Προεκλαμψία

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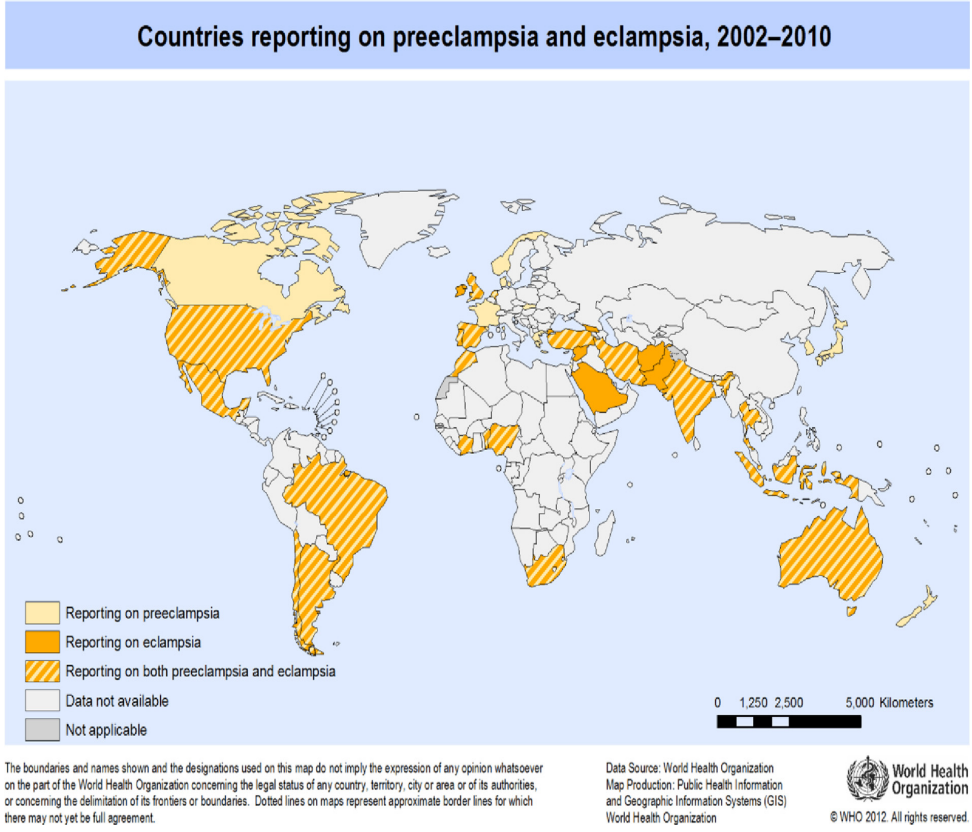
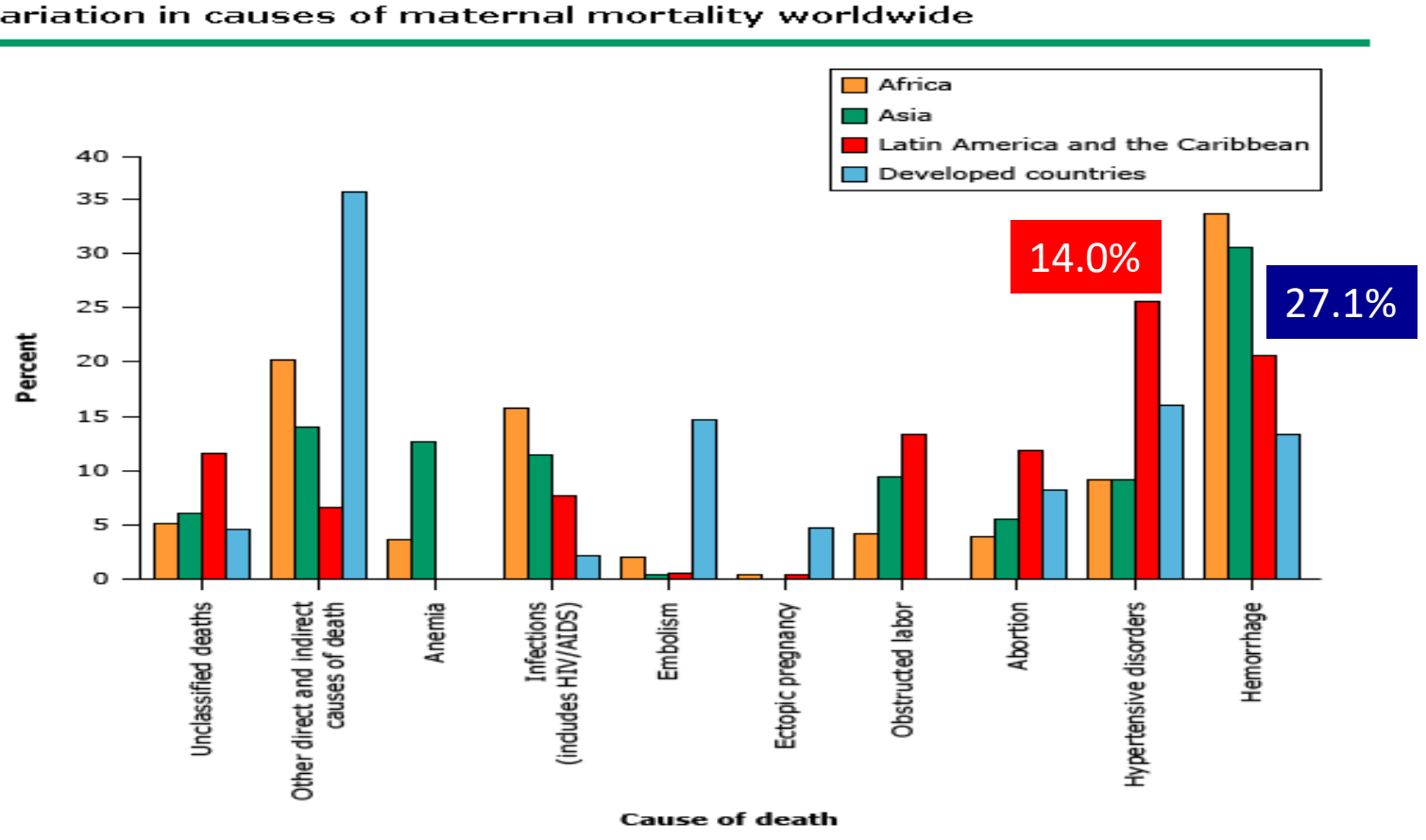
Προεκλαμψία



- **2% to 8%** of all pregnancies globally and about **3.4% in the United States**.
- **Over 10 million** women around the world **develop** pre-eclampsia annually
- **76 000** pregnant women **die** each year from pre-eclampsia and related hypertensive disorders globally
- **Every 7 minutes** one woman loses her life due to these often preventable conditions
- **500 000** babies die from pre-eclampsia and other hypertension disorders annually
- **Over 2.5 million** preterm births are caused by pre-eclampsia each year

http://prenataltesting.perkinelmer.com/total_partner/pre-eclampsia_screening
https://www.nichd.nih.gov/health/topics/preeclampsia/conditioninfo/risk

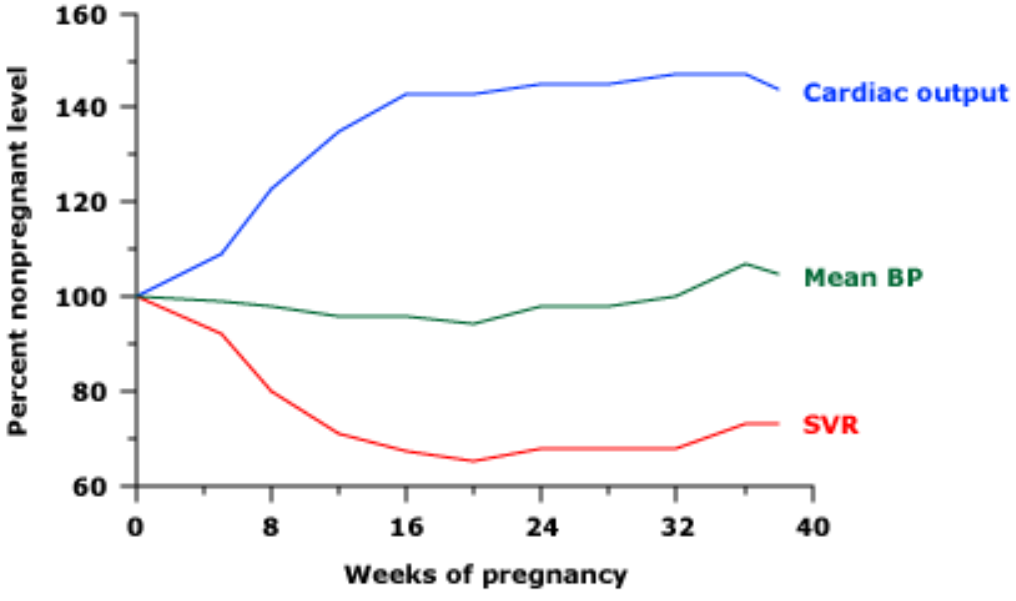
Προεκλαμψία



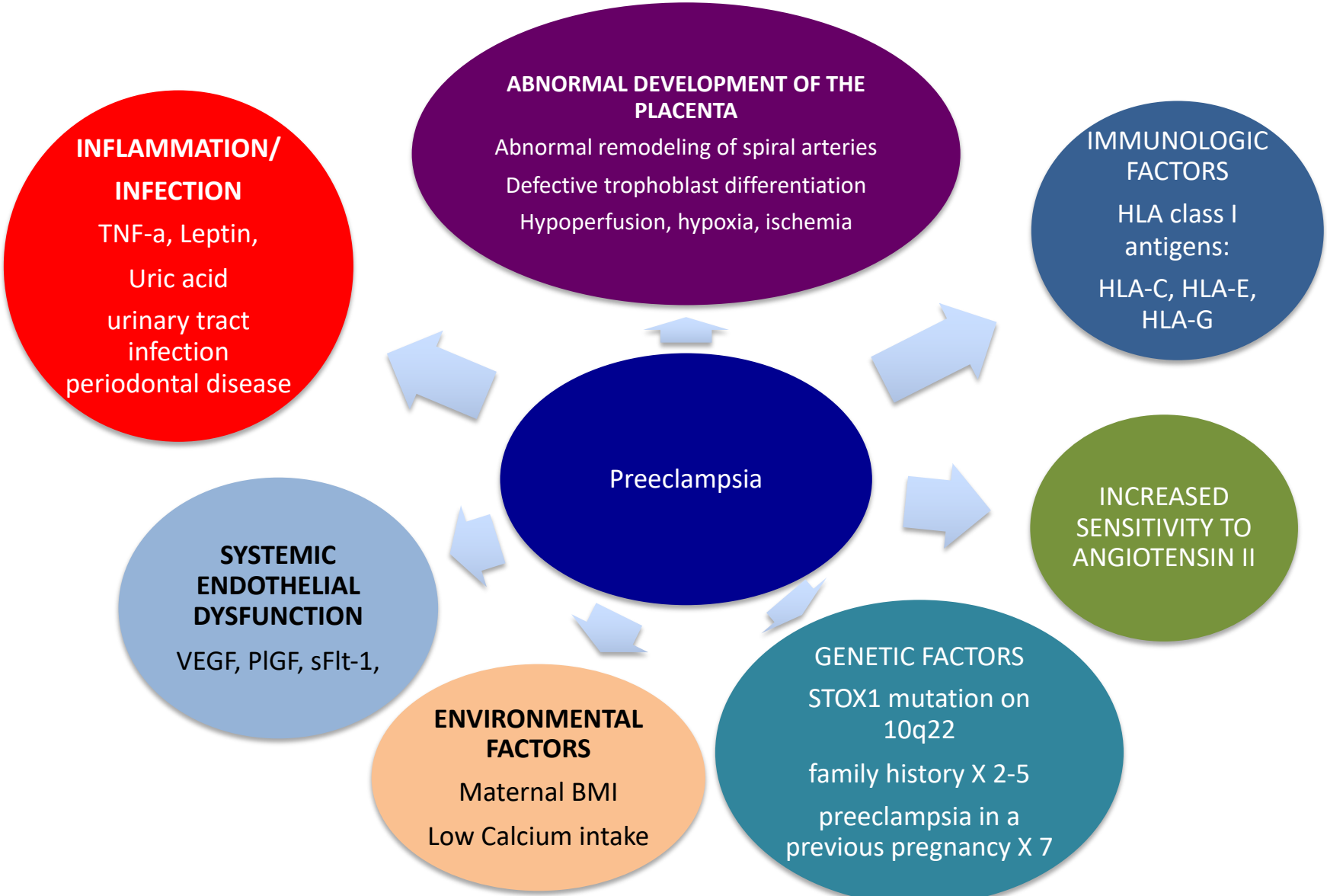
Say at al. www.thelancet.com/lancetgh Vol 2 June 2014

Blood Pressure (BP) = Cardiac Output (CO) x Systemic Vascular Resistance (SVR)

