Early Detection of Preeclampsia
in Antenatal Care Setting

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Grafik Tren Angka Kematian Ibu sejak 1992 sampai 2012 (Sumber: SDKI)

Angka Kematian Ibu Makin Meningkat

Sabtu , 23 April 2016

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25 Februari 2016 17:19 WIB *Category: Suara Kedu* *Dikunjungi: kali* A+ / A-

KESEPAKATAN: Kepala Perwakilan BKKBN Pemprov Jateng Condro Rini dan Rektor UM Magelang Eko Muh Widodo melakukan penandatanganan naskah kerja sama. (suaramerdeka.com/MH Habib Shaleh)

BERITA TERBARU

Revisi UU Pilkada Hanya Berkutat Pada Syarat Pencalonan

23 April 2016 14:00 WIB

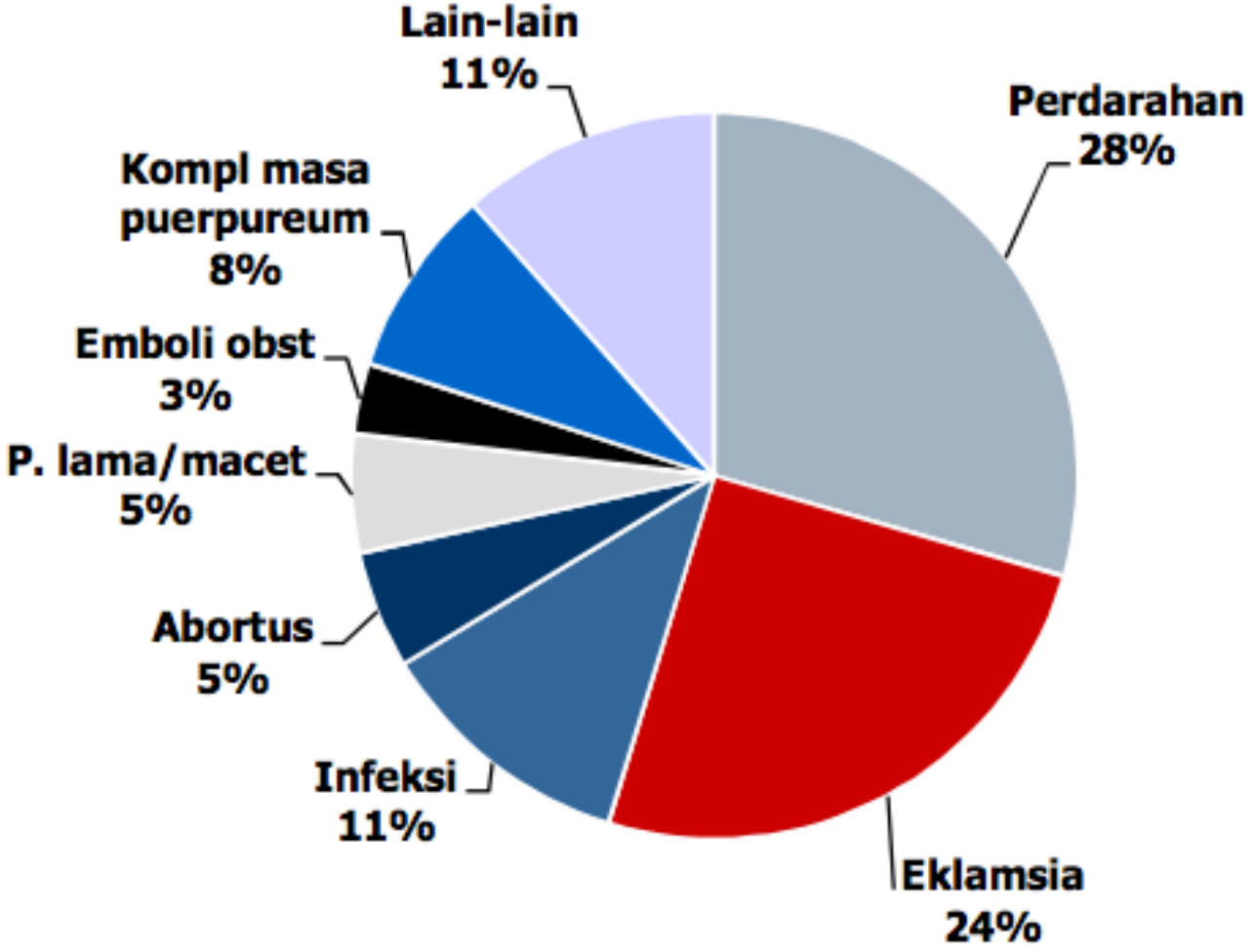
Fly Over Palur Dikelola Bersama Karanganyar - Sukoharjo

23 April 2016 13:45 WIB

Fraksi Partai Gerindra Apresiasi Kinerja BIN

23 April 2016 13:30 WIB

Penyebab Kematian Ibu



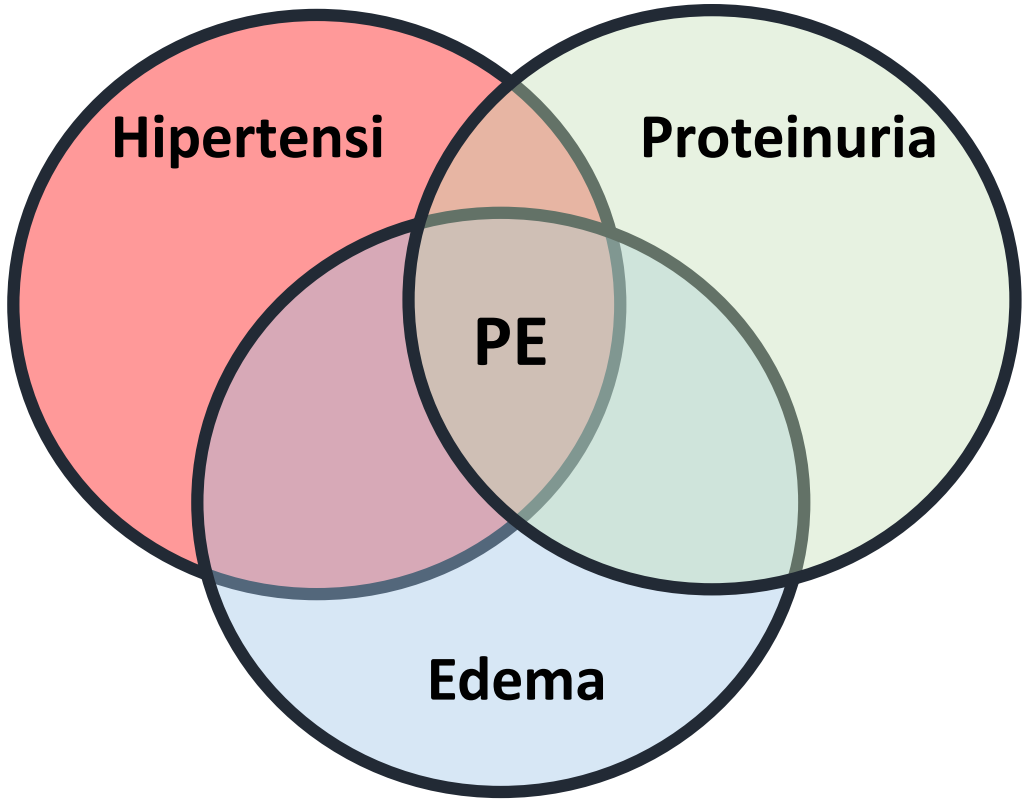
Sumber: Departemen Kesehatan,

Definitions Of Pregnancy-related Hypertensive Disorders

There are **four major hypertensive disorders** related to pregnancy:

1. Hipertensi Kronik/ Chronic hypertension
2. Hipertensi Gestasional/ Gestational hypertension
3. **Preeklamsia-eklamsia/ Preeclampsia-eclampsia**
4. Preeclampsia superimposed on chronic hypertension

Perkembangan Definisi Preeklamsi



Definisi Preeklamsia - Terdahulu

- **Preeklamsia** (**ringan**)
  - Tekanan darah > 140/90 mmHg
  - Proteinuria > 0,3 g/24 jam
- **Preeklamsia Berat**
  - Tekanan darah > 160/110 mmHg
  - Proteinuria > 5 g/24 jam
  - Sindroma HELLP
  - Gejala Sistem Saraf Pusat

Definisi Preeklamsia - Terbaru

- **Preeklamsia tanpa gejala berat** (**definisi terbaru**)
  - Tekanan darah > 140/90 mmHg
  - Proteinuria > 300 mg/ 24 jam ATAU dipstick 1+ ATAU rasio protein/kreatinin > 0,3
- **Tidak adanya proteinuria <u>dengan</u>**
  - Platelet < 100.000
  - Kreatinin > 1,1
  - Peningkatan Tes Fungsi Hati
  - Gejala Sistem Saraf Pusat

Pengertian baru Preeklamsia

- **Preeklamsia berat** = salah satu dari:
  - Tekanan darah >160/110 → harus di terapi dalam 1 jam
  - platelet <100000 → Kenaikan LFT
  - Kreatinin >1.1
  - Edema paru
  - Gejala sistem saraf pusat

