Pregnancy & Hypertension

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Objectives

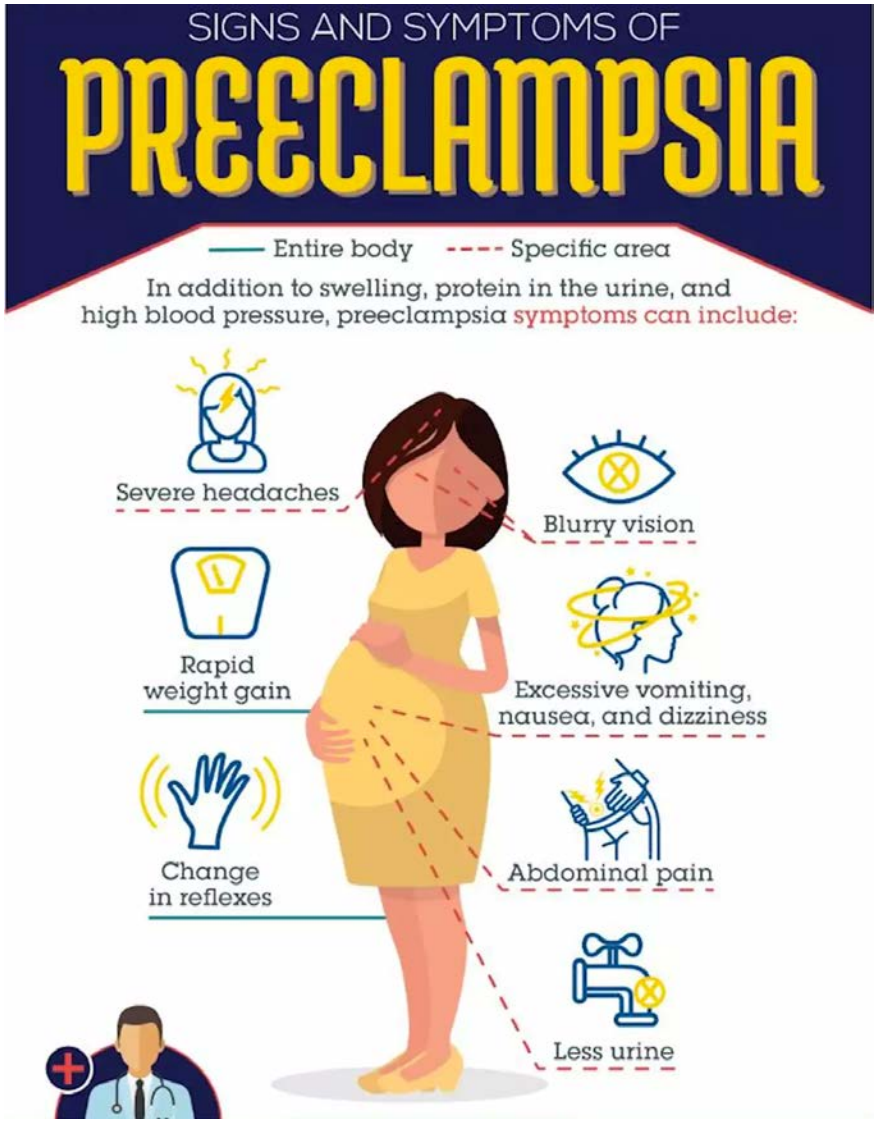
- Definition
- Prediction and prevention
- Management- hospital, outpatient
- Post pregnancy care

