Pre-eclampsia screening

PlGF1-2-3

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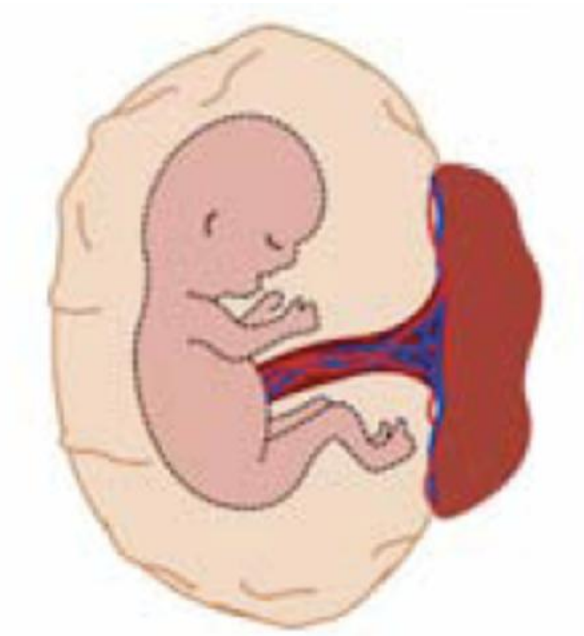
Prenatal screening

How is the baby?

Aneuploidies
- T21
- T18
- T13

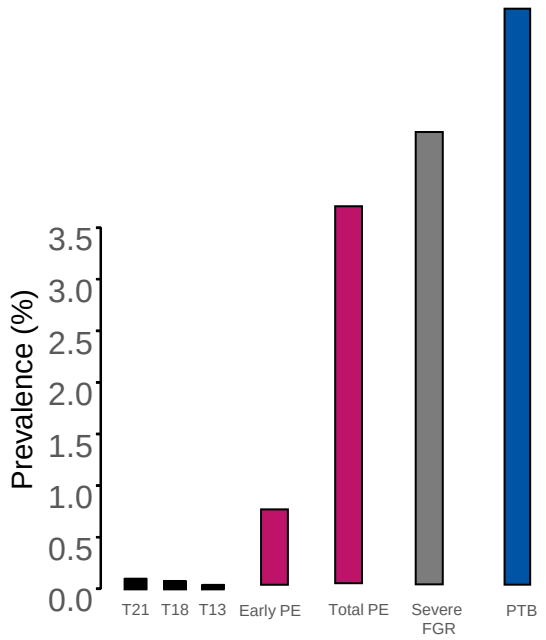


How is the placenta?

Placental insufficiencies:
- Pre-eclampsia
- Fetal Growth Restriction
- Preterm Birth
- Stillbirth

Making a real difference – Placental health

Aneuploidies vs Placental insufficiencies



- Pre-eclampsia is much more common than all aneuploidies combined.
- Both mother and the baby is affected.

Placental Insufficiency is present in virtually every major obstetrical syndrome.
Romero, *Am J Obstet Gynecol. 2011*

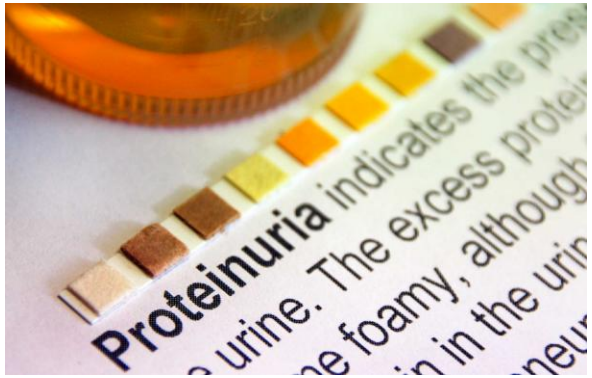
What is pre-eclampsia

Pre-eclampsia, a multisystem disorder of pregnancy, clinically defined by:

1. Hypertension (Diastolic BP >90 mmHg)
2. Protein in the urine (>0,3 g/24hours)

ISSHP Guideline for PE definition

- ✓ Symptoms appear after 20th week of gestation (=too late for preventive actions).
- ✓ Pre-eclampsia is associated preterm birth and fetal growth restriction.
- ✓ Women with a previous pre-eclampsia have a 3-4 times higher risk for cardiovascular disorders later in life.



Costs related to Pre-eclampsia

80 % of all pre-eclampsia related costs from Early-PE.

Estimated burden in UK £180m

- ✓ **Early PE (£144m)**
  - **Delivery = NICU**
  - **Cost per case = £24,000**
- ✓ **Late PE (£36m)**
  - **Cost per case : £1,500**

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Definitions

Placental Maternal

Very early Pre-eclampsia

- Delivery needed
  <32 weeks
- Prevalence
  0.2%

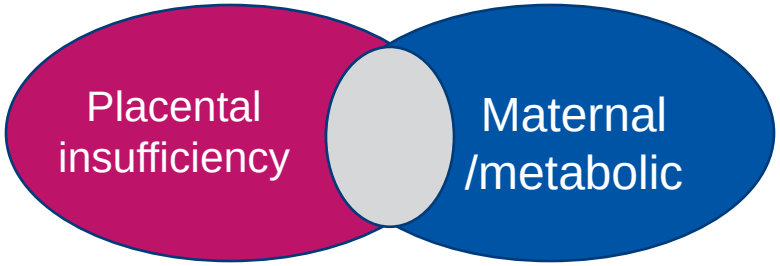
Preterm Pre-eclampsia

- Delivery needed
  <37 weeks
- Prevalence
  0.7%

Term Pre-eclampsia

- Delivery needed
  ≥37 week
- Prevalence
  2%

Fetal Growth restriction PTB (preterm birth)



