A close-up portrait of a woman with light brown hair and numerous freckles across her face. She is looking slightly to the right with a gentle expression. The background is a soft, out-of-focus white.

PRE-ECLAMPSIA SCREENING WITH PIGF 1-2-3™ KIT

**PRENATAL SCREENING SOLUTIONS
FROM THE GLOBAL LEADER
IN MATERNAL-FETAL HEALTH**

Brochure not for distribution in the USA

The PerkinElmer logo consists of a stylized blue 'P' followed by the company name.

PerkinElmer
For the Better

A NEW ERA IN PRE-ECLAMPSIA CARE WITH THE PIGF 1-2-3™ KIT



The next step in screening and treatment for pre-eclampsia

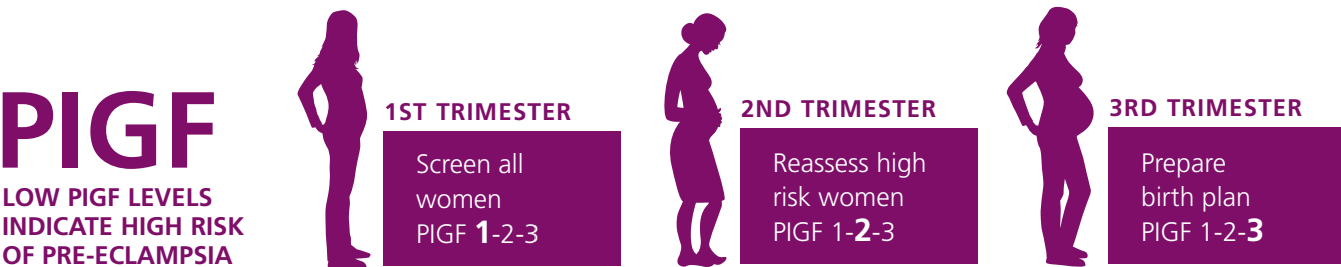
Pre-eclampsia is a complication of pregnancy marked by high blood pressure and protein in the urine. Left untreated, pre-eclampsia can lead to eclampsia, a serious condition that can, in some cases, lead to death. Pre-eclampsia also affects blood flow to the placenta, often leading to growth-restricted or prematurely born babies. Avoiding this condition would bring substantial improvements to maternal and fetal health.

Today women expect doctors to offer effective prenatal care based on the latest research evidence and screening solutions. They want the best care possible throughout pregnancy.

