) was used in Gothenburg.

### 2.1 | Statistical analyses

Method comparisons were performed using Deming regression analysis and the software Method Validator (Metz, France). The three methods were compared pairwise using linear regression and Deming analysis.

### 2.2 | Ethics statement

The study was performed according to the Helsinki Declaration and informed consent was obtained. Confidentiality aspects such as data encryption and storage comply with the General Data Protection Regulation and with ethical committee requirements. This study has been granted national ethical approval by the Uppsala Ethics Committee (2018/231, 2020-00319, 2022-05690-02) on July 4, 2018, February 12, 2020, and November 21, 2022 and national biobank approval at Uppsala Biobank (18237 22018 231).

## 3 | RESULTS

### 3.1 | General characteristics of the population

The women included were part of the IMPACT study, a population-based cohort. All women were living in Uppsala County, including both urban and rural areas. In the county, the prevalence of preeclampsia is around 3%, 80% of the pregnant population is born in the Nordic countries, mean age at pregnancy is 30 years, 5% are smokers, mean body mass index at the beginning of pregnancy is 25 kg/m<sup>2</sup>, and 47% have an education of more than 12 years.<sup>16</sup>

### 3.2 | Method comparison Perkin Elmer and Roche Diagnostics

The Roche Diagnostics method gave approximately 80% higher values than the Perkin Elmer method. The 95% confidence interval [CI] of the intercept was not significantly different from 0 and the methods showed an *r* value for the correlation of 0.966 (Figure 1).

$\text{PIGF}_{\text{PerkinElmer}} = 0.553$  (95% CI 0.518–0.588) \*  $\text{PIGF}_{\text{Roche}} - 1.112$  (95% CI  $-2.773$  to 0.550);  $r = 0.966$ , mean difference  $-24.6$  (95% CI  $-26.4$  to  $-22.8$ ).

$\text{PIGF}_{\text{Roche}} = 1.809$  (95% CI 1.694–1.923) \*  $\text{PIGF}_{\text{PerkinElmer}} + 2.010$  (95% CI  $-0.877$  to 4.897);  $r = 0.966$ , mean difference 24.6 (95% CI 22.8–26.4).

### 3.3 | Method comparison Perkin Elmer and Thermo Fisher

The Thermo Fisher method gave close to 50% higher values than the Perkin Elmer method. The 95% CI of the intercept was not significantly different from 0 and the methods showed an *r* value for the correlation of 0.945 (Figure 2).

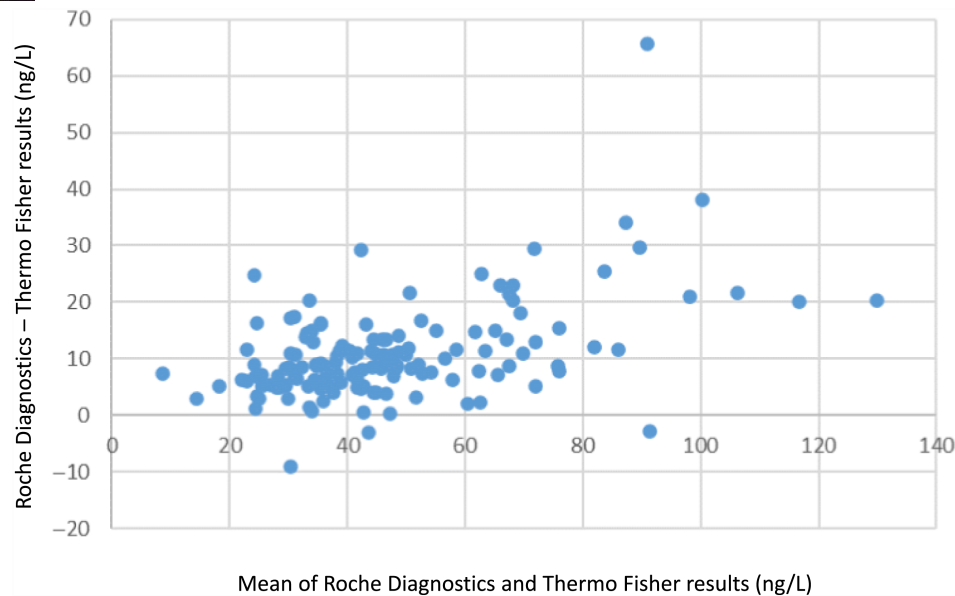
$\text{PIGF}_{\text{PerkinElmer}} = 0.673$  (95% CI 0.618–0.729) \*  $\text{PIGF}_{\text{ThermoFisher}} - 0.199$  (95% CI  $-2.292$  to 1.894);  $r = 0.945$ , mean difference  $-13.8$  ( $-15.1$  to  $-12.6$ ).