Preeklamsia

Hipertensi DENGAN proteinuria

atau

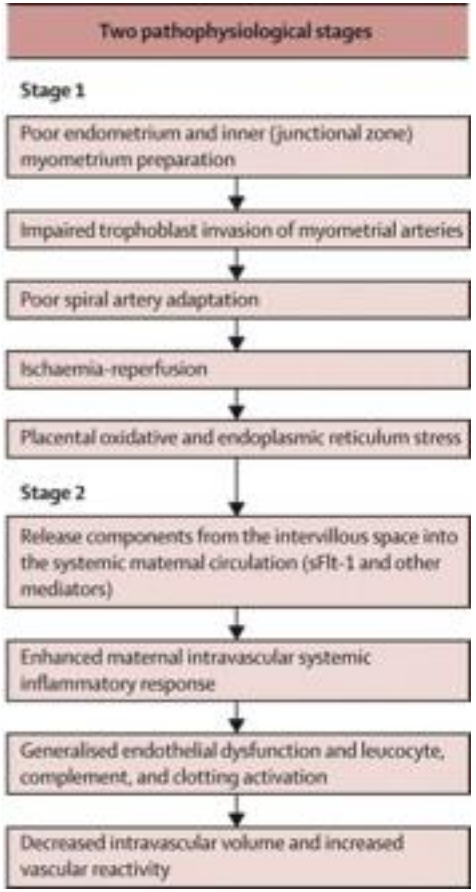
Hipertansi tanpa proteinuria

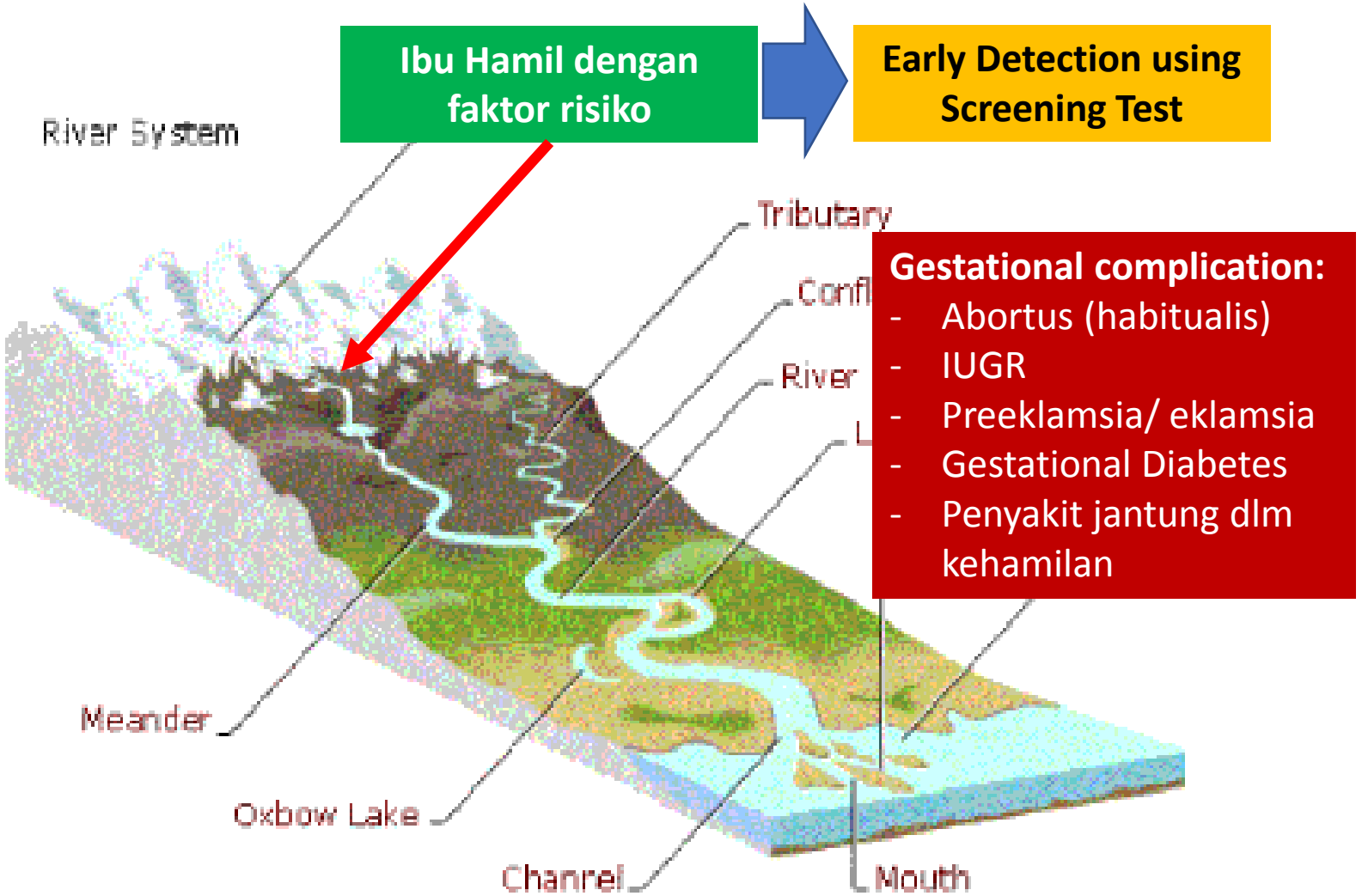
40% akan berkembang menjadi preeklamsia klasik

Eclampsia

- **Eclampsia** is the occurrence of seizures that cannot be attributed to other causes in a woman with preeclampsia

Konsep Hulu – Hilir ANC





Introduction

- Preeclampsia is a **multi-system progressive disorder** characterized by the **new onset** of **hypertension** and **proteinuria**, or **hypertension** and **significant end-organ dysfunction** in the last half of pregnancy or postpartum

SBP ≥140 mmHg or DBP ≥90 mmHg on two occasions at least four hours apart after 20 weeks of gestation in a previously normotensive patient

If SBP is ≥160 mmHg or DBP 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)

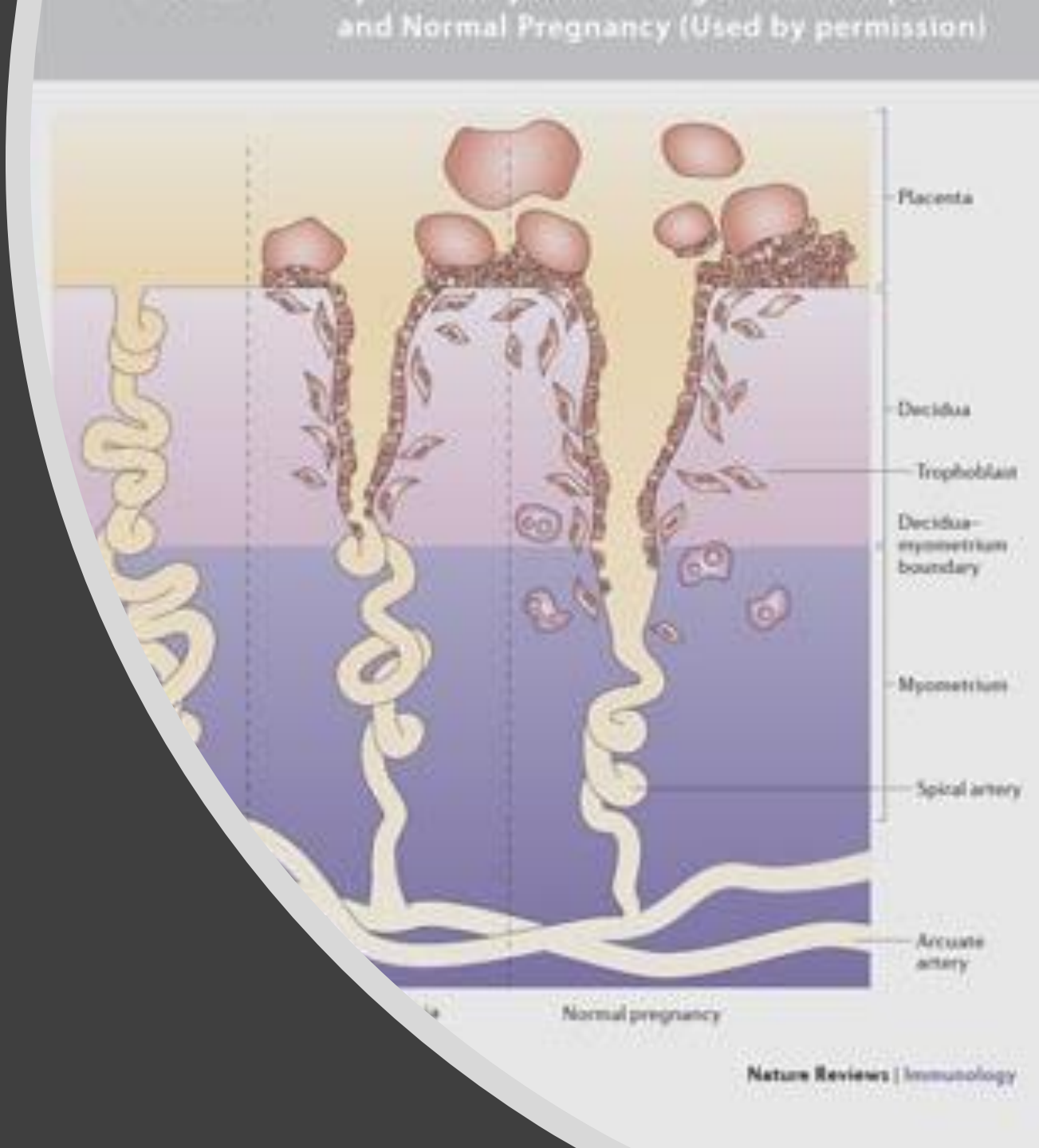
OR dipstick ≥1+ if a quantitative measurement is unavailable

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 with the new onset of any of the following (with or without proteinuria):

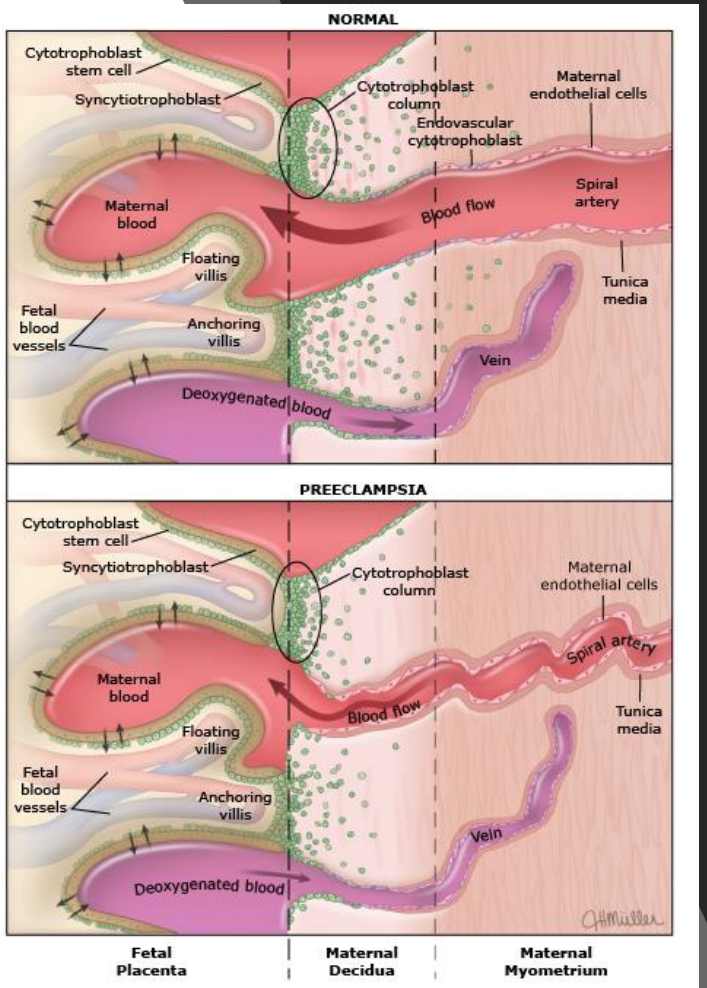
- Platelet count <100,000/microL
- Serum creatinine >1.1 mg/dL (97.2 micromol/L) or doubling of the creatinine concentration in the absence of other renal disease
- Liver transaminases at least twice the upper limit of the normal concentrations for the local laboratory
- Pulmonary edema
- Cerebral or visual symptoms (eg, new-onset and persistent headaches not responding to usual doses of analgesics*; blurred vision, flashing lights or sparks, scotomata)

Introduction

The **genesis** of the disease is laid down in **early pregnancy** and is characterized anatomically by **abnormal remodeling** of the maternal spiral arteries at the placental site.