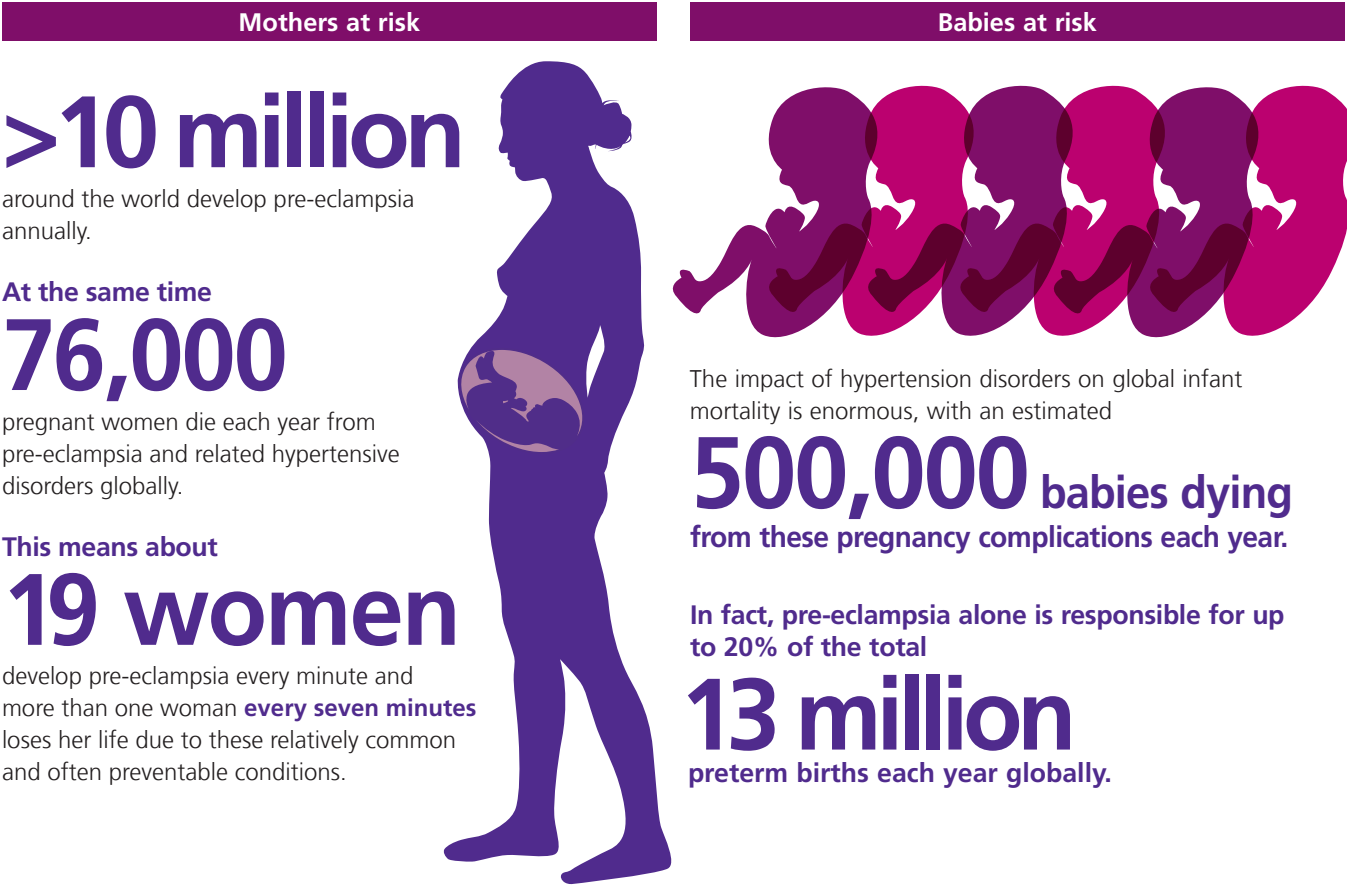
When it comes to pre-eclampsia, the growing consensus among caregivers and researchers is that timing matters more than ever. The earlier you identify women as having a high risk for pre-eclampsia, the better the outcome for mother and child.

PIGF 1-2-3™ – the 2nd-generation PIGF assay

PerkinElmer's PIGF 1-2-3 assay is the most sensitive first-trimester screening kit for pre-eclampsia to date.^[2] When used in combination with a comprehensive first trimester screening program that includes maternal medical history and mean arterial blood pressure, women at high risk for pre-eclampsia can be identified long before symptoms appear. The PIGF 1-2-3™ assay can also be used in the second and third trimester of pregnancy for effective reassessment, monitoring or diagnosis.^[3]



The global burden of pre-eclampsia



UNDERSTANDING PRE-ECLAMPSIA – CAUSE AND EFFECT

Early and preterm pre-eclampsia – poor placentation

While the direct cause of pre-eclampsia is unknown, researchers agree that if symptoms such as high blood pressure and proteinuria occur between 20 and 37 weeks, there is a high risk that the placenta will be adversely affected. Early onset pre-eclampsia is also associated with preterm birth and fetal growth restriction, with prematurity accounting for most pre-eclampsia-related healthcare costs. If HELLP syndrome or eclampsia occur alongside pre-eclampsia, ICU care is inevitable.

