

Preeclampsia

*For better maternal
and fetal care*

[Introduction to preeclampsia](#)



[Elecsys[®] sFlt-1/PIGF](#)



[Short term prediction and
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Introduction to preeclampsia

- Preeclampsia is a serious multi-system complication of pregnancy, occurring in 3 – 5% of pregnancies^{1,2}
- Preeclampsia is defined as new-onset of hypertension and proteinuria after 20 weeks of gestation³
- Preeclampsia is one of the leading causes of maternal and perinatal morbidity and mortality worldwide⁴



Pathogenesis



Complications



Today's challenge

“Preeclampsia is a common and potentially serious condition that presents a continuing challenge to clinicians due to the variable features and lack of diagnostic tests.”

Prof. Andrew Shennan, St. Thomas Hospital, London, UK



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Introduction to preeclampsia

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Pathogenesis

The cause of preeclampsia is not fully understood, but there is growing evidence that angiogenic growth factors such as placental growth factor (PlGF) and soluble fms-like tyrosine kinase-1 (sFlt-1) play a major role in the development of preeclampsia.⁴

Circulating levels of sFlt-1 and PlGF are altered in women who develop preeclampsia.

Hypertension and proteinuria are the diagnostic criteria for preeclampsia but they are only symptoms of the pathophysiologic changes that occur in the disorder.



Complications



Today's challenge



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Pathogenesis



Complications

Amongst others the most common complications of preeclampsia include:

For the mother:

- Eclampsia – Preeclampsia in combination with generalized seizures
- Convulsions
- Kidney damage / Kidney failure
- Abruptio placentae
- Antepartum hemorrhage
- Cerebrovascular bleeding

For the fetus:

- Fetal growth retardation
- Low birth weight
- Kidney damage / Kidney failure
- Premature birth
- Antepartum hemorrhage
- Stillbirth



Today's challenge



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Pathogenesis



Complications



Today's challenge

Clinical management can be challenging due to:

- A lack of effective treatment options other than delivery⁴
- The necessity of a reliable tests to predict preeclampsia and related complications and to assess disease severity and progression^{4,5}
- The necessity to balance maternal and fetal risks¹