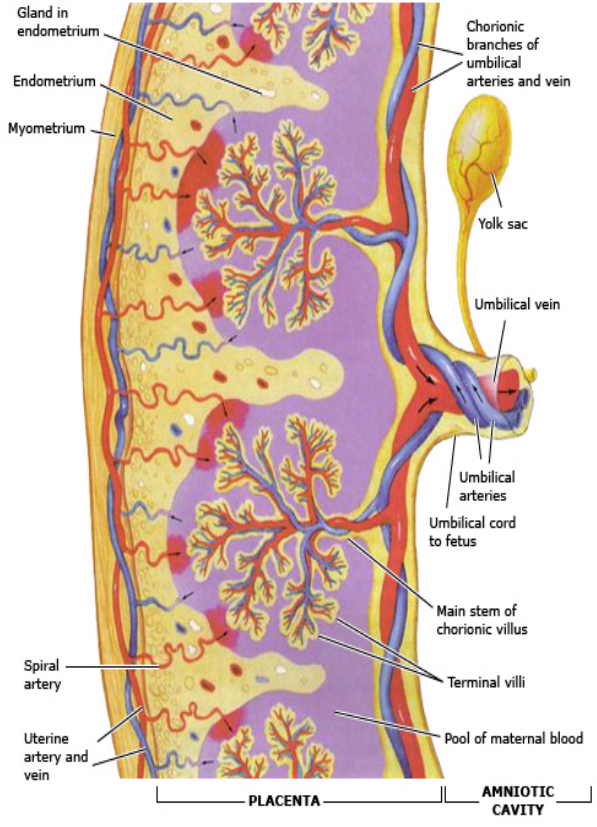
Hemodynamic changes in normal pregnancy



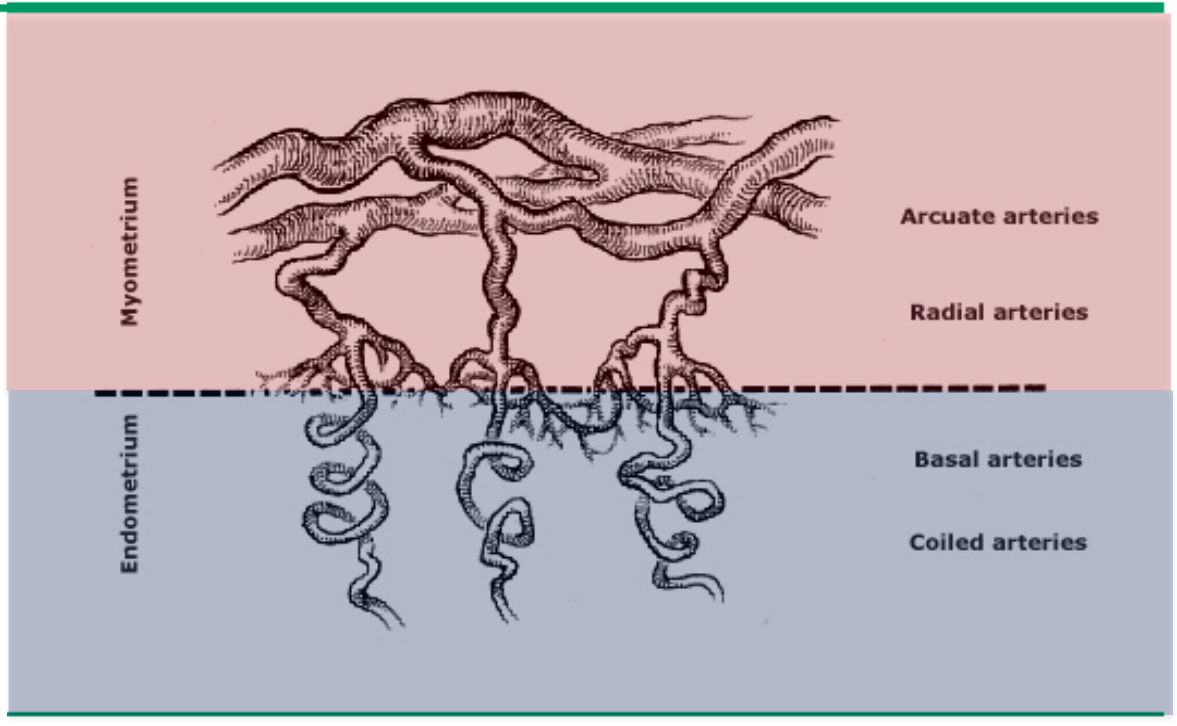
Normal pregnancy is characterized by an increase in cardiac output, a reduction in systemic vascular resistance, and minimal change in mean blood pressure. These changes are associated with a 10- to 15-beat/minute increase in heart rate.


ABNORMAL DEVELOPMENT OF THE PLACENTA
Abnormal remodeling of spiral arteries
Defective trophoblast differentiation
Hypoperfusion, hypoxia, ischemia
INFLAMMATION/ INFECTION
TNF-a, Leptin,
Uric acid
urinary tract infection
periodontal disease
IMMUNOLOGIC FACTORS
HLA class I antigens:
HLA-C, HLA-E, HLA-G
Preeclampsia
SYSTEMIC ENDOTHELIAL DYSFUNCTION
VEGF, PlGF, sFlt-1,
INCREASED SENSITIVITY TO ANGIOTENSIN II
ENVIRONMENTAL FACTORS
Maternal BMI
Low Calcium intake
GENETIC FACTORS
STOX1 mutation on 10q22
family history X 2-5
preeclampsia in a previous pregnancy X 7

Placental vasculature

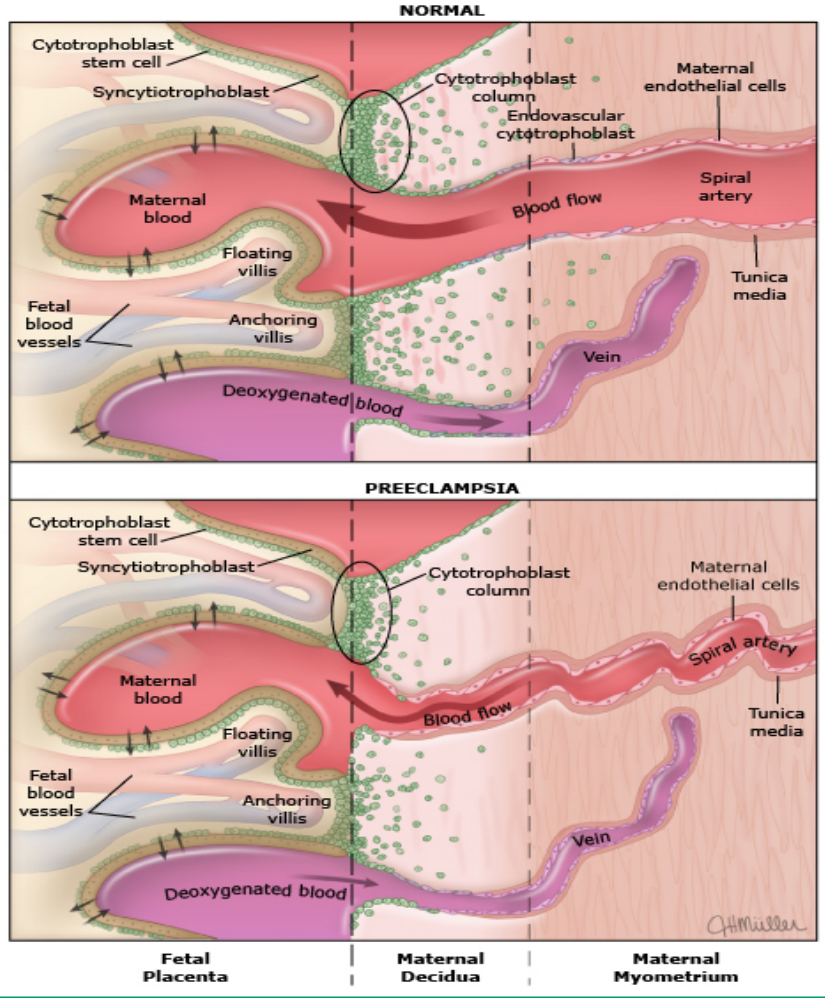


Stereographic representation of myometrial and endometrial arteries in the macaque



Above are shown parts of myometrial arcuate arteries from which myometrial radial arteries course toward the endometrium. There are found larger endometrial coiled arteries and smaller endometrial basal arteries.

ΠΛΑΚΟΥΝΤΟΠΟΙΗΣΗ



Ο σχηματισμός του πλακούντα αρχίζει με την εμφύτευση της βλαστοκύστης στο ενδομήτριο την 10η ημέρα μετά τη γονιμοποίηση του ωαρίου

Τροφοβλάστη → δομικό στοιχείο του πλακούντα

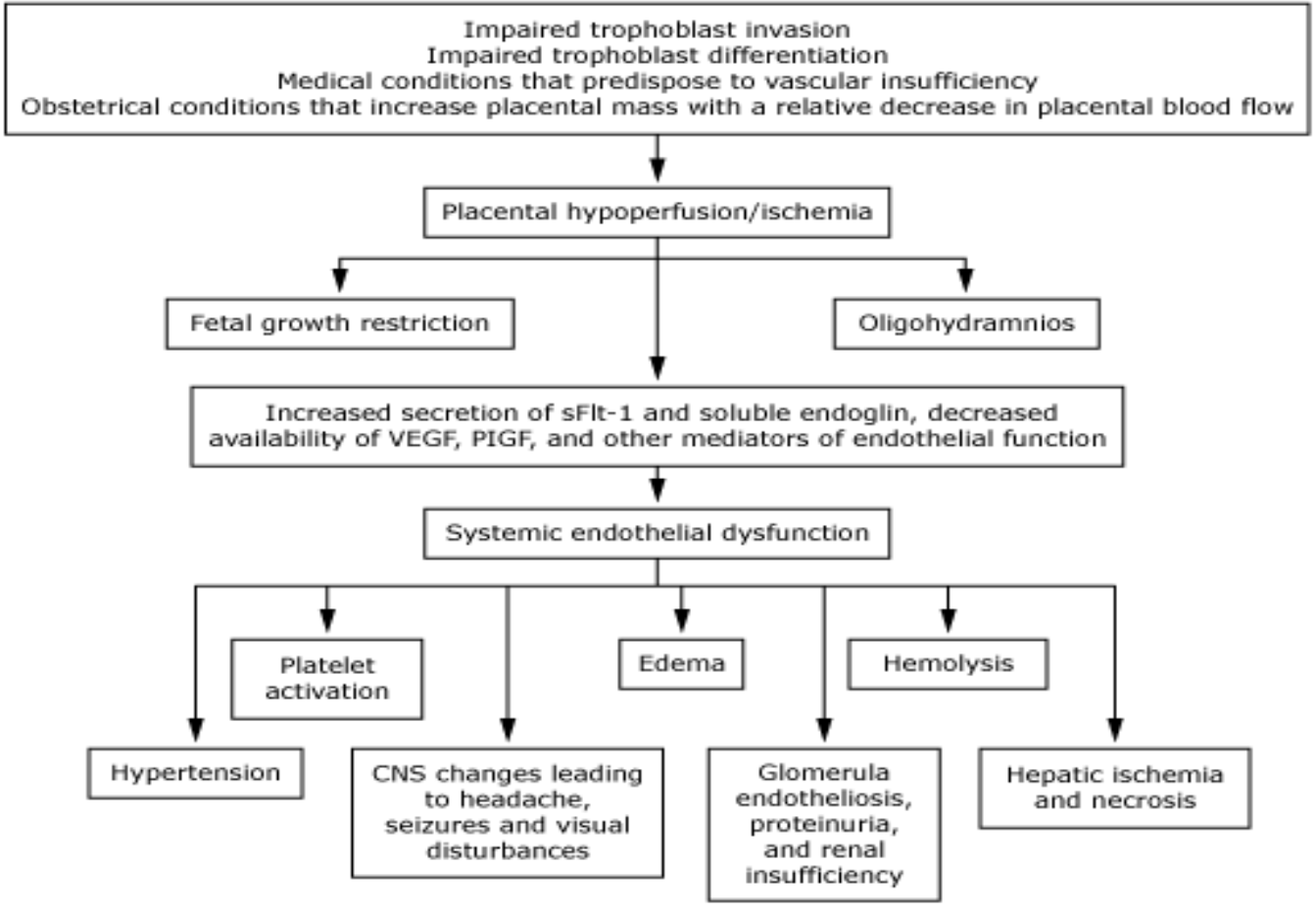
- Κύτταρο-τροφοβλάστη
- Συγκύτιο-τροφοβλάστη

- Πολυάριθμες διακλαδιζόμενες μονάδες (χοριακές λάχνες)

Οι κυτταροτροφοβλάστες μεταναστεύουν στον αυλό των σπειροειδών αρτηριών και σταδιακά αντικαθιστούν το **ενδοθήλιο** των αγγείων αυτών και **τμήμα του μυϊκού τους τοιχώματος**.

Οι αλλαγές αυτές που συμβαίνουν στο αγγειακό δίκτυο της μήτρας μεταμορφώνουν τα αγγεία σε ένα **σύστημα μειωμένων αντιστάσεων / χαμηλής πίεσης και μεγάλης ροής** ώστε να αυξηθεί η παροχή αίματος και να καλυφθούν οι αυξανόμενες ανάγκες του εμβρύου και του πλακούντα

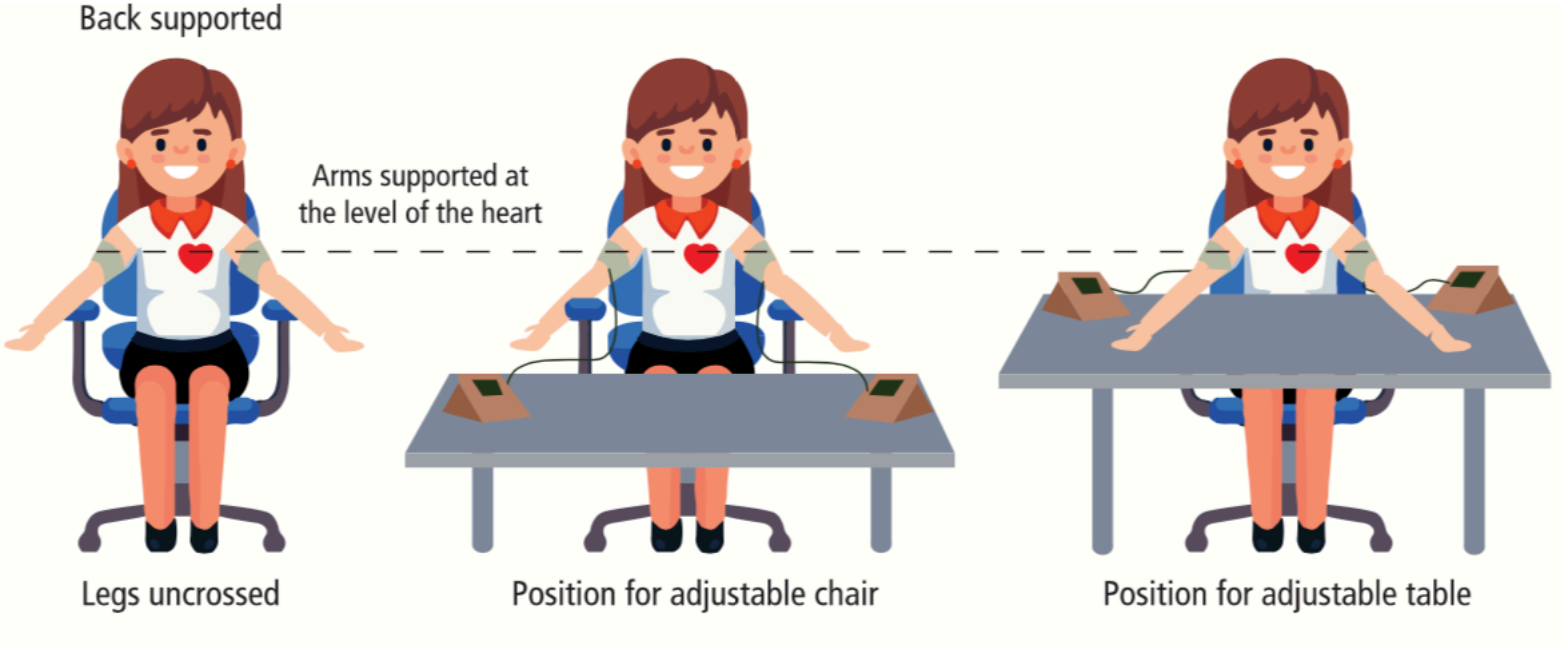
Παθογένεση προεκλαμψίας



DEFINITIONS / DIAGNOSTIC CRITERIA

Blood pressure

Severity	systolic BP (mmHg)	diastolic BP (mmHg)
Mild	140-150	90-100
Moderate	150-159	100-109
Severe	≥160	≥110


Back supported
Arms supported at
the level of the heart
Legs uncrossed
Position for adjustable chair
Position for adjustable table

ΥΠΕΡΤΑΣΙΚΕΣ ΔΙΑΤΑΡΑΧΕΣ ΤΗΣ ΚΥΗΣΗΣ

ΥΠΕΡΤΑΣΗ ΤΗΣ ΚΥΗΣΗΣ **Gestational hypertension**	• Πρωτοεμφανιζόμενη συστολική αρτηριακής πίεσης ≥140 mmHg ή διαστολική αρτηριακή πίεση ≥90 mmHg χωρίς πρωτεϊνουρία ή σημεία προσβολής τελικών οργάνων • Ανάπτυξη μετά την 20ή εβδομάδα της κύησης σε γυναίκες με γνωστό ιστορικό φυσιολογικής ΑΠ πριν από την εγκυμοσύνη. • Η αρτηριακή πίεση είναι αυξημένη τουλάχιστον δύο φορές σε μεσοδιάστημα τουλάχιστον 4 ωρών
ΠΡΟΕΚΛΑΜΨΙΑ/ΕΚΛΑΜΨΙΑ **Preeclampsia-eclampsia**	
ΧΡΟΝΙΑ/ΠΡΟΥΠΑΡΧΟΥΣΑ ΥΠΕΡΤΑΣΗ **Chronic (preexisting) hypertension**	• Συστολική πίεση ≥140 mmHg ή / και διαστολική πίεση ≥90 mmHg • προηγείται της εγκυμοσύνης • ή είναι παρούσα τουλάχιστον δύο φορές πριν από την 20ή εβδομάδα της κύησης • ή παραμένει περισσότερο από 12 εβδομάδες μετά τον τοκετό
ΠΡΟΕΚΛΑΜΨΙΑ ΣΕ ΕΔΑΦΟΣ ΧΡΟΝΙΑΣ /ΠΡΟΥΠΑΡΧΟΥΣΑΣ ΥΠΕΡΤΑΣΗΣ **Preeclampsia-eclampsia superimposed upon chronic hypertension**	Εμφάνιση πρωτεϊνουρίας, δυσλειτουργία τελικών οργάνων ή και τα δύο μετά τις 20 εβδομάδες κύησης σε γυναίκα με χρόνια / προϋπάρχουσα υπέρταση.

