Preeclampsia – Screening and prevention?

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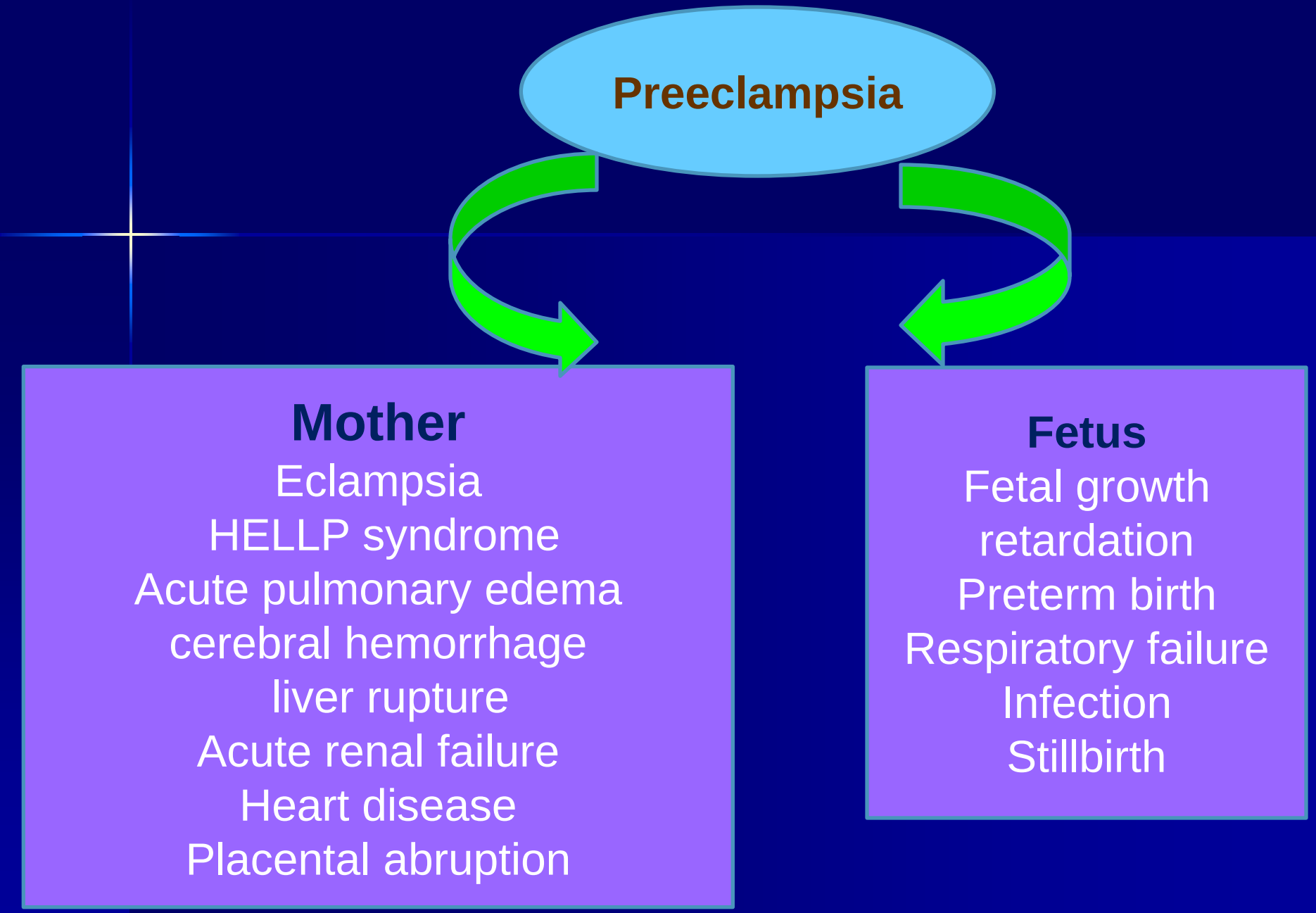
Preeclampsia

- Preeclampsia (PE) is a syndrome of multiple disfunctional organ due to reduced blood perfusion to sustain the growing fetus, after **v**asoconstriction and activate intravascular factors
- Incidence 2-6%, Vietnam: 2,34- 4%