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Elecsys[®] sFlt-1/PIGF

The first available automated diagnostic tests



-  **Hypoxic placenta**
-  **Normal pregnancy**
-  **Preeclampsia**

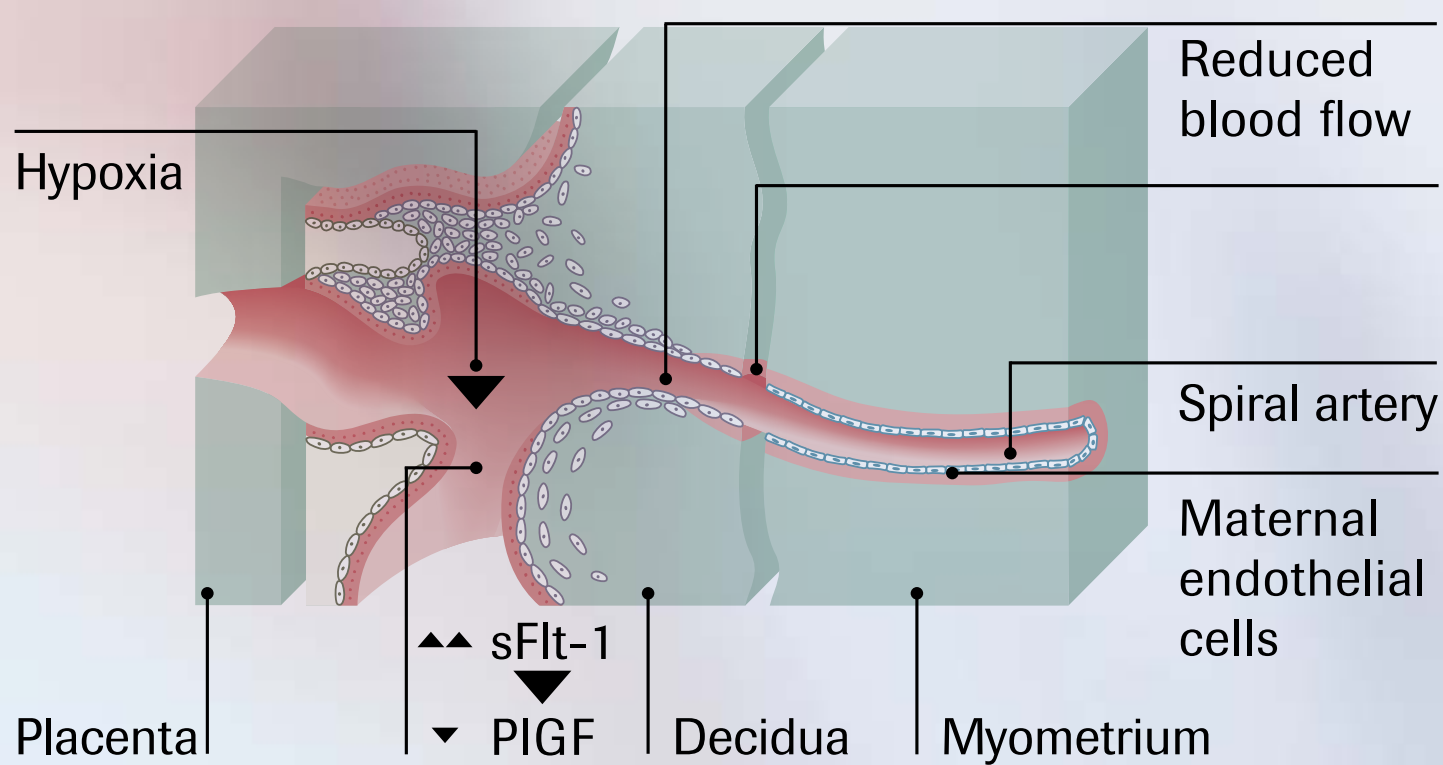
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Elecsys[®] sFlt-1/PIGF

The first available automated diagnostic tests



Hypoxic placenta



Normal pregnancy



Preeclampsia



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The first available automated diagnostic tests