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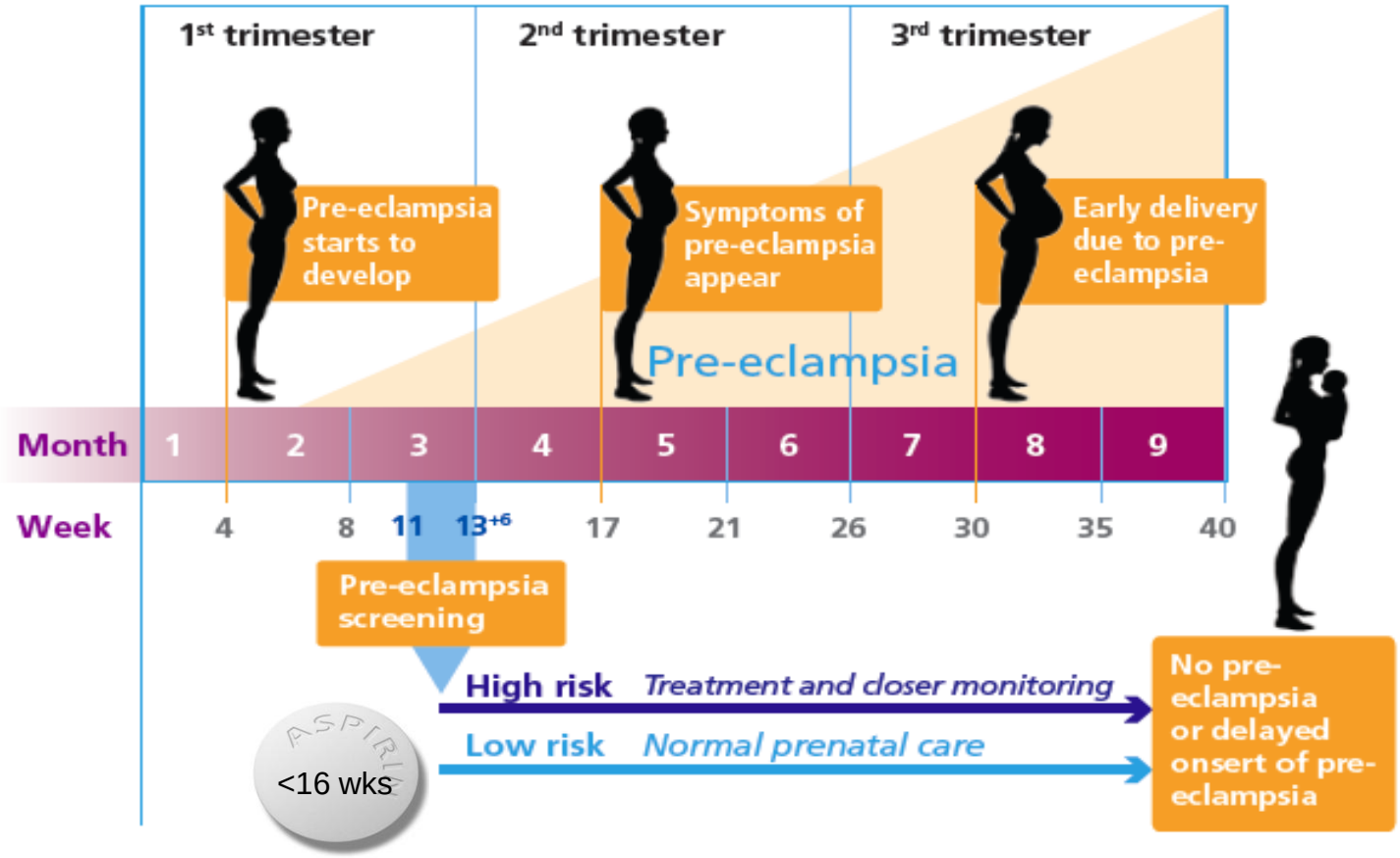
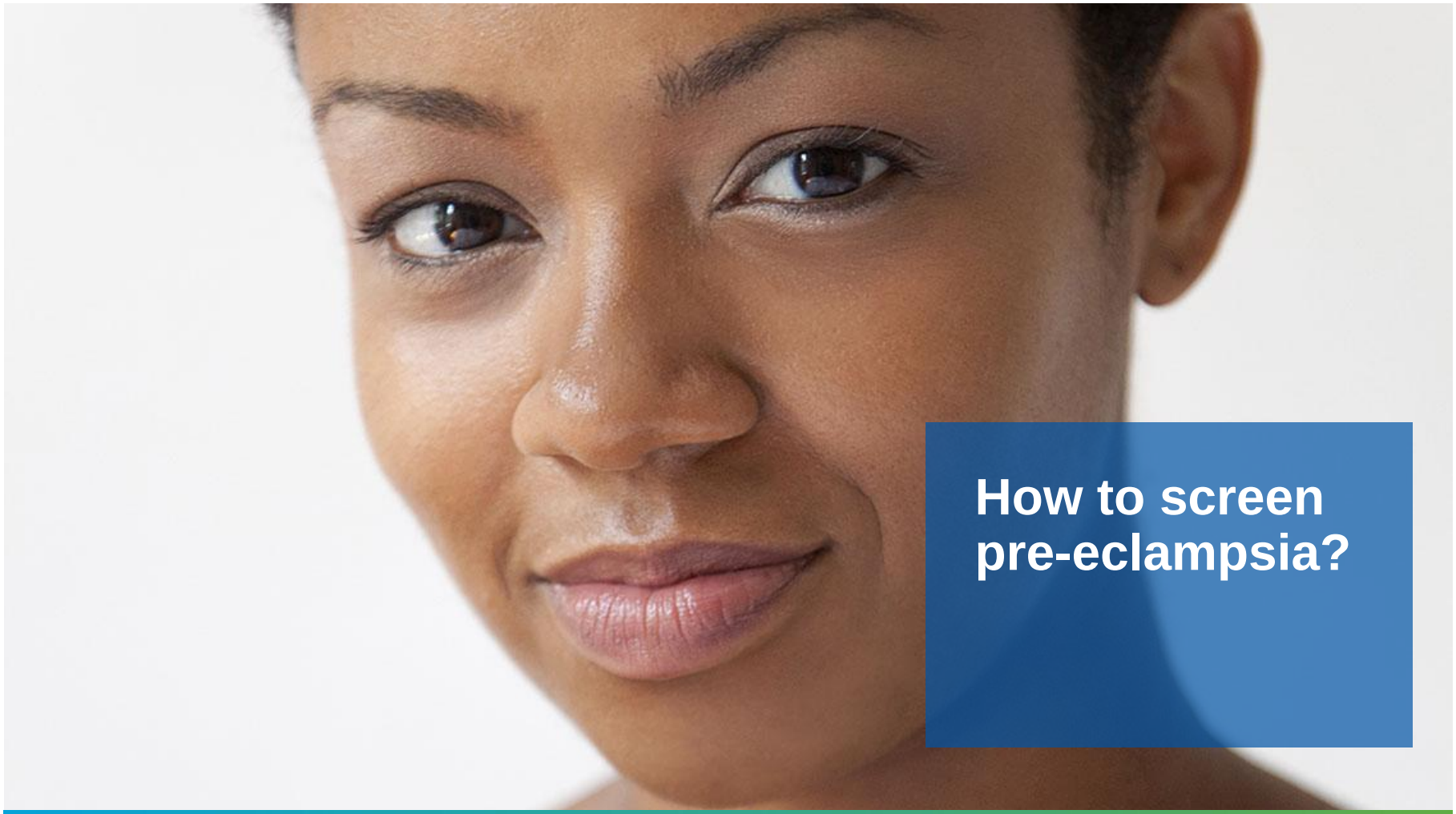
Optimal timeline for screening and prevention