American College of Obstetricians and Gynecologists, Task Force on Hypertension in Pregnancy. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. Obstet Gynecol 2013; 122:1122

Κριτήρια διάγνωσης Προεκλαμψίας

Systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg on two occasions at least four hours apart after 20 weeks of gestation in a previously normotensive patient
If systolic blood pressure is ≥160 mmHg or diastolic blood pressure is ≥110 mmHg, confirmation within minutes is sufficient
and
Proteinuria ≥0.3 g in a 24-hour urine specimen or protein/creatinine ratio ≥0.3 (mg/mg)(30 mg/mmol)
Dipstick ≥1+ if a quantitative measurement is unavailable
OR
New-onset hypertension with the new onset of any of the following (with or without proteinuria):
Platelet count <100,000/microL
Serum creatinine >1.1 mg/dL (97.2 micromol/L) or doubling of the creatinine concentration in the absence of other renal disease
Liver transaminases at least twice the upper limit of the normal concentrations for the local laboratory
Pulmonary edema
Cerebral or visual symptoms (eg, new-onset and persistent headaches not responding to usual doses of analgesics*; blurred vision, flashing lights or sparks, scotomata)

American College of Obstetricians and Gynecologists, Task Force on Hypertension in Pregnancy. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. Obstet Gynecol 2013; 122:1122

Κριτήρια διάγνωσης Προεκλαμψίας

Uteroplacental dysfunction

- fetal growth restriction
- abnormal umbilical artery Doppler waveform analysis
- stillbirth

FIGO adopts the definition of PE as provided by the International Society for the Study of Hypertension in Pregnancy (ISSHP).

Προεκλαμψία: Παράγοντες κινδύνου

Past history of preeclampsia	RR 8.4, 95% CI 7.1-9.9
Pregestational diabetes	RR 3.7, 95% CI 3.1-4.3
Chronic hypertension	RR 5.1, 95% CI 4.0-6.5
Systemic lupus erythematosus	RR 1.8, 95% CI 1.5-2.1
Antiphospholipid syndrome	RR 2.8, 95% CI 1.8-4.3
Prepregnancy body mass index >25	RR 2.1, 95% CI 2.0-2.2
body mass index (BMI) >30	RR 2.8, 95% CI 2.6-3.1
Chronic kidney disease (CKD)	RR 1.8, 95% CI 1.5-2.1
Multifetal pregnancy	RR 2.9, RR 2.6-3.1
First pregnancy (nulliparity)	RR 2.1, 95% CI 1.9-2.4
A family history of preeclampsia in a first-degree relative	RR 2.90, 95% CI 1.70-4.93
Prior pregnancy complications associated with placental insufficiency	
fetal growth restriction	RR 1.4, 95% CI 0.6-3.0
abruption	RR 2.0, 95% CI 1.4-2.7
stillbirth	RR 2.4, 95% CI 1.7-3.4
Advanced maternal age	
maternal age ≥35	RR 1.2, 95% CI 1.2-2.0
maternal age ≥40	RR 1.5, 95% CI 1.2-2.0
Use of assisted reproductive technology	RR 1.8, 95% CI 1.6-2.1

Bartsch E, et al. BMJ. 2016

Table 1 Maternal Complications in Preeclampsia

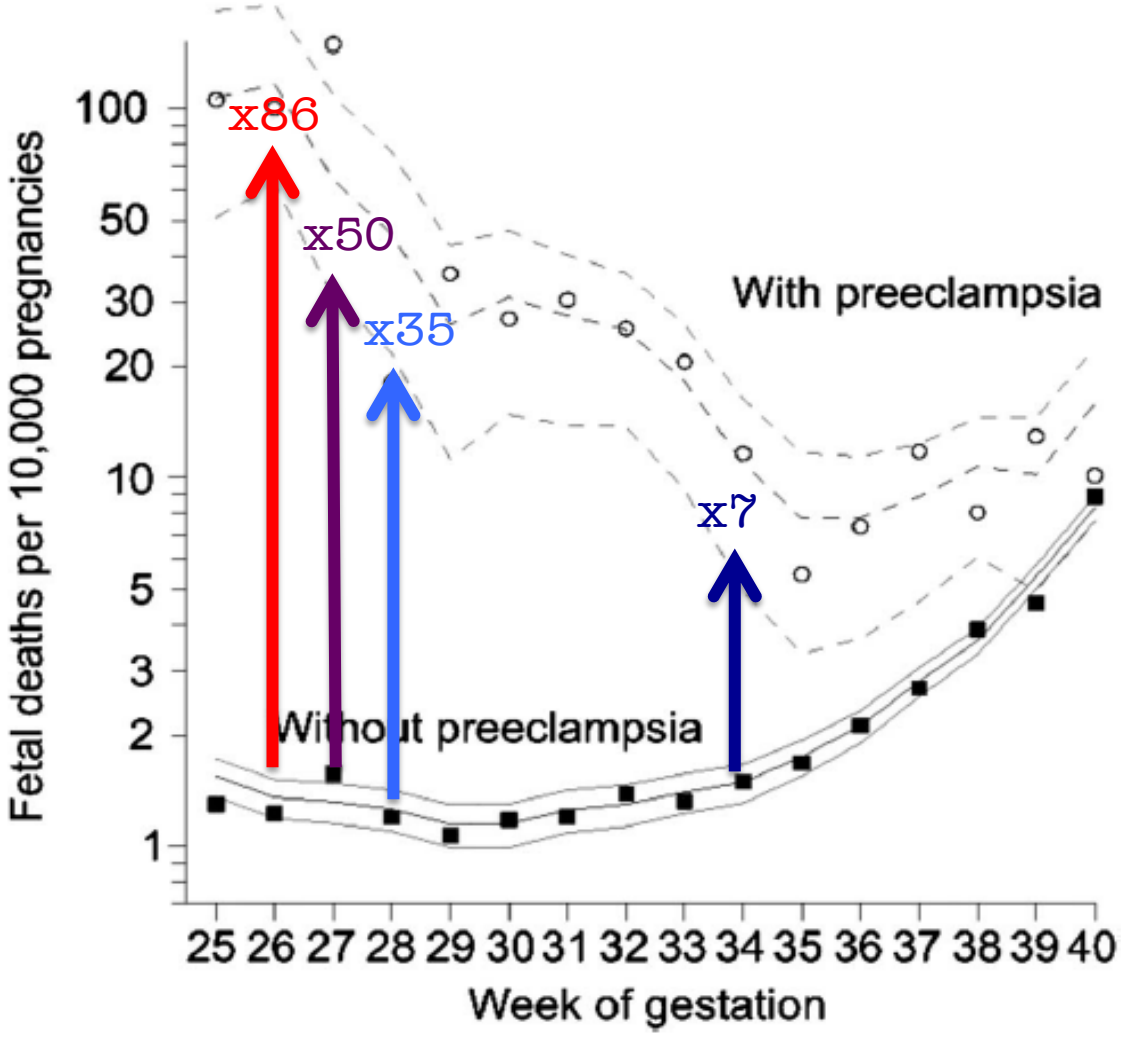
Acute
Eclampsia
Stroke
Abruptio placentae/disseminated intravascular coagulation
HELLP syndrome
Liver hemorrhage/rupture
Pulmonary edema/aspiration
Adult respiratory distress syndrome
Acute renal failure
Death
Long-term
Chronic hypertension
Diabetes mellitus
Chronic renal failure
Coronary artery disease
Neurologic deficit
Premature death

HELLP, hemolysis, elevated liver enzymes, low platelets.

Ghulmiyyah L., et al. Semin Perinatol. 2012

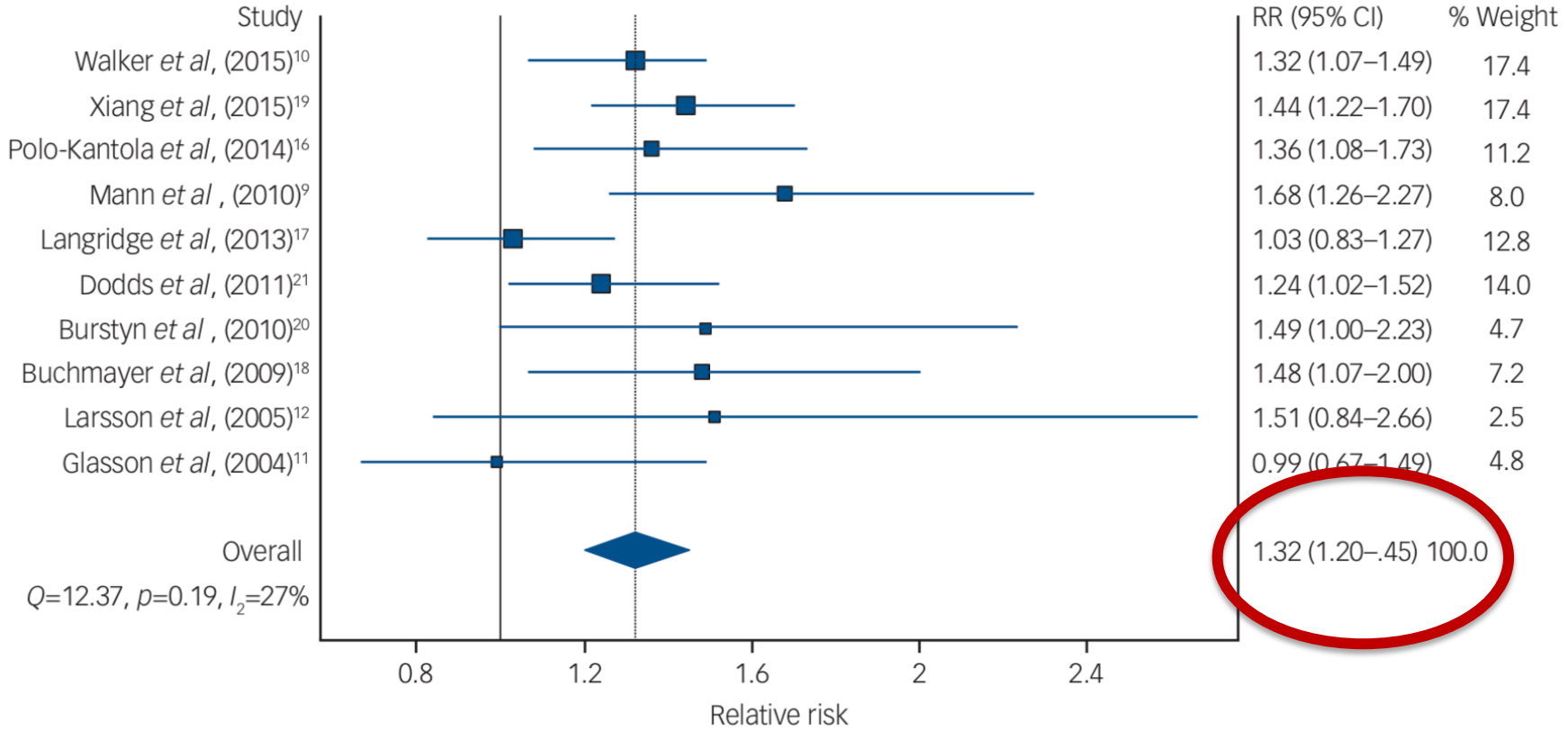
Fetal complications

- FGR
- Oligohydramnios
- preterm birth medically or obstetrically indicated
- Increased perinatal morbidity and mortality

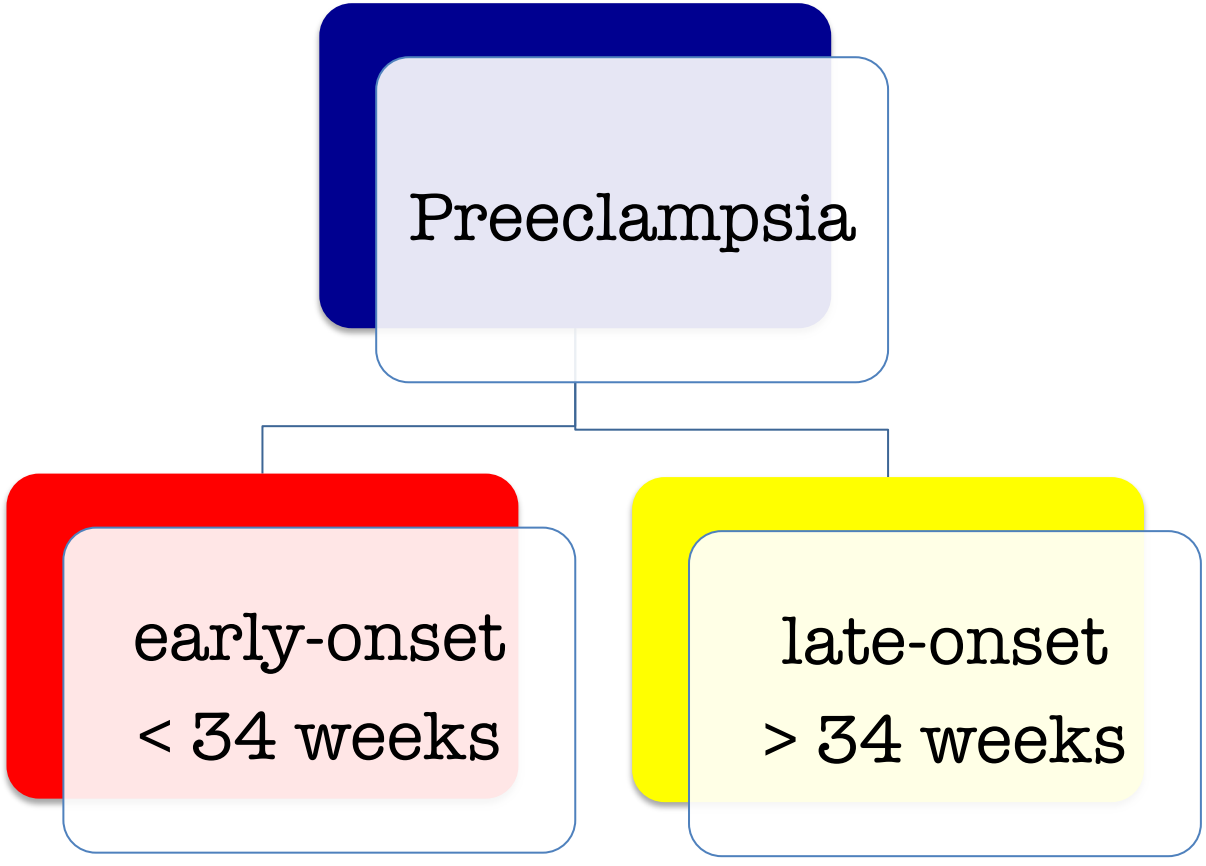


Harmon QE, et al. Obstet Gynecol. 2015

Pre-eclampsia and the risk of Autism Spectrum Disorder



Dachew BA et al. Br J Psychiatry. 2018



Valensise H, et al. Hypertension. 2008, Lisonkova S, et al. Am J Obstet Gynecol. 2013, Mifsud W, et al. Fetal Diagn Ther. 2014