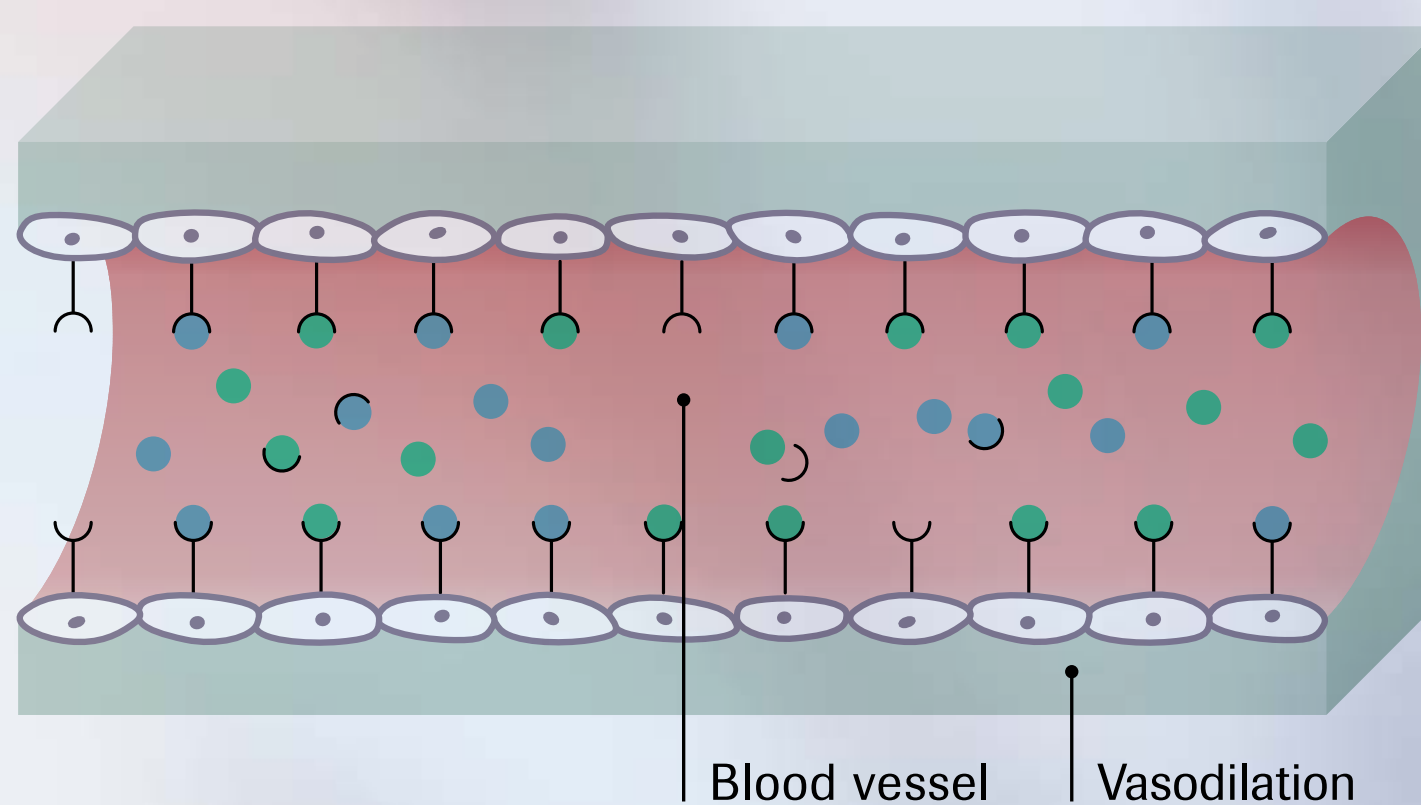


Hypoxic placenta



Normal pregnancy

Flt-1 sFlt-1 VEGF PIGF



Preeclampsia



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Elecsys[®] sFlt-1/PIGF

The first available automated diagnostic tests



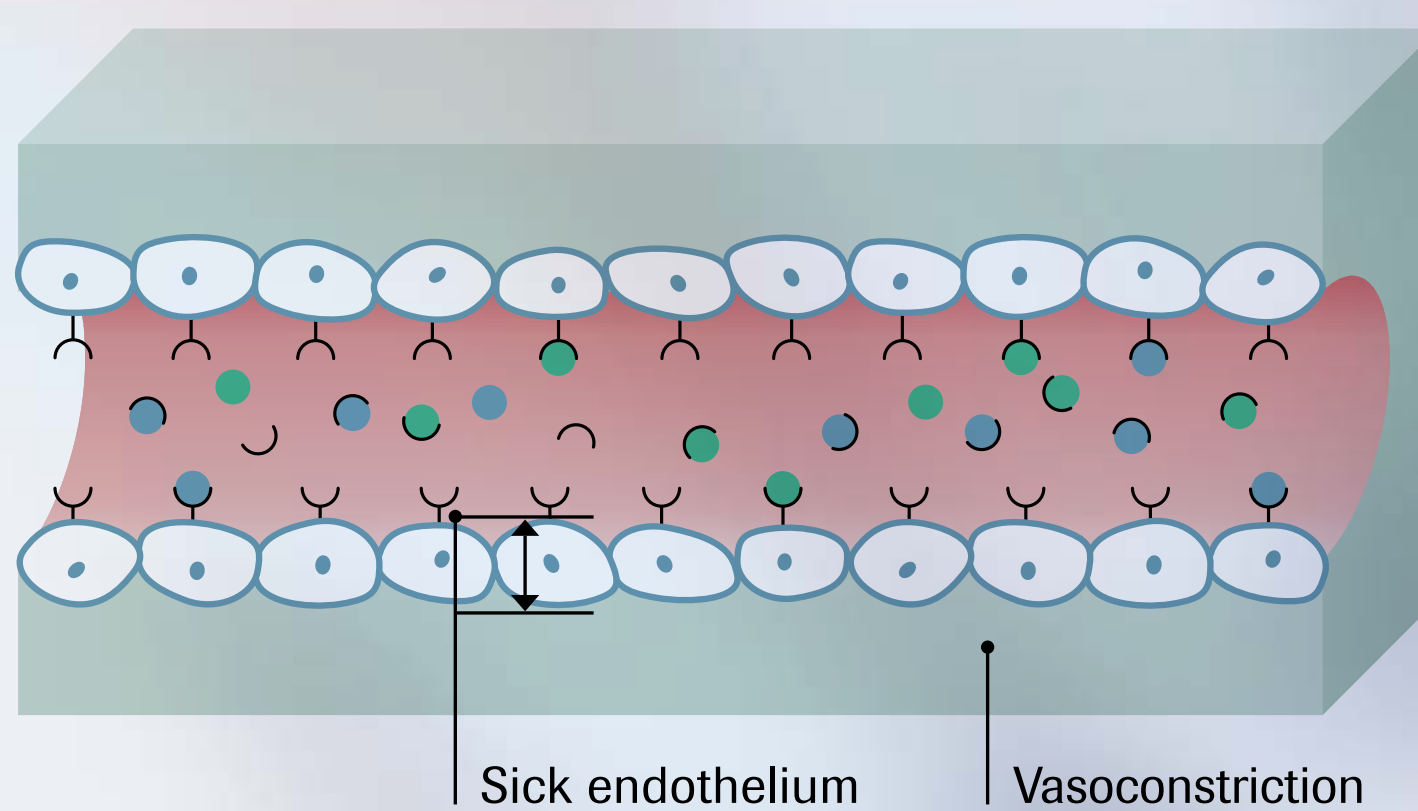
Hypoxic placenta



Normal pregnancy



Preeclampsia



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Short term prediction and diagnosis of preeclampsia

“Preeclampsia by itself cannot be treated, but the clear stratification of risk can trigger concrete actions, such as the close monitoring of the mother and fetus as well as the referral to a specialist delivery unit offering intensive care.”

Prof. Holger Stepan, University of Leipzig, Germany

Early onset preeclampsia – gestational week 20 – 33+6 days

sFlt-1/PIGF ≥ 85	▶	Diagnosis	▶	99.5 % specificity the woman has preeclampsia <i>Sensitivity: 88.0 %</i>
sFlt-1/PIGF < 85 ≥ 38	▶	Prediction rule-in within next 4 weeks	▶	38.6 % PPV the woman is at high risk to develop preeclampsia within the next 4 weeks