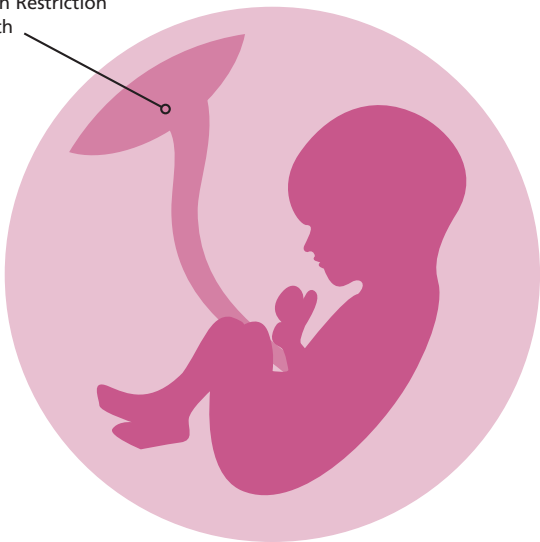
The good news is that aspirin treatment is highly effective in the prevention of early and preterm pre-eclampsia.^[4, 5]

Term pre-eclampsia – maternal origin and cardiac dysfunction

New evidence suggests that if pre-eclampsia develops after 37 weeks (term pre-eclampsia), the resulting condition is more closely related to cardiac and metabolic dysfunction in the mother than poor placentation per se.^[6,7] In fact, according to some researchers, term pre-eclampsia is a completely different pregnancy complication than early and pre-term pre-eclampsia. The alternative view is that pre-eclampsia is a spectrum disorder in which all women eventually develop the condition if the pregnancy is continued indefinitely.^[8, 9]

Placental insufficiencies

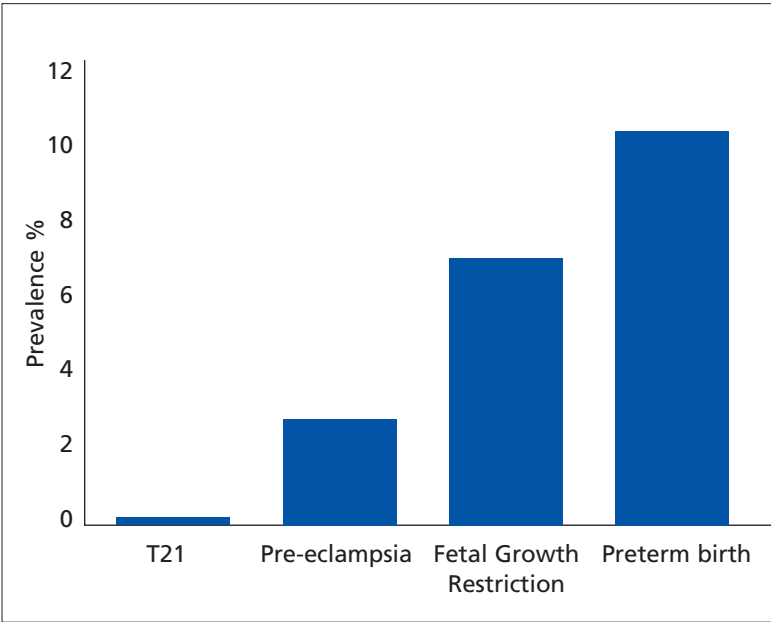
- 1 Pre-eclampsia
- 2 Fetal Growth Restriction
- 3 Preterm birth
- 4 Stillbirth



“Placental insufficiency is present in virtually every major obstetrical syndrome”
ROMERO, AM J OBSTET GYNECOL. 2011.

Placental insufficiencies are much more common than Down syndrome.

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



VERY EARLY PRE-ECLAMPSIA

- Delivery needed <32 weeks
- Prevalence 0.2%

EARLY ONSET PRE-ECLAMPSIA

- Delivery needed <34 weeks
- Prevalence 0.4%

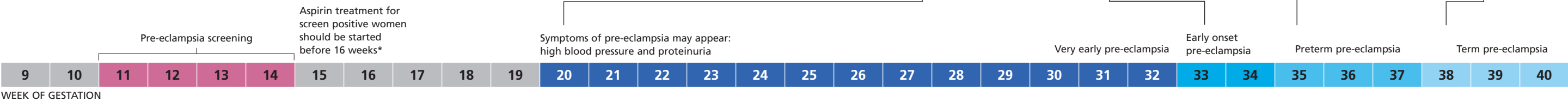
PRETERM PRE-ECLAMPSIA

- Delivery needed <37 weeks
- Prevalence 0.7%

TERM PRE-ECLAMPSIA

- Delivery needed ≥37 weeks
- Prevalence 2%

Timeline of pre-eclampsia screening, aspirin treatment and onset of different pre-eclampsia types.