$\text{PIGF}_{\text{ThermoFisher}} = 1.485$  (95% CI 1.363–1.607) \*  $\text{PIGF}_{\text{PerkinElmer}} + 0.296$  (95% CI  $-2.784$  to 3.375);  $r = 0.945$ , mean difference 13.8 (95% CI 12.6–15.1).

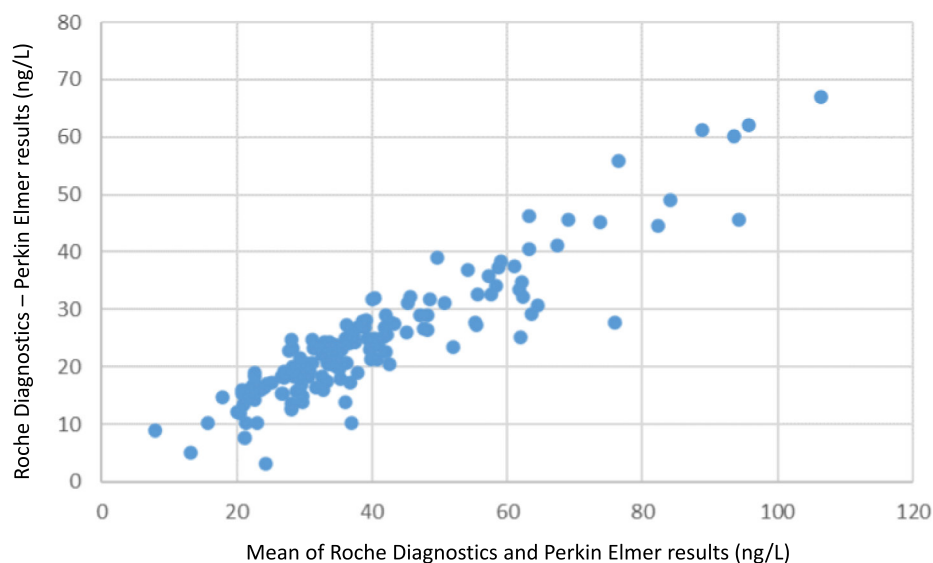
### 3.4 | Method comparison Roche Diagnostics and Thermo Fisher

The Roche Diagnostics method gave approximately 24% higher values than the Thermo Fisher method. The 95% CI of the intercept was not significantly different from 0 and the methods showed an *r* value for the correlation of 0.937 (Figure 3).

$\text{PIGF}_{\text{Roche}} = 1.237$  (95% CI 1.113–1.361) \*  $\text{PIGF}_{\text{ThermoFisher}} + 0.840$  (95% CI  $-3.684$  to 5.363);  $r = 0.937$ , mean difference 10.8 (95% CI 9.4–12.1).



**FIGURE 1** Bland Altman plot showing the mean of Roche Diagnostics and Thermo Fisher placental growth factor results on the x-axis and the difference between Roche Diagnostics and Thermo Fisher results on the y-axis. The values are shown in ng/L.



