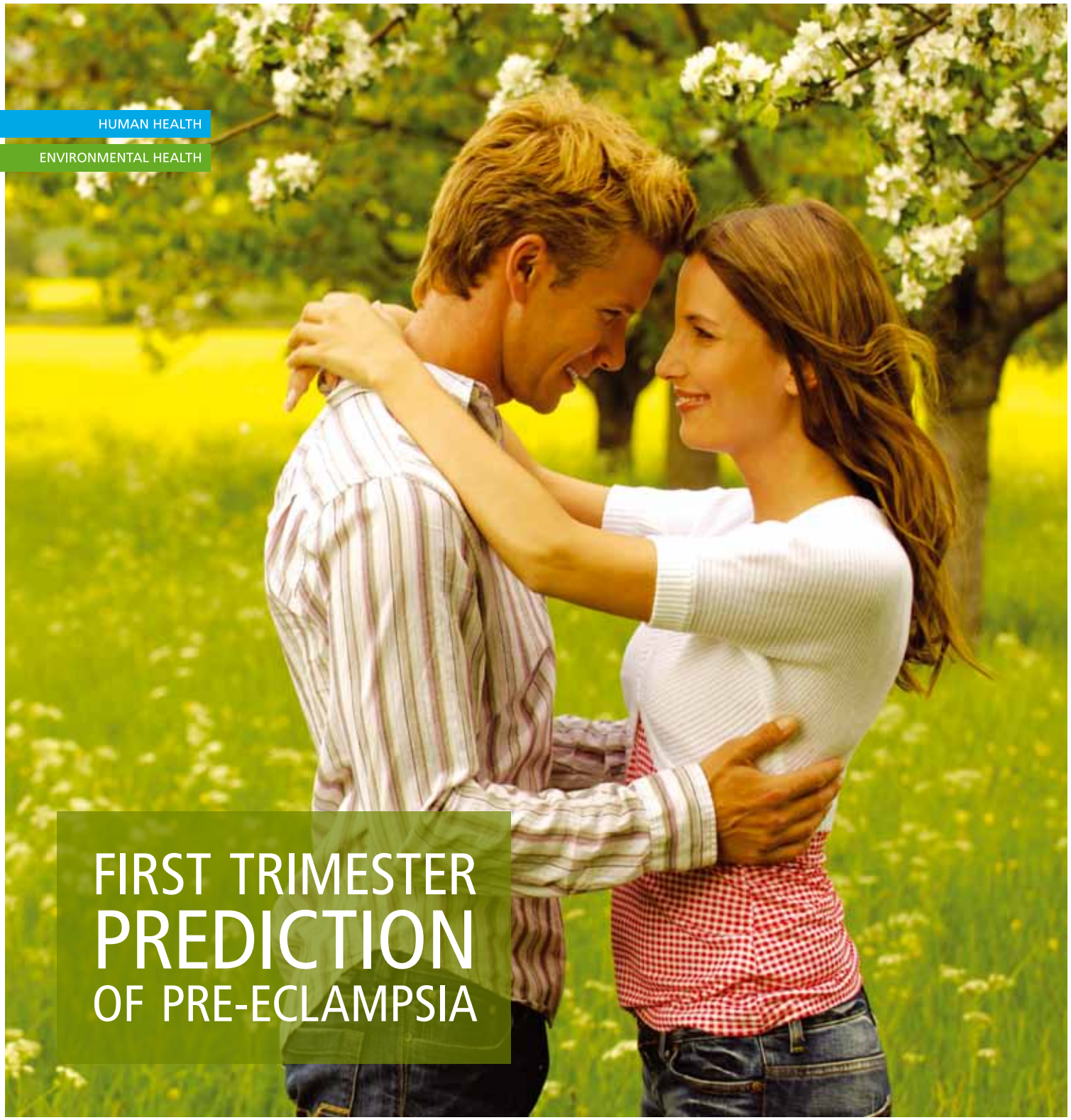
HUMAN HEALTH

ENVIRONMENTAL HEALTH

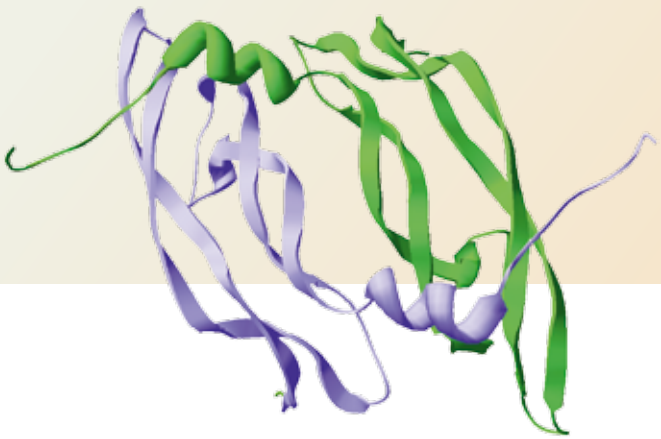


FIRST TRIMESTER PREDICTION OF PRE-ECLAMPSIA

DELFIA® XPRESS PlGF ASSAY

PerkinElmer®
For the Better

PlGF ASSAY KIT



Earlier identification of women at high risk for pre-eclampsia

Prediction before symptoms appear

DELFIA® Xpress PlGF is the first placental growth factor (PlGF) assay designed for use as an aid in screening pregnant women for pre-eclampsia in the first trimester. Pregnancies destined to develop pre-eclampsia are typically associated with reduced levels of PlGF in maternal serum samples. Since this reduction is already visible in the first trimester, PlGF assay helps to identify women at high risk for pre-eclampsia at an early stage of pregnancy.

Early screening is valuable for early-onset pre-eclampsia prediction

Early onset pre-eclampsia means that the delivery of the baby is needed before 34 weeks of pregnancy because the disorder is having an adverse effect on the mother´s or the baby´s condition. Although less common than the late form of the disorder, early onset pre-eclampsia contributes most to the mortality and morbidity statistics. PlGF is predictive of both early and late pre-eclampsia, but is most sensitive and specific as a marker of the early-onset form.