Definitions

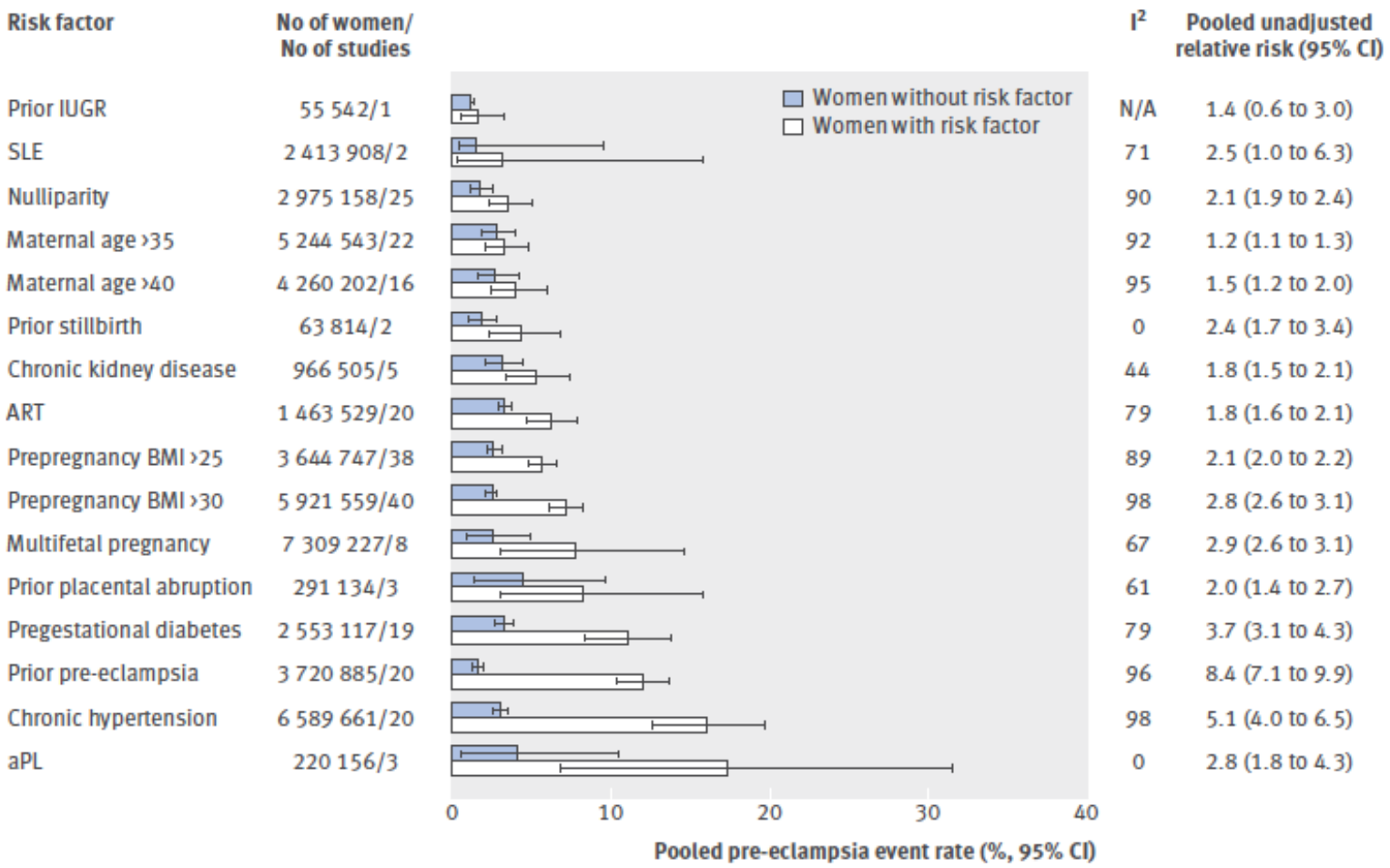
Disorder	Definition
Chronic Hypertension	HT confirmed before pregnancy or before 20/40
Gestational Hypertension	De novo HT (SBP ≥140 DBP≥90) after 20/40
Preeclampsia	GHT and evidence of one or more organ involvement - renal, liver, haematological, neurological, pulmonary oedema, uteroplacental dysfunction *proteinuria no longer essential criteria for diagnosis
Preeclampsia superimposed on chronic hypertension	Chronic HT with 1 or more PE features after 20 weeks gestation

Adapted from SOMANZ guidelines for the management of hypertensive disorders of pregnancy 2014

- Globally the incidence of preeclampsia is 3-10% (Jeyabalan et al Nutr rev 2013)
- Incidence in Australia 3-3.3% (Thornton et al AJOG 2013)
- Data from The Royal Women's Hospital shows preeclampsia and related complications account for 15% of maternal mortality and 10% of perinatal mortality (thewomens.org,au)



Risk factors



Bartsch *et al* BMJ 2016

Early prediction

- FMF algorithm: combines maternal history and biomarkers at 11-14 weeks gestation to determine risk of PET
  - Maternal characteristics, medical history and obstetric history
  - Maternal mean arterial pressure,
  - Uterine arterial pulsatility index
  - PAPP-A and PlGF
- https://fetalmedicine.org/research/assess/preeclampsia/first-trimester

How good is the screening?