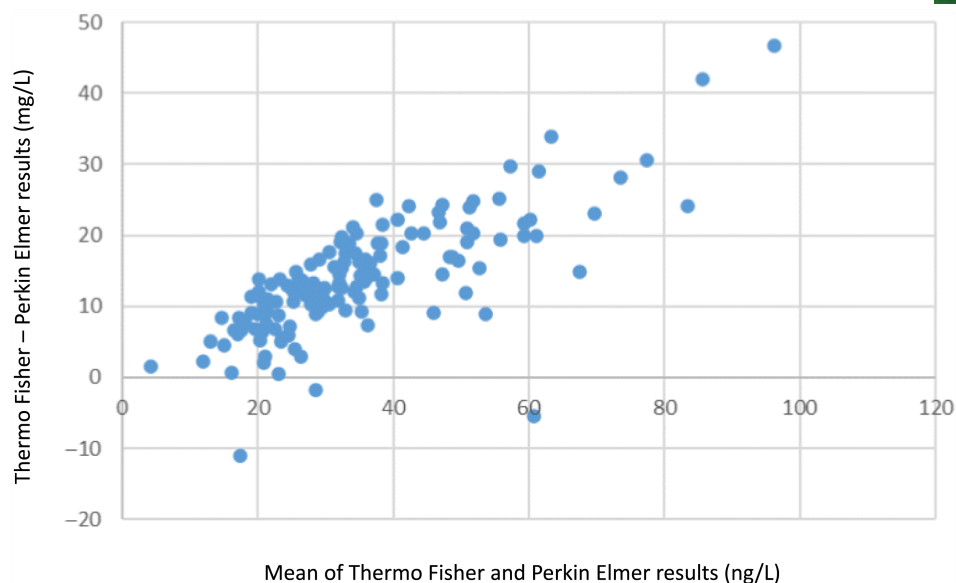
**FIGURE 2** Bland Altman plot showing the mean of Roche Diagnostics and Perkin Elmer placental growth factor results on the x-axis and the difference between Roche Diagnostics and Perkin Elmer results on the y-axis. The values are shown in ng/L.

$PIGF_{\text{ThermoFisher}} = 0.808 \text{ (95\% CI } 0.726\text{--}0.891) * PIGF_{\text{Roche}} - 0.679$   
(95\% CI  $-4.456$  to  $3.099$ );  $r=0.937$ , mean difference  $-10.8$  (95\% CI  $-12.1$  to  $-9.4$ ).

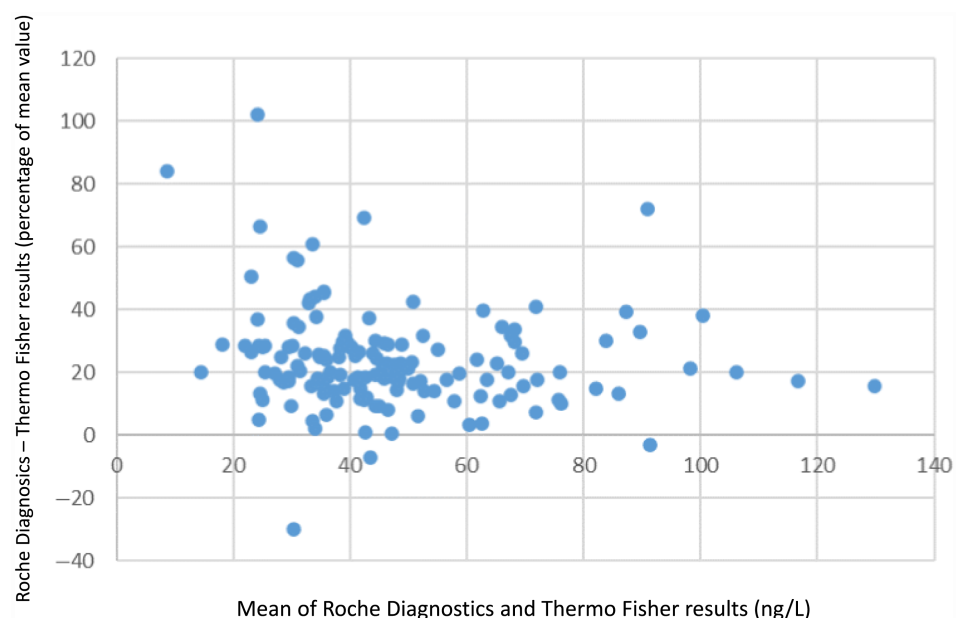
## 4 | DISCUSSION

In the present study we show that the choice of PIGF method has a clear impact on the PIGF results. However, the  $r$  values were high, indicating that it might be possible to convert the PIGF results to allow for the comparison and merging of data generated by the three assays used in this study (see [Figures 4–6](#)).