What is PlGF?

Protein produced by the placenta*

Growth factor active in angiogenesis and endothelial cell growth

Reduced maternal serum concentration of PlGF has been shown in a high proportion of pregnancies destined to develop pre-eclampsia.

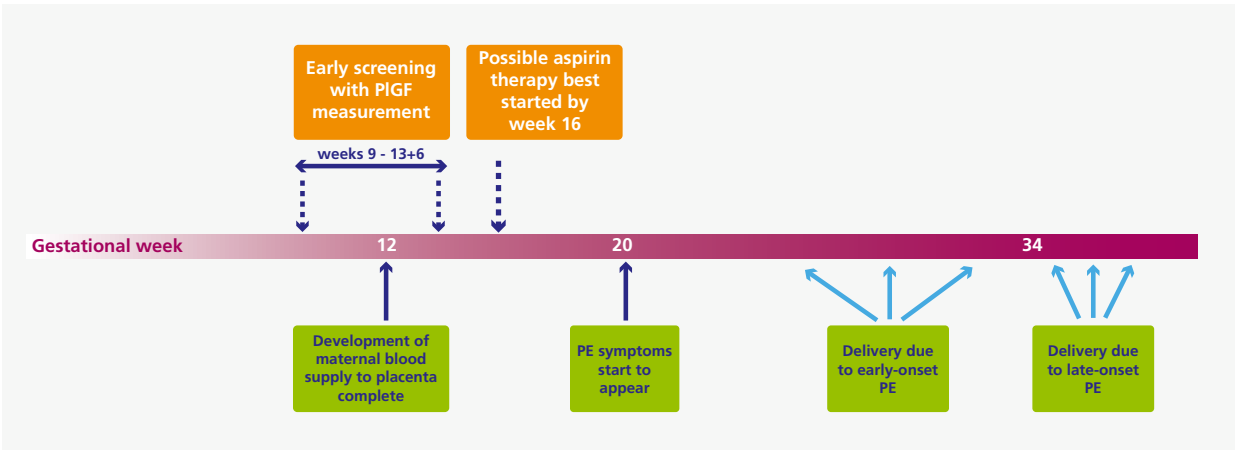
*Also detected in heart, lung, muscle and adipose tissue.

POTENTIAL FOR BETTER OUTCOMES OF PREGNANCY

Although there is no proven effective method for the prevention of pre-eclampsia, identification of affected pregnancies in the first trimester opens up a time window that is potentially very valuable and can ultimately lead to improved pregnancy outcome.

Identification at the end of the first trimester allows

- Increased surveillance of high risk pregnancies
- Earlier diagnosis of the clinical signs of the disease
- Earlier identification of the associated intra uterine growth restriction (IUGR)
- Wider ranging intervention possibilities



Early screening with PlGF measurement between 9 and 13+6 weeks opens a window of opportunity before pre-eclampsia symptoms appear.