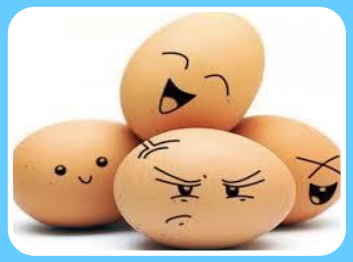

Preeclampsia
Mother
Eclampsia
HELLP syndrome
Acute pulmonary edema
cerebral hemorrhage
liver rupture
Acute renal failure
Heart disease
Placental abruption
Fetus
Fetal growth
retardation
Preterm birth
Respiratory failure
Infection
Stillbirth

Preclampsia

- PE is main cause of maternal mortality of 16% in developing countries, 29% in Vietnam (2011), 25% in 32 Southern provinces (2013)
- Morethan 50% of PE mortality can be prevented *(Berg et al 2005)*
- Perinatal death by Preeclampsia: 25%

- 32 provinces in the south 25%

Prevention

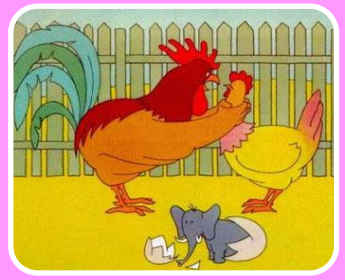


Level 1: Screening

- identification of high-risk PE pregnancies
- Early screening

Level 2: Early prediction of PE – Prevent to severe PE

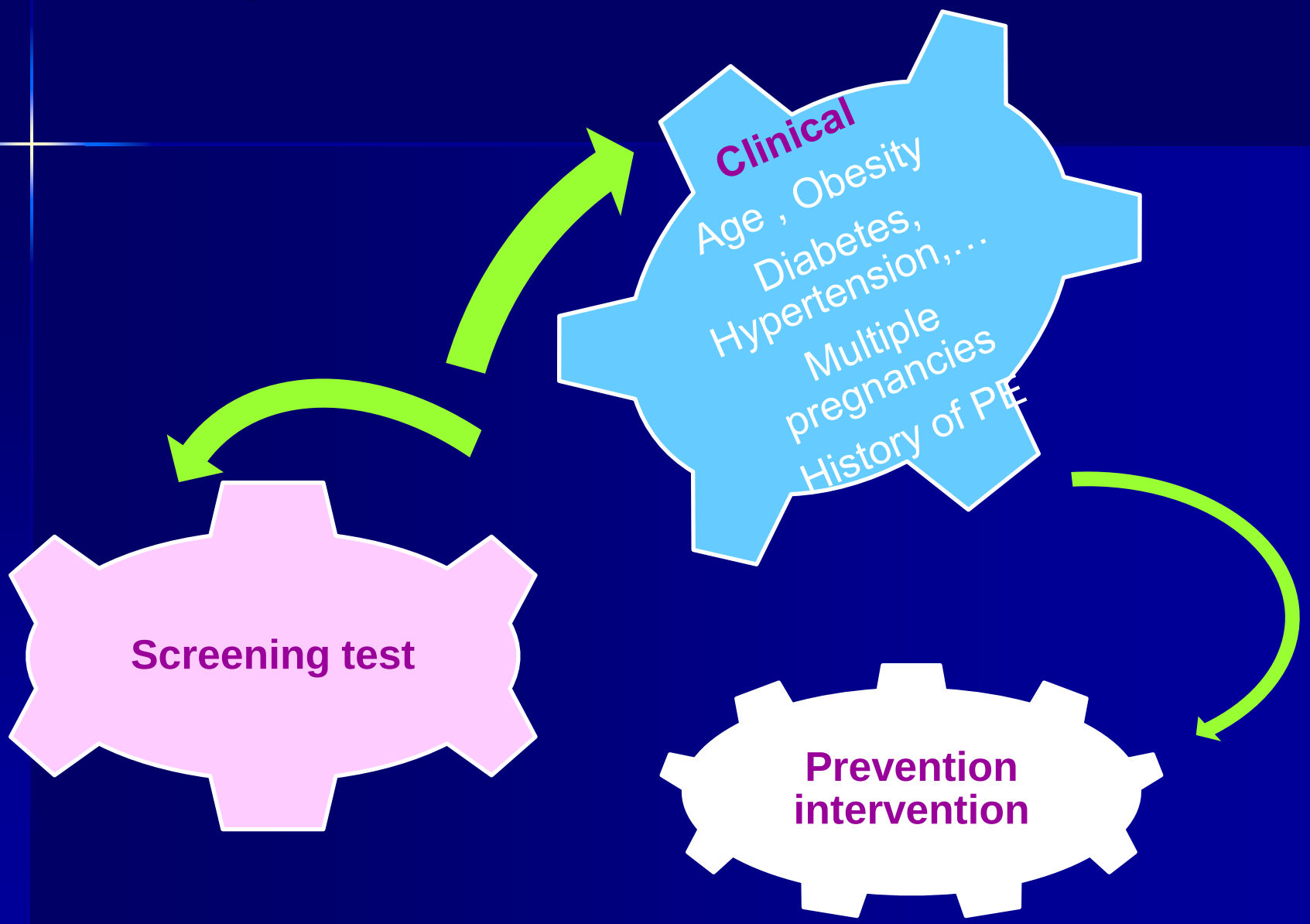
- Regular check-ups
- Intensified monitoring and handle appropriately, timely