Placental growth factor is currently used in prediction models for preeclampsia and all different platforms are used in, for example, the Fetal Medicine Foundation model.<sup>13,17,18</sup> However, the focus has not been on comparing individual serum sample aliquots with all three major clinically used PIGF methods during first trimester. There are some studies comparing PIGF concentrations collected late in pregnancy.<sup>19,20</sup> One previous study, where the authors studied PIGF and VEGF R1 in pregnant women with preeclampsia/HELLP syndrome (hemolysis, elevated liver enzymes, low platelets), revealed differences in PIGF calibration between the Roche Diagnostics and Thermo Fisher methods during late pregnancy.<sup>21</sup> The median gestational length was 32 weeks for the



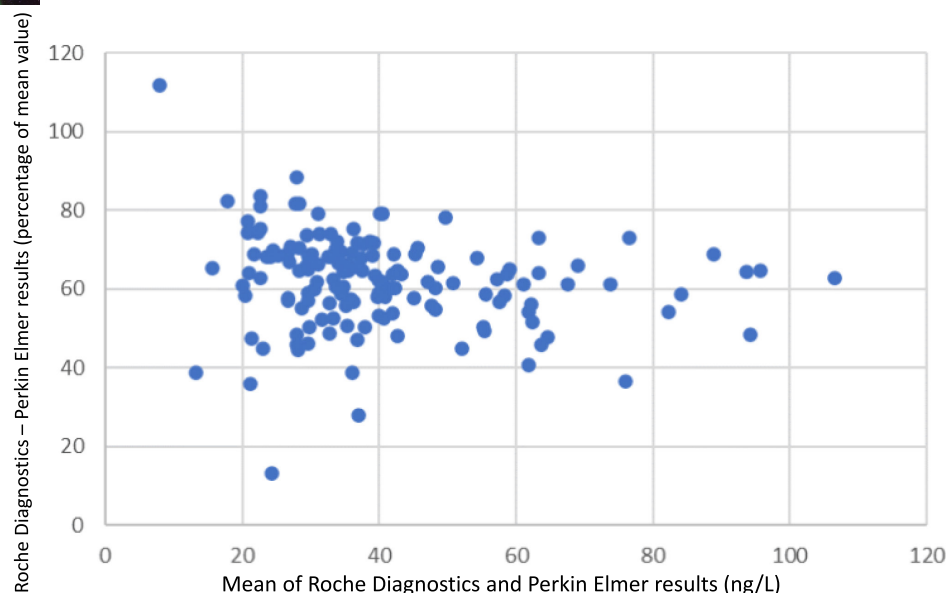
**FIGURE 3** Bland Altman plot showing the mean of Thermo Fisher and Perkin Elmer placental growth factor results on the x-axis and the difference between Thermo Fisher and Perkin Elmer results on the y-axis. The values are presented in ng/L.



**FIGURE 4** Bland Altman plot showing the mean of Roche Diagnostics and Thermo Fisher placental growth factor results on the x-axis and the difference between Roche Diagnostics and Thermo Fisher results on the y-axis. The difference on the y-axis is presented as percentages of the mean values.

early-onset preeclampsia group and 38 weeks for the late-onset group. Soluble VEGF R1 (or sFlt-1) binds to PIGF and could potentially interfere by hiding the antibody-binding epitopes when analyzing PIGF. Soluble VEGF R1 increases rapidly during pregnancy.<sup>9</sup> The ratio between PIGF and VEGF R1 will therefore vary depending on the gestational week and the presence of preeclampsia. Depending on the binding sites of the antibodies in the assays, this may interfere with the results of individual assays. Hence, the relationships between different PIGF methods in previous

preeclampsia studies may not be valid when used for early pregnancy prediction. Another factor that makes it difficult to use data from method comparisons from different gestational weeks is that PIGF is glycosylated. Glycosylation is the most common of the post-translational modifications of proteins. Glycosylation affects antibody binding for antibodies that are bound to glycosylated regions influencing the assay results.<sup>22</sup> Previous studies have shown that the glycosylation varies with week of gestation. The changes in transferrin glycosylation can increase disialotransferrin



**FIGURE 5** Bland Altman plot showing the mean of Roche Diagnostics and Perkin Elmer placental growth factor results on the x-axis and the difference between Roche Diagnostics and Perkin-Elmer results on the y-axis. The difference on the y-axis is presented as percentages of the mean values.