- Predicted
  - 90% of early PE
  - 75% pre-term PE
  - 41% term PE
- False positive rate 10%

Tan *et al* Ultrasound Obstet and Gynecol 2018

Prevention

The NEW ENGLAND JOURNAL of MEDICINE

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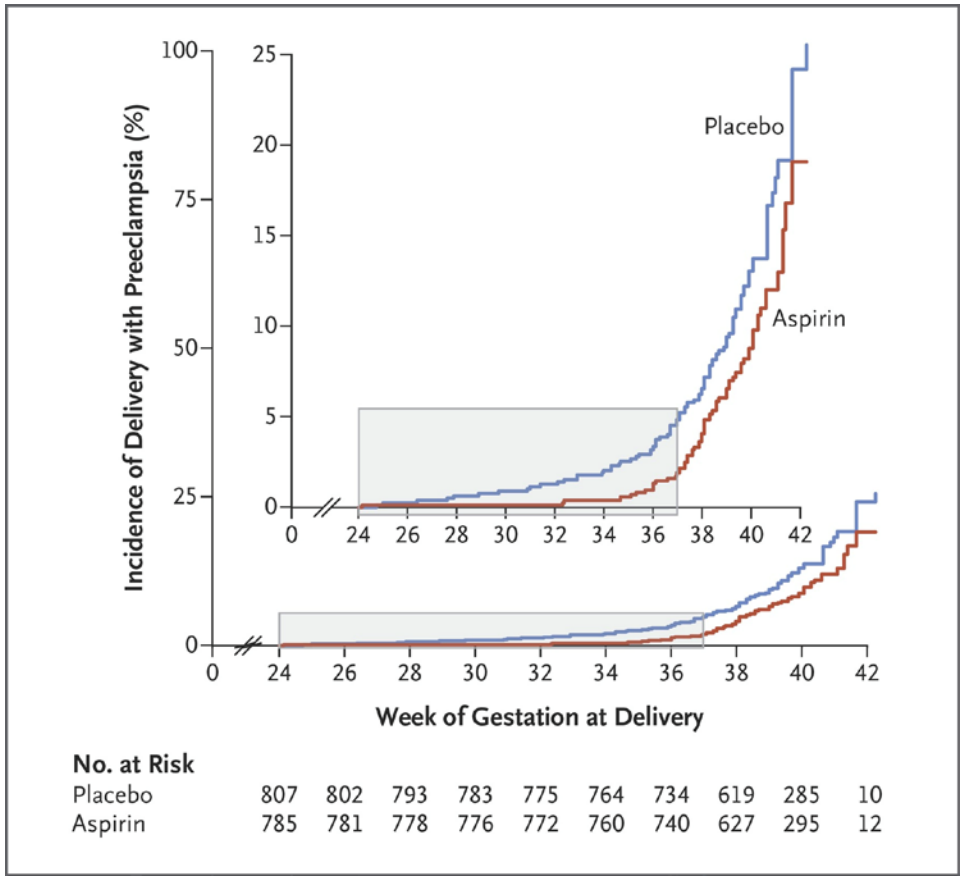
Aspirin versus Placebo in Pregnancies at High Risk for Preterm Preeclampsia

Daniel L. Rolnik, M.D., David Wright, Ph.D., Liona C. Poon, M.D., Neil O'Gorman, M.D., Argyro Syngelaki, Ph.D., Catalina de Paco Matallana, M.D., Ranjit Akolekar, M.D., Simona Cicero, M.D., Deepa Janga, M.D., Mandeep Singh, M.D., Francisca S. Molina, M.D., Nicola Persico, M.D., Jacques C. Jani, M.D., Walter Plasencia, M.D., George Papaioannou, M.D., Kinneret Tenenbaum-Gavish, M.D., Hamutal Meiri, Ph.D., Sveinbjorn Gizurarson, Ph.D., Kate Maclagan, Ph.D., and Kypros H. Nicolaides, M.D.