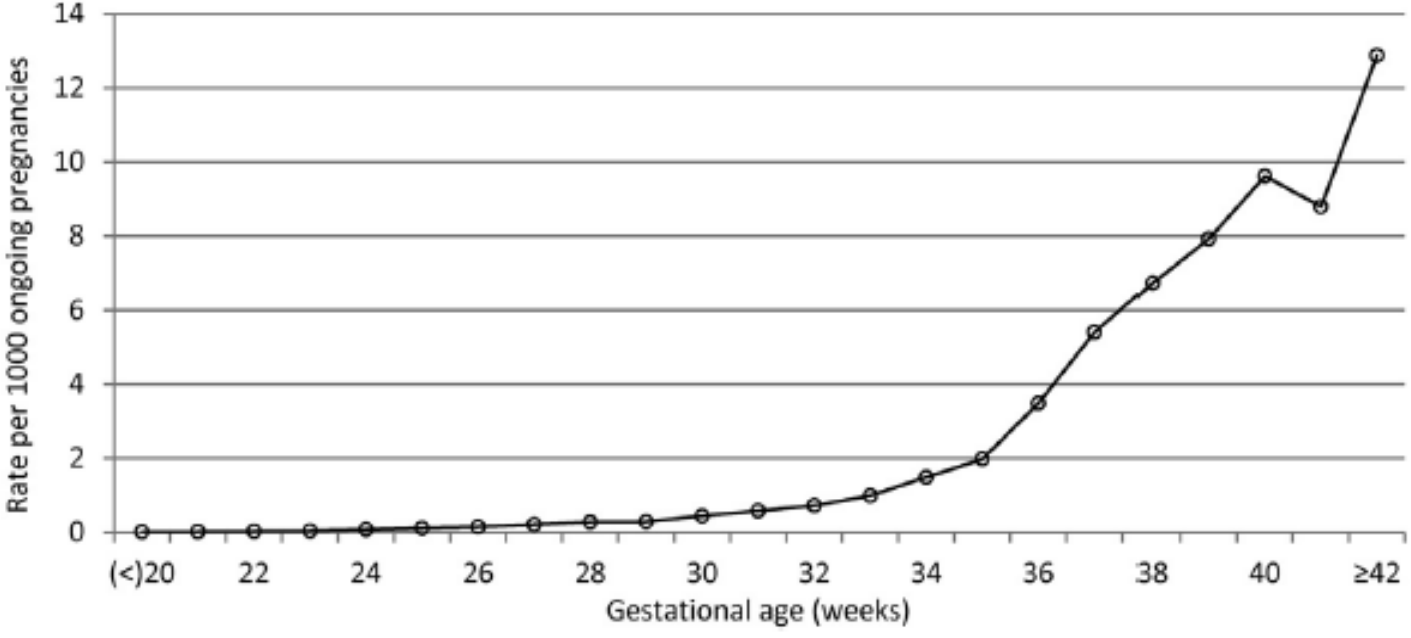
Preeclampsia: 3.11 %

Early-onset: 0.38 %

Late-onset: 2.72 %

FIGURE

Gestational age–specific incidence of preeclampsia, singleton deliveries, Washington State, 2003-2008



Lisonkova. Early- vs late-onset preeclampsia. Am J Obstet Gynecol 2013.

1. Early-onset PE (with delivery at <34+0 weeks of gestation)

2. Preterm PE (with delivery at <37+0 weeks of gestation)

3. Late-onset PE (with delivery at ≥34+0 weeks of gestation)

4. Term PE (with delivery at ≥37+0 weeks of gestation).

SCREENING

NICE National Institute for Health and Care Excellence

Η πρόβλεψη προεκλαμψίας μπορεί να βασιστεί μόνο σε παράγοντες κινδύνου από το ατομικό και μαιευτικό ιστορικό της μητέρας.

Αυξημένος κίνδυνος: 1 παράγοντας υψηλού κινδύνου ή τουλάχιστον 2 παράγοντες μετρίου κινδύνου

Οι παράγοντες υψηλού κινδύνου περιλαμβάνουν:

- Υπερτασική νόσος σε προηγούμενη εγκυμοσύνη
- Χρόνια νεφρική νόσος
- Αυτοάνοσα νοσήματα, όπως ο συστηματικός ερυθηματώδης λύκος ή το αντιφωσφολιπιδικό σύνδρομο
- Διαβήτης τύπου 1 ή τύπου 2
- Χρόνια υπέρταση

Οι παράγοντες μετρίου κινδύνου περιλαμβάνουν:

- Πρώτη εγκυμοσύνη
- Ηλικία μητέρας άνω των 40 ετών
- Χρονικό διάστημα μεταξύ δύο εγκυμοσυνών άνω των 10 ετών
- Δείκτης Μάζας Σώματος (BMI) 35 kg / m2 ή περισσότερο κατά την πρώτη επίσκεψη
- οικογενειακό ιστορικό προεκλαμψίας
- πολύδυμη κύηση.

150 mg aspirin, καθημερινά μετά το τελευταίο γεύμα της ημέρας, από τις 12 εβδομάδες έως τις 37 εβδομάδες κύησης.

https://www.nice.org.uk/guidance/qs35/chapter/Quality-statement-2-Antenatal-assessment-of-pre-eclampsia-risk

Clinical Risk Factors and Aspirin Use*

Level of Risk	Risk Factors	Recommendation
High†	• History of preeclampsia, especially when accompanied by an adverse outcome • Multifetal gestation • Chronic hypertension • Type 1 or 2 diabetes • Renal disease • Autoimmune disease (ie, systemic lupus erythematosus, the antiphospholipid syndrome)	Recommend low-dose aspirin if the patient has one or more of these high-risk factors
Moderate‡	• Nulliparity • Obesity (body mass index greater than 30) • Family history of preeclampsia (mother or sister) • Sociodemographic characteristics (African American race, low socioeconomic status) • Age 35 years or older • Personal history factors (eg, low birth weight or small for gestational age, previous adverse pregnancy outcome, more than 10-year pregnancy interval)	Consider low-dose aspirin if the patient has more than one of these moderate-risk factors§
Low	• Previous uncomplicated full-term delivery	Do not recommend low-dose aspirin

*Includes only risk factors that can be obtained from the patient's medical history. Clinical measures, such as uterine artery Doppler ultrasonography, are not included.

†Single risk factors that are consistently associated with the greatest risk of preeclampsia. The preeclampsia incidence rate would be approximately 8% or more in a pregnant woman with one or more of these risk factors.

‡A combination of multiple moderate-risk factors may be used by clinicians to identify women at high risk of preeclampsia. These risk factors are independently associated with moderate risk of preeclampsia, some more consistently than others.

§Moderate-risk factors vary in their association with increased risk of preeclampsia.

Modified from LeFevre, ML. U.S. Preventive Services Task Force. Low-dose aspirin use for the prevention of morbidity and mortality from preeclampsia: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med 2014;161(11):819–26.

ULTRASOUND
in Obstetrics & Gynecology

isuog.org

Multicenter screening for pre-eclampsia by maternal factors and biomarkers at 11–13 weeks' gestation: comparison with NICE guidelines and ACOG recommendations

N. O'Gorman et al., UOG 2017

Table 1 Detection rate of pre-eclampsia (PE) delivering < 32, < 37 and ≥ 37 weeks' gestation in validation dataset using previously developed screening algorithm[5] based on maternal factors and combinations of biomarkers, and using recommendations of National Institute of Health and Care Excellence (NICE)[1] and American College of Obstetricians and Gynecologists (ACOG)[2,3]

	DR (%) of PE with delivery at:		
Screening method	*< 32 weeks*	*< 37 weeks*	*≥ 37 weeks*
FMF algorithm (FPR = 10%)			
Maternal factors	53 (28–77)	41 (28–54)	37 (30–45)
Maternal factors plus:			
MAP	71 (44–90)	47 (34–61)	37 (30–45)
UtA-PI	82 (57–96)	61 (47–73)	39 (32–47)
PAPP-A	59 (33–82)	47 (34–61)	37 (30–44)
PlGF	88 (64–99)	63 (49–75)	39 (32–46)
MAP, UtA-PI	94 (71–100)	71 (58–82)	41 (34–49)
MAP, PAPP-A	76 (50–93)	49 (36–63)	40 (33–48)
MAP, PlGF	88 (64–99)	69 (56–81)	43 (36–51)
UtA-PI, PAPP-A	82 (57–96)	66 (53–78)	40 (33–48)
UtA-PI, PlGF	100 (80–100)	75 (62–85)	39 (32–47)
PlGF, PAPP-A	88 (64–99)	66 (53–78)	39 (32–47)
MAP, UtA-PI, PAPP-A	94 (71–100)	69 (56–81)	42 (35–50)
MAP, PAPP-A, PlGF	88 (64–99)	69 (56–81)	43 (36–51)
MAP, UtA-PI, PlGF	100 (80–100)	75 (62–85)	43 (35–50)
UtA-PI, PAPP-A, PlGF	100 (80–100)	75 (62–85)	38 (31–46)
MAP, UtA-PI, PAPP-A, PlGF	100 (80–100)	80 (67–89)	43 (35–50)
NICE[1] (FPR = 10.2%)	41 (18–67)	39 (27–53)	34 (27–41)
ACOG[2] (FPR = 64.2%)	94 (71–100)	90 (79–96)	89 (84–94)
ACOG aspirin[3] (FPR = 0.2%)	6 (1–27)	5 (2–14)	2 (0.3–5)

Values in parentheses are 95% CI. DR, detection rate; FPR, false-positive rate; MAP, mean arterial pressure; PlGF, placental growth factor; PAPP-A, pregnancy-associated plasma protein-A; UtA-PI, uterine artery pulsatility index.

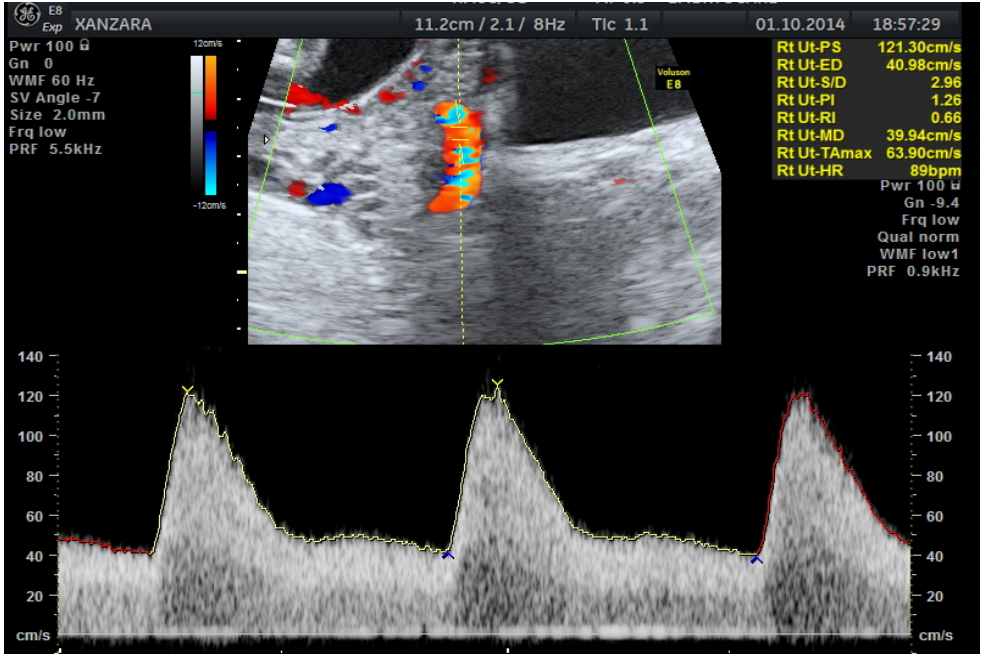
ΠΡΟΒΛΕΨΗ ΠΡΟΕΚΛΑΜΨΙΑΣ

Εκτίμηση της ροής αίματος στα μητριαία αγγεία

- **Διακοιλιακό υπερηχογράφημα στις 11-13 εβδ.**

- **Ταυτοποίηση μητριαίων**
  - Οβελιαία τομή τραχήλου
  - Έγχρωμο Doppler
  - Κίνηση ηχοβολέα στα δύο πλάγια
  - Αρτηρίες στο ύψος του έσω τραχ. στομίου

- **Θύρα δείγματος**: 2 mm καλύπτει όλο το αγγείο
- **Γωνία πρόσκρουσης:** < 30^0
- **Μέγιστη ταχύτητα ροής:** > 60 cm/s
- **Μέσο PI:** αριστερό + δεξιό/2



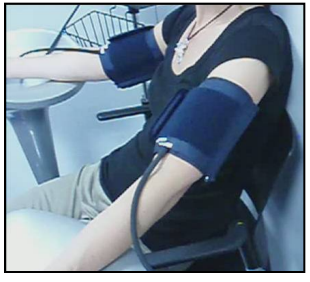
Υπερηχογράφημα 1ου τριμήνου κύησης - Προεκλαμψία