**FIGURE 6** Bland Altman plot showing the mean of Thermo Fisher and Perkin Elmer placental growth factor results on the x-axis and the difference between Thermo Fisher and Perkin Elmer results on the y-axis. The difference on the y-axis is presented as percentages of the mean values.

by approximately 50% before delivery.<sup>23</sup> This means that the correlation between different immunoassays may vary with week of gestation.

We investigated the potential instruments for PIGF testing in Sweden and evaluated those supplied by three of the largest suppliers used clinically in Sweden and internationally: PerkinElmer, Roche Diagnostics, and Thermo Fisher.

As of 2022 PIGF is a recommended biomarker in several international guidelines for preeclampsia management.<sup>24</sup> In theory, the PIGF assays could be centralized to a single laboratory in Sweden,

but it would lead to longer test-turnaround times and additional costs for transportation. Considering turnaround times, costs, and the number of PIGF assays needed to test all pregnant women in a first-trimester preeclampsia prediction model, PIGF testing will most likely continue at a county level. Hence, PerkinElmer, Roche Diagnostics, or Thermo Fisher instrumentation would be chosen depending on the laboratory instrumentation available in the county. This means that there is a need to convert test results from one platform to the others to allow for a comparable cut-off /threshold level.



To be able to use results from different manufacturers it is important to know the difference in slopes and intercepts between the methods. This is also of importance when interpreting results from scientific publications conducted with various PIGF methods. The linear regression equations presented in this article can be used as a direct translation between different commonly used PIGF platforms to facilitate the incorporation of PIGF into clinical prediction models. A strength of this study is that it used the same aliquot for all three methods and the samples were handled in the same way for all three assays. The samples were also from the preferred gestational age span (gestational weeks 12–14) for preeclampsia prediction.<sup>25</sup>

We acknowledge that our study has limitations. One limitation is that the samples were frozen and thawed twice to ensure that they were handled identically for all three assays. The extra freezing–thawing cycle could influence the results but would most probably not affect the relation of the results between the different platforms.<sup>26</sup> We also acknowledge that all immunoassays can show lot-to-lot variation. In this study only one lot was used. All females recruited were Swedish residents with mainly Caucasian ethnicity, so it is uncertain whether the results are applicable to other ethnic groups, especially since the number of samples ( $n=150$ ) was limited. However, the high correlation is a strong indication that the results can be transferred to larger populations.

The different calibrations will most likely occasionally cause erroneous conclusions. It would therefore be valuable to have an international reference material to reduce method differences. However, this may take years to obtain and until then we need to use equations to align the results of the different methods when they are used in prediction algorithms.

## 5 | CONCLUSION

Our results indicate that the commercial analytic platforms produced by Perkin Elmer, Roche Diagnostics, and Thermo Fisher for determining circulating PIGF concentrations have different calibrations. Despite this, there is good agreement between the three methods, which may allow for converting and then comparing results obtained from the different platforms. We encourage future research to develop conversion equations so that PIGF results from different manufacturers can be used interchangeably in first-trimester preeclampsia prediction models.

## AUTHOR CONTRIBUTIONS

AL, YC, AKW, and AS conceived and designed the study. AL, UG, and GO collected all data. AL, YC, and AKW analyzed the data. YC and AL wrote the manuscript and all authors provided intellectual input and approved the manuscript.

## ACKNOWLEDGMENTS

We thank Liza Oraha, MSc, Perkin Elmer, Roche Diagnostics, and Thermo Fisher for providing the PIGF reagents for the study. We

also thank Associate Professor Erik Hunter for his valuable language check.