Level 3: Effective treatment – Complication Prevention

- Termination
- Supportive treatment
- Admission to specialised perinatal care hospital safely

Level 1 prevention



Level 1 prevention

- Early screening

Level 1 prevention

- WHO recommendation2012 on level 1 prevention

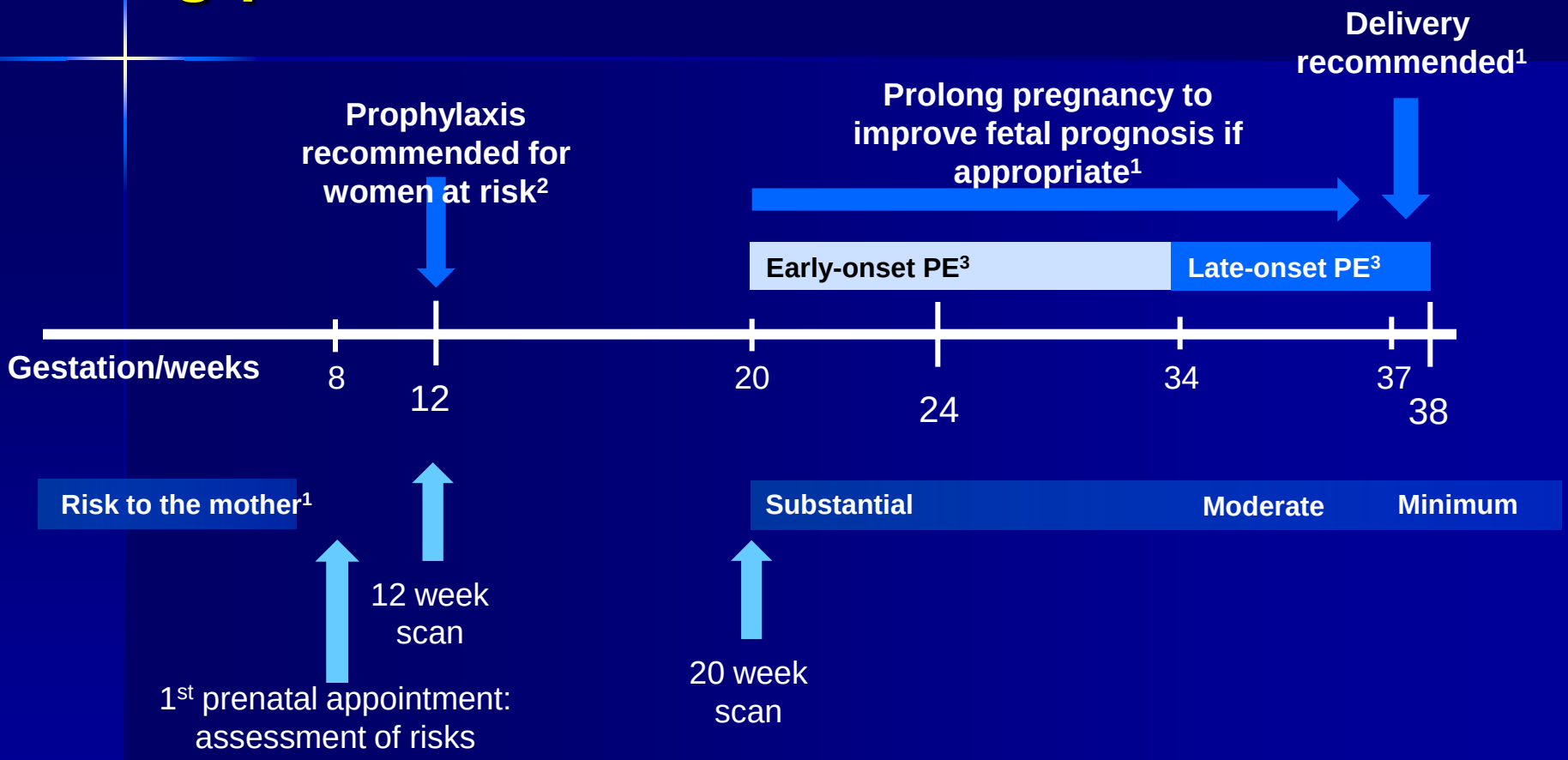
  Low dosage of Aspirine, before 20 gestional week