- Signs of pre-eclampsia can be detected by screening tests **early** in pregnancy (11-13+6 wks).
- If the risk of pre-eclampsia is found to be high, treatment to **delay or prevent the disease** can be started right away[..]



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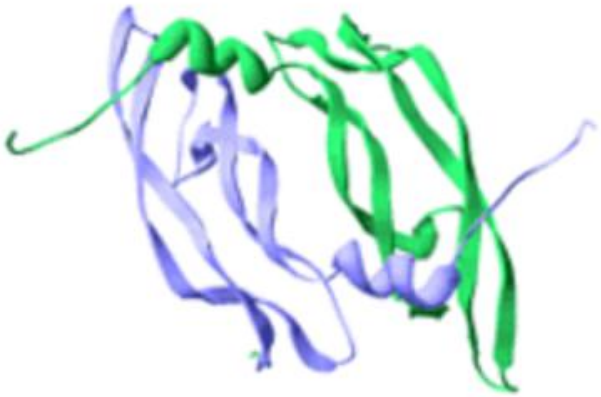
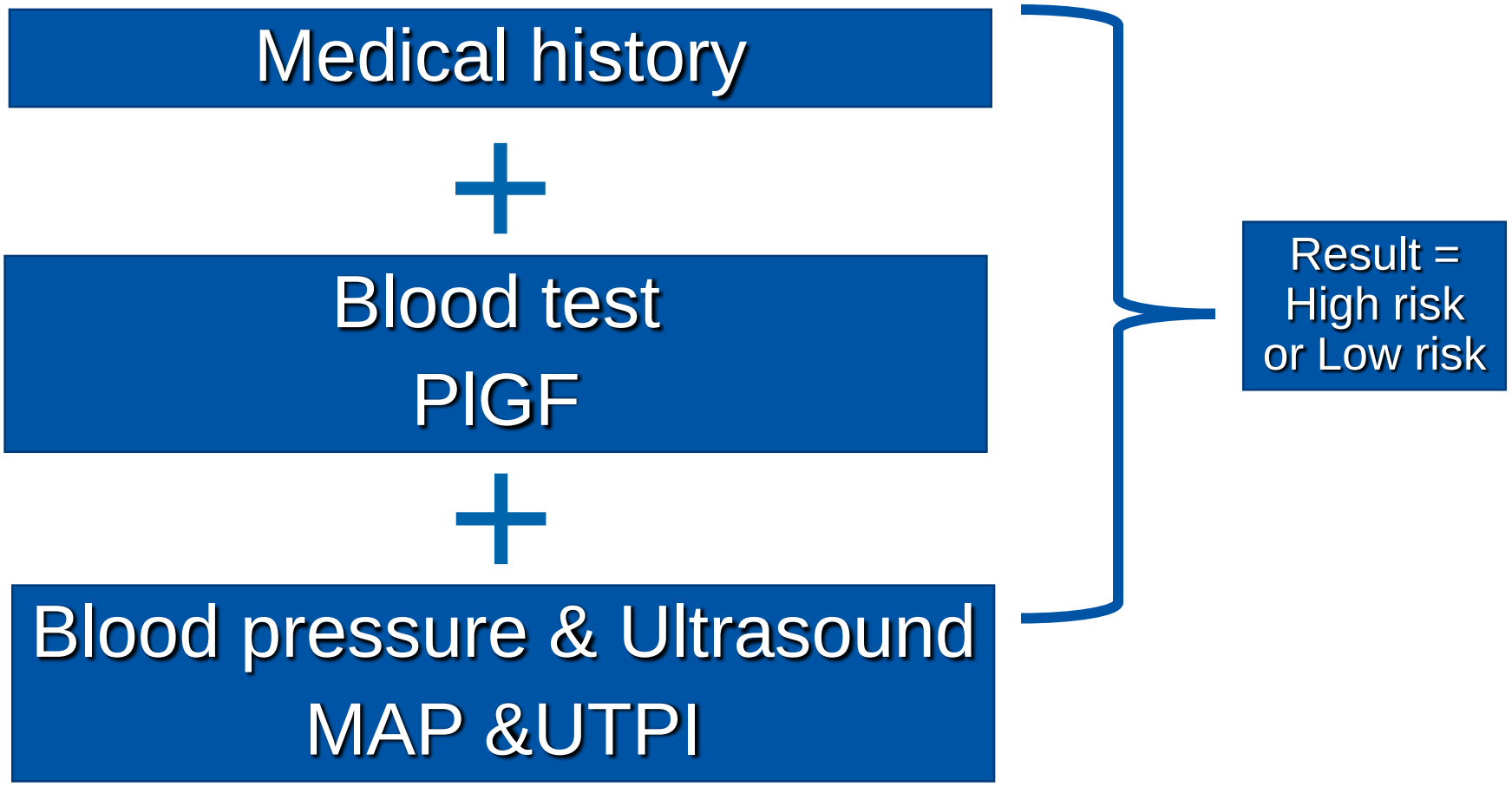
PlGF 1-2-3, validated marker for screening