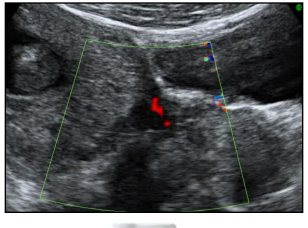
Prediction of preeclampsia

FMF algorithm

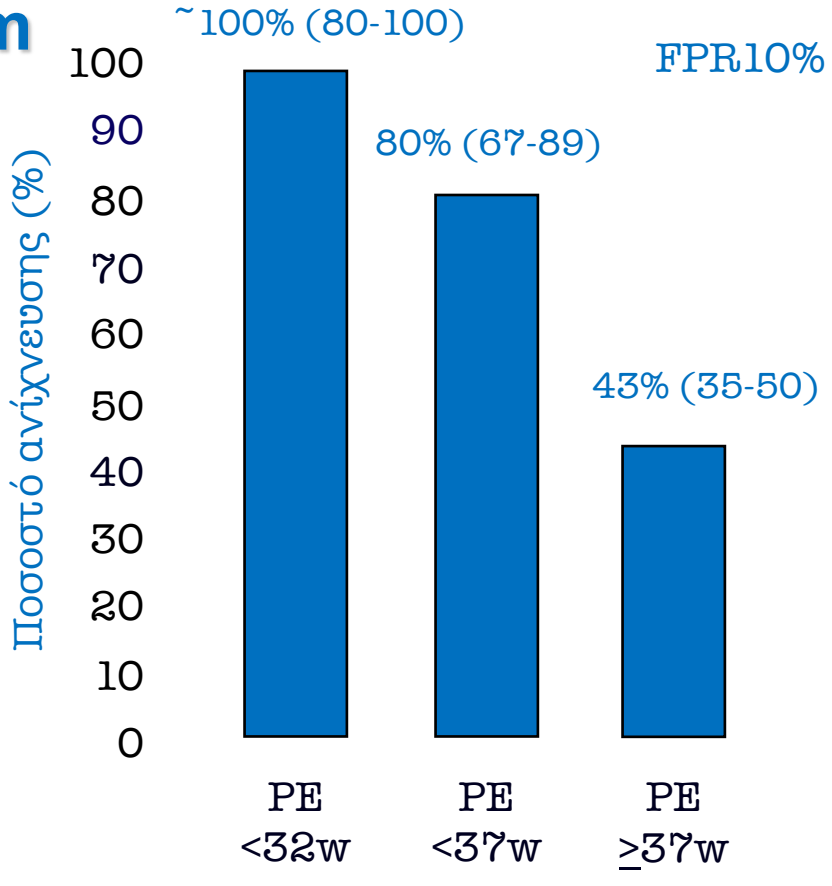
Maternal risk factors

- Age: every 10 years above 30 y
- Weight: every 10 kg above 70 kg
- Racial origin
  Afro-Caribbean
  South Asian
- Obstetric history
  First pregnancy
  Previous preeclampsia
- Family history of preeclampsia
- Conception by IVF
- Chronic hypertension
- Diabetes mellitus
- Autoimmune : SLE / APS





1st trimester combined test



FMF algorithm: Ιστορικό, ΜΑΠ, PI μητριαίων, PLGF, PAPP-A

O' Gorman et al. Am J Obstet Gynecol 2016; 214: 103

The NEW ENGLAND JOURNAL of MEDICINE
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Aspirin versus Placebo in Pregnancies at High Risk for Preterm Preeclampsia

Screening at 11-13 wks
n = 26,941

High-risk for preterm PE
n = 2,971

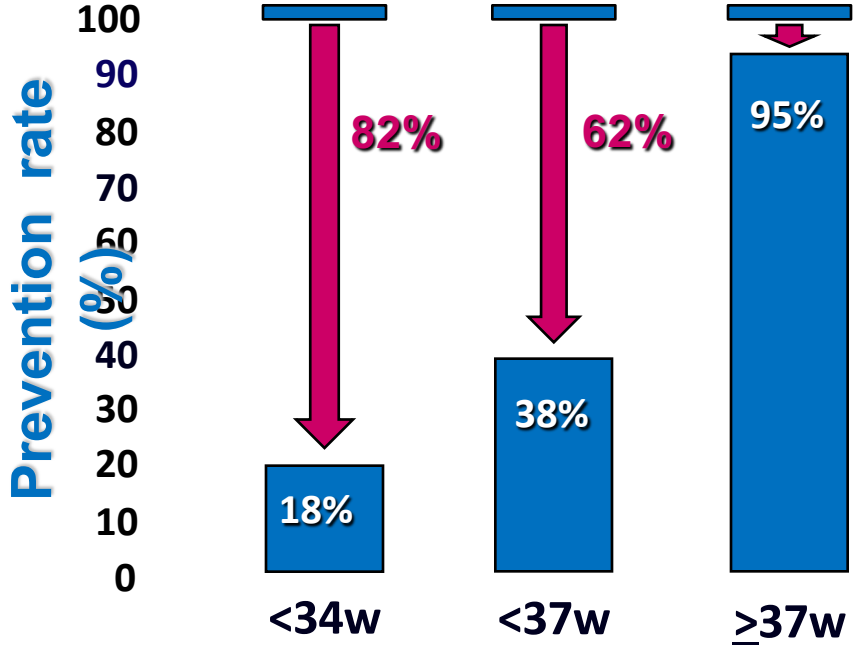
Randomized n = 1,776 (66%)

Aspirin
n = 800

Placebo
n = 824

funded by EU FP7 ASPRE project

Prevention of preeclampsia



Rolnik DL, et al. N Engl J Med 2017;377:613-622.

Management

Αντιμετώπιση της προεκλαμψίας

Gestational age	Management	Delivery
<34 weeks	Conservative if no features of severe disease	• 37 weeks • as soon as they develop preeclampsia with severe features • eclampsia (whether or not the cervix is favorable)
34 - 36 weeks	• Uncertain • Conservative management reasonable	37 weeks
≥37 weeks (term pregnancies)	DELIVERY	

- National Collaborating Centre for Women's and Children's Health. Hypertension in Pregnancy: The Management of Hypertensive Disorders During Pregnancy, RCOG Press, London 2010
- American College of Obstetricians and Gynecologists, Task Force on Hypertension in Pregnancy, Obstet Gynecol. 2013
- ACOG committee opinion no. 560: Medically indicated late-preterm and early-term deliveries. American College of Obstetricians and Gynecologists, Obstet Gynecol. 2013

In a patient with preeclampsia, the presence of one or more of the following indicates a diagnosis of "preeclampsia with severe features"

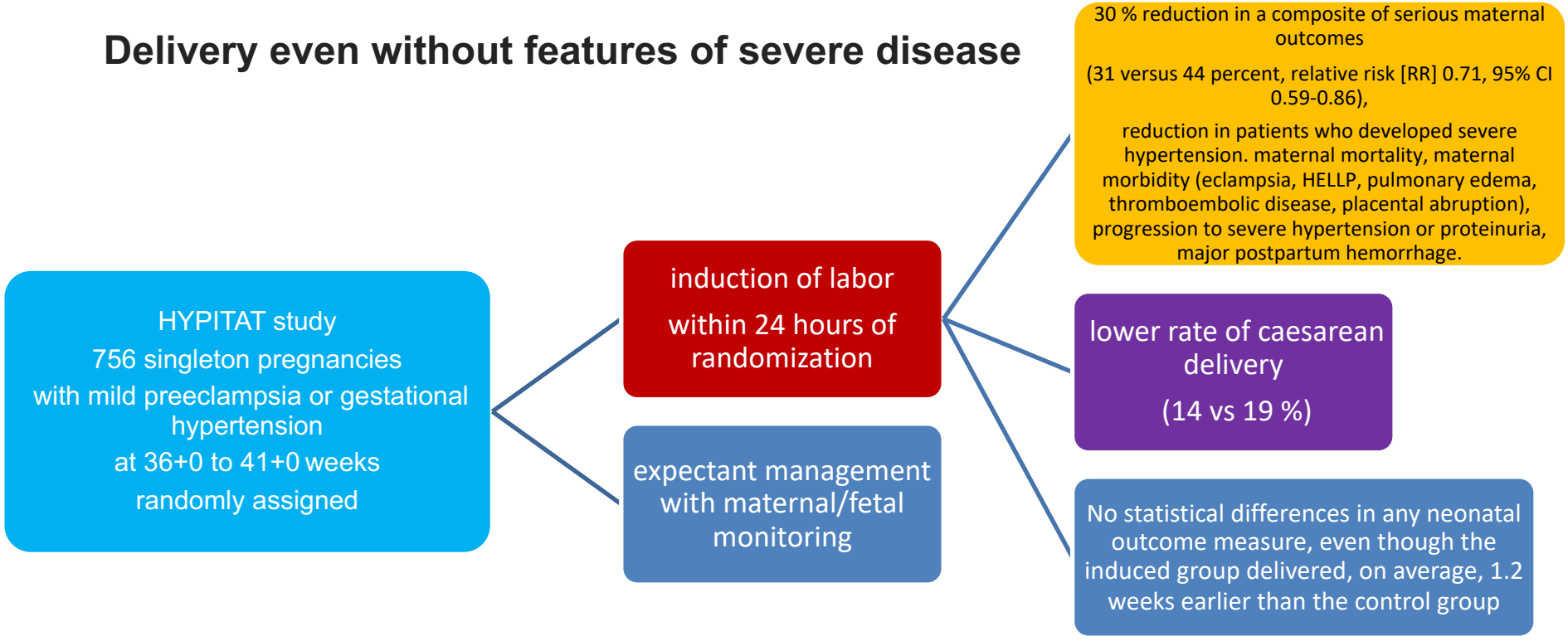
Severe blood pressure elevation:
Systolic blood pressure ≥160 mmHg or diastolic blood pressure ≥110 mmHg on 2 occasions at least 4 hours apart while the patient is on bedrest (antihypertensive therapy may be initiated upon confirmation of severe hypertension, in which case criteria for severe blood pressure elevation can be satisfied without waiting until 4 hours have elapsed)
Symptoms of central nervous system dysfunction:
New-onset cerebral or visual disturbance, such as: ▪ Photopsia, scotomata, cortical blindness, retinal vasospasm ▪ Severe headache (ie, incapacitating, "the worst headache I've ever had") or headache that persists and progresses despite analgesic therapy and not accounted for by alternative diagnoses
Hepatic abnormality:
Severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by an alternative diagnosis or serum transaminase concentration ≥2 times the upper limit of the normal range, or both
Thrombocytopenia:
<100,000 platelets/microL
Renal abnormality:
Renal insufficiency (serum creatinine >1.1 mg/dL [97.2 micromol/L] or a doubling of the serum creatinine concentration in the absence of other renal disease)
Pulmonary edema

In contrast to older criteria, the 2013 criteria do not include proteinuria >5 g/24 hours and fetal growth restriction as features of severe disease.

PREECLAMPSIA WITHOUT FEATURES OF SEVERE DISEASE

General approach - Term pregnancies ≥ 37 weeks:

Delivery even without features of severe disease

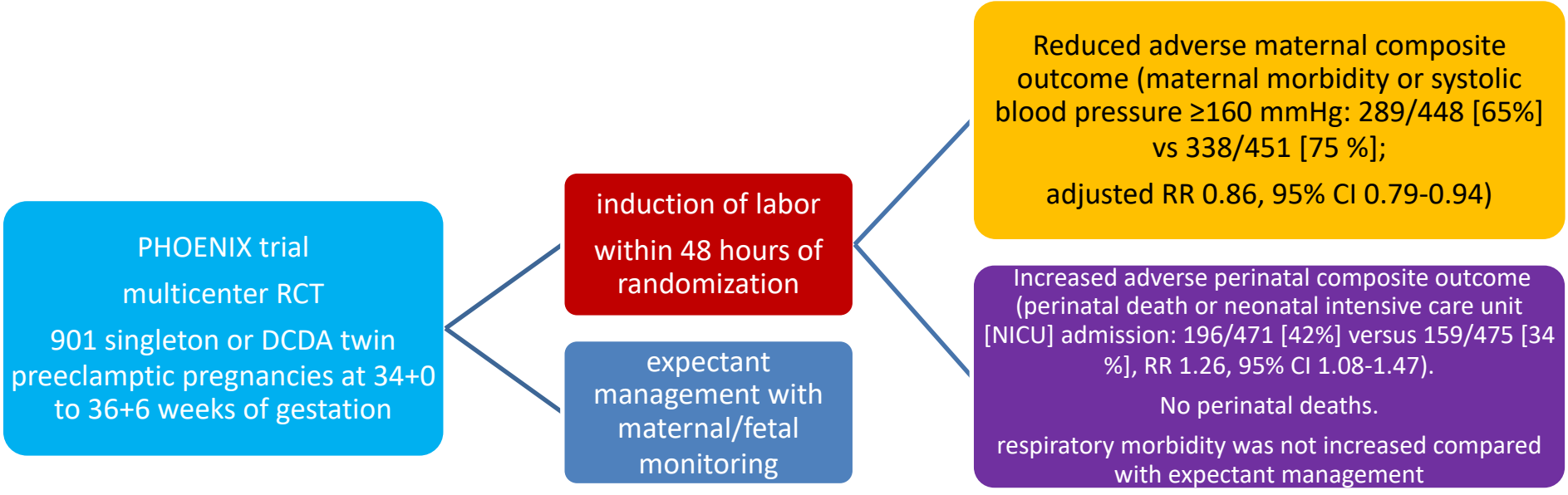


Koopmans CM, et al. Lancet. 2009

PREECLAMPSIA WITHOUT FEATURES OF SEVERE DISEASE

Preterm pregnancies: Expectant management

34+0 to 36+6 weeks: less consensus about the optimum management of preeclampsia without features of severe disease and stable maternal and fetal condition



Chappell LC, et al. Lancet. 2019

Expectant management of preterm preeclampsia with severe features

Onset in the second trimester : high maternal morbidity and fetal mortality

25 - 63 % of mothers managed expectantly:

- HELLP syndrome (Hemolysis, Elevated Liver enzymes, Low Platelets),
- renal insufficiency
- placental abruption
- pulmonary edema
- eclampsia

Short-term consequences

Perinatal survival	
<22+6 weeks	2 %
23+0 to 23+6 weeks	13 %
24+0 to 24+6 weeks	33 %
25+0 to 26+0 weeks	60 %

The median prolongation of pregnancy : 5 days (range 0 to 25 days)

The limits of viability vary among hospitals and are impacted by factors other than gestational age, such as gender, birth weight, and administration of antenatal corticosteroids, and these factors should be considered when counseling individual patients