Abnormal placentation in preeclampsia



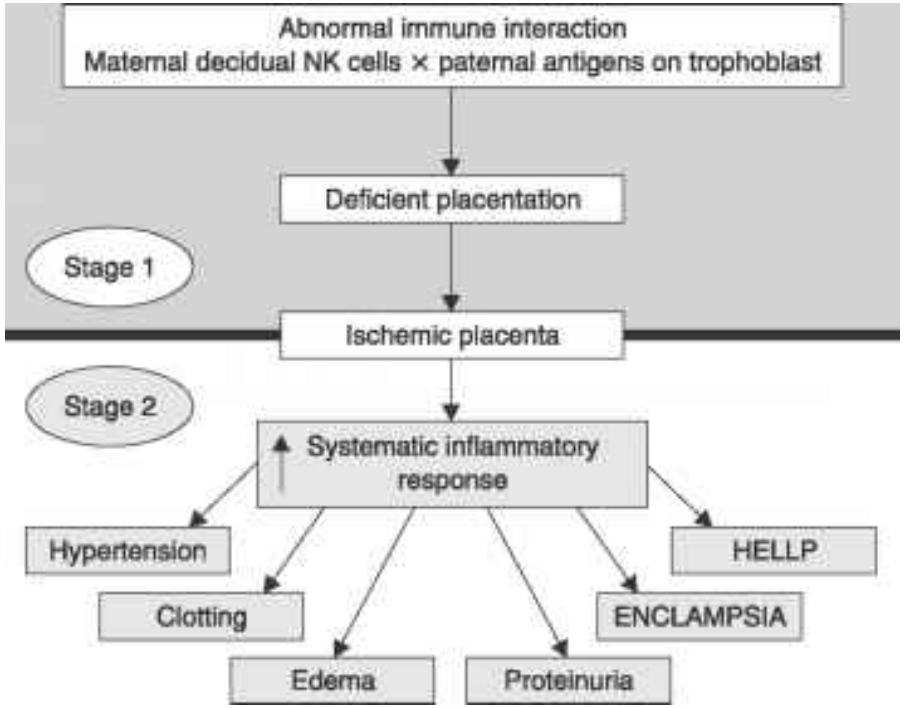
Exchange of oxygen, nutrients, and waste products between the fetus and mother depends on **adequate placental perfusion** by maternal vessels.

In **normal placental** development, invasive cytotrophoblasts of fetal origin invade the maternal spiral arteries, transforming them from small-caliber resistance vessels to high-caliber capacitance vessels capable of providing placental perfusion adequate to sustain the growing fetus. During the process of vascular invasion, the cytotrophoblasts differentiate from an epithelial phenotype to an endothelial phenotype, a process referred to as "pseudovasculogenesis" or "vascular mimicry" (Upper panel).

In **preeclampsia**, cytotrophoblasts fail to adopt an invasive endothelial phenotype. Instead, invasion of the spiral arteries is shallow and they remain small caliber, resistance vessels (Lower panel).

Introduction

- Preeclampsia **cannot reliably be predicted as no tests available in early pregnancy can accurately** distinguish women who will go on to develop preeclampsia from those who will not
  - For this reason, **obstetric care providers focus primarily on early clinical detection of the disease**: All pregnant women are monitored for evidence of preeclampsia at each of their prenatal visits.