- Placental Growth Factor.
- Plays a role in placental development.
- Predictive value in 1st, 2nd and 3rd trimester(s).
- Low levels indicate high risk.



Principle of combined pre-eclampsia screening



MAP = Mean Arterial Pressure
UTPI = Uterine Artery Pulsatility Index

PRE-ECLAMPSIA SCREENING IN 1st TRIMESTER

Record medical history

- First pregnancy?
- Previous or family history with pre-eclampsia?
- Ethnicity
- Chronic hypertension?
- Smoking?
- Weight AND height.

Blood test PlGF 1-2-3

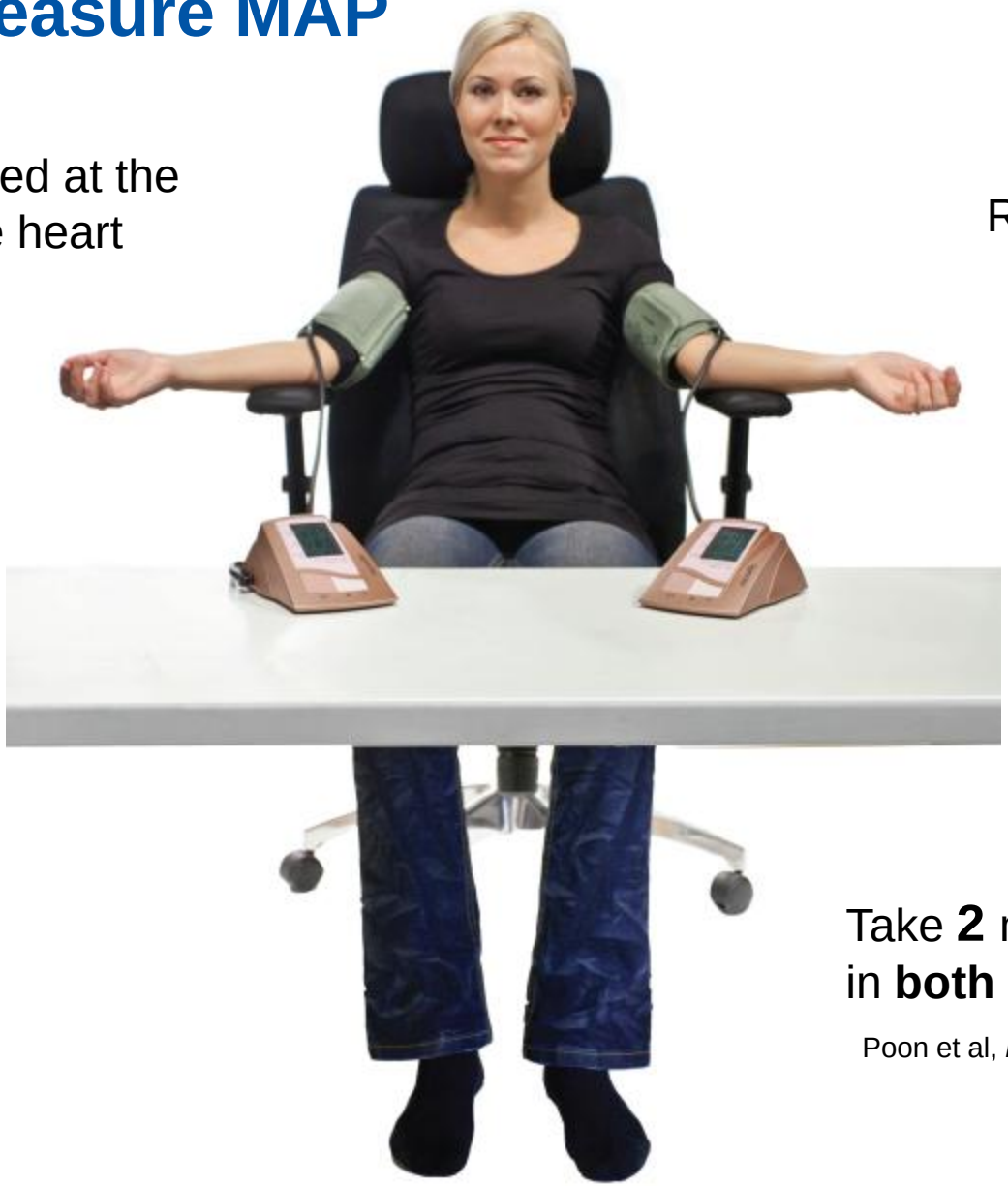
Measure blood pressure

Ultrasound

If accessible, measure uterine artery doppler ultrasound.

How to measure MAP

Arms supported at the level of the heart



Right cuff size:
S, M, L

Take **2** measurements in **both** arms.

Poon et al, *Fetal Diagn Ther 2012*

Both feet on the floor

Blood Pressure monitors for pre-eclampsia

Manufacturer	Model
Microlife	Watch BP Home
Microlife	BPA200
Microlife	3AS1-2
Omron	Mit-ELITE

List of all validated monitors:
http://www.dableducational.org/sphygmomanometers/devices_2_sbpm.html#ArmTable

How does the combined PE screening perform?