Expectant management of preterm preeclampsia with severe features

Long - term consequences: Pre-eclampsia Eclampsia Trial Amsterdam (PETRA) study

216 children born after expectant management of severe hypertensive complications of pregnancy

onset between 24 and 34 weeks of gestation

singleton gestations

91% were SGA at birth

mean gestational age at delivery: 31.4 weeks

neurodevelopmental outcome at age 4.5 years

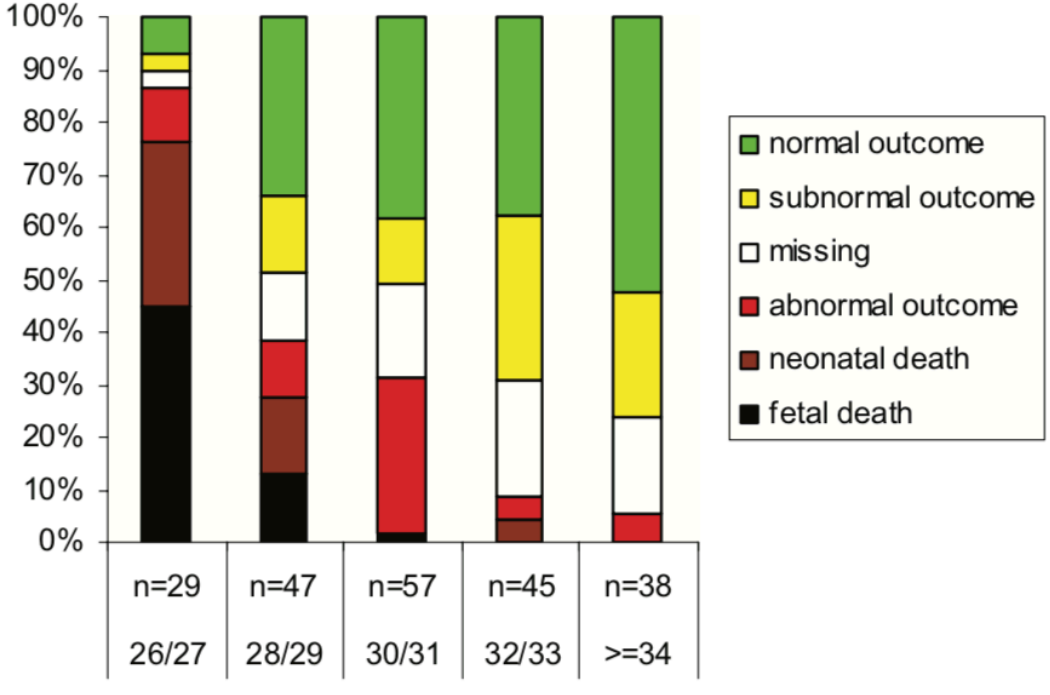
Major outcomes were:

- At 4.5 years corrected age, an increased frequency of IQ values that were either subnormal (78 to 93) or abnormal (<78; **30 vs 16%** in the general population) was identified.
- **54 %** of the children had normal results on all tests of developmental outcome.
- **7%** of the children were attending special education classes, which is approximately seven times as many as the nationwide rate of 1% at that age in The Netherlands.
- There were no blind or deaf children in the cohort

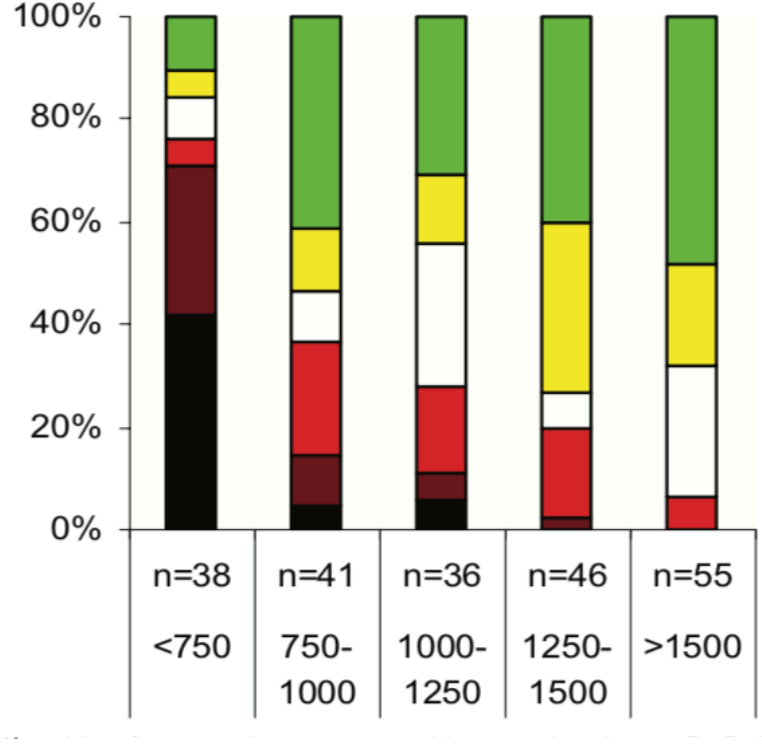
van Wassenaer AG, et al. Am J Obstet Gynecol. 2011

Expectant management of preterm preeclampsia with severe features

Long - term consequences: Pre-eclampsia Eclampsia Trial Amsterdam (PETRA) study



Relasionship of composite outcome with gestational age



Relasionship of composite outcome with birthweight

van Wassenaer AG, et al. Am J Obstet Gynecol. 2011

Contraindications to beginning or continuing expectant management

Maternal :

- Hemodynamic instability (shock)
- Persistent severe hypertension unresponsive to medical therapy
- Symptoms of severe disease – Severe headache (ie, incapacitating, "the worst headache of my life") or persistent progressive headache (despite a dose of an analgesic), characteristic vision abnormalities, or epigastric/right upper quadrant pain unresponsive to analgesics
- Motor deficit or altered sensorium
- Pulmonary edema
- Renal failure
- Stroke
- Myocardial infarction.

ACOG Practice Bulletin No. 202: Gestational Hypertension and Preeclampsia.Obstet Gynecol. 2019

Contraindications to beginning or continuing expectant management

Maternal :

Laboratory abnormalities, such as:

- Aminotransferases increasing over 6 to 12 hours and reaching levels twice the upper limit of normal
- Progressive decrease in platelet count to less than 100,000 cells/microL
- Coagulopathy in the absence of an alternative explanation
- New or worsening renal dysfunction (serum creatinine greater than 1.1 mg/dL or twice baseline)
- Maternal request for immediate delivery.
- Eclampsia.

Obstetric :

- Placental abruption
- Preterm labor
- Preterm prelabor rupture of membranes

ACOG Practice Bulletin No. 202: Gestational Hypertension and Preeclampsia.Obstet Gynecol. 2019

Contraindications to beginning or continuing expectant management

Fetal :

- **Fetal demise**

- **Abnormal fetal testing** (eg, nonreactive nonstress test or abnormal biophysical profile score; growth restriction with absent/reversed diastolic flow on umbilical artery Doppler or abnormal ductus venosus waveform)

- **Estimated fetal weight less than the fifth percentile for gestational age**. Although ACOG considered fetal growth restriction defined as an estimated weight <10th percentile as an indication for delivery in the past, in the setting of normal fetal parameters (eg, amniotic fluid volume, Doppler findings, antenatal fetal testing), in 2019 they suggested that continuation of expectant management may be reasonable in the absence of other maternal and fetal criteria

- **Oligohydramnios** (amniotic fluid index <5.0 cm or single deepest vertical pocket <2.0 cm)

- **Fetus without expectation for survival** at the time of maternal diagnosis (eg, lethal anomaly, extreme prematurity).

ACOG Practice Bulletin No. 202: Gestational Hypertension and Preeclampsia.Obstet Gynecol. 2019

Αντιμετώπιση της προεκλαμψίας

Preeclampsia with features of severe disease : DELIVERY

Delivery minimizes the risk of development of serious maternal and fetal complications

- cerebral hemorrhage
- hepatic rupture
- renal failure
- pulmonary edema
- seizure
- bleeding related to thrombocytopenia
- abruptio placenta
- fetal growth restriction

With the exception of fetal growth restriction, **any of these life-threatening complications can occur suddenly**

American College of Obstetricians and Gynecologists, Task Force on Hypertension in Pregnancy, Obstet Gynecol. 2013

Components of conservative management	
Patient education	All women with preeclampsia should be aware of the signs and symptoms at the severe end of the disease spectrum and should monitor fetal movements daily
Activity	Strict bedrest is unnecessary (associated with an increased risk of venous thromboembolism)
Laboratory follow-up	• platelet count • serum creatinine • liver enzymes (at least weekly in women without severe features) repeated urinary protein estimations are not useful once the threshold of 300 mg/24 for the diagnosis of preeclampsia has been exceeded
Treatment of hypertension	The use of antihypertensive drugs to control mild hypertension (defined as systolic blood pressure <160 mmHg and diastolic blood pressure <110 mmHg) in the setting of preeclampsia does not alter the course of the disease or diminish perinatal morbidity or mortality, and should be avoided
Assessment of fetal growth	
Antenatal corticosteroids	<34 weeks of gestation Betamethasone two doses of 12 mg im 24 hours apart
Seizure prophylaxis (mangesium sulfate)	reduces the risk of eclampsia (RR 0.42, 95% CI 0.26-0.67)

WHEN TO TREAT HYPERTENSION

Severe hypertension — systolic blood pressure ≥160 mmHg and/or diastolic blood pressure ≥110 mmHg persisting for ≥15 minutes

- to reduce the risk of maternal stroke and heart failure and other serious maternal complications.
- initiated as soon as reasonably possible and within 30 to 60 minutes.

WHEN TO TREAT HYPERTENSION

Nonsevere hypertension

No consensus as to the **optimal blood pressure threshold** for initiating therapy of nonsevere hypertension to prevent development of severe hypertension

Management of pregnancy with gestational hypertension

	Degree of hypertension	
	Hypertension: BP of 140/90 – 159/109 mmHg	**Severe hypertension: BP of ≥ 160/110 mmHg**
Admission to hospital	Do not routinely admit to hospital	Admit, but if BP falls below 160/110 mmHg then manage as for hypertension
Antihypertensive pharmacological treatment	Offer pharmacological treatment if BP remains above 140/90 mmHg	Offer pharmacological treatment to all women
Target blood pressure once on antihypertensive treatment	Aim for BP of 135/85 mmHg or less	Aim for BP of 135/85 mmHg or less
Blood pressure measurement	Once or twice a week (depending on BP) until BP is 135/85 mmHg or less	Every 15–30 minutes until BP is less than 160/110 mmHg
Dipstick proteinuria testing [a]	Once or twice a week (with BP measurement)	Daily while admitted
Blood tests	Measure full blood count, liver function and renal function at presentation and then weekly	Measure full blood count, liver function and renal function at presentation and then weekly
Fetal assessment	Offer fetal heart auscultation at every antenatal appointment Carry out ultrasound assessment of the fetus at diagnosis and, if normal, repeat every 2 to 4 weeks, if clinically indicated Carry out a CTG only if clinically indicated	Offer fetal heart auscultation at every antenatal appointment Carry out ultrasound assessment of the fetus at diagnosis and, if normal, repeat every 2 weeks, if severe hypertension persists Carry out a CTG at diagnosis and then only if clinically indicated

INITIAL MANAGEMENT OF ALL PATIENTS WITH PREECLAMPSIA WITH SEVERE FEATURES

- **Admission to the Labor and Delivery Unit** (or similar unit with equivalent monitoring and resources)
- Administration of a course of **antenatal corticosteroids**
- **Seizure prophylaxis**
- **Blood pressure monitoring**
- Accurate recording of **fluid intake and urine output**
- **Laboratory studies**
- **Assessment of fetal well-being**

Admission to the Labor and Delivery Unit

The patient may need to be monitored in this intensive setting for as long as **48 hours**

After several hours of observation, she can be transferred to a setting with less intensive care if **all of the following are present**:

•She is asymptomatic

•Her blood pressure is stable at a safe level without labile elevations into the severe range

•Her laboratory test results are in the normal range or improving

•Fetal testing is reassuring

ΚΟΡΤΙΚΟΕΙΔΗ

Χορηγείται σε κάθε περίπτωση επαπειλούμενου πρόωρου τοκετού σε ηλικία κύησης μεταξύ **24^{+0} και 33^{+6}** με σκοπό να μειωθεί η νεογνική νοσηρότητα (αναπνευστική δυσχέρεια, εγκεφαλική αιμορραγία, νεκρωτική εντεροκολίτιδα, μηχανικός αερισμός) και θνητότητα.

Σε περίπτωση που τελικά ο τοκετός δεν ολοκληρωθεί και μετά από τουλάχιστον 2 εβδομάδες από την αρχική χορήγηση κορτικοειδών και τεθεί εκ νέου η διάγνωση του επαπειλούμενου πρόωρου τοκετού (μεταξύ 24^{+0} και 33^{+6} εβδομάδων) συστήνεται να χορηγηθεί ένα επαναληπτικό σχήμα.

ΙΜ Βηταμεθαζόνη 12mg×1×2μέρες

Practice Bulletin No. 171: Management of Preterm Labor ACOG Obstet Gynecol. 2016

Seizure prophylaxis

Candidates for seizure prophylaxis

Magnesium sulfate should be used for the prevention of seizures in women with preeclampsia with severe features.

- MAGPIE trial (magnesium sulfate for prevention of eclampsia trial) / 10,000 patients
- The largest randomized placebo-controlled trial that evaluated outcomes by severity of disease,
- The frequency of eclampsia in women with preeclampsia without severe features was 0.7 percent with prophylaxis versus 1.6 percent without prophylaxis (RR 0.42, 95% CI 0.26-0.67);
- Approximately 100 women with preeclampsia without severe features and approximately 60 women with preeclampsia with severe features would need to be treated to prevent one seizure.
- Although not statistically significant, prophylaxis also **reduced the risk of maternal death** in women without severe features of preeclampsia (RR 0.54, 95% CI 0.20-1.45; 6/3758 [0.16 percent] versus 11/3710 [0.30 percent] without treatment).
- Seizure prophylaxis does not prevent progression of disease unrelated to convulsions.

Lancet. 2002, Obstet Gynecol. 2020

Magnesium sulfate

1. Magnesium sulfate for seizure prophylaxis is usually initiated at the onset of labor or induction, or prior to and throughout the duration of a cesarean delivery

2. It is usually not administered to stable antepartum patients, but is sometimes given to women with preeclampsia with severe features while they are being considered for expectant management.

3. Prolonged antepartum therapy (more than five to seven days) should be avoided as it has been associated with adverse effects on fetal bones when it was administered for long-term tocolysis

IV $MgSO_4$ 4g σε 15' (1,5amp $MgSO_4$ σε 100ml NS) Φόρτιση
IV $MgSO_4$ 1g/h (10amp $MgSO_4$ σε 900ml NS με 40ml/h) Συντήρηση

Παρακολούθηση: αντανακλαστικά/ αναπνοές/ πίεση/ σφύξεις ανά 4 ώρες
επίπεδα ανά 6 ώρες (μέγιστο 8mg/dL)

Αντίδοτο: IV Γλυκονικό ασβέστιο 1g σε 10' (1 amp 10ml 10%)

ACOG Practice Bulletin No. 202: Gestational Hypertension and Preeclampsia. Obstet Gynecol. 2019;133(1):e1.

The American College of
Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS

Serum Magnesium Concentration and Toxicities

Serum Magnesium Concentration			
mmol/L	**mEq/L**	**mg/dL**	**Effect**
2–3.5	4–7	5–9	Therapeutic range
>3.5	>7	>9	Loss of patellar reflexes
>5	>10	>12	Respiratory paralysis
>12.5	>25	>30	Cardiac arrest

Data from Duley L. Magnesium sulphate regimens for women with eclampsia: messages from the Collaborative Eclampsia Trial. Br J Obstet Gynaecol 1996;103:103–5 and Lu JF, Nightingale CH. Magnesium sulfate in eclampsia and preeclampsia: pharmacokinetic principles. Clin Pharmacokinet 2000;38:305–14.