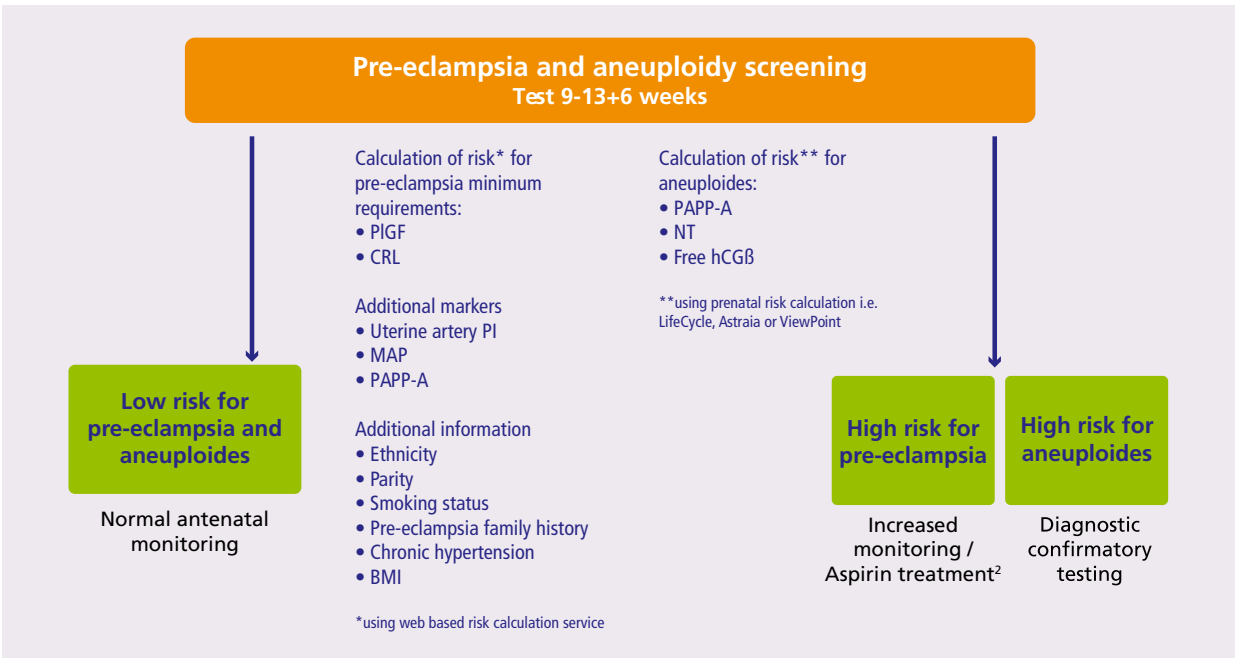
Aspirin treatment before 16 weeks effective in preventing pre-eclampsia

Within the past few years, treatment with aspirin (acetylsalicylic acid, ASA) during pregnancy has been shown to have a moderate but significant effect on the risk of pre-eclampsia. As a therapy, low dose aspirin has a number of attractions, among them the low cost and free availability of the drug throughout the world. A recent meta-analysis focused particularly on the time at which the therapy was started. The reduction in pre-eclampsia (as well as IUGR) was significantly greater when started before 16 weeks of gestation rather than after 20 weeks[2].

Pre-eclampsia screening at 9 to 13+6 weeks is now a practical proposition

The affordable way to start pre-eclampsia screening

Now, using the DELFIA Xpress PlGF assay and the established DELFIA Xpress instrument, laboratories and clinics can perform risk assessment for pre-eclampsia without major hardware investment. Pre-eclampsia testing and aneuploidy testing can be carried out simultaneously, and even using the same maternal serum sample.
A laboratory running PlGF alongside PAPP-A and Free hCGβ can deal with 10,000 samples per year. Processing time is 30 minutes and patient results are delivered at 1.5 minute intervals.



Possible testing procedures for laboratories performing preeclampsia screening alongside first trimester aneuploidy screening.

ONE COMPACT INSTRUMENT FOR ANEUPLOIDY AND PRE-ECLAMPSIA SCREENING

DELFIA® Xpress has been developed to streamline workflows in laboratories and clinics providing prenatal screening services. The instrument is already in use for aneuploidy screening in more than 40 countries.

DELFIA Xpress is a compact table-top instrument offering a range of benefits critical for operational efficiency.