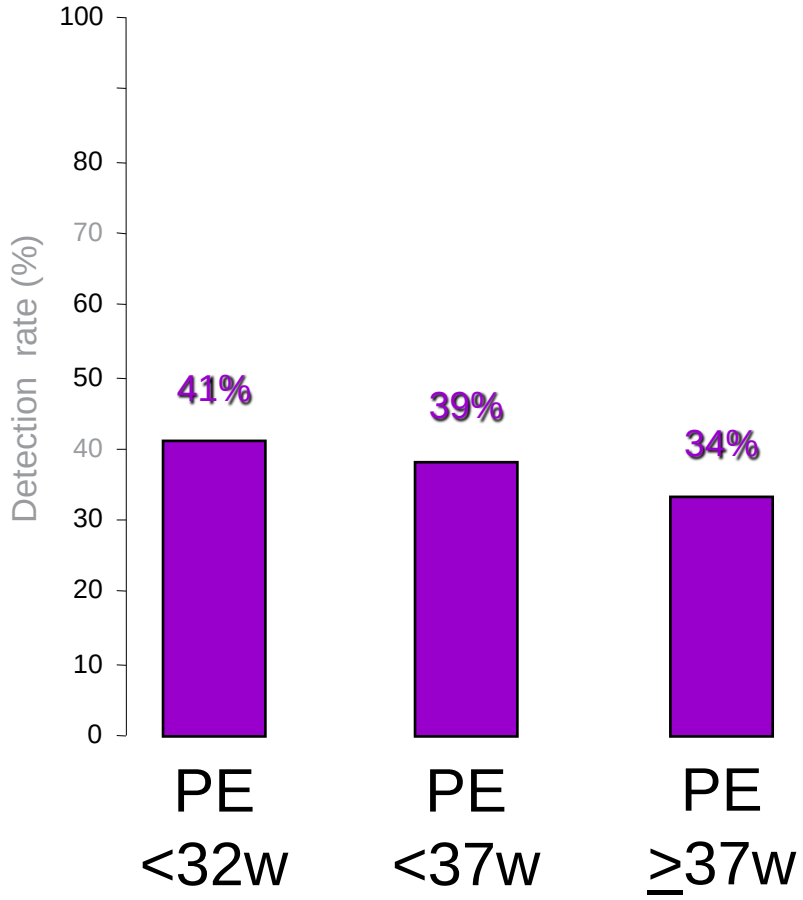
Parameters	Very Early PE	Preterm-PE
History with:	DR % PE<32 weeks	DR% PE<37weeks
PlGF + PAPP-A	88 %	66 %
PlGF + MAP	88 %	69 %
PlGF + MAP+UTPI	100 %	75 %
PlGF + PAPP-A+ MAP+UTPI	100 %	80 %

O' Gorman 2017 *Ultrasound Obstet Gynecol*

Screening without Doppler ultrasound is a good alternative if access is limited.