Antihypertensive agents used for urgent blood pressure control in pregnancy

Drug	Initial dose	Follow-up
Labetalol	20 mg IV gradually over 2 minutes.	Repeat BP measurement at 10-minute intervals: ▪ If BP remains above target level at 10 minutes, give 40 mg IV over 2 minutes. ▪ If BP remains above target level at 20 minutes, give 80 mg IV over 2 minutes. ▪ If BP remains above target level at 30 minutes, give 80 mg IV over 2 minutes. ▪ If BP remains above target level at 40 minutes, give 80 mg IV over 2 minutes. Cumulative maximum dose is 300 mg. If target BP is not achieved, switch to another class of agent.
	A continuous IV infusion of 1 to 2 mg/minute can be used instead of intermittent therapy or started after 20 mg IV dose. Requires use of programmable infusion pump and continuous noninvasive monitoring of blood pressure and heart rate.	Adjust dose within this range to achieve target blood pressure. Cumulative maximum dose is 300 mg. If target BP is not achieved, switch to another class of agent.

Hydralazine	5 mg IV gradually over 1 to 2 minutes.* Adequate reduction of blood pressure is less predictable than with IV labetalol.	Repeat BP measurement at 20-minute intervals: ▪ If BP remains above target level at 20 minutes, give 5 or 10 mg IV over 2 minutes, depending on the initial response. ▪ If BP remains above target level at 40 minutes, give 10 mg IV over 2 minutes, depending on the previous response. Cumulative maximum dose is 30 mg. If target BP is not achieved, switch to another class of agent.
Nifedipine extended release	30 mg orally.	If target BP is not achieved in 1 to 2 hours, another dose can be administered. If target BP is not achieved, switch to another class of agent.
Nifedipine immediate release*	10 mg orally. May be associated with precipitous drops in BP in some women, with associated FHR decelerations for which emergency cesarean delivery may be indicated. As such, this regimen is not typically used as a first-line option and is usually reserved only for women without IV access. If used, FHR should be monitored while administering short-acting nifedipine.	Repeat BP measurement at 20-minute intervals: ▪ If BP remains above target at 20 minutes, give 10 or 20 mg orally, depending on the initial response. ▪ If BP remains above target at 40 minutes, give 10 or 20 mg orally, depending on the previous response. If target BP is not achieved, switch to another class of agent.

Ουσία	Α-μεθυλ-ντόπα (Aldomet 250 – 500)	Νιφεδιπίνη βραδείας δράσης (Adalat CR / 60 mg)	Λαμπεταλόλη (Trandate 100)
Τρόπος δράσης	Κεντρική δράση Αναστολέας DOPA-decarboxylate Α2-αγωνιστική δράση, κεντρικά	Αποκλειστής διαύλων ασβεστίου	Α1-αποκλειστής Β1-αποκλειστής
Δοσολογία	500 – 3gr 3 δόσεις	30-120 mg 2 δόσεις	200-1200 mg 2-3 δόσεις
FDA class	B	C	C
Παρενέργειες	Υπνηλία Αιμόλυση Αύξηση ηπατικών Κατάθλιψη	Αναστολή τοκετού	FGR
Αντενδείξεις	Ηπατική ανεπάρκεια Κατάθλιψη	Υπόταση (συνδυασμός με MgSO4)	Άσθμα Βραδυκαρδία

Υπέρταση στη Λοχεία

i. **Διακοπή methyl-dopa (κατάθλιψη)**

ii. Όλα τα φάρμακα περνούν στο μητρικό γάλα

iii. Ασφαλή θεωρούνται:

- Λαμπεταλόλη
- Νιφεδιπίνη
- Καπτοπρίλη
- Εναλαπρίλη

HELLP

HELLP is an acronym that refers to a syndrome characterized by

1. Hemolysis (with a microangiopathic blood smear)
2. Elevated Liver enzymes
3. Low Platelet count

0.1 to 0.2 % of pregnancies overall

10 to 20 % of women with severe preeclampsia/eclampsia.

HELLP

Precise criteria for HELLP are necessary for research purposes and for predicting maternal complications. We require the presence of all of the following criteria to diagnose HELLP (Tennessee classification)
:

●Microangiopathic hemolytic anemia with characteristic schistocytes (also called helmet cells) on blood smear . Other signs suggestive of hemolysis include an elevated indirect bilirubin level and a low serum haptoglobin concentration (≤25 mg/dL).

●Platelet count ≤100,000 cells/microL.

●Total bilirubin ≥1.2 mg/dL (20.52 micromol/L; hemolysis results in an increase in indirect bilirubin).

●Serum AST >2 times upper limit of normal for local laboratory (usually >70 international units/L). Some investigators obtain alanine aminotransferase (ALT) levels instead of, or in addition to, AST levels. An advantage of the AST is that it is a single test that reflects both hepatocellular necrosis and red cell hemolysis.

HELLP / Maternal outcome

- Disseminated intravascular coagulation (DIC) – 21 %
- Abruptio placentae – 16 %
- Acute renal failure – 8 %
- Pulmonary edema – 6%
- Subcapsular liver hematoma – 1%
- Retinal detachment – 1 %

Sample Order Set for Severe Intrapartum or Postpartum Hypertension, Initial First-line Management With Labetalol I

- Notify physician if systolic blood pressure (BP) mea- surement is greater than or equal to 160 mm Hg or if diastolic BP measurement is greater than or equal to 110 mm Hg.
- Institute fetal surveillance if undelivered and fetus is viable.
- If severe BP elevations persist for 15 minutes or more, administer labetalol (20 mg intravenously [IV] for more than 2 minutes).
- Repeat BP measurement in 10 minutes and record results.
- If either BP threshold is still exceeded, administer labetalol (40 mg IV for more than 2 minutes). If BP is below threshold, continue to monitor BP closely.
- Repeat BP measurement in 10 minutes and record results.

Sample Order Set for Severe Intrapartum or Postpartum Hypertension, Initial First-line Management With Labetalol II

If either BP threshold is still exceeded, administer labetalol (80 mg IV for more than 2 minutes). If BP is below threshold, continue to monitor BP closely.

Repeat BP measurement in 10 minutes and record results.

If either BP threshold is still exceeded, administer hydralazine (10 mg IV for more than 2 minutes). If BP is below threshold, continue to monitor BP closely.

Repeat BP measurement in 20 minutes and record results.

If either BP threshold is still exceeded, obtain emergency consultation from maternal–fetal medicine, internal medicine, anesthesia, or critical care subspecialists.

Sample Order Set for Severe Intrapartum or Postpartum Hypertension, Initial First-line Management With Labetalol III

- Give additional antihypertensive medication per specific order.

- Once the aforementioned BP thresholds are achieved, repeat BP measurement

i. every 10 min for 1 hour
ii. then every 15 min for 1 hour
iii. then every 30 miN for 1 hour
iv. and then every hour for 4 hours

- Institute additional BP timing per specific order.

Acute therapy

Nifedipine, a dihydropyridine calcium channel blocker, is used extensively to treat hypertension in pregnancy, both in the acute as well as in the chronic setting. There are several different formulations of nifedipine:

•Preferred formulation – An extended-release tablet (30 mg), which lasts 24 hours and is known as nifedipine XL or CR or ER.

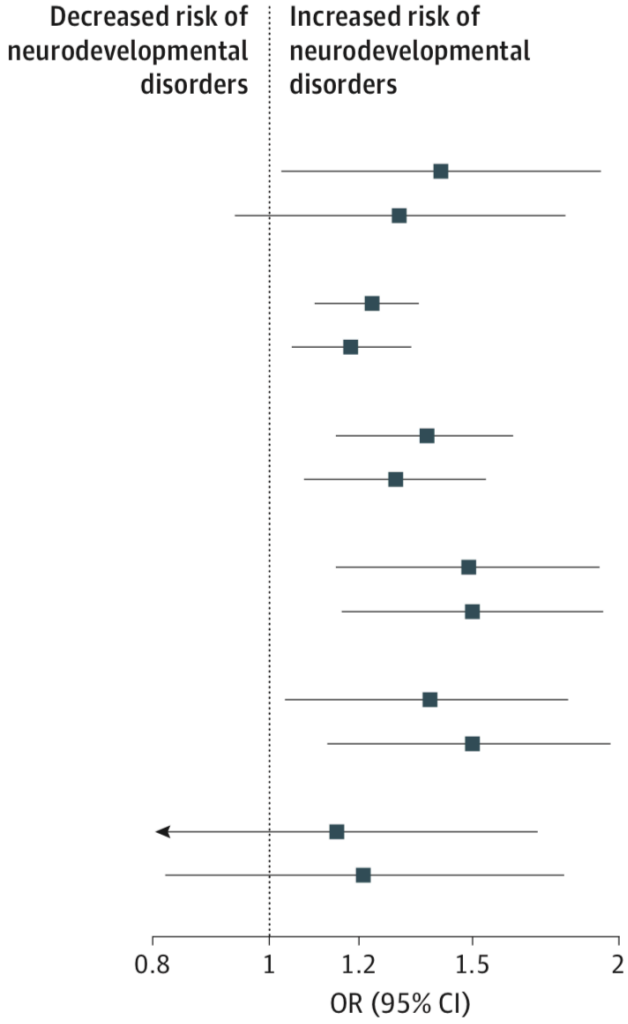
•An intermediate-acting tablet (10 or 20 mg; in some countries, this is known as nifedipine retard), which has a more delayed onset and is usually prescribed two or three times a day.

•A rapid-onset, short-acting capsule (10 mg), which lowers blood pressure within 30 to 60 minutes. (In the United States, the FDA/package insert notes that "Nifedipine capsules should not be used for the acute reduction of blood pressure"

Long-term oral therapy: nifedipine XL or CR or ER.

Association of Preeclampsia in Term Births with Neurodevelopmental Disorders in Offspring

Outcome by analysis	OR (95% CI)
Cerebral palsy	
Crude	1.41 (1.03-1.93)
Adjusted	1.30 (0.94-1.80)
ADHD	
Crude	1.23 (1.10-1.39)
Adjusted	1.18 (1.05-1.33)
ASD	
Crude	1.37 (1.15-1.62)
Adjusted	1.29 (1.08-1.54)
Epilepsy	
Crude	1.49 (1.15-1.92)
Adjusted	1.50 (1.16-1.93)
Intellectual disability	
Crude	1.38 (1.04-1.81)
Adjusted	1.50 (1.13-1.97)
Vision or hearing loss	
Crude	1.15 (0.78-1.70)
Adjusted	1.21 (0.82-1.79)

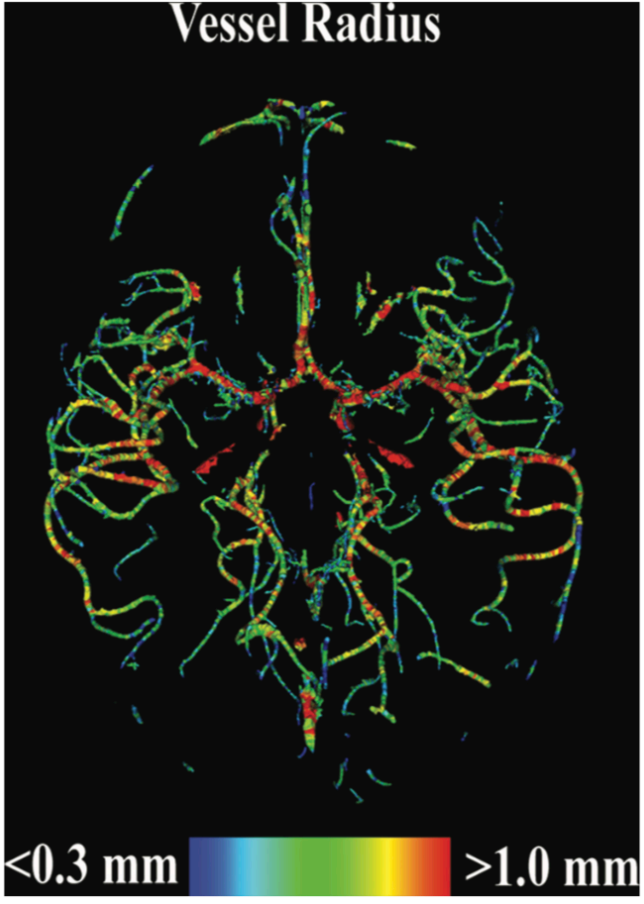


Adjusted for

- sex
- year of birth
- mother's age
- parity
- marital status
- maternal and paternal educational levels
- parental immigrant status

Sun BZ et al. JAMA Psychiatry. 2020

Altered brain structural and vascular anatomy in pre-eclamptic pregnancies



Preeclapmsia (*n* = 10; 5 male, 5 female)
VS
uncomplicated pregnancy (*n* = 10; 5 male, 5 female)

matched for

- Gestational age at birth
- sex
- 7–10 years of age
- Height
- weight

MR imaging to identify brain structural and vascular anatomic differences

Ratsep MT et al. Am J Neuroradiol. 2016

Adjusted mean brain regional volumes (percentage of full intracranial volume)

Brain Region	Control (n = 10) (mean) (SE)	PE (n = 10) (mean) (SE)	P Value[d]
Full intracranial volume (mL)	1431.7 (33.6)	1495.5 (33.6)	.201
Cerebellum[b]	8.72 (0.21)	9.58 (0.21)	.010
Frontal lobe[b]	16.62 (0.39)	17.08 (0.39)	.422
Occipital lobe[b]	6.25 (0.18)	6.58 (0.18)	.213
Parietal lobe[b]	9.41 (0.26)	9.75 (0.26)	.364
Temporal lobe[b]	8.98 (0.15)	9.65 (0.15)	.007
Left accumbens[c]	0.03 (0.001)	0.03 (0.001)	.993
Right accumbens[c]	0.03 (0.001)	0.03 (0.001)	.986
Left amygdala[c]	0.09 (0.003)	0.10 (0.003)	.023
Right amygdala[c]	0.11 (0.002)	0.12 (0.002)	.012
Brain stem[c]	1.27 (0.04)	1.40 (0.04)	.015
Left caudate[c]	0.20 (0.01)	0.21 (0.01)	.843
Right caudate[c]	0.20 (0.01)	0.21 (0.01)	.490
Left cerebral cortex[c]	23.25 (0.41)	24.39 (0.41)	.071
Right cerebral cortex[c]	24.42 (0.46)	25.39 (0.46)	.158
Left cerebral white matter[c]	13.42 (0.37)	13.96 (0.37)	.320
Right cerebral white matter[c]	12.17 (0.33)	12.85 (0.33)	.168
Left hippocampus[c]	0.21 (0.01)	0.23 (0.01)	.166
Right hippocampus[c]	0.22 (0.01)	0.23 (0.01)	.247
Left lateral ventricle[c]	0.34 (0.07)	0.36 (0.07)	.873
Right lateral ventricle[c]	0.31 (0.05)	0.32 (0.05)	.941
Left pallidum[c]	0.11 (0.004)	0.12 (0.004)	.327
Right pallidum[c]	0.12 (0.004)	0.12 (0.004)	.257
Left putamen[c]	0.31 (0.01)	0.32 (0.01)	.446
Right putamen[c]	0.34 (0.01)	0.34 (0.01)	.594
Left thalamus[c]	0.36 (0.01)	0.38 (0.01)	.335
Right thalamus[c]	0.41 (0.01)	0.42 (0.01)	.396

Enlarged left and right amygdalae are also commonly seen in autism spectrum disorder[30] and are associated with an increased incidence of temporal lobe epilepsy

enlarged amygdalae are associated with increased anxiety.