*PerkinElmer does not endorse or make recommendations with respect to research, medication, or treatments. All information presented is for informational purposes only and is not intended as medical advice. For country-specific recommendations please consult your local health care professional.



FROM MATERNAL FACTORS TO EFFECTIVE COMBINED SCREENING

The right combination

The combined screening program for pre-eclampsia is the most effective way to identify women at high risk of pre-eclampsia in the early stages of pregnancy. The program consists of the PIGF 1-2-3™ blood test, maternal medical history assessment, mean arterial blood pressure measurement and, if available, uterine artery Doppler ultrasonography.

1st trimester – perfect timing

The timeframe for pre-eclampsia screening is the first trimester, when low-dose aspirin therapy shows the best results in the prevention of pre-eclampsia. To achieve maximum effectiveness, aspirin therapy should be started before 16 weeks of gestation among women at high risk of pre-eclampsia.^[10]

Four simple steps

The combined screening program is made up of four simple steps that require short training and minimal additional investment in equipment for screening programs.

- 1. Record medical history, weight and height.
- 2. Take blood sample for measuring PIGF 1-2-3™.
- 3. Measure blood pressure 2 times from both arms simultaneously.
- 4. If accessible, measure uterine artery Doppler pulsatility index.

Medical history – a priori risk

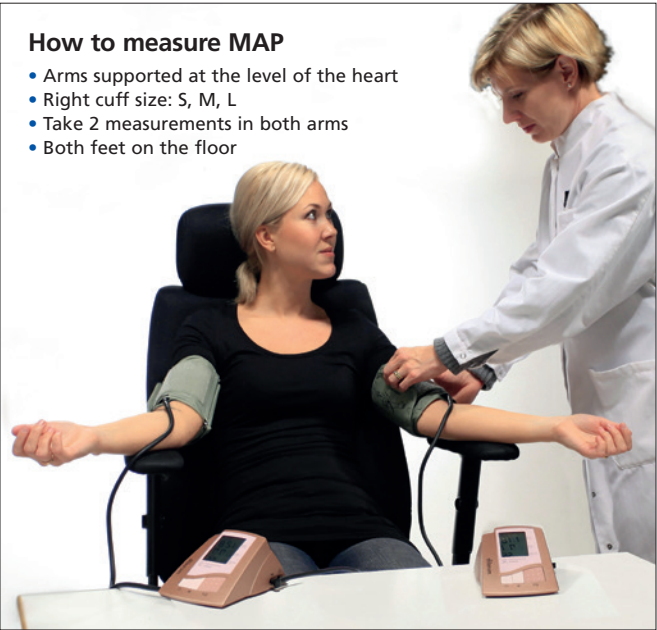
The traditional method of screening for pre-eclampsia has been based on asking women a series of questions during their first pregnancy visit.^[11,12] This method considers each risk factor as an independent and unrelated event. The more effective approach to defining maternal a priori risk uses an algorithm that determines the relative importance of each risk factor and their interrelationship.^[13]

PIGF 1-2-3 blood test

The high-sensitivity PIGF 1-2-3™ assay can be performed as early as the first trimester, at 11–13⁺6 weeks. The blood sample is analysed using the same PerkinElmer instrument that is used for aneuploidy screening. No additional blood sample is required as the same sample can be used both to screen for pre-eclampsia and for aneuploidy screening. Women with an elevated risk of pre-eclampsia show a lower maternal serum level of placental growth factor (PIGF).

Mean arterial blood pressure – MAP

When mean arterial blood pressure (MAP) is used as a pre-eclampsia screening marker, it is important to use the standardised protocol for MAP measurement. The blood pressure (BP) should be measured two times from both arms simultaneously using two blood pressure monitors. The blood pressure should be recorded from both arms because of significant non-pathological inter-arm variations.^[14]



How to measure MAP

- Arms supported at the level of the heart
- Right cuff size: S, M, L
- Take 2 measurements in both arms
- Both feet on the floor

RECORD MEDICAL HISTORY

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

BLOOD TEST PIGF 1-2-3

MEASURE BLOOD PRESSURE

Take 2 measurements from both arms simultaneously

Ultrasound If accessible, measure uterine artery Doppler pulsatility index.