Results – NICE

National Institute for Health and Clinical Excellence



NICE: FPR 10.2%

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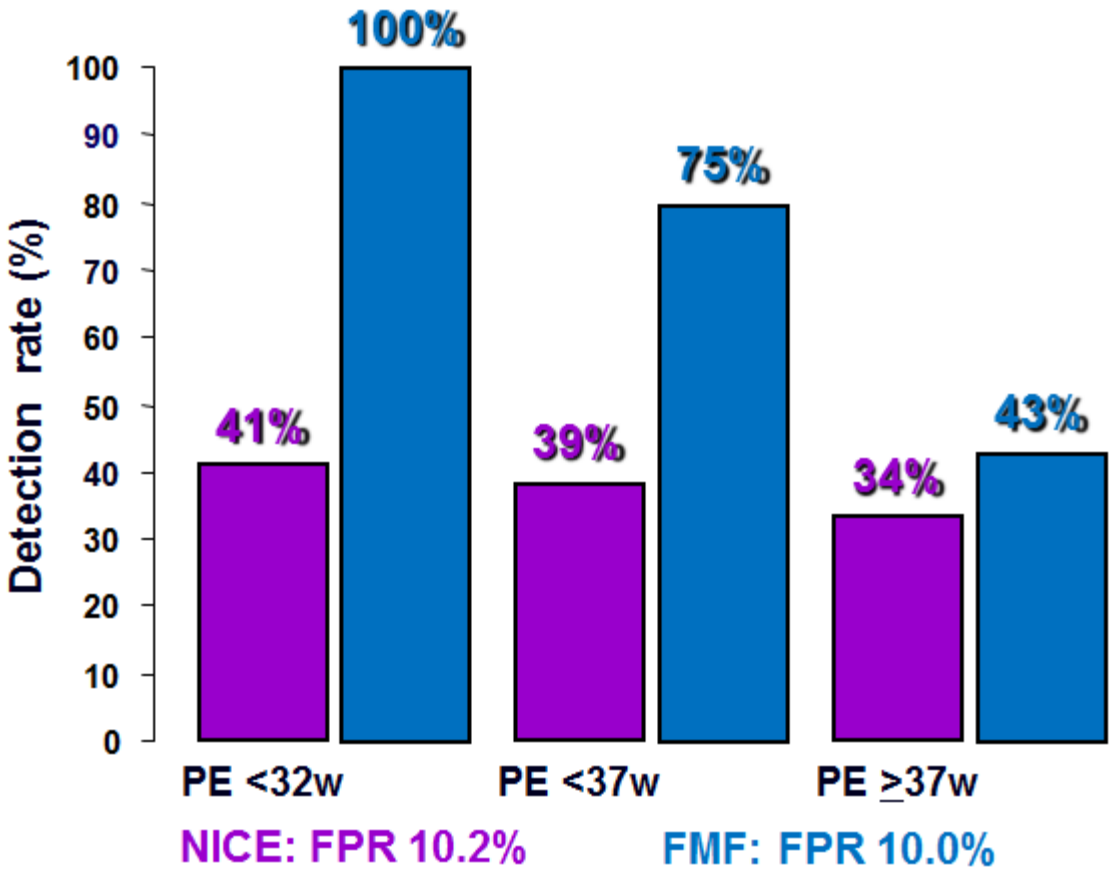
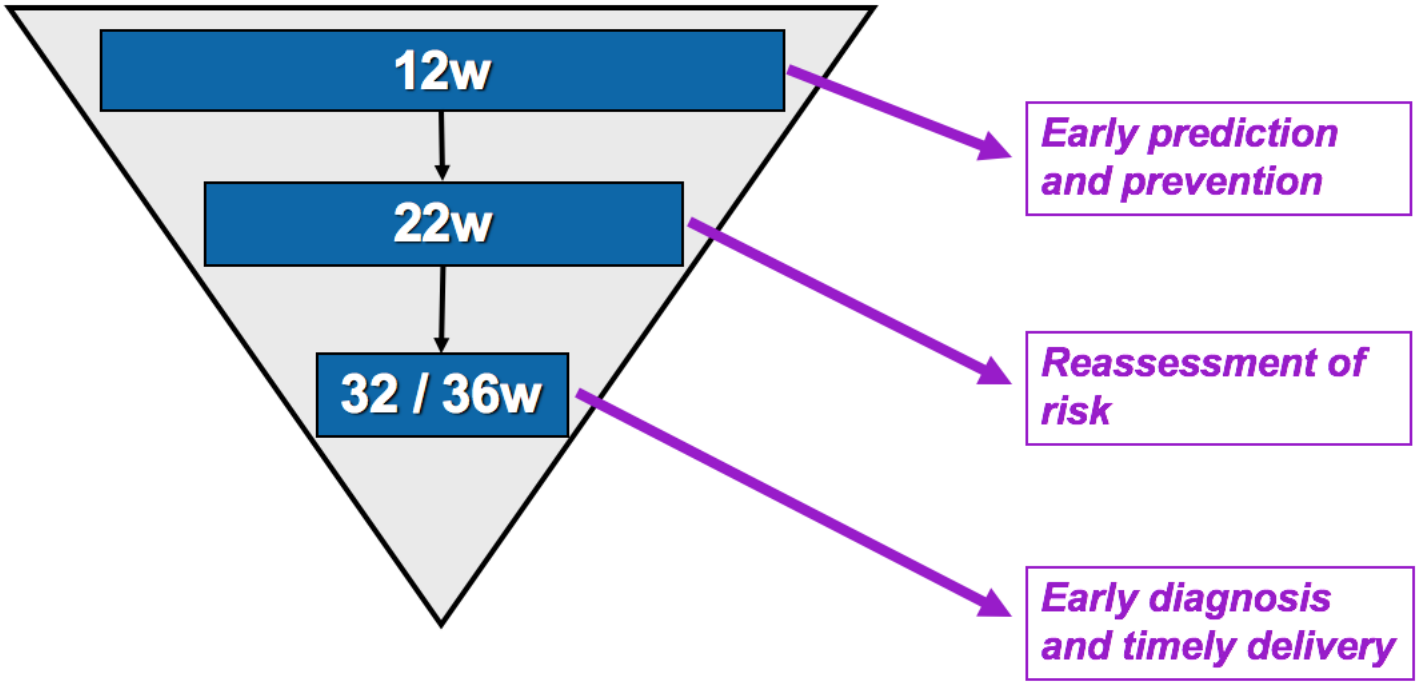
Combined pre-eclampsia screening has a superior performance



Superior performance is achieved with combined pre-eclampsia screening method especially with preterm and very early pre-eclampsia.

O'Gorman et al. Multicenter screening for preeclampsia by maternal factors and biomarkers at 11-13 weeks gestation: comparison to NICE guidelines and ACOG recommendations Ultrasound Obstet Gynecol 2017 – in press

Screening through pregnancy with PlGF 1-2-3

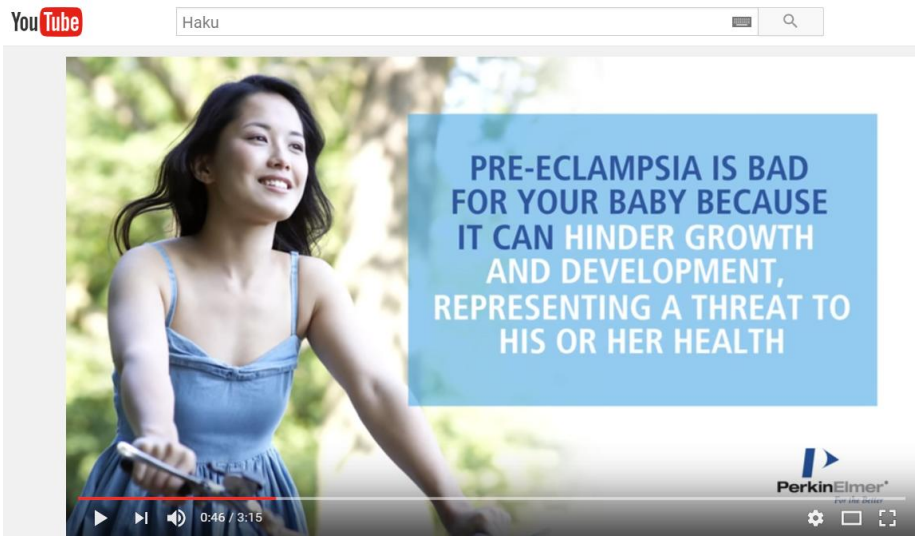


Courtesy of Fetal Medicine Foundation, Ranjit Akolekar

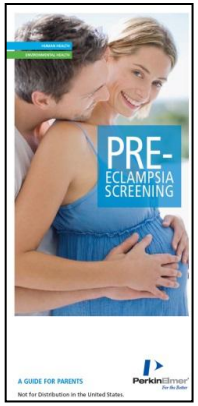
What women need to know?