Level 2 prevention: Early PE diagnosis, early prediction of severe PE

The diagnosis of mild PE and severe PE may be WRONG because the symptoms of mild PE may progress rapidly to severe PE

Williams Obstetrics, 23rd edition, 2010

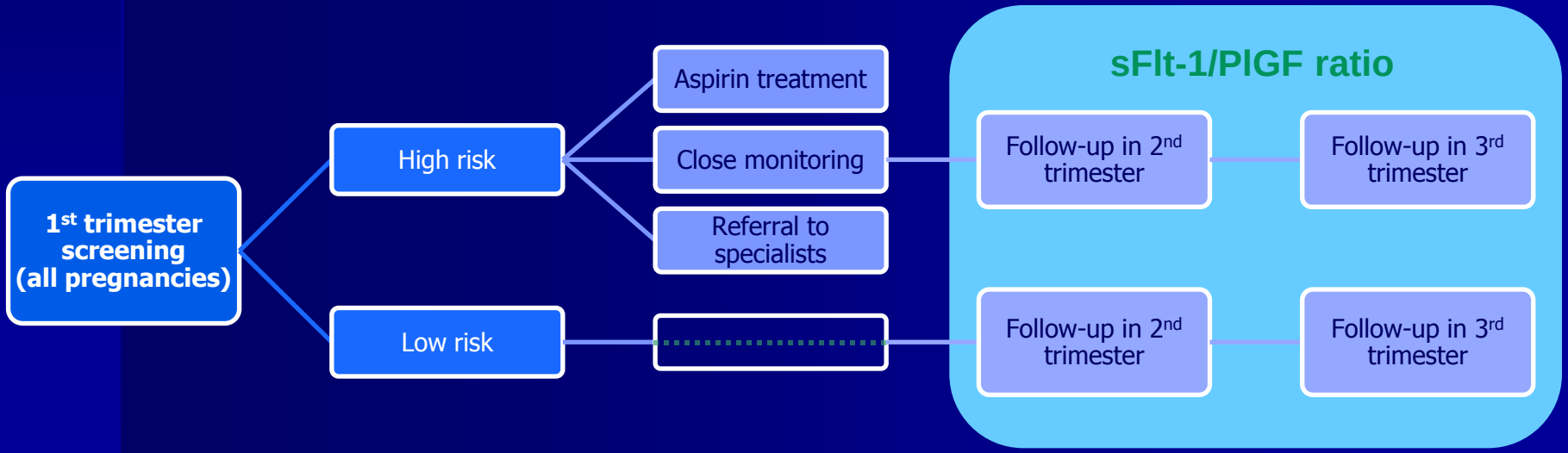
Đánh giá lâm sàng trên thai phụ
Quyết định lâm sàng trong quản lý tiền sản giật



[1] Steegers EAP et al. *Lancet* 2010;376:631–44
[2] Hypertension in pregnancy: the management of hypertensive disorders during pregnancy, 2011, NICE guidelines

Level 1 prevention be an additional testing step for level 2,3 prevention

- Level 1 prevention be an additional testing step for level 2, 3 to identify high risk patients they will receive a closer follow-up or will be referred to a higher level of care
- **Level 2,3 prevention remain useful independently from the level 1 prevention results whenever there is a suspicion of Preeclampsia**



Improved preeclampsia diagnosis and risk stratification with the Roche sFlt-1/PlGF assay