## FUNDING INFORMATION

This work was supported by The Healthcare Board, Region Västra Götaland (YC, 931960, 968567, 979810), The Swedish Medical Society (YC, 2022), The Gothenburg Society of Medicine (YC, GLS-973367), Frimurarfonden Barnhusdirektionen Foundation (YC, GLS 7000991), Wilhelm and Martina Lundgren foundation (YC 2018–2094), Hjalmar Svensson Foundation (YC, 2021), Mary von Sydow Foundation (YC, 2021), Regional research funds Uppsala/Örebro region (LB, AK RFR-839171, 930161), Center for clinical research, Falun (LB, CKFUU 795621, 895291) and Region Skåne Research funds (SH, 2020–0281). The study was also financed by grants from the Swedish state under the agreement between the Swedish government and the county councils, the ALF agreement (YC, ALFGBG-77860, 75710; AS, ALFStockholm-590448).

## CONFLICT OF INTEREST STATEMENT

Perkin Elmer, Roche Diagnostics and Thermo Fisher provided reagents used in this study for the analysis of placental growth factor free of charge. Roche Diagnostics and Thermo Fisher also contributed to analyses of placental growth factor (labor costs). YC is currently an employee of AstraZeneca.

## ORCID

Ylva Carlsson  <https://orcid.org/0000-0002-1414-7279>

Anna Sandström  <https://orcid.org/0000-0003-2879-4271>

## REFERENCES

- Chappell LC, Cluver CA, Kingdom J, Tong S. Pre-eclampsia. *Lancet*. 2021;398:341–354.
- Mol BWJ, Roberts CT, Thangaratinam S, Magee LA, de Groot CJM, Hofmeyr GJ. Pre-eclampsia. *Lancet*. 2016;387:999–1011.
- Grunewald C, Esscher A, Lutvica A, Paren L, Saltvedt S. Mödradöd i Sverige: Vården hade många gånger kunnat vara bättre - Lärdomar från 11 års extern kollegial granskning. [Maternal deaths in Sweden: diagnostics and clinical management could be improved]. In Swedish. *Lakartidningen*. 2019;116:FPL4.
- Organization WWH. In: Committee WGAAbtGR, ed. *WHO Recommendations for Prevention and Treatment of Pre-Eclampsia and Eclampsia*. World Health Organization; 2011.
- Rolnik DL, Wright D, Poon LC, et al. Aspirin versus placebo in pregnancies at high risk for preterm preeclampsia. *N Engl J Med*. 2017;377:613–622.
- Akolekar R, Syngelaki A, Poon L, Wright D, Nicolaides KH. Competing risks model in early screening for preeclampsia by biophysical and biochemical markers. *Fetal Diagn Ther*. 2013;33:8–15.
- Gu Y, Lewis DF, Wang Y. Placental productions and expressions of soluble endoglin, soluble fms-like tyrosine kinase receptor-1, and placental growth factor in normal and preeclamptic pregnancies. *J Clin Endocrinol Metab*. 2008;93:260–266.
- Kingdom J, Huppertz B, Seaward G, Kaufmann P. Development of the placental villous tree and its consequences for fetal growth. *Eur J Obstet Gynecol Reprod Biol*. 2000;92:35–43.
- Palm M, Basu S, Larsson A, Wernroth L, Akerud H, Axelsson O. A longitudinal study of plasma levels of soluble fms-like tyrosine kinase 1 (sFlt1), placental growth factor (PIGF), sFlt1: PIGF ratio and