Being screened for risk of pre-eclampsia is an important step you can take to protect the health of yourself and your baby.

Waiting room video - for parents to be:



https://www.youtube.com/watch?v=DYCnuNmLeeI



Patient flyer

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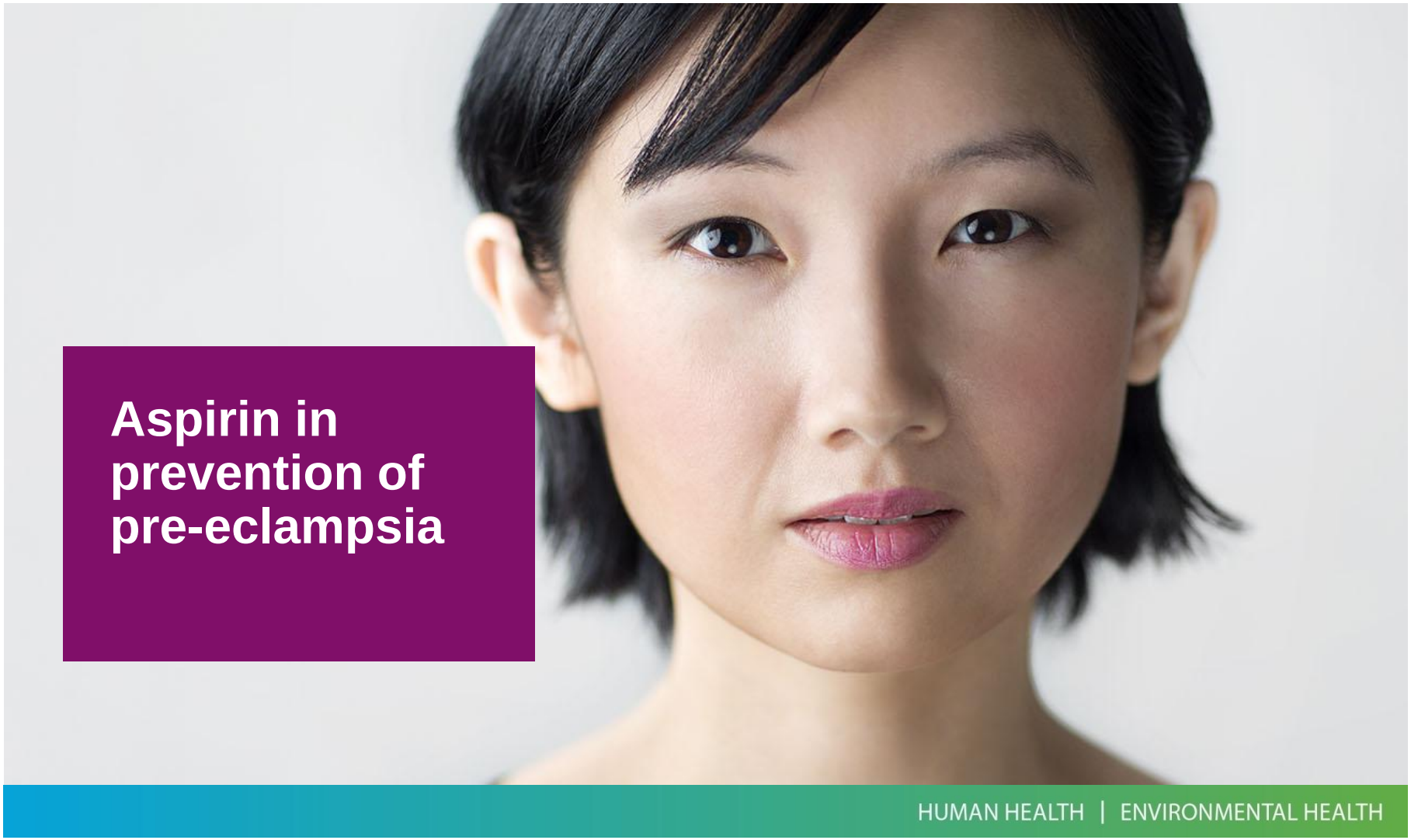

Aspirin in prevention of pre-eclampsia

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Aspirin story

funded by EU FP7
ASPRE
project

Aspirin has been used to help prevent pre-eclampsia, but evidence supporting the effectiveness has been mixed.

ASPRE study was conducted to bring final, level A1 evidence to the matter.

Facts about ASPRE trial:

- ✓ The largest, multicenter, randomized, placebo controlled trial.
- ✓ Funded by European union FP7.
- ✓ Principal investigator, Professor Kypros Nicolaides, founder of FMF.
- ✓ ASPRE chose PerkinElmer PlGF 1-2-3 assay for screening.

ASPRE study design

~30,000 women

Combined pre-eclampsia screening at 11-13 wks
History+PlGF1-2-3+MAP+UTPI

High risk

Placebo

Aspirin

Aspirin treatment in ASPRE

funded by EU FP7 ASPRE project

			Reference
Dose	150 mg	*A dose response effect of aspirin is demonstrated. A high proportion (30%) of population is non responsive to aspirin if given at lower doses.*	*Caron et al 2009* *Bujold et al 2015*
Start	12 weeks	*Aspirin is effective if given to high risk women before 16 weeks of gestation.*	*Bujold et al 2010* *Roberge et al 2011*
Finish	36 weeks	*Avoid potential hemorrhage for neonate*	De Beradis 2012
Time	Bed time	*Lower incidence of PE when aspirin taken at bedtime compared to morning or afternoon.*	*Ayala et al 2013*

ASPRE results – publication submitted

Publication expected summer 2017.

ASPRE results are likely to change treatment guidelines and reimbursement policies worldwide

PlGF 1-2-3 improves T21 screening

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1T QUAD

The Fetal Medicine Foundation
FMF approved

Effective 1st trimester aneuploidy screening even when NT is not available.