- Providing health economic benefits for pregnancies

PE management

Diagnosis based on non-specific symptoms is insufficient for the correct management of patients with PE

PE is a **leading cause of maternal and fetal/neonatal morbidity and mortality worldwide** [1]

1

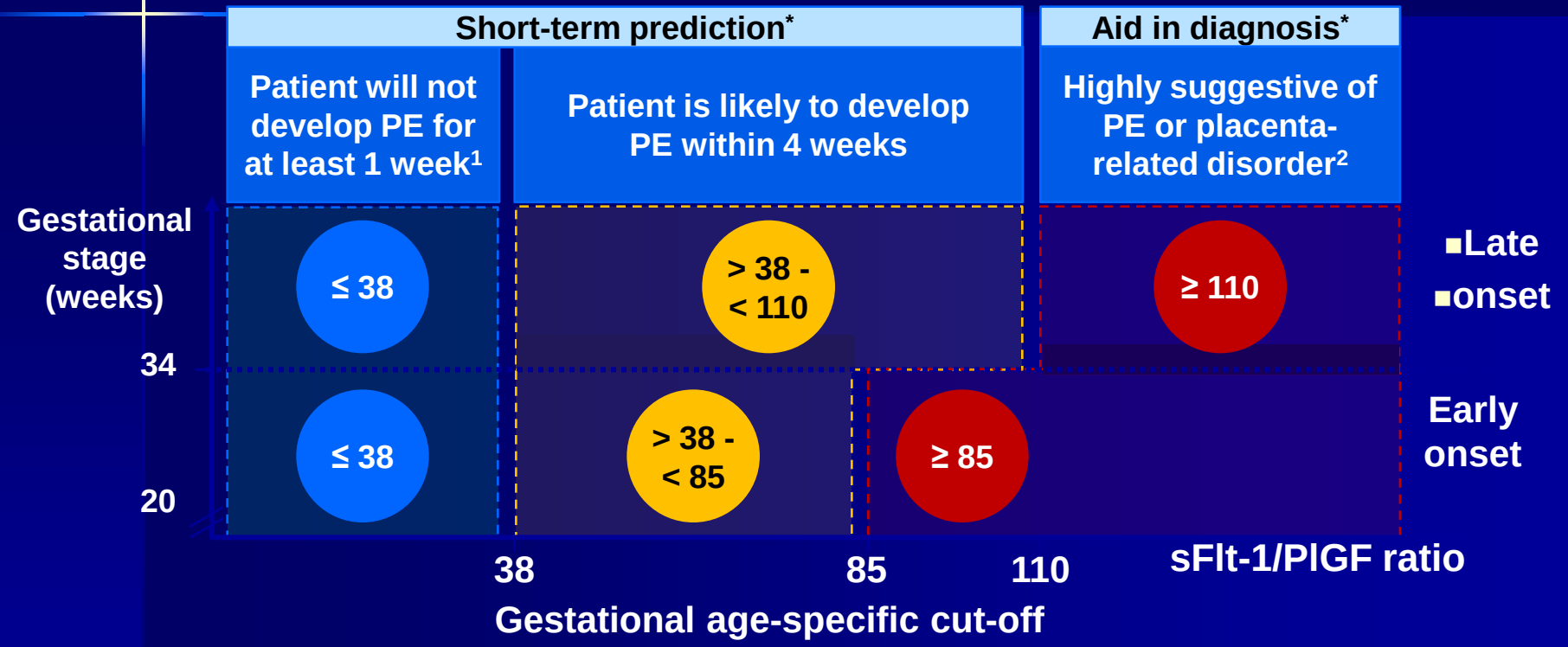
Clinical diagnosis is based currently on the determination of **blood pressure** and **proteinuria**[1]

- Proteinuria testing is prone to inaccuracies and PE complications can occur prior to the appearance of proteinuria[1]
- Since 2013 guidelines have been updated to support the diagnosis of PE on the basis of hypertension and other symptoms of maternal organ dysfunction (including ACOG[2], ISSHP[3])

1. Stepan, H., et al. (2015). *Ultrasound Obstet Gynecol* 45, 241-246
2. ACOG Task Force on Hypertension in Pregnancy (2013). *Obst & Gynecol* 122,1122-1131
3. Tranquilli, A.L., et al. (2014). *Pregnancy Hypertens* 4, 97–104