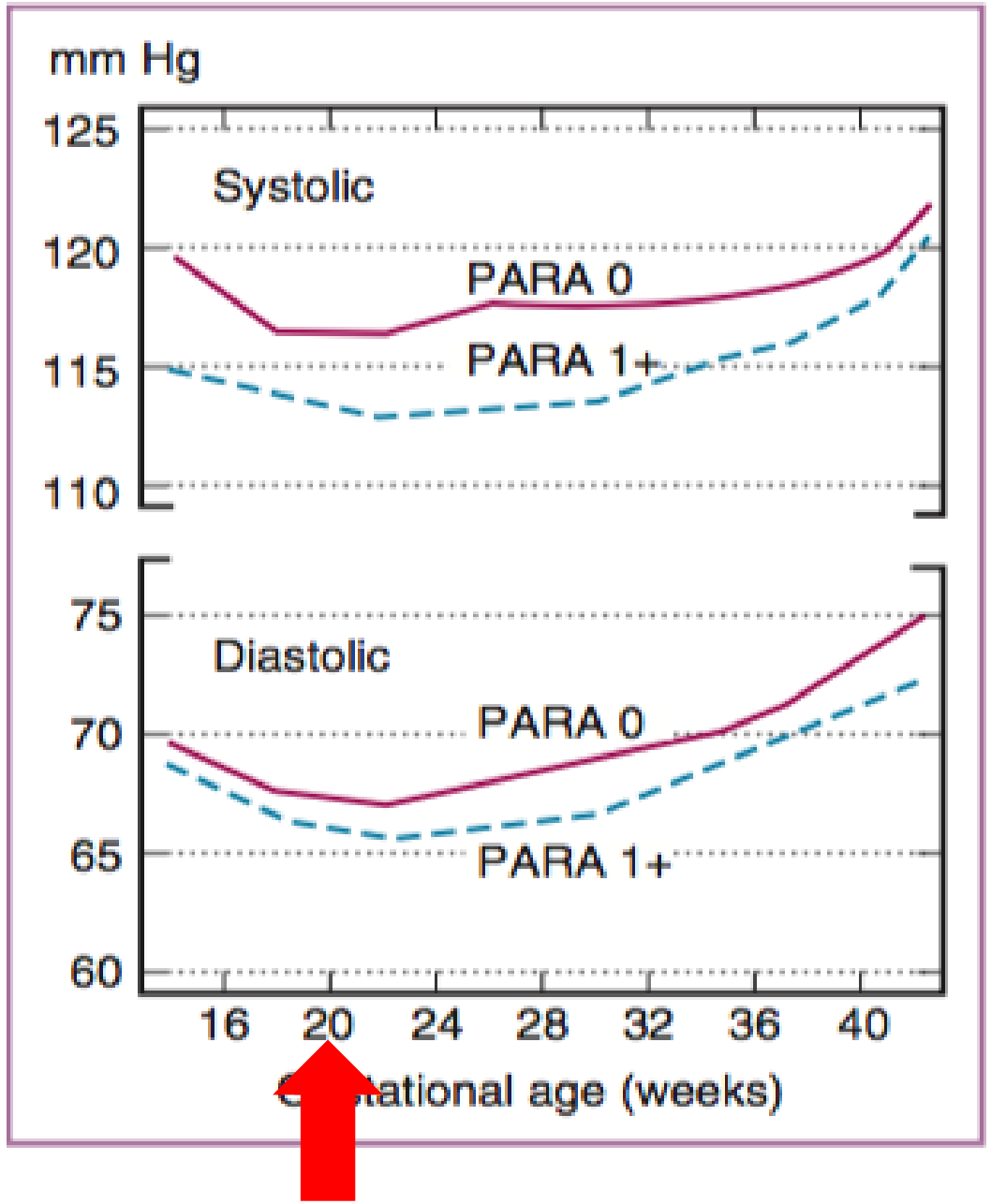
Clinical Approach

Universal routine blood pressure measurement in pregnancy

Identifying women at high risk

Early prenatal assessments of women at high risk

Interventions to reduce risk

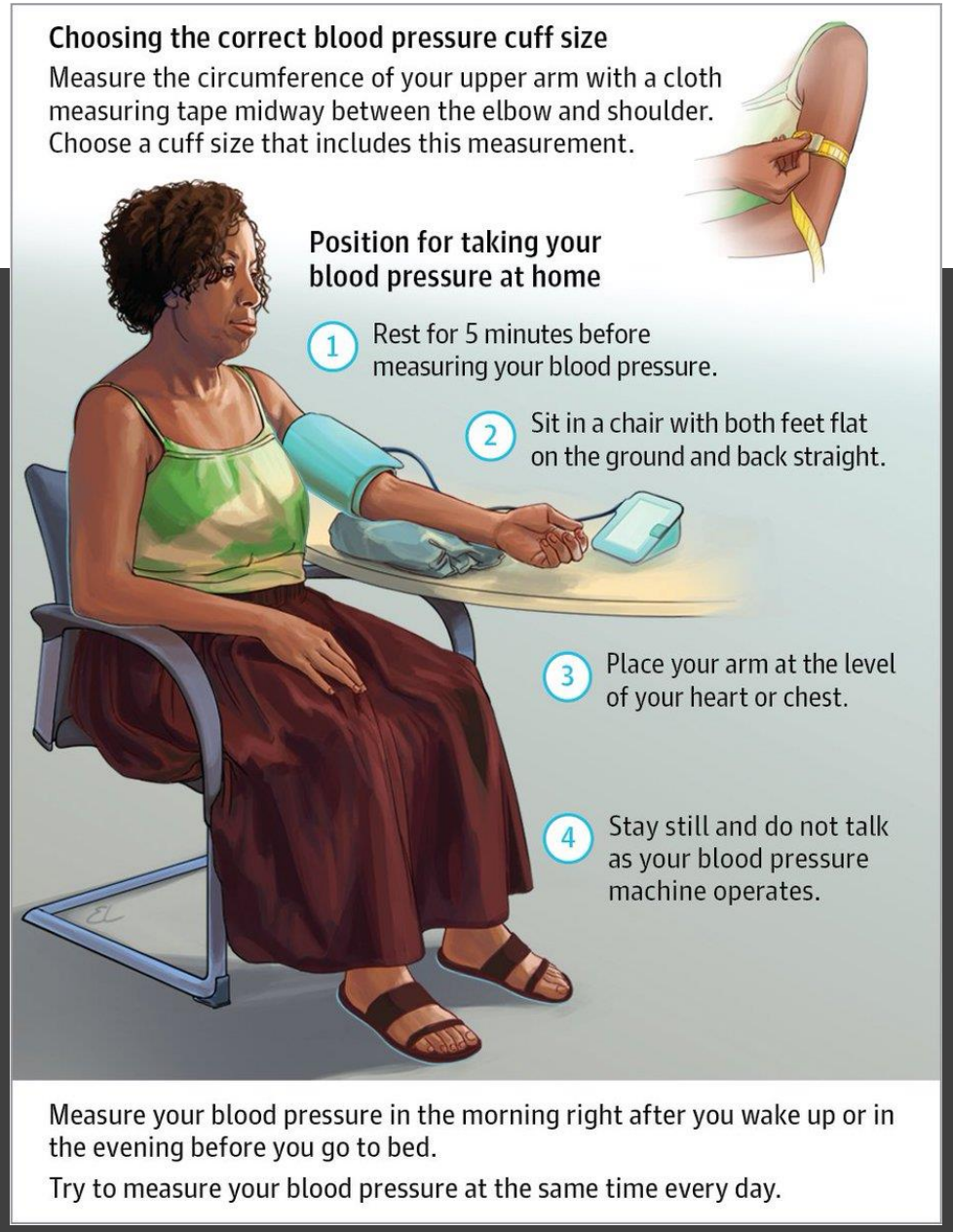


Universal routine blood pressure measurement in pregnancy

- US Preventive Services Task Force (USPSTF): **all pregnant women are at risk for preeclampsia** and should be **screened by measurement of blood pressure** at all provider visits throughout pregnancy
  - Although preeclampsia is not diagnosed before 20 weeks of gestation, early measurements establish the patient's baseline blood pressure

Hipertensi dalam Kehamilan

Hipertensi	**Sistolik ≥ 140 mmHg** **Diastolik ≥ 90 mmHg**
Prehipertensi	**Sistolik 120 – 139 mmHg** **Diastolik 80 – 89 mmHg**
Normotensi	**Sistolik 90 – 120 mmHg** **Diastolik 60 – 80 mmHg**
Hypotensi	**Sistolik ≤ 90 mmHg** **Diastolik ≤ 90 mmHg**

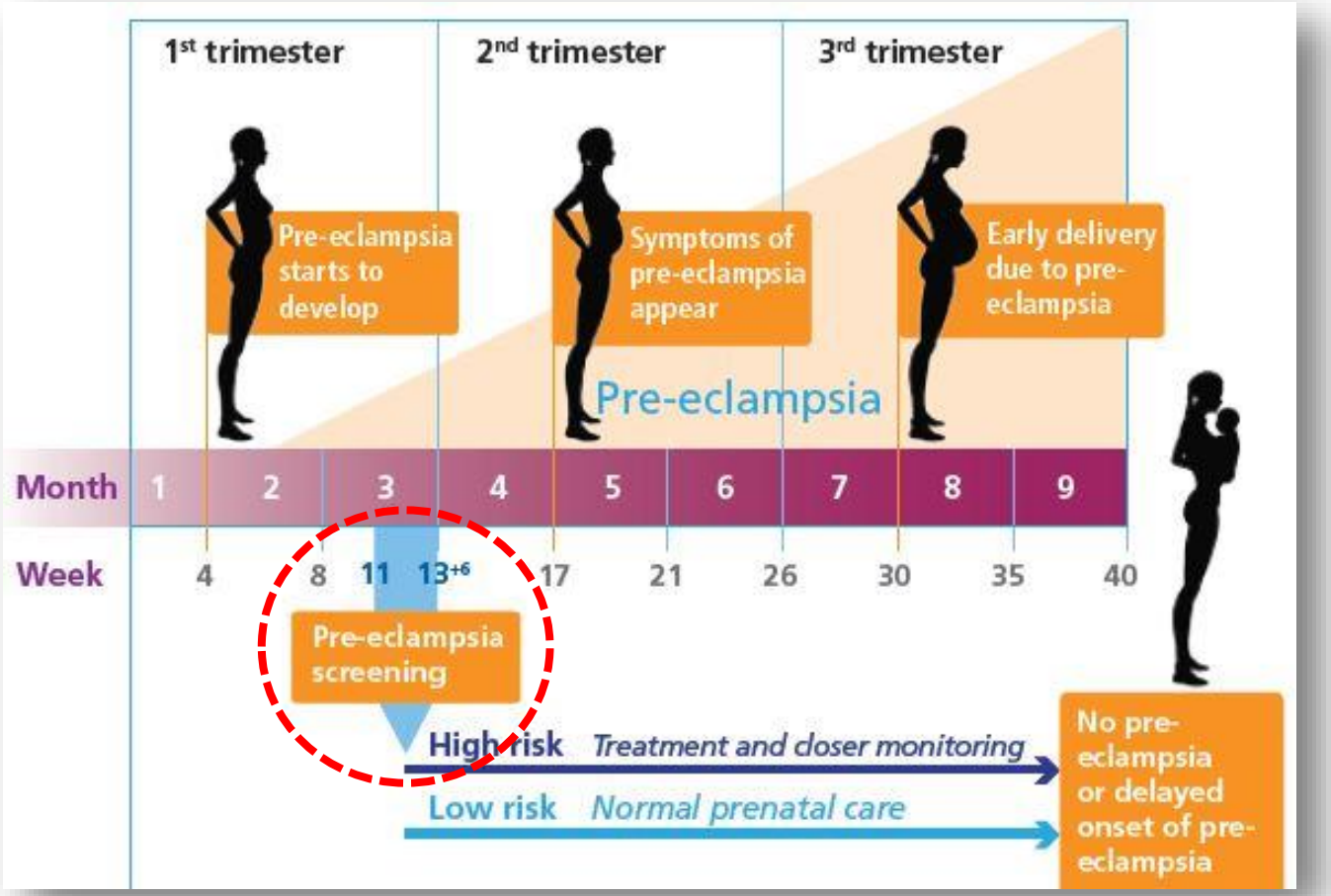


Accurate assessment of blood pressure

- Choose an appropriately sized cuff: width of bladder 40 percent of circumference and encircling 80 percent of the upper arm. Use a large adult cuff in women with an upper-arm circumference of 35 to 44 cm, and use a thigh cuff if the upper-arm circumference is 45 to 52 cm. If an automated device is used, it should have been validated in a pregnant population [48]. If an auscultatory method is used, the first audible sound (Korotkoff I) is the systolic pressure and the disappearance of sound (Korotkoff V) is the diastolic pressure [49]. However, if sounds are audible with the cuff deflated, which can happen in pregnant women, then Korotkoff IV should be used [47]. Caffeine or nicotine within 30 minutes of measurement can increase readings.

Identifying women at high risk

- Pregnant women **should be evaluated early in pregnancy for risk factors** for **preeclampsia**.
    - Early assessment is particularly important for women who are planning to receive pregnancy care and deliver in a low-risk setting (eg, midwifery practice, birthing center, home birth), which would be contraindicated if preeclampsia develops.



Identifying women at high risk

Clinical factors that have been associated with an increased risk of developing preeclampsia

High risk:

- Previous pregnancy with preeclampsia, especially early onset and with an adverse outcome
- Multifetal gestation
- Chronic hypertension
- Type 1 or 2 diabetes mellitus
- Renal disease
- Autoimmune disease (antiphospholipid syndrome, systemic lupus erythematosus)

Moderate risk

- Nulliparity
- Obesity (body mass index [BMI]>30 kg/m2)
- Family history of preeclampsia in mother or sister
- Age ≥35 years
- Sociodemographic characteristics (African American, low socioeconomic level)
- Personal risk factors (eg, history of low birth weight or small for gestational age, previous adverse pregnancy outcome,>10-year pregnancy interval)

Interventions to reduce risk

- **Most** risk factors for preeclampsia **are not modifiable**
  - avoiding pre-pregnancy obesity and excessive gestational weight gain are notable exceptions.
  - Obese women can reduce their risk of developing preeclampsia by losing weight before pregnancy and limiting weight gain during pregnancy
  - Women who are not obese can reduce their risk of developing preeclampsia by not exceeding Institute of Medicine recommendations for gestational weight gain

Faktor – faktor Risiko Preeklamsia

Faktor maternal	Inheren	• Umur < 20 atau 35–40 • Nulliparitas • Diri/kel. Dg. riw. PE atau peny. Kardiovaskular • Wanita yg terlahir PJT
	Kondisi medis	• Obesitas • Hipertensi Kronik • Peny Ginjal kronis • DM (IR, type 1, dan GDM) • APS • Peny Jaringan Ikat (SLE dsb) • Thrombophilia • Stress

	Kehamilan Spesifik	• Kehamilan majemuk
		• Oocyte donation
		• UTI
		• Janin dg kelainan
		  • Mola Hydatidosa
		  • Hydrops fetalis
		  • Anomali Structural

Faktor Paternal	Paparan dg semen & sperma terbatas	• Barrier contraception • Pertama kali menjadi ayah • Donor insemination
	Suami dg riwayat preeklampsia dengan pasangan terdahulu	

Lancet 2001;357:209–15

Interventions to reduce risk

- **Daily Low-dose aspirin** (100 to 150 mg in the 12th or 13th week of gestation
  - **Early therapy** (before 16 weeks) may be **important** since the **pathophysiologic** features of **preeclampsia develop early** in **pregnancy**
  - For women at low risk for development of preeclampsia, available evidence does not support use of low-dose aspirin for prevention of preeclampsia, but a modest (approximately 10 percent) reduction in the risk of preeclampsia and its sequelae (growth restriction, preterm birth) is possible for women at moderate to high risk of developing the disease

Daily Low-dose aspirin Evidence of efficacy

- In one 2017 meta-analysis (45 trials, almost 21,000 women at increased risk of preeclampsia), aspirin initiated at ≤16 weeks:
  - reduced the risk of preeclampsia (relative risk [RR] 0.57, 95% CI 0.43-0.75)
  - severe preeclampsia (RR 0.47, 95% CI 0.26-0.83)
  - fetal growth restriction (RR 0.56, 95% CI 0.44-0.70) [30]
  - The reductions were lower or insignificant with initiation after 16 weeks
  - The authors also noted a dose-dependent effect whereby the optimum aspirin dose appeared to be 100 to 150 mg of aspirin rather than a lower dose

Am J Obstet Gynecol. 2017 Feb;216(2):110-120.e6. doi: 10.1016/j.ajog.2016.09.076. Epub 2016 Sep 15.

The role of aspirin dose on the prevention of preeclampsia and fetal growth restriction: systematic review and meta-analysis.