Aspirin reduces the risk of Preeclampsia

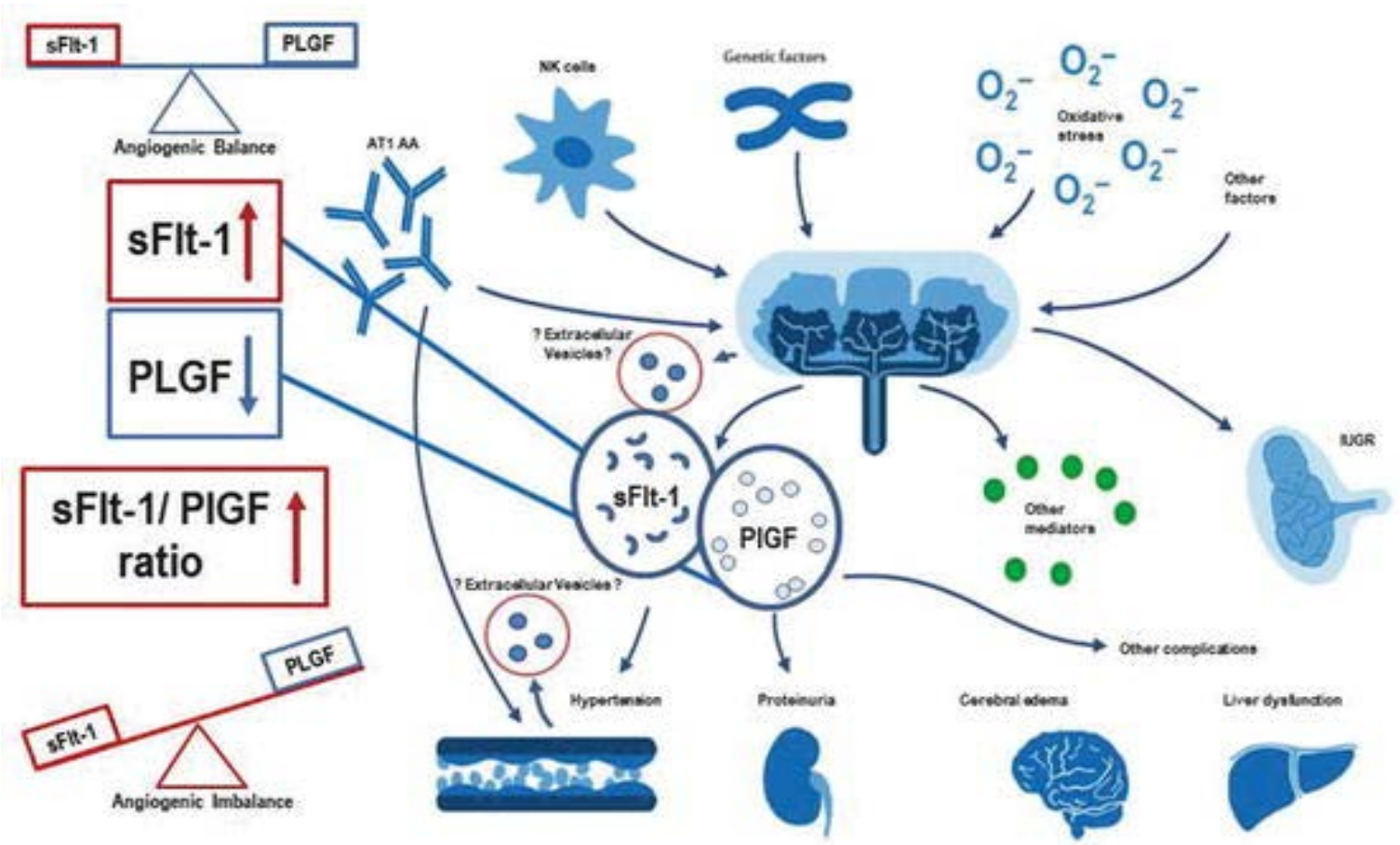


Risk of Preeclampsia

Placebo 4.3%

Aspirin 1.6%

sFlt-1 and PlGF are angiogenic markers of normal pregnancy



The sFLT-1:PlGF ratio

- sFLT-1:PlGF ratio cut-off of **< 38** has important short term negative predictive value (Verloheren *et al* NEJM 2016)

- Useful **RULE OUT** test in suspected preeclampsia

Table 2. Validation of a Cutoff Point of 38 for the sFlt-1:PlGF Ratio in Predicting Preeclampsia.*

Preeclampsia	Development Cohort	Validation Cohort
	percent (95% CI)	
Within 1 wk		
Negative predictive value: rule out	98.9 (97.3–99.7)	99.3 (97.9–99.9)
Sensitivity	88.2 (72.5–96.7)	80.0 (51.9–95.7)
Specificity	80.0 (76.1–83.6)	78.3 (74.6–81.7)
Within 4 wk		
Positive predictive value: rule in	40.7 (31.9–49.9)	36.7 (28.4–45.7)
Sensitivity	74.6 (62.5–84.5)	66.2 (54.0–77.0)
Specificity	83.1 (79.3–86.5)	83.1 (79.4–86.3)

Verlohren *et al*- NEJM 2016

Anti-hypertensive therapy

Drug	Dose	Action	Contraindications	Practise Points
Methyl dopa Clonidine	250-750mg tds 75-300µg tds	Central	Depression	Slow onset of action over 24 hours, dry mouth, sedation, depression, blurred vision Withdrawal effects: rebound hypertension
Labetalol Oxprenolol	100-400mg q8h 20-160 mg q8h	β Blocker with mild alpha vasodilator effect β Blocker with intrinsic sympathomimetic activity	Asthma, chronic airways limitation	Bradycardia, bronchospasm, headache, nausea, scalp tingling (labetalol only) which usually resolves within 24 hours
Nifedipine	20mg -60 mg slow release bd	Ca channel antagonist	Aortic stenosis	Severe headache in first 24 hours Flushing, tachycardia, peripheral oedema, constipation
Prazosin	0.5-5 mg q8h	α blocker		Orthostatic hypotension especially after first dose
Hydralazine	25-50 mg q8h	Vasodilator		Flushing, headache, nausea, lupus-like syndrome