ISSHP: International society for the study of hypertension in pregnancy; ACOG: American college of obstetricians and gynecologists

The sFlt-1/PlGF ratio gestational age-specific cut-offs for the short-term prediction and diagnosis of preeclampsia



*Used in addition to other accepted diagnostic tools and clinical information

1. Zeisler, H., et al. (2016).*N Engl J Med* 374(1), 13-22
2. Verlohren et al (2014). *Hypertension* 63, 346-352

The sFlt-1/PlGF ratio supports the rule-out of PE within 1 week in women with suspected PE

Allowing cost-savings

A cut-off of 38 allows the 'rule-out' of PE within 1 week of start visit:

- **reassuring patients and the physicians**
- **saving resources and hospitalisation costs**

Short-term prediction of PE / eclampsia / HELLP syndrome Rule-out within 1 week (Validation cohort, n = 550)[2]*	
cut-off sFlt-1/PlGF	**38**
NPV (95% CI)	**99.3%** (97.9 – 99.9)
Sensitivity (95% CI)	**80.0%** (51.9 - 95.7)
Specificity (95% CI)	78.3% (74.6 - 81.7)

CI: Confidence interval; NPV: Negative predictive value; HELLP: Hemolysis, elevated liver enzymes, low platelets
* Complete data results (1,050 subjects)

1. Hund, M., et al. (2014). *BMC Pregnancy and Childbirth* 14, 324
2. Zeisler, H., et al. (2016). *N Engl J Med* 374(1), 13-22

The sFlt-1/PlGF ratio supports the rule-in of PE within 4 weeks in women suspected of PE

Allowing timely patient management

- **A cut-off of 38 allows the 'rule-in' of PE within 4 weeks – enabling focus on the right patients**

Short-term prediction of PE / eclampsia / HELLP syndrome Rule-in within 4 weeks (Validation cohort, n = 550)[1*]	
sFlt-1/PlGF ratio cut-off	**38**
PPV (95% CI)	**36.7**% (28.4-45.7)
Sensitivity (95% CI)	66.2% (54.0-77.0)
Specificity (95% CI)	**83.1%** (79.4–86.3)

CI: Confidence interval; PPV: Positive predictive value;
* Complete data results (1,050 subjects)

1. Zeisler, H., et al. (2016). *N Engl J Med* 374(1), 13-22

Early diagnosis of PE might have clinical and health economic benefits

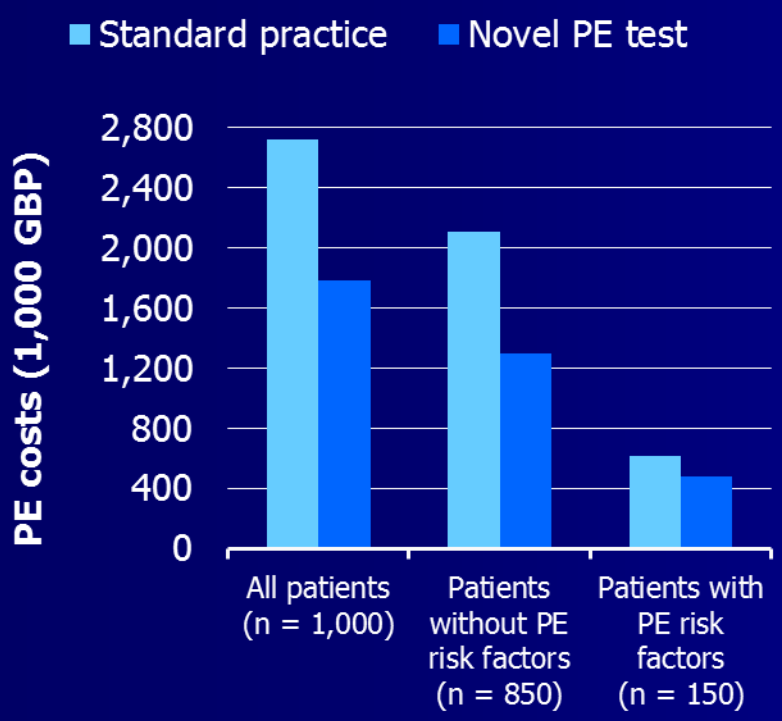
Methods and standard of care

- Budget impact model, a decision-analytic software tool comparing two PE testing paradigm scenarios:
  - UK/German standard practice including blood test, urine tests, blood pressure measures and uterine artery Doppler ultrasound
  - UK/German standard practice + measures of PIGF, sFlt-1 (Elecsys® platform) from week 20