Approved blood pressure monitors for pre-eclampsia screening	
Manufacturer	Model
Microlife®	WatchBP Home
Microlife®	BP A200
Microlife®	3AS1-2
Microlife®	CRADLE VSA
Omron®	MIT-Elite

Monitors that are not listed here can also be used if they have been validated for pre-eclampsia, or declared identical with a validated model.

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Uterine artery Doppler pulsatility index (UTPI) ultrasound

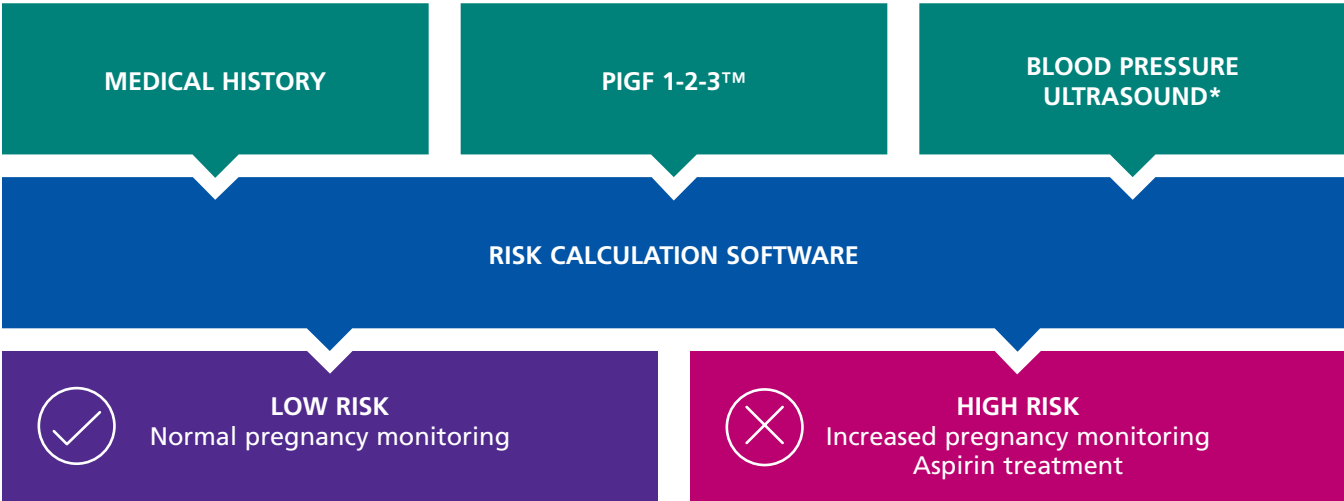
The uterine artery Doppler pulsatility index (UTPI) can be measured between 11–13⁺⁶ weeks via a transvaginal or transabdominal ultrasound. Please refer to the Fetal Medicine Foundation's guidelines for the detailed protocol and certificates of competence.^[15]

Automatic risk assessment

Specialised software generates a unique patient risk profile and report based on maternal risk factors, PIGF 1-2-3™ test results and biophysical information. Depending on access and availability, other marker combinations can also be used to screen for pre-eclampsia.

Procedure for 1T transabdominal UTPI measurement:

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



*Risk calculation can be performed without ultrasound if access is limited” as in example below.

Combined pre-eclampsia screening – the first step to better detection

When it comes to effectively predicting pre-eclampsia, the combined screening program outperforms screening methods that rely only on maternal history.