Roberge S[1], Nicolaides K[2], Demers S[1], Hyett J[3], Chaillet N[4], Bujold E[5].

Author information

Abstract

BACKGROUND: Preeclampsia and fetal growth restriction are major causes of perinatal death and handicap in survivors. Randomized clinical trials have reported that the risk of preeclampsia, severe preeclampsia, and fetal growth restriction can be reduced by the prophylactic use of aspirin in high-risk women, but the appropriate dose of the drug to achieve this objective is not certain.

OBJECTIVE: We sought to estimate the impact of aspirin dosage on the prevention of preeclampsia, severe preeclampsia, and fetal growth restriction.

STUDY DESIGN: We performed a systematic review and meta-analysis of randomized controlled trials comparing the effect of daily aspirin or placebo (or no treatment) during pregnancy. We searched MEDLINE, Embase, Web of Science, and Cochrane Central Register of Controlled Trials up to December 2015, and study bibliographies were reviewed. Authors were contacted to obtain additional data when needed. Relative risks for preeclampsia, severe preeclampsia, and fetal growth restriction were calculated with 95% confidence intervals using random-effect models. Dose-response effect was evaluated using meta-regression and reported as adjusted R^2. Analyses were stratified according to gestational age at initiation of aspirin (≤16 and >16 weeks) and repeated after exclusion of studies at high risk of biases.

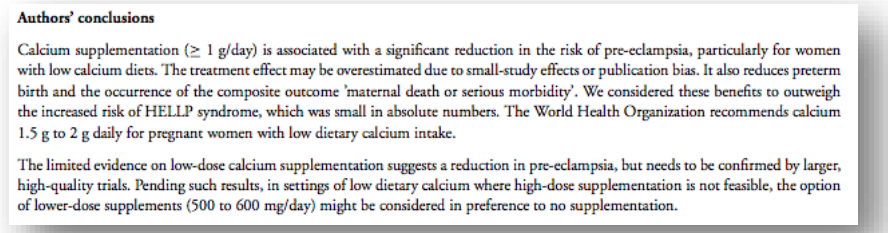
RESULTS: In all, 45 randomized controlled trials included a total of 20,909 pregnant women randomized to between 50-150 mg of aspirin daily. When aspirin was initiated at ≤16 weeks, there was a significant reduction and a dose-response effect for the prevention of preeclampsia (relative risk, 0.57; 95% confidence interval, 0.43-0.75; P < .001; R^2, 44%; P = .036), severe preeclampsia (relative risk, 0.47; 95% confidence interval, 0.26-0.83; P = .009; R^2, 100%; P = .008), and fetal growth restriction (relative risk, 0.56; 95% confidence interval, 0.44-0.70; P < .001; R^2, 100%; P = .044) with higher dosages of aspirin being associated with greater reduction of the 3 outcomes. Similar results were observed after the exclusion of studies at high risk of biases. When aspirin was initiated at >16 weeks, there was a smaller reduction of preeclampsia (relative risk, 0.81; 95% confidence interval, 0.66-0.99; P = .04) without relationship with aspirin dosage (R^2, 0%; P = .941). Aspirin initiated at >16 weeks was not associated with a risk reduction or a dose-response effect for severe preeclampsia (relative risk, 0.85; 95% confidence interval, 0.64-1.14; P = .28; R^2, 0%; P = .838) and fetal growth restriction (relative risk, 0.95; 95% confidence interval, 0.86-1.05; P = .34; R^2, not available; P = .563).

CONCLUSION: Prevention of preeclampsia and fetal growth restriction using aspirin in early pregnancy is associated with a dose-response effect. Low-dose aspirin initiated at >16 weeks' gestation has a modest or no impact on the risk of preeclampsia, severe preeclampsia, and fetal growth restriction. Women at high risk for those outcomes should be identified in early pregnancy.

KEYWORDS: aspirin; fetal growth restriction; meta-analysis; meta-regression; preeclampsia; pregnancy; systematic review

Calcium supplementation **Evidence of efficacy**

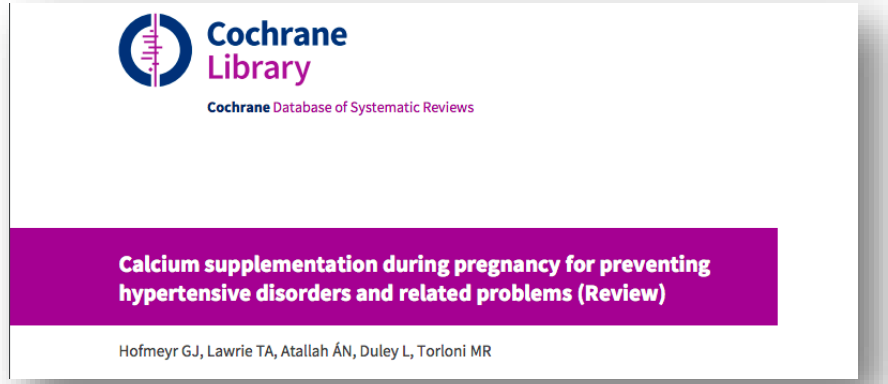
- Low dietary calcium intake is associated with hypertension in the general population
- In populations **where baseline dietary calcium intake** is **low**, WHO recommends **1500 to 2000 mg elemental calcium supplementation per day** for pregnant women to reduce the risk of preeclampsia, particularly among those at higher risk of developing hypertension
  - 2.5 g of calcium carbonate or 4.75 g of calcium citrate contains about 1 g elemental calcium



Authors' conclusions

Calcium supplementation (≥ 1 g/day) is associated with a significant reduction in the risk of pre-eclampsia, particularly for women with low calcium diets. The treatment effect may be overestimated due to small-study effects or publication bias. It also reduces preterm birth and the occurrence of the composite outcome 'maternal death or serious morbidity'. We considered these benefits to outweigh the increased risk of HELLP syndrome, which was small in absolute numbers. The World Health Organization recommends calcium 1.5 g to 2 g daily for pregnant women with low dietary calcium intake.

The limited evidence on low-dose calcium supplementation suggests a reduction in pre-eclampsia, but needs to be confirmed by larger, high-quality trials. Pending such results, in settings of low dietary calcium where high-dose supplementation is not feasible, the option of lower-dose supplements (500 to 600 mg/day) might be considered in preference to no supplementation.



Cochrane Library

Cochrane Database of Systematic Reviews

Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems (Review)

Hofmeyr GJ, Lawrie TA, Atallah ÁN, Duley L, Torloni MR

Weight loss
Evidence of efficacy

- In overweight and obese women, prepregnancy weight loss is recommended as it has a variety of reproductive, pregnancy, and overall health benefits.
- In particular, cohort studies of women who underwent bariatric surgery suggest that weight loss in obese women significantly reduces the risk of preeclampsia
- In addition, a cohort study of women with preeclampsia found weight loss between pregnancies reduced the risk of recurrent preeclampsia in women who were normal weight, overweight, or obese

Obstet Gynecol. 2010 Sep;116(3):667-72. doi: 10.1097/AOG.0b013e3181ed74ea.

Recurrent preeclampsia: the effect of weight change between pregnancies.

Mostello D[1], Jen Chang J, Allen J, Luehr L, Shyken J, Leet T.

Author information

Abstract

OBJECTIVE: To estimate whether the risk of recurrent preeclampsia is affected by interpregnancy change in body mass index (BMI).

METHODS: We conducted a population-based cohort study using Missouri maternally linked birth certificates for 17,773 women whose first pregnancies were complicated by preeclampsia. The women were placed into three groups: those who decreased their BMIs, those who maintained their BMIs, and those who increased their BMIs between their first two pregnancies. The primary outcome was recurrent preeclampsia in the second pregnancy. Adjusted risk ratios and 95% confidence intervals were calculated using Poisson regression analysis.

RESULTS: The overall rate of recurrent preeclampsia in women who decreased their BMIs between pregnancies was 12.8% (risk ratio 0.70, confidence interval 0.60-0.81) compared with 14.8% if BMI was maintained and 18.5% in those who increased their BMIs (risk ratio 1.29, confidence interval 1.20-1.38). Within the normal weight, overweight, and obese weight categories, women who decreased BMI between pregnancies were less likely to experience recurrent preeclampsia. Women in all weight categories who increased their BMIs between pregnancies were more likely to experience recurrent preeclampsia.

CONCLUSION: Interpregnancy weight reduction decreases the risk of recurrent preeclampsia and should be encouraged in women who experience preeclampsia.

LEVEL OF EVIDENCE: II.

Probably Ineffective Interventions
to Reduce Preeclampsia

- **Vitamin C and E supplements**
  - We recommend not prescribing antioxidant supplementation with vitamin C and/or E for prevention of preeclampsia
  - Meta-analyses of nine such trials involving a total of almost 20,000 women confirmed this finding and also found that supplementation was associated with **a slightly increased risk of gestational hypertensio**n (relative risk [RR] 1.11, 95% CI 1.05-1.17), but this could have been the result of multiple statistical comparisons
  - Two trials included in a meta-analysis noted that supplementation was associated with an **increased risk of premature rupture of membranes** (RR 1.73, 95% CI 1.34-2.23)
- **Vitamin D supplements**
  - The combination of vitamin D and calcium resulted in a lower risk of preeclampsia than not receiving this intervention (RR 0.51, 95% CI 0.32-0.80; three trials; 1114 women, moderate quality), but this **may have been related to calcium supplementation in calcium-deficient women.**
- **Folic acid supplementation**
  - recommended to reduce the occurrence of **neural tube defect**s
- **Fish oil supplements**
  - The 2016 Evidence Report/Technology Assessment by the Agency for Healthcare Research and Quality analysis of randomized trials concluded that maternal supplementation with n-3 (also called omega-3) long-chain polyunsaturated fatty acids (n-3 PUFA; ie, eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA]) did not reduce the incidence of fetal growth restriction/small for gestational age (SGA) infants in high-risk populations or gestational hypertension in normal-risk or high-risk populations [92].
  - A multicenter randomized trial not included in the assessment **found no reduction in preeclampsia**