sFlt-1/PIGF < 38	▶	Prediction rule-out for the next 1 week	▶	99.1 % NPV the woman will not develop preeclampsia for the next 1 week

Late onset preeclampsia – gestational week 34 to end of pregnancy

sFlt-1/PIGF ≥ 110	▶	Diagnosis	▶	95.5 % specificity the woman has preeclampsia <i>Sensitivity: 58.2 %</i>
sFlt-1/PIGF < 110 ≥ 38	▶	Prediction rule-in within next 4 weeks	▶	38.6 % PPV the woman is at high risk to develop preeclampsia within the next 4 weeks
sFlt-1/PIGF < 38	▶	Prediction rule-out for the next 1 week	▶	99.1 % NPV the woman will not develop preeclampsia for the next 1 week







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Facing unmet medical needs

Medical value of Elecsys[®] preeclampsia immunoassays



-  **Short term prediction**
-  **Diagnosis**
-  **Differential diagnosis**
-  **Disease severity**

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REFERENCES



Short term prediction

The sFlt-1/PIGF ratio can be used to predict preeclampsia in women with signs or symptoms of the disease.⁶

- **sFlt-1/PIGF ratio < 38: Rule out preeclampsia for 1 week**
- **sFlt-1/PIGF ratio ≥ 38: Rule in preeclampsia within 4 weeks**