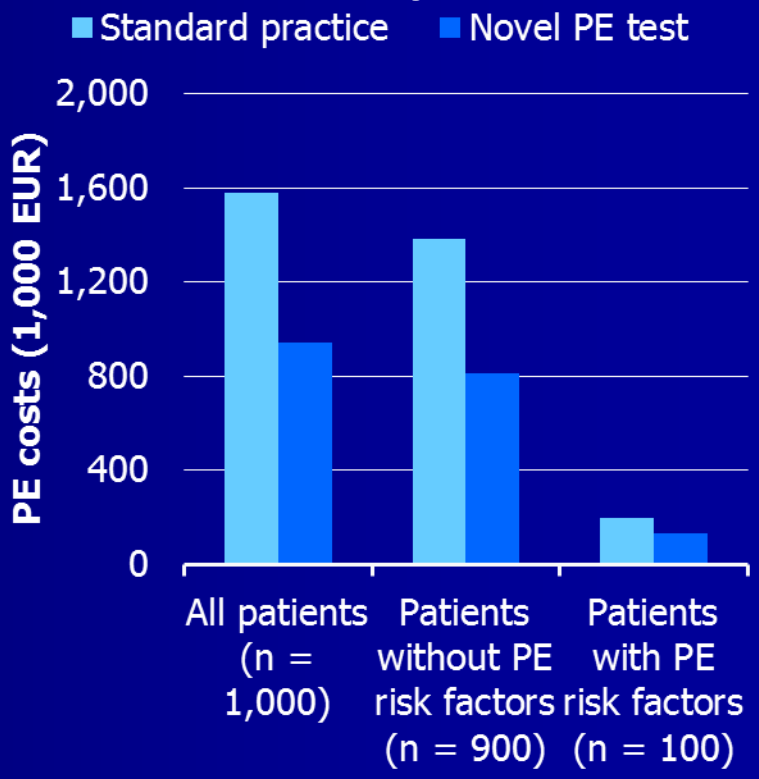
- Both the NICE and DGGG guidelines require that physicians stratify patients as high risk for PE when the patient's pregnancy is confirmed and health status assessed
- Patients at high risk of PE are more frequently controlled until PE can be diagnosed starting from week 20

By using the novel PE test in the UK, the NHS could save GBP 730 million annually and in Germany, national savings could reach EUR 436 million annually

Budget impact of novel PE test in the UK



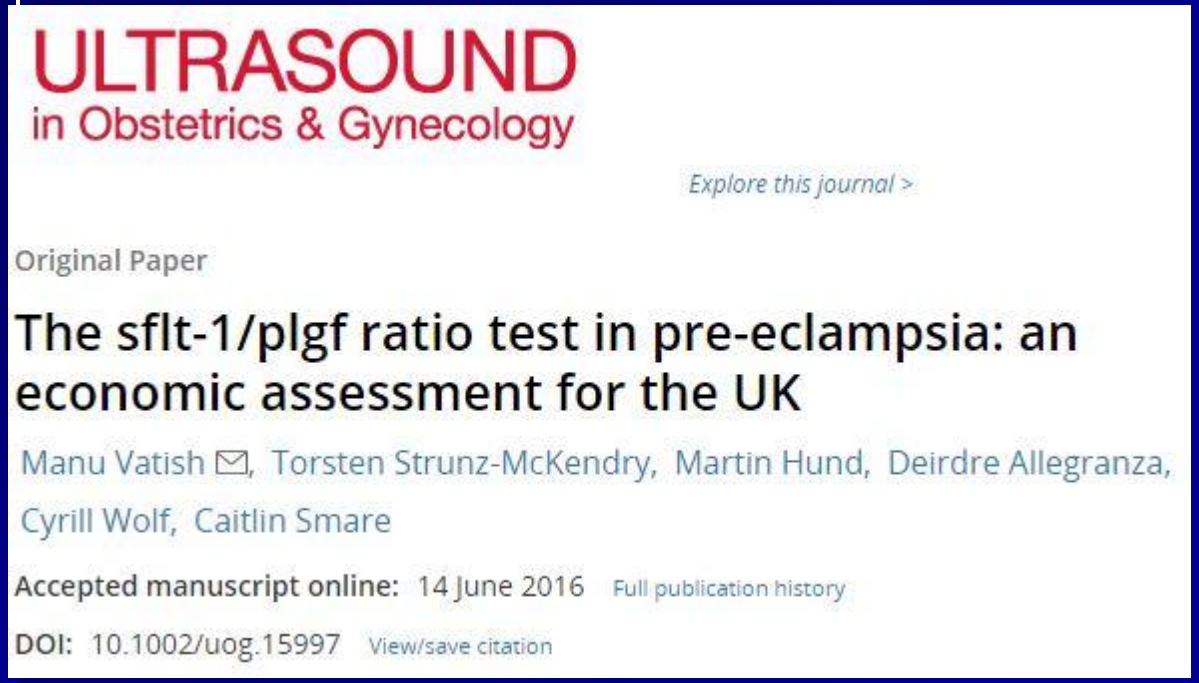
Budget impact of novel PE test in Germany