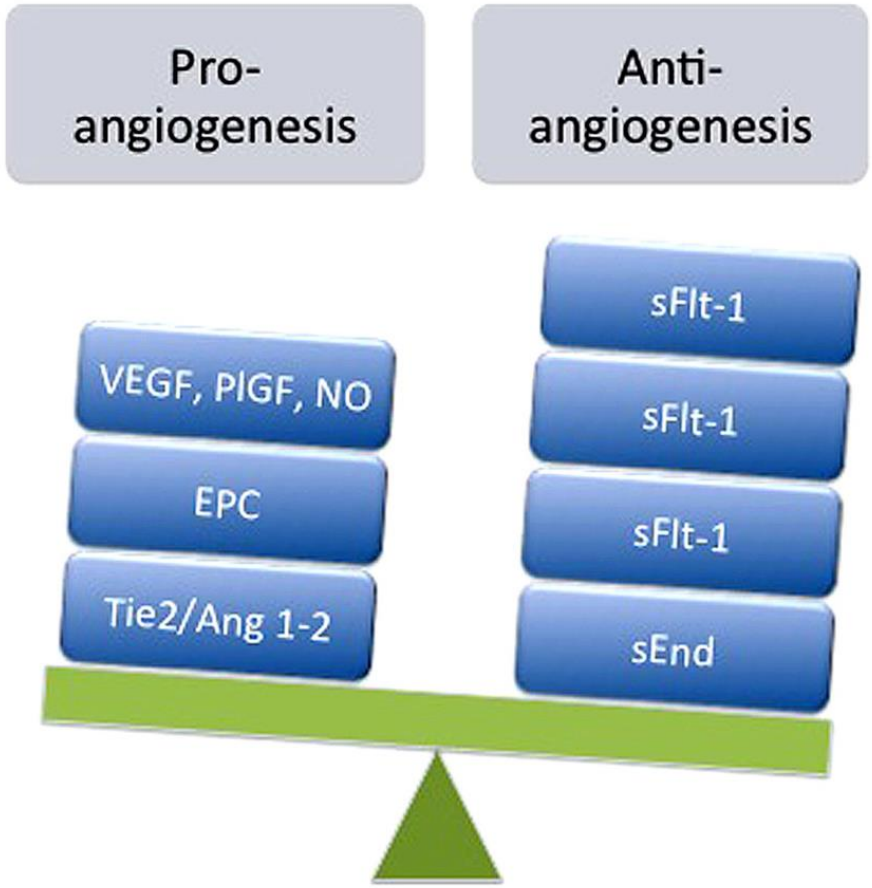
Probably Ineffective Interventions
to Reduce Preeclampsia

- **Diet**
  - **No beneficial** results have been demonstrated from these interventions, which include nutritional advice, protein and energy supplements, protein and **energy restriction** (in obese women), **magnesium supplementation**, and **salt restriction**
- **Nitric oxide donors**
  - **Preeclamptic women** may be **deficient** in **nitric oxide**, which mediates vasodilatation and inhibits platelet aggregation.
  - Systematic review concluded that there is **no high-quality evidence** that administration of **nitric oxide donors (glyceryl trinitrate) prevents preeclampsia**
- **Antihypertensive drugs**
  - In randomized trials, lowering blood pressure with **antihypertensive** medications (**including diuretics) did not reduce** the frequency of **preeclampsia** or **improve fetal** or **pregnancy outcome**
- **Behavioral changes**
  - There is **no strong evidence** that **exercise** and **physical activity** affect the risk of developing preeclampsia.
  - **Bedrest** or **restricted physical activity** is **not recommended** for prevention of preeclampsia, as it is ineffective and bedrest **increases the risk of venous thromboembolism**

Investigational Approaches
Screening tests - Biomarkers

Angiogenic modulators

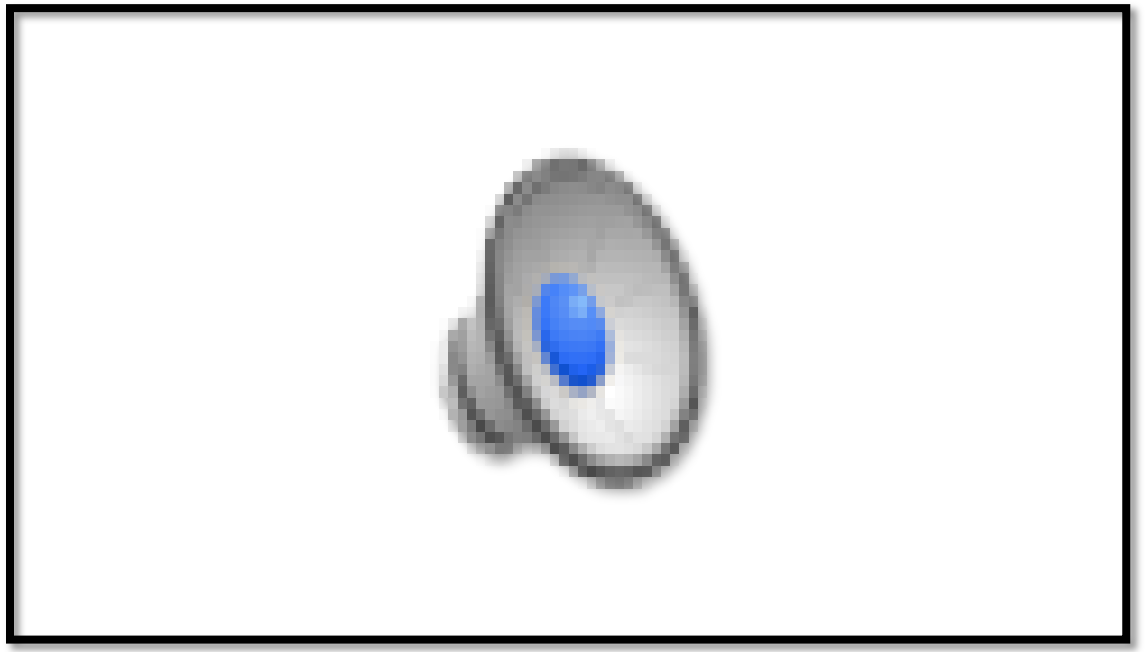
- Mammalian placentation requires extensive angiogenesis for the establishment of a suitable vascular network to supply oxygen and nutrients to the fetus.
- A variety of **proangiogenic** (VEGF, PlGF) and **antiangiogenic factors** (sFlt-1) are elaborated by the developing placenta, and the balance among these factors is important for normal placental development.
- Increased production of antiangiogenic factors disturbs this balance and results in the systemic endothelial dysfunction characteristic of preeclampsia

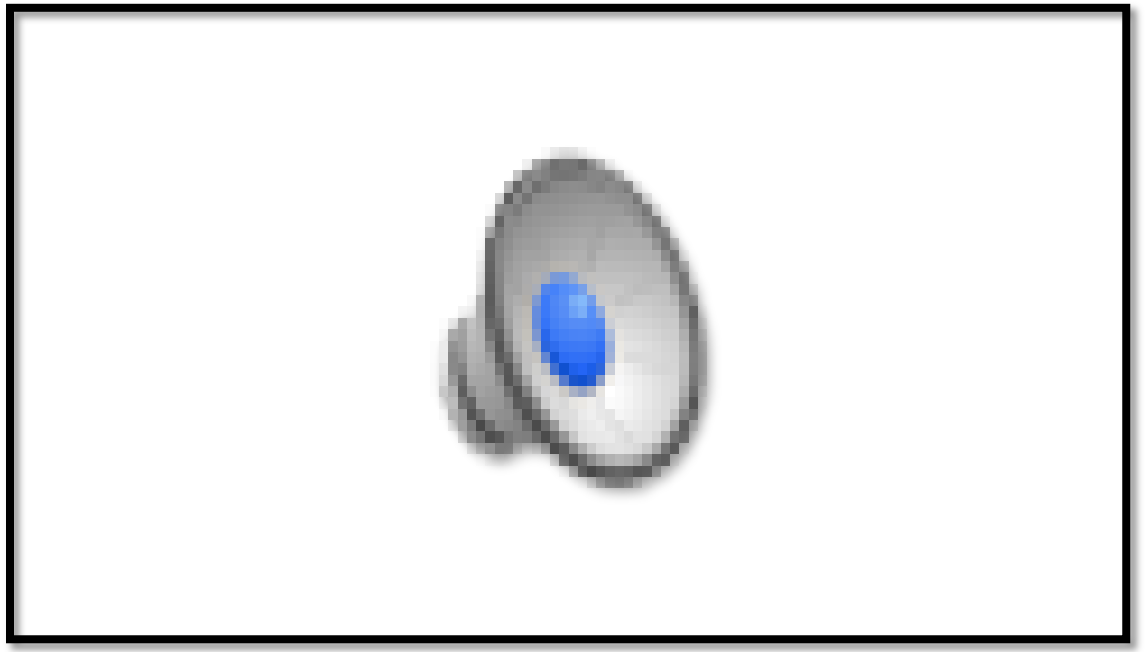


Investigational Approaches

Screening tests - Uterine artery Doppler velocimetry

- Meta-analyses show that uterine artery Doppler analysis can predict women at increased risk of preeclampsia
  - Most experts do not recommend these studies for screening in early pregnancy: false-positive rate of this test is quite high
- Impedance to flow in the uterine arteries normally decreases as pregnancy progresses.
  - Increased impedance for gestational age is an early radiographic feature of preeclampsia and likely reflects high downstream resistance due to defective differentiation of trophoblast, which leads to defective invasion of spiral arteries and failure of these vessels to transform into low resistance vessels