Short term prediction of preeclampsia

Rule out within 1 week (n = 1,050)⁶

sFlt-1/PIGF ratio	< 38
NPV (95% CI)	99.1% (98.2 – 99.6)
Sensitivity (95% CI)	85.7% (72.8 – 94.1)
Specificity (95% CI)	79.1% (76.5 – 81.6)

Short term prediction of preeclampsia

Rule in within 4 weeks (n = 1,050)⁶

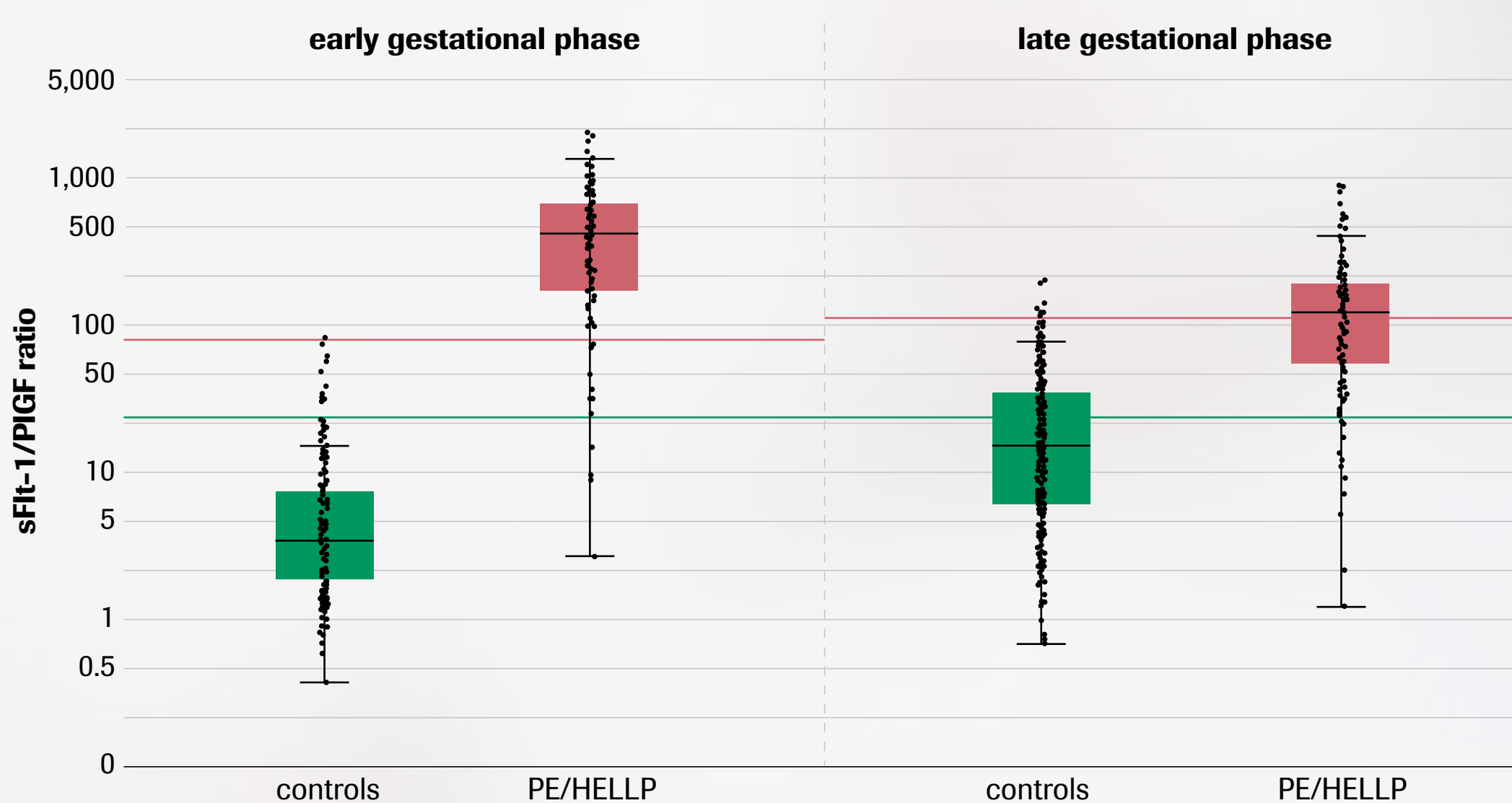
sFlt-1/PIGF ratio	≥ 38
PPV (95% CI)	38.6% (32.6 – 45.0)
Sensitivity (95% CI)	70.3% (61.9 – 77.8)
Specificity (95% CI)	83.1% (80.5 – 85.5)

