# Screening and prevention of preeclampsia

**Liona Poon**
**MBBS MRCOG MD(Res) Cert RCOG (Maternal and Fetal Med)**
**Associate Professor**
**The Chinese University of Hong Kong**

# Prediction of PE

## Adopted in PWH

### High risk factors

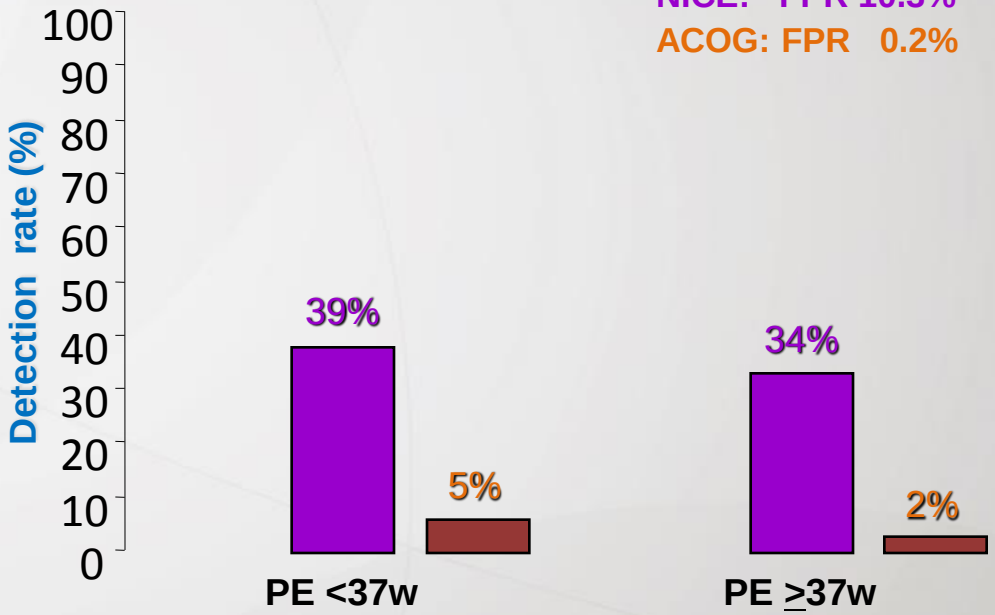
- Hypertensive disease in a previous pregnancy
- Chronic renal disease
- Chronic hypertension
- Diabetes mellitus
- Autoimmune disease such as SLE or APS

### Moderate risk factors

- First pregnancy
- Age ≥ 40 years
- Body mass index ≥ 35 kg/m$^2$
- Inter-pregnancy interval > 10 years
- Family history of preeclampsia

### ACOG 2013: High-risk in need of aspirin

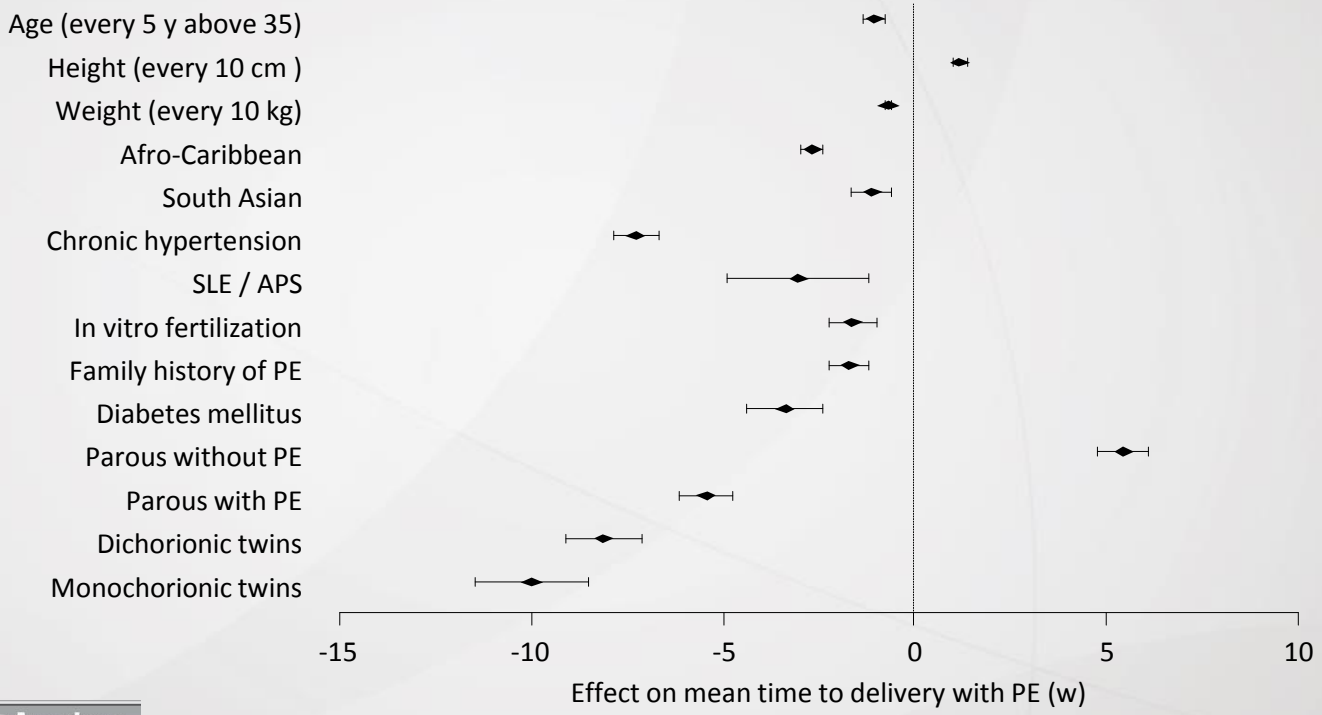
- Preeclampsia in ≥2 previous pregnancies
- Preeclampsia <34w in previous pregnancy