Hadker N, Garg S, et al. (2010). *J Med Econ 13*(4):728-37; Hadker N, Garg S, et al. (2013). *Hypertens Pregnancy 32*(2): 105–119

Economic assessment of the sFlt-1/PlGF ratio in preeclampsia

A UK NHS payer perspective



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Original Paper

The sflt-1/plgf ratio test in pre-eclampsia: an economic assessment for the UK

Manu Vatish ✉, Torsten Strunz-McKendry, Martin Hund, Deirdre Allegranza, Cyrill Wolf, Caitlin Smare

Accepted manuscript online: 14 June 2016 Full publication history

DOI: 10.1002/uog.15997 View/save citation

Đánh giá tác động kinh tế của tỉ số sFlt-1/PlGF trên thai phụ nghi ngờ TSG ở Anh

Ultrasound Obstet Gynecol 2016

- NHS, National Health Service; PlGF, placental growth factor; sFlt-1, soluble fms-like tyrosine kinase-1

Level 3 prevention

- Severe PE treatment to prevent effectively maternal and fetal complications

When termination??

Clinical study

- **The value of the ratio sFlt-1 / PlGF in prediction pregnant outcome of early –onset preeclampsia in 28-32 gestational week**

Principle investigator: Diem Tuyet Hoang

Quang Thanh Le

Study site: Tudu hospital

Trial design

- Prospective cohort study
- Sample size: 342
- Gestation age : 28-32 week

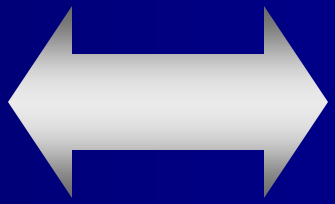
Conclusion

- In women with PE presenting at<32 weeks, circulating sFlt-1/PlGF ratio predicts adverse outcomes occurring within 1-7 weeks. The accuracy of this test is sustantially better than that of current approaches and may be useful in risk stratification and management.
- Pregnancy can prolong within 1.2 weeks in women group with sFlt-1/PlGF ratio ≥85
- Pregnancy can prolong 7.48 weeks in women group with sFlt-1/PlGF ratio < 85

PE – E treatment

Termination is the best way

Termination **so EARLY**



Termination **so LATE**

FETUS

MOTHER

	Mother	Fetus
Immediately intervention (within 72 hours) *One of these symptoms*	Uncontrolled hypertension Eclampsia Platelets <100,000 AST, ALT> 2 times higher + epigastric pain, Lower right flank, Acute Pulmonary edema renal failure Headache, , visual disturbances Placental abruption	Late downturn Biophysical profile<4, two occasions ≥4 hour apart Amniotic fluid index<2 Impaired fetal growth <5th gestational weight Reversed diastolic wave of the umbilical artery
Monitoring *One of these symptoms*	controlled hypertension Oliguria be solved merely by infusion AST, ALT increase 2 times higher than normal but no epigastric pain, Lower right flank	Biophysical profile > 6 Amniotic fluid index >2 Impaired fetal growth >5th gestational weight

Cambridge university, 2007
Pre-eclampsia Etiology and clinical Practice

Summary

- PE is obstetric complication
- Main cause of maternal and perinatal mortality
- Morethan 50% of PE mortality can be prevented
- Preventing and predicting PE well help to reduce maternal and perinatal mortality in Vietnam

Thank you