CI = Confidence Interval, NPV = Negative Predictive Value, PPV = Positive Predictive Value



Diagnosis

sFlt-1/PIGF ratio for aid in diagnosis of preeclampsia ⁷



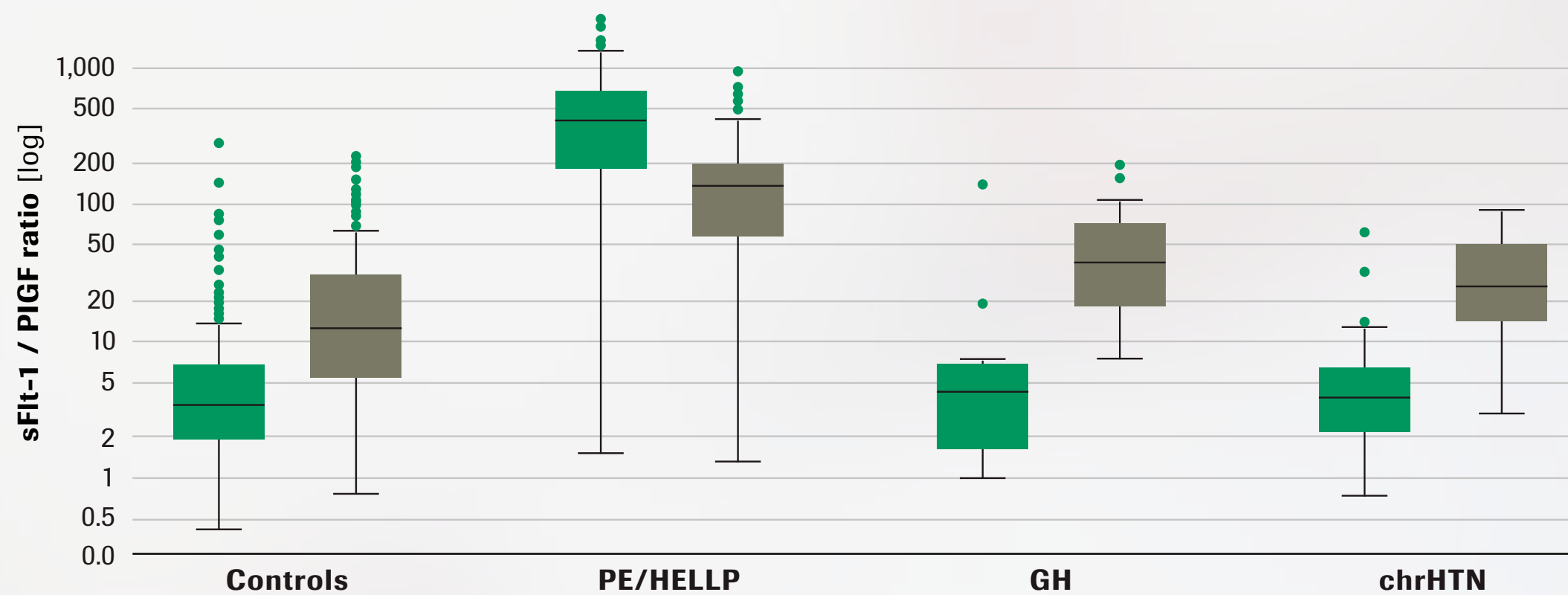
PE/HELLP = preeclampsia / HELLP syndrome; sFlt-1/PIGF ratio cut-offs for early gestational phase: 33 / 85; sFlt-1/PIGF ratio cut-offs for late gestational phase: 33 / 110