The effectiveness of pre-eclampsia screening also depends on marker combination.^[13]

Parameters	Very Early PE	Preterm PE
Medical history with:	Detection rate	Detection rate
PIGF + PAPP-A	88 %	66 %
PIGF + MAP	88 %	69 %
PIGF + MAP + UTPI	100 %	75 %
PIGF + PAPP-A + MAP + UTPI	100 %	80 %

Medical history and blood test can help to identify 88% of very early pre-eclampsia cases and 66% of preterm pre-eclampsia cases. Similar detection rates can be achieved with medical history, PIGF 1-2-3™ and MAP. If UTPI is available, the detection rate is close to 100% for very early PE and between 75%–80% for preterm PE.^[13] These are examples and other combinations are possible. FPR (False Positive Rate) = 10% in this example.





WHAT DOCTORS NEED TO KNOW



Who should be screened for pre-eclampsia?

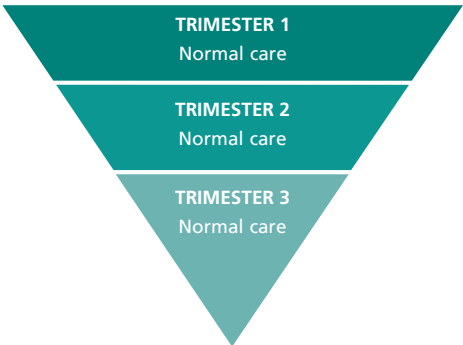
All pregnant women should be assessed early on in their pregnancy to prevent the development of pre-eclampsia. They should also have access to screening even if there are no maternal risk factors or history of pre-eclampsia. Why? The benefit of detecting and treating pre-eclampsia early in the pregnancy always outweighs the conventional wait-and-see approach to pre-eclampsia management.

What should women know?

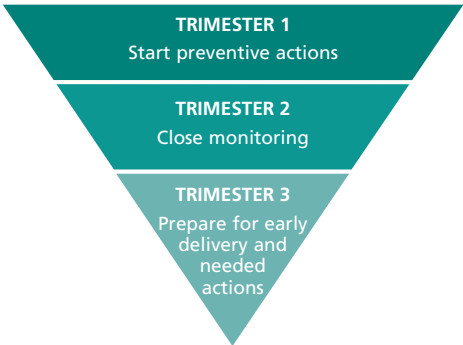
While pre-eclampsia screening is critical to protecting the health of mother and child, many women are unaware of pre-eclampsia or combined pre-eclampsia screening with the PIGF 1-2-3™ assay. They need to know that pre-eclampsia can affect any pregnancy. They should also be informed that some pregnancies are more at risk of developing pre-eclampsia than others. Combined pre-eclampsia screening with the PIGF 1-2-3™ assay is an effective way to assess this risk. In fact, women with a history of pre-eclampsia have a three to four times greater risk of developing chronic hypertension than mothers with no history of pre-eclampsia and double the risk of ischemic heart disease, venous thromboembolism and stroke.^[16]

What do the results mean?

Low risk
Low risk means that there is minimal risk of developing pre-eclampsia later in pregnancy. While it is possible to develop pre-eclampsia regardless of low risk status, the pregnancy can continue as normal and the mother can rest assured that there is little or no reason for concern.



High risk
If the risk of developing pre-eclampsia later in pregnancy is high, the doctor can start treatment at the optimum time and monitor the pregnancy more closely. While not all women in the high-risk group develop pre-eclampsia, doctors can now offer the best possible care early in the pregnancy and significantly improve the outcome for mother and child.



ASPREE – LOW-DOSE ASPIRIN IN THE PREVENTION OF PRE-ECLAMPSIA

Low-dose aspirin is effective in reducing the risk of pre-eclampsia – especially the early forms of the disease. The best results are achieved with a dose of 150 mg aspirin per day.^[17] In the ASPREE trial, aspirin treatment was started after PE screening at around 12 weeks and finished at 36 weeks. The trial results showed that the rate of developing early onset pre-eclampsia dropped by 82% and preterm pre-eclampsia by 62% among those women who received aspirin treatment and were at high risk of risk of developing the disease. To identify women in the high risk group, ASPREE employed a first-trimester combined screening program that included PerkinElmer's PIGF 1-2-3™ assay.