- The speed and convenience of random access
- The security associated with barcoded reagents and samples to ensure positive identification
- The reassurance from using reliable, proven DELFIA chemistry

DELFIA Xpress reagents for Maternal Health screening

- PlGF
- PAPP-A
- Free hCGβ
- hAFP
- uE3
- hCG

The PAPP-A and Free hCGβ assays and the DELFIA Xpress instrument are approved by the FMF for first trimester aneuploidy screening.

PlGF CONTRIBUTES TO GREATLY IMPROVED SCREENING PERFORMANCE

The traditional method of screening for pre-eclampsia is maternal history, for example, as recommended in the U.K.'s National Institute for Clinical Excellence (NICE) guidelines. However, screening as suggested by NICE would result in false positive rates of more than 64% in order to achieve a detection rate of around 90% for early pre-eclampsia[1]. This result is compatible with the 30 % detection rate at a 5 % false positive level suggested in an earlier work[5].

Detection rates closer to 90% with a combination of PlGF with other markers

Far better performance is attainable by combining maternal history with other serum and ultrasound marker results. The utility of maternal serum PlGF measurement in pre-eclampsia prediction has been confirmed in many studies. Case controlled studies suggest that by using this marker in combination with others, detection rates closer to 90% can be achieved with the false positive rate kept at 5%[3].

Marker combination	False positive rate	Detection rate		
		Early PE	**Late PE**	**PE total**
History	5%	40%	28%	28%
	10%	52%	43%	45%
PlGF	5%	33%	24%	26%
	10%	56%	32%	37%
PlGF+ PAPP-A	5%	48%	26%	30%
	10%	52%	31%	35%
History + PlGF	5%	56%	32%	36%
	10%	60%	49%	50%
History + PlGF+ PAPP-A	5%	60%	31%	39%
	10%	76%	48%	53%
History + PlGF + Uterine artery PI	5%	60%	31%	35%
	10%	80%	48%	54%
History + PlGF + PAPP-A + Uterine artery PI + MAP	5%	89%	39%	50%
	10%	96%	64%	69%
History + PlGF + Uterine artery PI + MAP	5%	90%	41%	47%
	10%	96%	63%	70%

Statistical analysis of data from Nicolaides[3,4] based on the sample material detailed below.

	Early PE	**Late PE**	**PE total**	**Unaffected**
Number of cases	25	94	119	604

History = body mass index, family history of PE, previous PE, ethnicity, smoking
MAP = mean arterial blood pressure
PI = pulsatility index

Pre-eclampsia prediction using risk calculation engine

For risk calculation based on a variety of markers, a web based pre-eclampsia risk calculation service is being offered by Prof Howard Cuckle. This service allows users to calculate a risk for both early onset (delivery before 34 weeks) and late onset pre-eclampsia (delivery at or later than 34 weeks) and obtain a printable patient report. The report will contain patient information, measurement results and risk estimations.

For more information on his Screen Info service please contact Prof Cuckle on hscuckle@screeninfo.co.uk.

Parameters that can be used to calculate the risk with the web based risk calculation service:

- Patient History
- PlGF (mandatory)
- PAPP-A
- CRL (mandatory) for dating of the pregnancy
- Uterine artery Pulsatility Index*
- Mean arterial blood pressure (MAP)

*Measured by health care professionals who have completed the Fetal Medicine Foundation internet based course on the 11-13 weeks scan and who have submitted four images, each showing color flow with normal or abnormal waveform of the uterine arteries, and who have had these images accepted by FMF. See http://www.fetalmedicine.com/fmf/online-education/01-11-136-weekscan.

An easy to use, but sophisticated web-based method

- Login at the risk calculation webpage - www.screeninfo.co.uk/eReports
- Enter patient info
- Enter MAP and uaDoppler
- Enter biochemistry results for PlGF and/or PAPP-A

The application generates both the prior risk and the risk based on all markers for both early onset (<34 weeks) and late onset (≥34 weeks) pre-eclampsia.

You can print out a risk report, and you can save the data for MoM QA/QC assessment

- No identifiable patient information will be retained by the application

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5 Yu et al. (2005)
An integrated model for the prediction of preeclampsia using maternal factors and uterine artery Doppler velocimetry in unselected low-risk women.
Am J Ostet Gynecol. 193 429-436.

ORDERING INFORMATION

6007-0010/6007-001C	DELFIA Xpress PlGF kit
3090-0010	PlGF Controls*
6000-0010	DELFIA Xpress instrument

* Under development.

Products are not available in the US, and may not have been licensed in accordance with Canadian law.

For more information, visit www.perkinelmer.com/pre-eclampsia

For information on availability of PerkinElmer products please contact your local representative.

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