Cerebellar and brain stem enlargements are common among small-for-gestational-age neonates at term.

Adjusted mean brain regional vascular diameters (mm)

Brain Region	Control (*n* = 10) (mean) (SE)	PE (*n* = 10) (mean) (SE)	*P* Value[d]
Cerebellum[b]	0.56 (0.01)	0.55 (0.01)	.417
Frontal lobe[b]	0.54 (0.01)	0.52 (0.01)	.112
Occipital lobe[b]	0.50 (0.01)	0.45 (0.01)	.004
Parietal lobe[b]	0.55 (0.01)	0.52 (0.01)	.025
Temporal lobe[b]	0.63 (0.01)	0.60 (0.01)	.128
Cerebral cortex[c]	0.57 (0.01)	0.55 (0.01)	.085
Cerebral white matter[c]	0.44 (0.02)	0.42 (0.02)	.454

Pre-eclampsia and the risk of Autism Spectrum Disorder

	Studies	OR	95% CI
Clinical classification			
Gestational hypertension	**9**	**1.37**	**1.21–1.54**
Pre-eclampsia	**11**	**1.43**	**1.31–1.55**
Chronic hypertension	**4**	**1.48**	**1.29–1.70**
Mixed	**3**	**1.37**	**1.13–1.67**
Overall		**1.42**	**1.34-1.50**

Confound Factor	
maternal age	No statistical significance
preterm birth	higher in HDP
PROM	No statistical significance
maternal education	No statistical significance
Sex differentiation	males increased the risk of ASD by 38% to females

Xu RT et al. Oncotarget. 2018

Association of Preeclampsia in Term Births with Neurodevelopmental Disorders in Offspring

- prospective, population-based cohort study
- singleton term pregnancies
- followed up to 5 years of age

Associations between preeclampsia in term pregnancies and

- cerebral palsy
- attention-deficit/hyperactivity disorder (ADHD),
- autism spectrum disorder (ASD),
- epilepsy,
- intellectual disability
- vision or hearing loss

Cohort Characteristics Among Term Singleton Live Births

Characteristic	Exposed to preeclampsia[a]	
	No (n = 952 492)	Yes (n = 28 068)
Gestational age, mean (SD), wk	39.8 (1.4)	39.3 (1.5)
Birth weight, mean (SD), g	3628 (494)	3463 (605)
Female sex	464 904 (48.8)	13 367 (47.6)
Mother married or with partner	875 701 (91.9)	25 584 (91.2)
Mother's age, y		
≤19	24 603 (2.6)	1056 (3.8)
20-24	161 504 (17.0)	5768 (20.6)
25-29	331 916 (34.8)	9792 (34.9)
30-34	295 853 (31.1)	7533 (26.8)
35-39	119 269 (12.5)	3308 (11.8)
≥40	19 323 (2.0)	611 (2.2)
Educational level, mean (SD)[b]		
Mother	4.6 (1.7)	4.6 (1.6)
Father	4.4 (1.7)	4.4 (1.7)
Immigrant parents	77 462 (8.1)	1462 (5.2)
First birth	382 486 (40.2)	17 064 (60.8)

Sun BZ et al. JAMA Psychiatry. 2020

ACOG COMMITTEE OPINION

Number 767

(Replaces Committee Opinion Number 692, September 2017)

- Η χρήση πρωτοκόλλων και τεκμηριωμένων κλινικών οδηγιών για τη διαχείριση ασθενών με προεκλαμψία και εκλαμψία έχει αποδειχθεί ότι βελτιώνει την περιγεννητική έκβαση.

- Εγκυμονούσες ή λεχωίδες με οξεία έναρξη, σοβαρή συστολική υπέρταση, σοβαρή διαστολική υπέρταση ή και τα δύο απαιτούν επείγουσα αντιυπερτασική θεραπεία.

- Συνιστάται στενή παρακολούθηση της μητέρας και του εμβρύου από ιατρό και νοσηλευτικό προσωπικό κατά τη θεραπεία της οξείας εμφάνισης της σοβαρής υπέρτασης.

- Μετά την αρχική σταθεροποίηση, η ομάδα θα πρέπει να παρακολουθεί στενά την αρτηριακή πίεση και να εφαρμόζει θεραπεία συντήρησης όπως απαιτείται.

ACOG COMMITTEE OPINION

Number 767

(Replaces Committee Opinion Number 692, September 2017)

Η ενδοφλέβια (IV) λαμπεταλόλη και η υδραλαζίνη θεωρούνται από καιρό φάρμακα πρώτης γραμμής για τη διαχείριση της οξείας εμφάνισης της σοβαρής υπέρτασης της κύησης και της λοχείας

Η από του στόματος άμεσης αποδέσμευσης νιφεδιπίνη μπορεί επίσης να θεωρηθεί ως θεραπεία πρώτης γραμμής, ιδιαίτερα όταν δεν υπάρχει πρόσβαση IV.

Η χρήση IV labetalol, IV υδραλαζίνης ή από του στόματος νιφεδιπίνης άμεσης αποδέσμευσης για τη θεραπεία της οξείας εμφάνισης της σοβαρής υπέρτασης δεν απαιτεί παρακολούθηση της καρδιάς.

Στη σπάνια περίπτωση που η IV bolus labetalol, η υδραλαζίνη ή η per os νιφεδιπίνη άμεσης αποδέσμευσης αποτυγχάνει να ανακουφίσει την οξεία έναρξη, τη σοβαρή υπέρταση και χορηγείται σε διαδοχικές κατάλληλες δόσεις, επανεμφανιζόμενη διαβούλευση με έναν αναισθησιολόγο, μη-εμβρυϊκό υποειδικό φάρμακο ή υποειδικός κρίσης συνιστάται παρέμβαση δεύτερης γραμμής.

Το θειικό μαγνήσιο δεν συνιστάται ως αντιυπερτασικός παράγοντας, αλλά το θειικό μαγνήσιο παραμένει το φάρμακο επιλογής για προφύλαξη κατάσχεσης για γυναίκες με οξεία έναρξη σοβαρής υπέρτασης κατά τη διάρκεια της εγκυμοσύνης και της περιόδου μετά τον τοκετό. Η έναρξη του μαγνησίου δεν πρέπει να καθυστερεί στη ρύθμιση της οξείας σοβαρής υπέρτασης. Συνιστάται ανεξάρτητα από το εάν ο ασθενής έχει υπέρταση κύησης με σοβαρά χαρακτηριστικά, προεκλαμψία με σοβαρά χαρακτηριστικά ή εκλαμψία.

Reported frequency of signs and symptoms of HELLP syndrome

Sign/symptom	Frequency, percent
Proteinuria	86 to 100
Hypertension	82 to 88
Right upper quadrant/epigastric pain	40 to 90
Nausea, vomiting	29 to 84
Headache	33 to 61
Visual changes	10 to 20
Jaundice	5

Indications for antihypertensive therapy

Not prescribe antihypertensive therapy for **mild hypertension** in the context of preeclampsia (consistently less than 150/100 mmHg).

The benefit of antihypertensive therapy in pregnant women with mild hypertension is a reduction in risk of developing severe hypertension which may not be sufficient to warrant exposing the fetus to the potential adverse effects from these drugs.

Lowering blood pressure does not affect the course of preeclampsia because the primary pathogenetic process is an abnormality of the placental vasculature that results in placental underperfusion, which, in turn, leads to release of factors that cause widespread maternal endothelial dysfunction with multiorgan dysfunction

Summary of maternal and neonatal outcomes in pregnancies complicated by eclampsia

Outcome	Frequency, percent
Abruption	7 to 10
Disseminated intravascular coagulation	7 to 11
Pulmonary edema	3 to 5
Acute renal failure	5 to 9
Aspiration pneumonia	2 to 3
Cardiopulmonary arrest	2 to 5
Liver hematoma	1
HELLP syndrome	10 to 15
Perinatal death	5.6 to 11.8
Preterm birth	50

Adapted from: Sibai, BM. Obstet Gynecol 2005; 105:402.

Complications of preeclampsia

Outcome measure	Normal blood pressure (percent)	Mild preeclampsia (percent)	Severe preeclampsia (percent)
Maternal			
Liver dysfunction	0.2	3.2	20.2
Kidney dysfunction	0.3	5.1	12.8
Placental abruption	0.7	0.5	3.7
Induced labor	12.1	41.5	58.7
Cesarean delivery	13.3	30.9	34.9
Delivery <34 weeks	3.2	1.9	18.5
Fetal or neonatal			
Growth restriction	4.2	10.2	18.5
Admission to NICU	12.9	27.3	42.6
Respiratory difficulty	3.8	3.2	15.7
Brain hemorrhage	0.2	0.5	0
Fetal death	0.9	0.5	0.9
Neonatal death	0.5	0.5	0.9

NICU: neonatal intensive care unit.

Πρόβλεψη και αντιμετώπιση της όψιμης προεκλαμψίας

Crude and AORs for birth outcomes following early- and late-onset preeclampsia, singleton deliveries, Washington State, 2003-2008

	Early-onset preeclampsia				Late-onset preeclampsia			
Birth outcomes	OR	95% CI	AOR	95% CI	OR	95% CI	AOR	95% CI
SGA (<10th percentile)	7.19	6.49–7.96	6.08	5.43–6.80	2.94	2.80–3.09	2.68	2.54–2.82
LGA (>90th percentile)	0.11	0.07–0.16	0.10	0.07–0.16	0.78	0.73–0.83	0.81	0.76–0.86
Fetal death	9.42	7.22–12.3	5.79	4.03–8.33	1.55	1.06–2.27	1.26	0.81–1.96
Neonatal death	12.84	9.63–17.1	11.44	8.07–16.4	1.31	0.78–2.19	1.09	0.61–1.96
Perinatal death	10.93	8.97–13.3	8.38	6.48–10.8	1.46	1.07–1.98	1.19	0.83–1.69
Perinatal death/morbidity[a]	19.07	17.08–21.29	16.41	14.48–18.60	2.37	2.11–2.67	2.02	1.78–2.28

For early-onset preeclampsia comparisons, all ongoing pregnancies at 20 weeks of gestation were included in the denominator; for late-onset preeclampsia comparisons, all ongoing pregnancies at 34 weeks of gestation were included in the denominator.

Lisonkova S, Am J Obstet Gynecol. 2013

	Immediate delivery (n=352)	Expectant monitoring (n=351)	Relative risk (95% CI)	Absolute risk difference (95% CI)
Primary outcome	4 (1%)	11 (3%)	0·36 (0·12 to 1·11)	2·0 (–0·2 to 4·5)
Thromboembolic process	1 (<1%)	1 (<1%)	1·00 (0·06 to 15·88)	0·0 (–1·3 to 1·3)
Pulmonary oedema	0 (0%)	0 (0%)	..	0·0 (–1·1 to 1·1)
HELLP syndrome	3 (1%)	6 (2%)	0·50 (0·13 to 1·98)	0·9 (–0·0 to 0·0)
Eclampsia	0 (0%)	2 (1%)	..	0·6 (–0·6 to 2·1)
Placental abruption	0 (0%)	2 (1%)	..	0·6 (–0·6 to 2·1)
Death	0 (0%)	0 (0%)	..	0·0 (–1·1 to 1·1)
Secondary outcomes				
Instrumental vaginal delivery	32 (9%)	34 (10%)	0·94 (0·59 to 1·49)	0·6 (–3·8 to 5·0)
Caesarean section	107 (30%)	114 (32%)	0·94 (0·75 to 1·16)	2·1 (–4·8 to 8·9)
Onset by caesarean section	27 (8%)	42 (12%)		
Caesarean section after induction or spontaneous onset of labour	80 (23%)	72 (21%)		

p=0·069

Broekhuijsen K. et al. Lancet. 2015

	Immediate delivery (n=352)	Expectant monitoring (n=351)	Relative risk (95% CI)	Absolute risk difference (95% CI)	Number needed to harm
Primary outcome	20/352 (5·7%)	6/351 (1·7%)	3·3 (1·4 to 8·2); p=0·005	4·0 (1·2 to 7·1)	25
Secondary outcomes					
5 min Apgar score <7	14/351 (4·0%)	10/350 (2·9%)	1·4 (0·6 to 3·1)	1·1 (–1·7 to 4·0)	..
Umbilical artery pH <7·05	6/270 (2·2%)	6/263 (2·3%)	2·0 (0·3 to 3·0)	0·1 (–2·9 to 2·8)	..
NICU admission	26/352 (7·4%)	13/350 (3·7%)	2·0 (1·0 to 3·8)	3·7 (0·3 to 7·2)	27
Perinatal death	0/352 (0·0%)	0/351 (0·0%)	..	0·0 (–1·1 to 1·1)	..
Suspected or confirmed infection or sepsis	36/351 (10·3%)	22/348 (6·3%)	1·6 (1·0 to 2·7)	3·9 (–0·2 to 8·1)	..
Hypoglycaemia (intravenous glucose)	64/350 (18·3%)	53/348 (15·2%)	1·2 (0·9 to 1·7)	3·1 (–2·5 to 8·6)	..
Transient tachypnoea of the newborn	20/349 (5·7%)	6/348 (1·7%)	3·3 (1·4 to 8·2)	4·0 (1·2 to 7·1)	25
Meconium aspiration syndrome	0/351 (0·0%)	1/349 (0·3%)	..	0·3 (–1·6 to 0·8)	..
Pneumothorax or pneumomediastinum	3/351 (0·9%)	1/348 (0·3%)	3·0 (0·3 to 28·5)	0·6 (–0·9 to 2·2)	..
Periventricular leucomalacia	4/303 (1·3%)	2/284 (0·7%)	1·9 (0·4 to 10·2)	0·6 (–1·4 to 2·7)	..
Intraventricular haemorrhage	3/339 (0·9%)	0/335 (0·0%)	..	0·9 (–0·.4 to 2·6)	..
Convulsions	4/351 (1·1%)	1/348 (0·3%)	4·0 (0·5 to 35·3)	0·9 (–0·6 to 2·6)	..
Necrotising enterocolitis	1/351 (0·3%)	0/348 (0·0%)	..	0·3 (–0·8 to 1·6)	..
Any neonatal morbidity*	131/267 (49·1%)	89/245 (36·3%)	1·4 (1·1 to 1·7)	12·7 (4·2 to 21·0)	8

Data are n (%). NICU=neonatal intensive care unit. *Classified as normal if umbilical artery pH was missing and other components were normal, classified as normal if periventricular leucomalacia or intraventricular haemorrhage, or both, were missing but no cerebral imaging had taken place; includes respiratory distress syndrome; some had more than one type of morbidity; not prespecified.

Broekhuijsen K. et al. Lancet. 2015

Προεκλαμψία

Σας ευχαριστώ