1T QUAD= PAPP-A, free hCGß, PlGF and AFP

With 1T Quad, you can achieve similar performance to 2T Triple test already in the first trimester (Johnson 2013).

FIRST TRIMESTER SCREENING 11-13+6 WEEKS

	Serum markers	Ultrasound	T21 Detection
Combined test	PAPP-A, free hCGβ	NT	87%
Combined Plus	PAPP-A, free hCGβ, PlGF	NT	90%
Expanded combined test	PAPP-A, free hCGβ, PlGF, AFP	NT	92%
1T QUAD (serum only)	PAPP-A, free hCGβ, PlGF, AFP	-	82%

NT=nuchal translucency ultrasound

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Huang et al Prenat Diagn. 2015, Donaldson et al 2013, Johnson *et al.*, 2012 , Pandya 2012, Wald 2012, Cowans 2010, Zaragoza, 2009.

Join Professor Kypros Nicolaides' webcast on pre-eclampsia screening

Monday, May 29 at 4:00 pm CET

Kypros Nicolaides, Professor at King's College Hospital, London, UK and founder of Fetal Medicine Foundation, FMF, will cover the following topics in his presentation:

Pre-eclampsia prediction and prevention

- Combined pre-eclampsia screening – the new way forward
- Optimal use of aspirin in the prevention of pre-eclampsia
- Highly anticipated ASPRE results

The webcast lasts 42-minutes and is followed by a live Q&A session.

Register at
http://info.perkinelmer.com/PEWebcast

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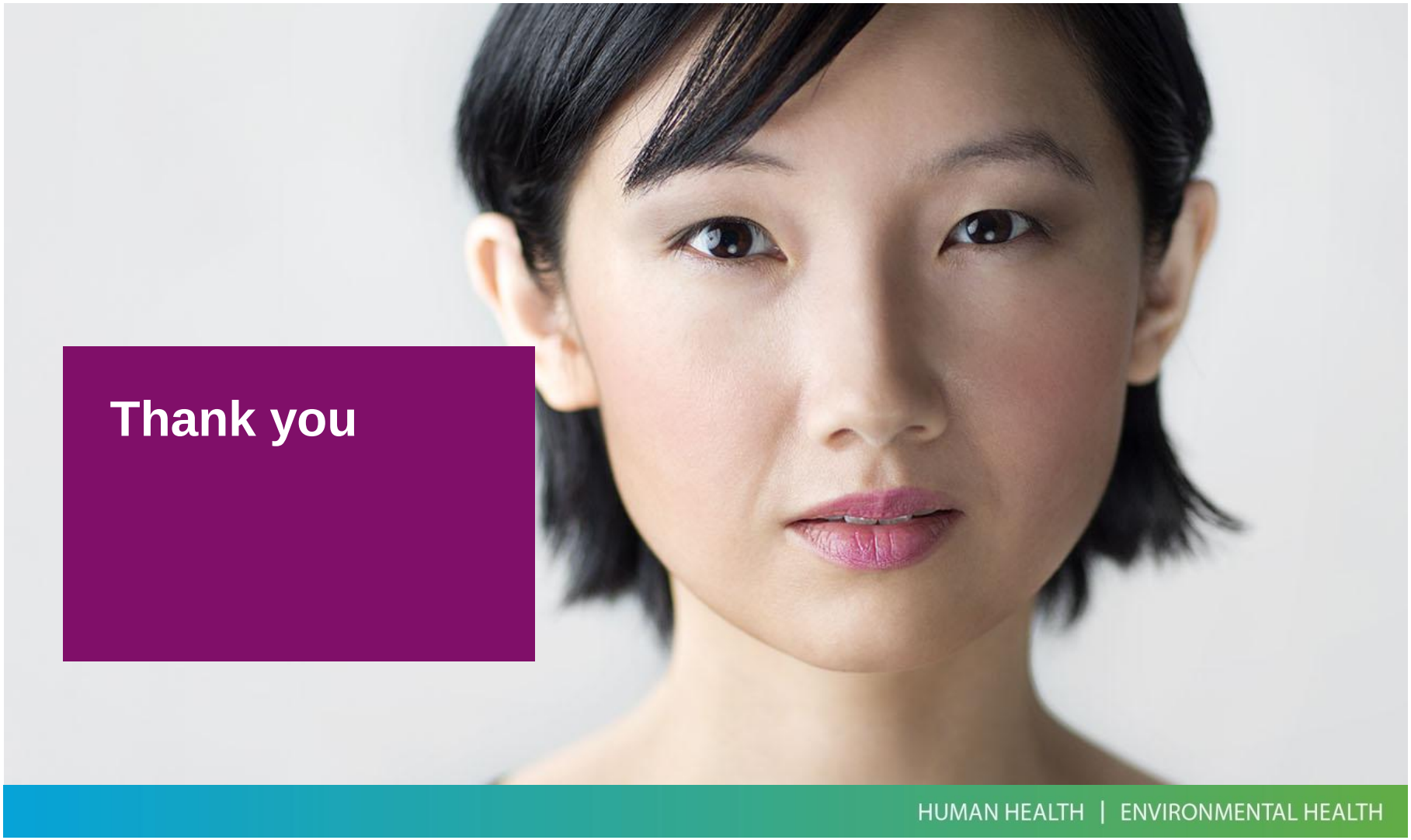

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How to perform uterine artery doppler

1T - Transabdominal ultrasound:

1. **Identify uterine arteries:**
2. **Obtain sagittal section of the cervix and use colour flow doppler**
3. **Rotate the transducer from side to side to identify uterine arteries at the level of the internal cervical os.**

Sampling gate:	**2 mm to cover whole vessel**
Angle of insonation:	less than 30º
Peak systolic velocity:	more than 60 cm/s
Mean PI:	average PI from the left and right arteries