Differential diagnosis

Angiogenic factors can support in the differential diagnosis of preeclampsia⁸

■ < 34 gestational weeks ■ ≥ 34 gestational weeks



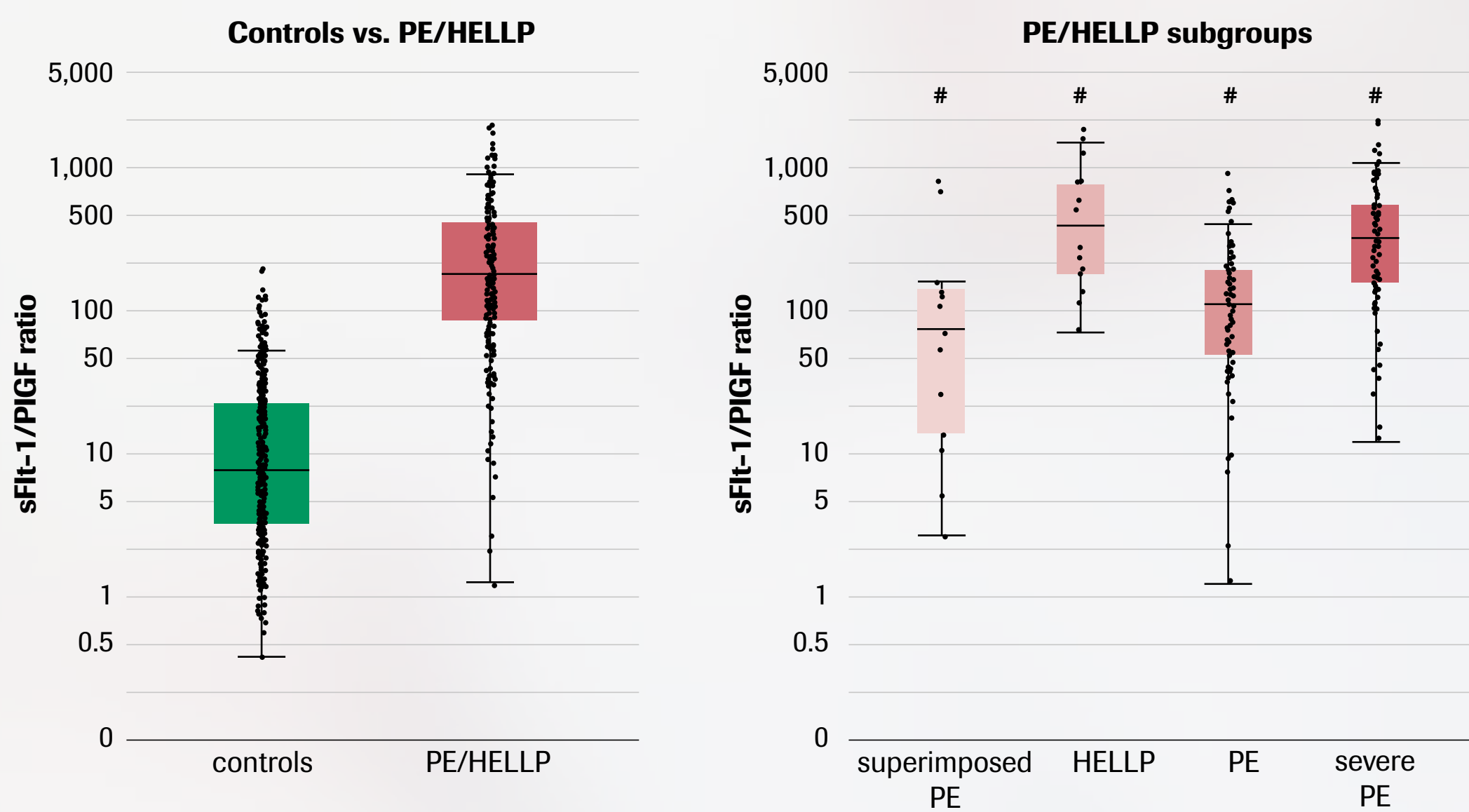
sFlt-1/PlGF ratio in PE/HELLP, GH, chrHTN, and healthy controls⁷
(PE = preeclampsia; HELLP = Hemolysis, Elevated Liver Enzymes, Low Platelets; GH = gestational hypertension; chrHTN = chronic hypertension)