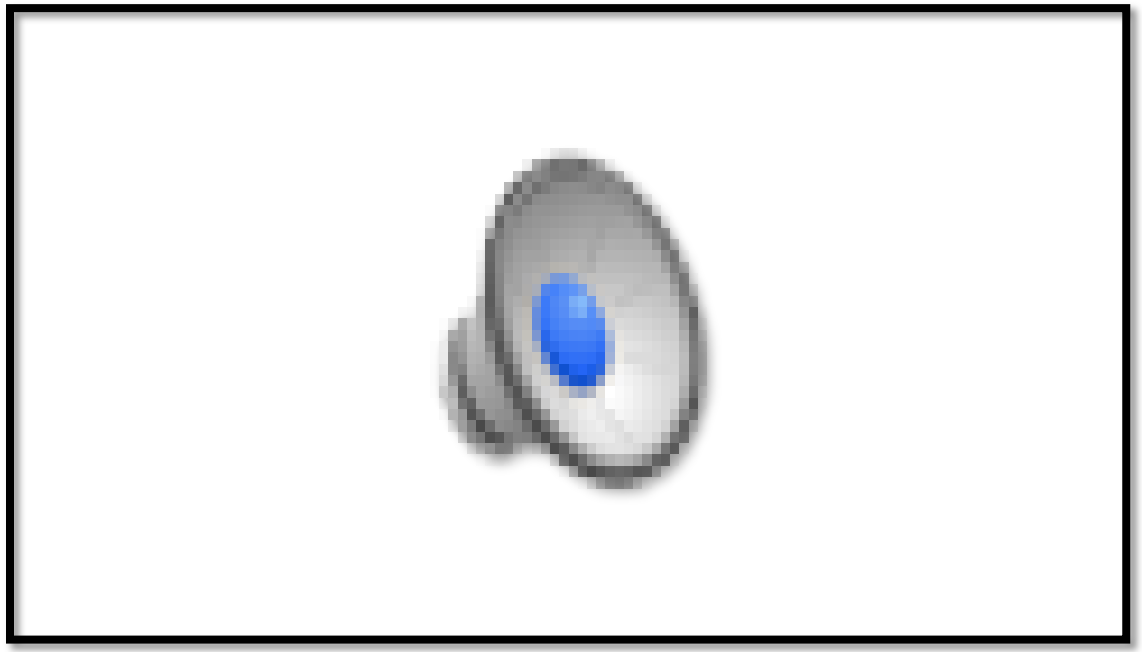


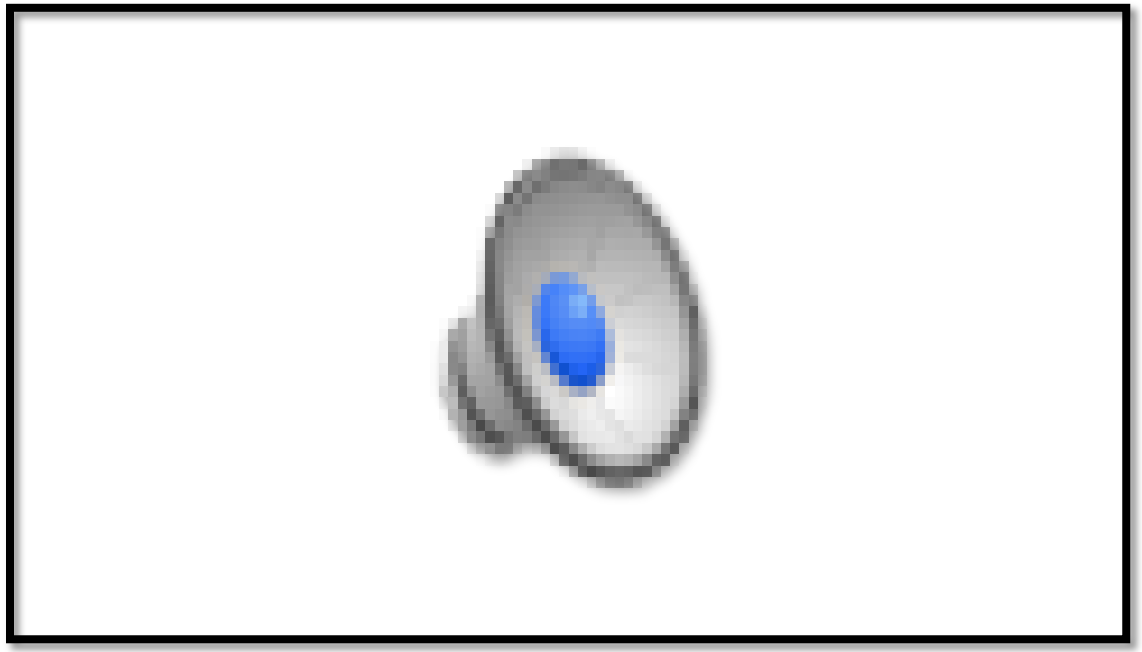
Doppler A. Uterina

Investigational Approaches

Screening tests - Uterine artery Doppler velocimetry

- Two types of uterine artery Doppler waveform analysis techniques have emerged for prediction of preeclampsia as well as other disorders associated with impaired placentation (eg, fetal growth restriction, pregnancy loss):
  1) presence or absence of diastolic notching (unilateral, bilateral) of the uterine arcuate vessels and
  2) flow waveform ratios (eg, high resistance or pulsatility index, systolic/diastolic ratio).





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Investigational Approaches

Screening tests - Uterine artery Doppler velocimetry

CMAJ. 2008 Mar 11;178(6):701-11. doi: 10.1503/cmaj.070430.

Use of uterine artery Doppler ultrasonography to predict pre-eclampsia and intrauterine growth restriction: a systematic review and bivariable meta-analysis.

Cnossen JS[1], Morris RK, ter Riet G, Mol BW, van der Post JA, Coomarasamy A, Zwinderman AH, Robson SC, Bindels PJ, Kleijnen J, Khan KS.

Author information

Abstract

BACKGROUND: Alterations in waveforms in the uterine artery are associated with the development of pre-eclampsia and intrauterine growth restriction. We investigated the predictive accuracy of all uterine artery Doppler indices for both conditions in the first and second trimesters.

METHODS: We identified relevant studies through searches of MEDLINE, EMBASE, the Cochrane Library and Medion databases (all records to April 2006) and by checking bibliographies of identified studies and consulting with experts. Four of us independently selected studies, extracted data and assessed study validity. We performed a bivariable meta-analysis of sensitivity and specificity and calculated likelihood ratios.

RESULTS: We identified 74 studies of pre-eclampsia (total 79,547 patients) and 61 studies of intrauterine growth restriction (total 41 131 patients). Uterine artery Doppler ultrasonography provided a more accurate prediction when performed in the second trimester than in the first-trimester. Most Doppler indices had poor predictive characteristics, but this varied with patient risk and outcome severity. An increased pulsatility index with notching was the best predictor of pre-eclampsia (positive likelihood ratio 21.0 among high-risk patients and 7.5 among low-risk patients). It was also the best predictor of overall (positive likelihood ratio 9.1) and severe (positive likelihood ratio 14.6) intrauterine growth restriction among low-risk patients.

INTERPRETATION: Abnormal uterine artery waveforms are a better predictor of pre-eclampsia than of intrauterine growth restriction. A pulsatility index, alone or combined with notching, is the most predictive Doppler index. These indices should be used in clinical practice. Future research should also concentrate on combining uterine artery Doppler ultrasonography with other tests.

Comment in

How useful is uterine artery Doppler ultrasonography in predicting pre-eclampsia and intrauterine growth restriction? [CMAJ. 2008]

Use of Doppler ultrasonography to predict pre-eclampsia. [CMAJ. 2008]

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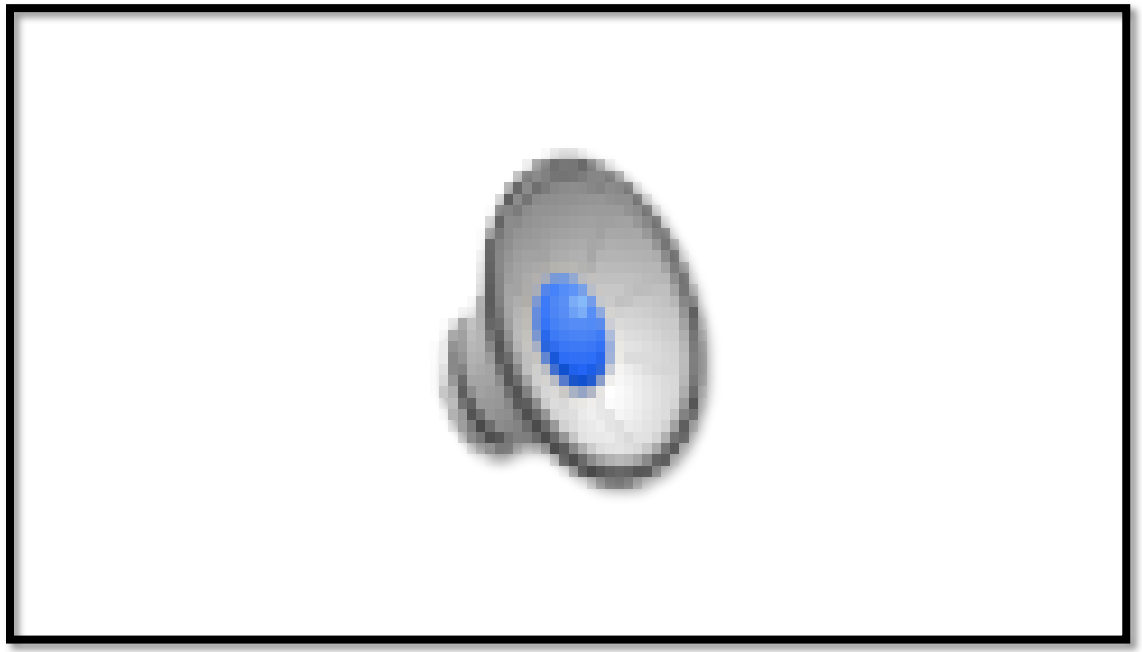
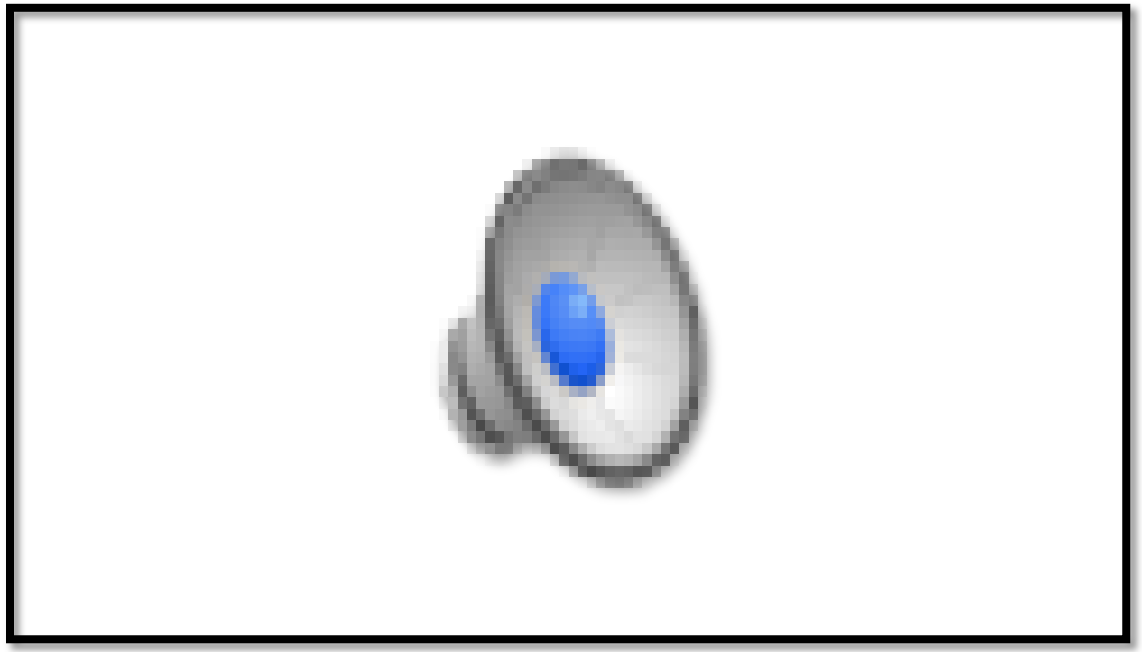
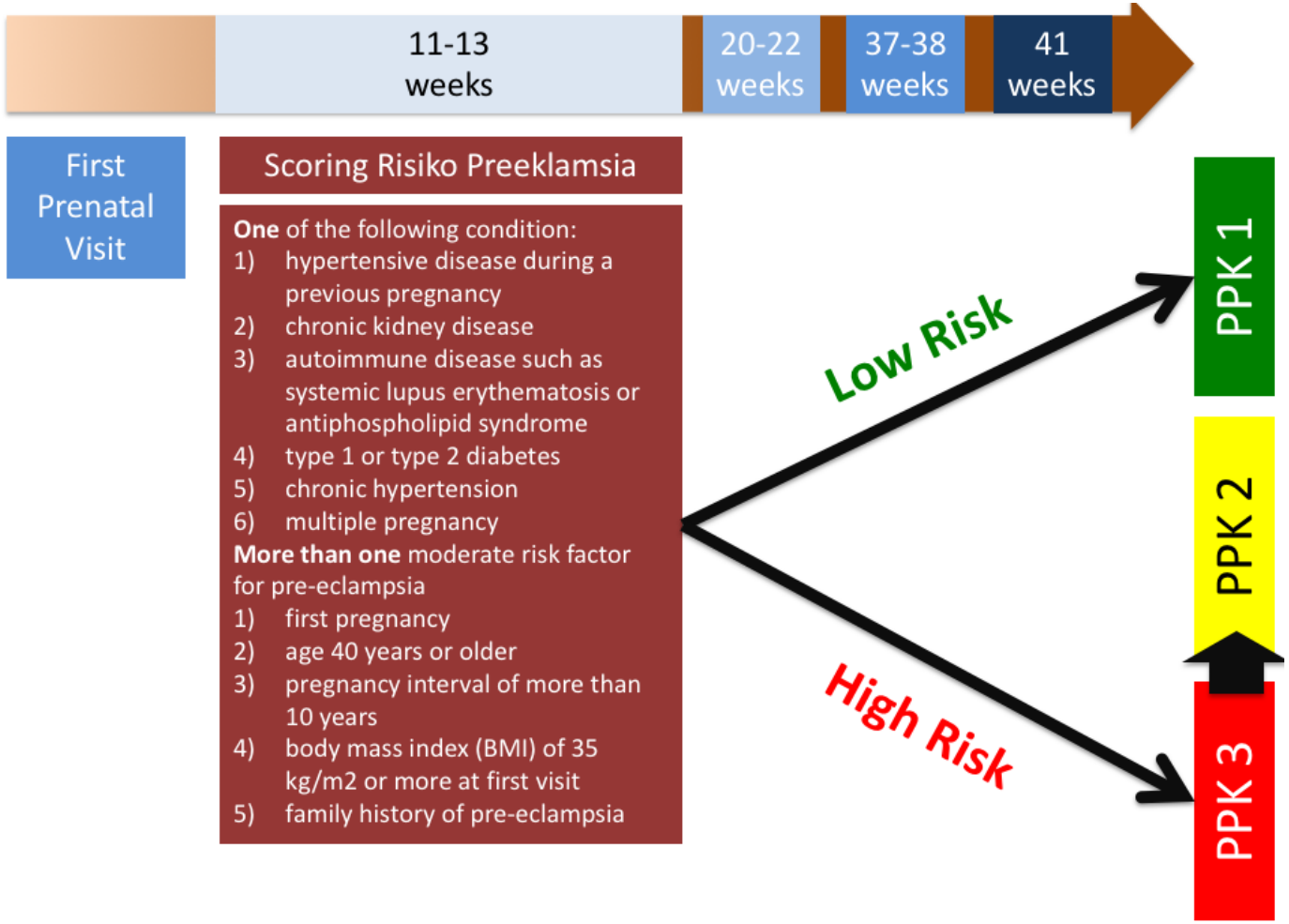