- vascular endothelial growth factor (VEGF-A) in normal pregnancy. *Acta Obstet Gynecol Scand*. 2011;90:1244-1251.
10. Romero R, Nien JK, Espinoza J, et al. A longitudinal study of angiogenic (placental growth factor) and anti-angiogenic (soluble endoglin and soluble vascular endothelial growth factor receptor-1) factors in normal pregnancy and patients destined to develop pre-eclampsia and deliver a small for gestational age neonate. *J Matern Fetal Neonatal Med*. 2008;21:9-23.
  11. Asvold BO, Vatten LJ, Romundstad PR, Jenum PA, Karumanchi SA, Eskild A. Angiogenic factors in maternal circulation and the risk of severe fetal growth restriction. *Am J Epidemiol*. 2011;173:630-639.
  12. O'Gorman N, Wright D, Poon LC, et al. Multicenter screening for pre-eclampsia by maternal factors and biomarkers at 11-13 weeks' gestation: comparison with NICE guidelines and ACOG recommendations. *Ultrasound Obstet Gynecol*. 2017;49:756-760.
  13. Tan MY, Syngelaki A, Poon LC, et al. Screening for pre-eclampsia by maternal factors and biomarkers at 11-13 weeks' gestation. *Ultrasound Obstet Gynecol*. 2018;52:186-195.
  14. Park HJ, Kim SH, Jung YW, et al. Screening models using multiple markers for early detection of late-onset preeclampsia in low-risk pregnancy. *BMC Pregnancy Childbirth*. 2014;14:35.
  15. Bergman L, Sandstrom A, Jacobsson B, et al. Study for improving maternal pregnancy and child outcomes (IMPACT): a study protocol for a Swedish prospective multicentre cohort study. *BMJ Open*. 2020;10:e033851.
  16. Petursdottir Maack H, Skalkidou A, Sjöholm A, et al. Maternal body mass index moderates antenatal depression effects on infant birthweight. *Sci Rep*. 2019;9:6213.
  17. Mazer Zumaeta A, Wright A, Syngelaki A, Maritsa VA, Da Silva AB, Nicolaides KH. Screening for pre-eclampsia at 11-13 weeks' gestation: use of pregnancy-associated plasma protein-a, placental growth factor or both. *Ultrasound Obstet Gynecol*. 2020;56:400-407.
  18. Poon LC, Shennan A, Hyett JA, et al. The International Federation of Gynecology and Obstetrics (FIGO) initiative on pre-eclampsia: a pragmatic guide for first-trimester screening and prevention. *Int J Gynaecol Obstet*. 2019;145(Suppl 1):1-33.
  19. Burke O, Benton S, Szafranski P, et al. Extending the scope of pooled analyses of individual patient biomarker data from heterogeneous laboratory platforms and cohorts using merging algorithms. *Pregnancy Hypertens*. 2016;6:53-59.
  20. Staff AC, Burke O, Benton S, et al. Maternal circulating PIGF concentrations and placenta-related pregnancy complications: first results from the CoLab AngF Study. *Pregnancy Hypertens*. 2013;3:59.
  21. Stepan H, Hund M, Dilba P, Sillman J, Schlembach D. Elecsys(R) and Kryptor immunoassays for the measurement of sFlt-1 and PIGF to aid preeclampsia diagnosis: are they comparable? *Clin Chem Lab Med*. 2019;57:1339-1348.
  22. Li L, Semenov AG, Feygina EE, et al. Diagnostic utility of total NT-proBNP testing by immunoassay based on antibodies targeting glycosylation-free regions of NT-proBNP. *Clin Chem Lab Med*. 2023;61:485-493.
  23. Kenan N, Larsson A, Axelsson O, Helander A. Changes in transferrin glycosylation during pregnancy may lead to false-positive carbohydrate-deficient transferrin (CDT) results in testing for riskful alcohol consumption. *Clin Chim Acta*. 2011;412:129-133.
  24. Guidelines N. PLGF-based testing to help diagnose suspected preterm pre-eclampsia. *Diagnostics Guidance [DG49]*. 2022;27 July 2022.
  25. Tan MY, Wright D, Syngelaki A, et al. Comparison of diagnostic accuracy of early screening for pre-eclampsia by NICE guidelines and a method combining maternal factors and biomarkers: results of SPREE. *Ultrasound Obstet Gynecol*. 2018;51:743-750.
  26. Cowans NJ, Alfthan H, Stenman UH, Spencer K. Stability of first trimester placental growth factor in serum and whole blood. *Prenat Diagn*. 2011;31:1193-1197.

**How to cite this article:** Carlsson Y, Sandström A, Bergman L, et al. Comparing the results from a Swedish pregnancy cohort using data from three automated placental growth factor immunoassay platforms intended for first-trimester preeclampsia prediction. *Acta Obstet Gynecol Scand*. 2023;00:1-8. doi:[10.1111/aogs.14615](https://doi.org/10.1111/aogs.14615)