Somanz guidelines 2014

Treatment Goals

Tight control group

27.5%

Developed severe hypertension

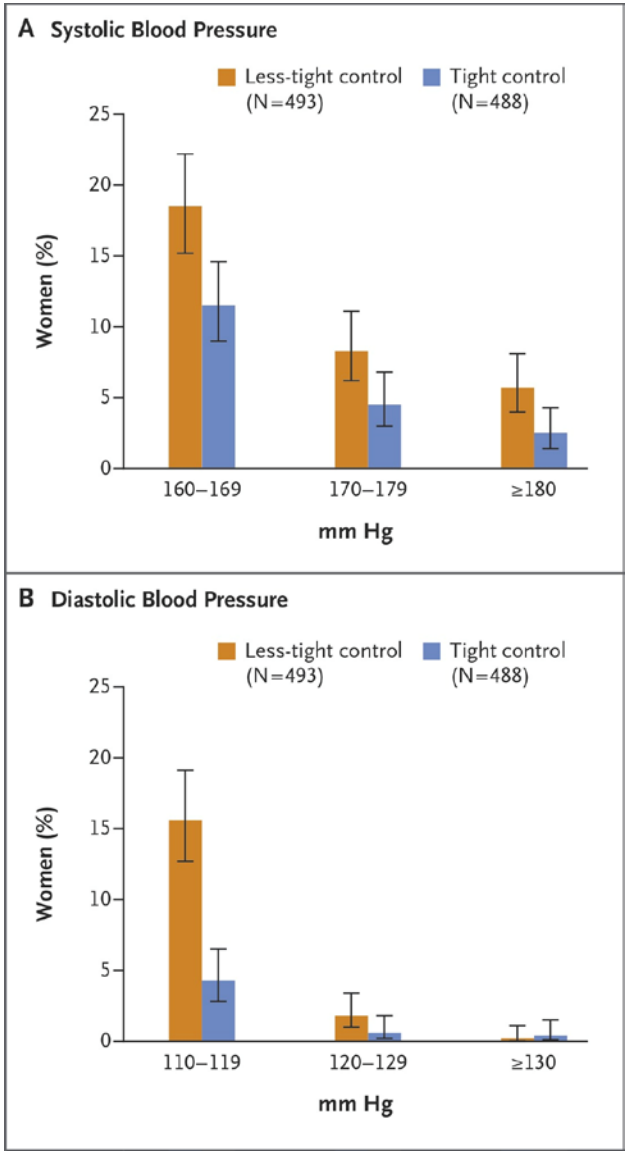
N= 488

Less-tight control group

40.6%

Developed severe hypertension

N=493



Magee *et al*, NEJM 2015- CHIPS trial

Acute treatment

- Severe HT: **ADMIT**
- Treat BP IV labetalol, hydralazine or diazoxide
  - Lancet- Easterling *et al:* Showed oral agents as good an IV esp oral nifedipine (short acting)
- Monitor bloods: FBC, EUC,LFTs
- MgSO4 for neurological irritability
- Management of VTE risk, fluid status
- Fetal monitoring
- Decision: Delivery, in-patient stay or discharge with regular day assessment follow-up depends on severity

Post-partum

- **5.7%** of preeclampsia cases present in the post-partum period
(Powles *et al* CMAJ 2017)
- BP peaks usually 3-6 days post-partum (NSAIDS, vascular tone restoration, excessive fluids). Can persist til 12 weeks
- **ACEI:** captopril, enalapril, quinapril
(Gaisin *et al*, 2020 EHJ, Ormesher *et al* 2020 Hypertension
  - Improved cardiac parameters at 6 months
  - Greater reduction in proteinuria at 6 months
- **Frusemide** 20-40 mg daily for 5 days
(Levine *et al* 2021 Hypertension)
  - Reduces MAP, number of antihypertensives on d/c and reduced length of time for BP normalisation
  - Long term use: detrimental to breast feeding

Risk of developing subsequent disease after Preeclampsia

Medical Condition	Relative Risk [95% CI]
Chronic Hypertension	3.70 [2.70-5.05]
Ischaemic Heart Disease	2.16 [1.86-2.52]
Cerebrovascular Disease	1.81 [1.45-2.27]
Peripheral Vascular Disease	1.87 [0.94-3.73]
Deep Vein Thrombosis	1.79 [1.37-2.33]
End Stage Renal Disease	4.3 [3.3-5.6]
Type II Diabetes	1.86 [1.22-2.84]
Elevated TSH	1.7 [1.1-1.7]
All Cancer	0.96 [0.73-1.27]

Bellamy *et al* 2006 BMJ

Can we make a difference?

- Follow up essential until normalization of parameters
  - 10% persistent HT at 3 months (Brown *et al* 2020 JAHA)
  - 25% persistent proteinuria at 3 months
- Educate regarding future risks and discuss prevention strategies in future pregnancy
- Children also affected (Turbeville *et al* AMJRP 2020)
- Current guidelines (SOMANZ)
  - Yearly optimization of CV RF- weight loss, smoking
  - Treat HT, lipids, glucose, check urine ACR + micro

Take Home Messages

1. Opportunity to offer early screening for PET (NIPT/Harmony tests with PE screening)
2. Early referral to commence prophylaxis in high risk groups
3. Tight BP control important during the pregnancy
4. New diagnostic tests and novel therapeutic agents being studied with good success (siRNA)
5. Don't forget about post-partum preeclampsia
6. It doesn't end with delivery there are long term consequences/RF that need monitoring