Investigational Approaches
Risk prediction models

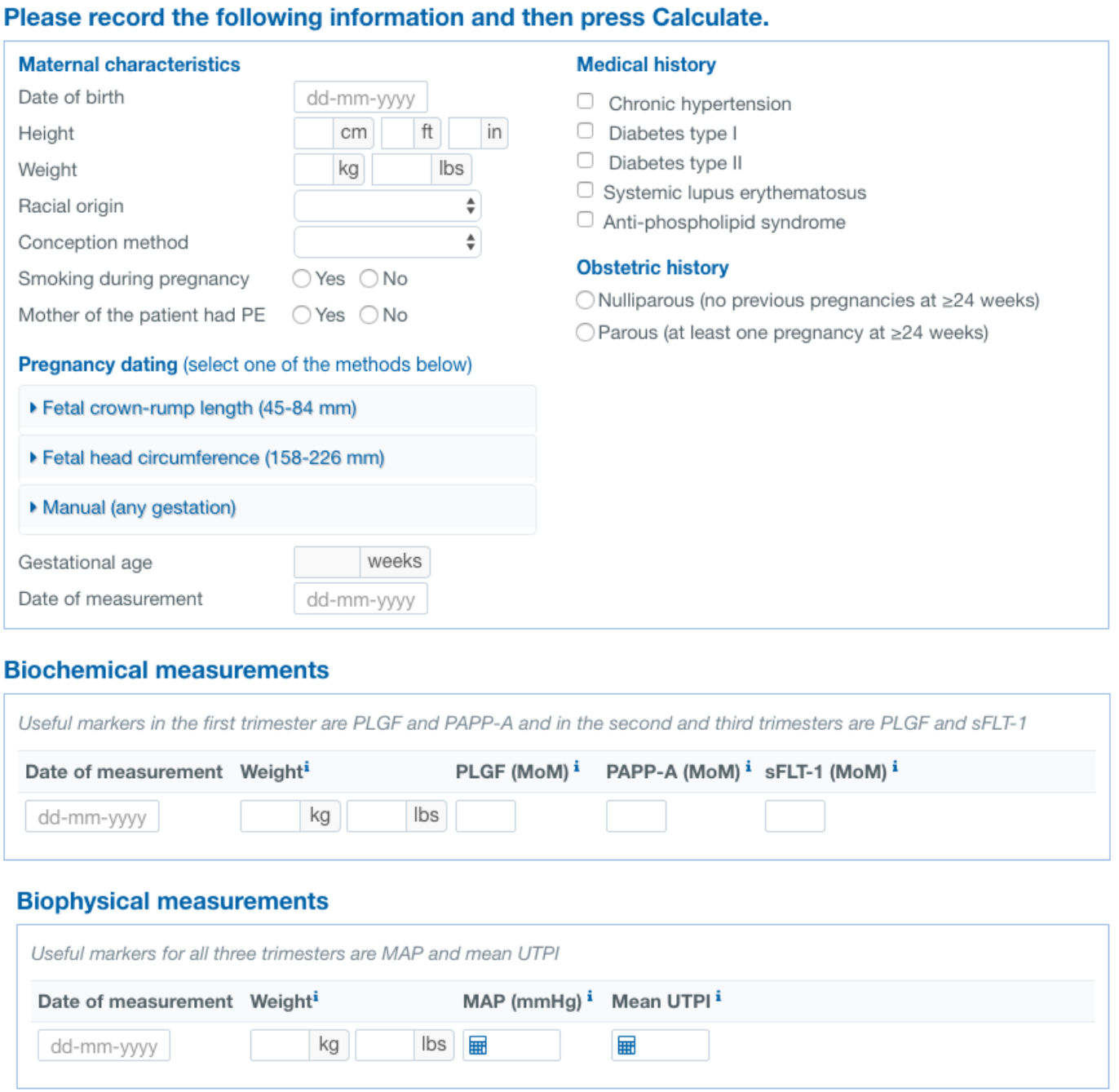
- Multiple risk factors for development of preeclampsia have been described
- The United States Preventive Services Task Force (USPSTF) risk criteria for **high risk** OR **moderate risk** of development of preeclampsia



Investigational Approaches
Risk assessment for preeclampsia

- This application allows estimation of risks of early-PE (delivery at<32 weeks gestation), preterm-PE (<37 weeks) and term-PE (≥37 weeks) by a combination of maternal factors and results of various biophysical and biochemical measurements made at different stages in pregnancy.
- The application allows calculation of risks for PE based on maternal factors alone and in combination with any of the biomarkers. Biophysical and biochemical markers should be obtained within the same gestational age block (11^{+0} to 14^{+1}, 19^{+0} to 24^{+6}, $30^{+0}$to 34^{+6}, 35^{+0} to 37^{+6} weeks)

https://fetalmedicine.org/research/assess/preeclampsia



Screening Tests Not Useful for Predicting Preeclampsia

- **Provocative biophysical tests:**
  - Aberrations in vascular responsiveness have formed the basis of several screening tests for the detection of pregnant women at risk for preeclampsia
  - Tests:
    - angiotensin II challenge test
    - roll-over test [supine pressor test]
    - isometric exercise test [hand-grip test]
- **Serum uric acid:**
  - Hyperuricemia is commonly seen in women with preeclampsia
    - Systematic review of five studies concluded that measurement of serum uric acid concentration before 25 weeks of gestation was not useful for predicting which women would develop preeclampsia

Screening Tests Not Useful
for Predicting Preeclampsia

- **Screening for inherited thrombophilias:**
  - Data from prospective cohort studies, indicates that inherited thrombophilias (such as Factor V Leiden mutation, prothrombin gene mutation, protein C or S deficiency, and antithrombin deficiency) are not associated with preeclampsia
    - therefore, screening pregnant women for inherited thrombophilias is not useful for predicting those at high risk of developing the disease
- **Screening for antiphospholipid antibodies:**
  - ospholipid antibodies:
  - APS is associated with the development of severe early preeclampsia. Prophylaxis with both low-dose aspirin and prophylactic-dose heparin starting at the end of the first trimester and continuing throughout pregnancy can decrease the rate of pregnancy complications (including preeclampsia) and improve pregnancy outcome in women with APS
  - Screening the general obstetric population for antiphospholipid antibodies regardless of past pregnancy and thrombotic history is not useful

Terima Kasih