While aspirin treatment is not a cure for pre-eclampsia, fewer women need to suffer from this serious disease if low-dose aspirin is administered early in the pregnancy.^[5]

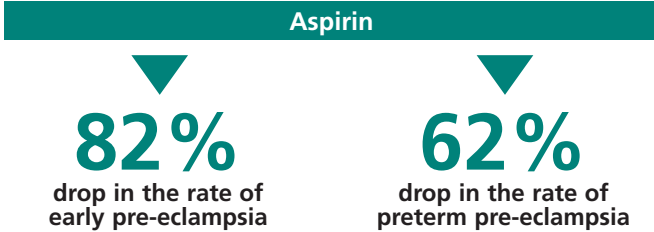
Dose	150 mg	A dose response effect of aspirin is demonstrated. A high proportion (1/3) of the population is non-responsive to aspirin at lower doses. ^[18,19]
Start	12 weeks	Aspirin is effective if given to high risk women before 16 weeks of gestation. ^[4,10]
Finish	36 weeks	Avoid potential hemorrhage for neonate. ^[20]
Time	Bed time	Lower incidence of PE when taken at bedtime compared to morning or afternoon. ^[21]

Aspirin treatment according to ASPREE study design^[5]

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Combined pre-eclampsia screening at 11–13⁺6 weeks



What makes ASPREE special?

ASPREE was the biggest prospective, randomized, placebo-controlled trial ever on the prophylactic use of aspirin in women at increased risk of pre-eclampsia. Funded by the European Union and administered by the Fetal Medicine Foundation, more than 30,000 pregnancies were studied in the UK, Belgium, Italy, Spain, Greece and Israel. No other clinical study on low-dose aspirin and pre-eclampsia matches the scale and scope of ASPREE.



WHAT LABORATORIES NEED TO KNOW



Choose PIGF 1-2-3™ and enter a new era

PerkinElmer's high-sensitivity PIGF 1-2-3™ kit is the only assay that can offer the level of accuracy and precision required by the ground-breaking ASPRE trial.

PIGF 1-2-3™ is also the first assay optimized for first-trimester screening of pre-eclampsia, which makes it the logical choice in the new era of improved pre-eclampsia management.

PIGF 1-2-3™ – the ASPRE assay

- Options for 48 and 96 test kits
- Sensitivity 1.9 pg/ml
- 20 min incubation time with DELFIA® Xpress
- Native pregnancy serum CE-IVD controls
- Clinical validity demonstrated in the ASPRE study
- Same CE-IVD assay kit is applicable in 1st, 2nd and 3rd trimesters
- Proven DELFIA® technology

	PerkinElmer PIGF 1-2-3™	Company A	Company B
LoD	1.9 pg/mL	3.0 pg/mL	3.6 pg/mL
LoQ	3.3 pg/ml	10 pg/ml	6.9 pg/ml

The ASPRE study chose PerkinElmer DELFIA®Xpress and PIGF 1-2-3™ assay, because sensitivity and precision matters in screening.^[22]



To find out more about ASPRE, go to ASPRE.perkinelmer.com

SENSITIVITY	PRECISION
CLINICAL VALIDITY	CHOICE OF EXPERTS ASPRE
ACCURACY OF RESULTS CAN BE ENSURED IN 1T WHEN THE CLINICALLY RELEVANT PIGF LEVEL IS VERY LOW	



PIGF 1-2-3™ assay



DELFIA® Xpress

Complete panel of prenatal screening and maternal-fetal health markers on DELFIA platforms

PIGF 1-2-3™
sFlt-1*
PAPP-A
Free hCGβ
PAPP-A / Free hCGβ Dual
hAFP
hAFP / Free hCGβ Dual
hCG
uE3
InhA
PIGF Controls
Maternal Health Control early

*In development

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PerkinElmer is committed to advancing maternal-fetal health

With more than 10 million prenatal screens performed annually on our solutions, PerkinElmer is the globally recognized leader in maternal fetal health. Our complete screening and diagnostic solutions, combining clinically proven assays, equipment and informatics, are devoted to supporting the needs of all women worldwide. PerkinElmer is committed to leveraging this knowledge to advance the science of maternal fetal health and expand the capabilities of laboratory specialists and clinicians now, and in the future.



PerkinElmer – Your complete screening solution provider

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