Disease severity

Higher sFlt-1/PIGF ratio is associated with a higher severity of the diseases.

sFlt-1/PIGF ratio for aid in diagnosis of preeclampsia ⁷



P < 0.001 multigroup comparison PE subgroups

Novel innovative biomarkers

Precise, consistent, reliable

“We hope that early identification of women at high risk of developing preeclampsia will allow healthcare professionals to prevent the most serious effects of the disease and avoid unnecessary expenditure by healthcare systems on excessive medical treatment or unnecessary hospital admission prompted by inadvertently positive diagnoses based on current standard of clinical practice”

Prof. Harald Zeisler, University of Vienna, Austria



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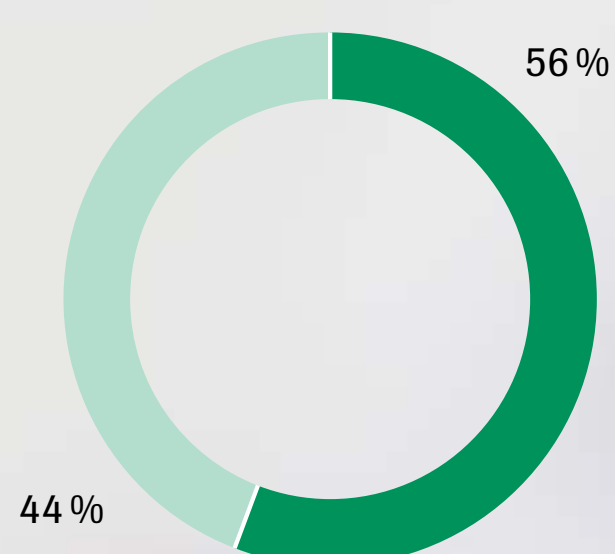


sFlt-1/PIGF assay could allow cost-savings

In a recent model, adding the Elecsys® sFlt-1/PIGF ratio to the standard diagnostic method improved risk stratification with a significant reduction of false positive and false negative diagnosis. This could enable reductions in direct hospital costs and resource use with savings of 540 – 1,215 USD per patient.⁹

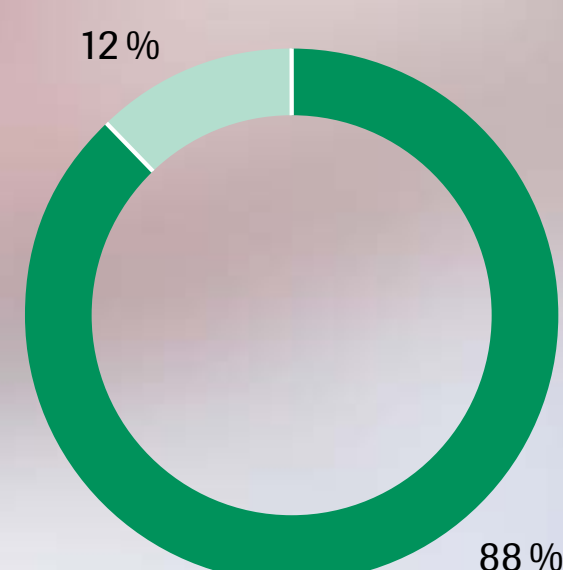
Standard approach

- True positive and negative
- False positive and negative



New approach (adding sFlt-1/PIGF)

- True positive and negative
- False positive and negative



By using the novel preeclampsia test in the UK, the National Health Service (NHS) could save GBP 730 million annually and in Germany, national savings could reach EUR 436 million annually.^{10,11}



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