NICE: FPR 10.3%
ACOG: FPR 0.2%

# Prediction of PE

## Maternal characteristics

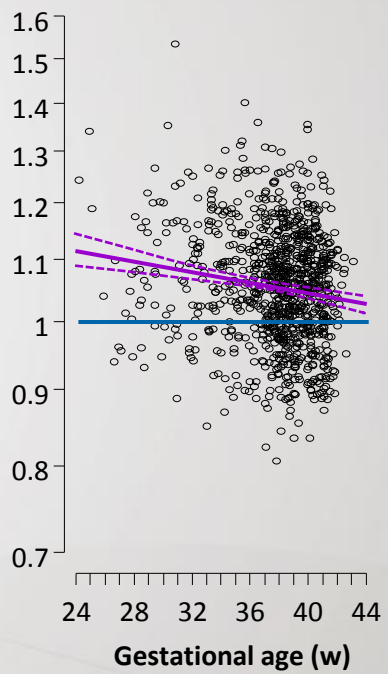



Wright et al. Competing risks model in screening for preeclampsia by maternal characteristics and medical history. AJOG 2015;213:62

# Prediction of PE

## Mean arterial pressure

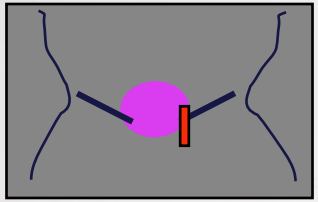

- Device: Validated automated devices, calibrated at regular intervals.
- Method: Women rested for 5 minutes, arms supported at the level of the heart.
- Cuff size: Small (<22 cm), normal (22-32 cm) or large (33-42 cm), depending on the mid-arm circumference.
- Both arms: Take average of two measurements in each arm.

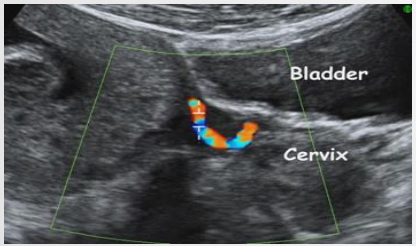


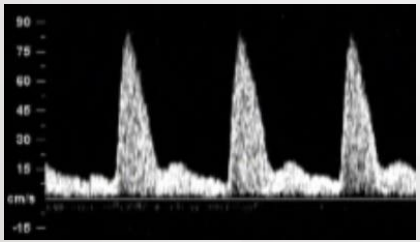

Poon et al. Fetal Diagn Ther 2012

# Prediction of PE

## Uterine artery PI





### 1st trimester – transabdominal ultrasound

Identify the uterine arteries

-Obtain a sagittal section of the cervix and use colour Doppler

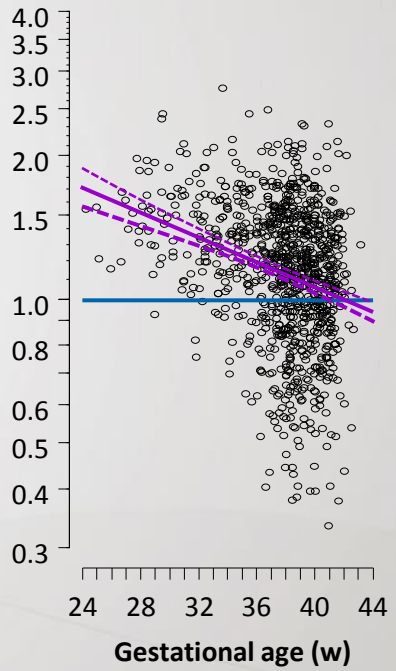
-Fixing the probe in the midline then tilt the transducer from side to side to identify the uterine arteries at the level of the internal cervical os

Sampling gate: 2 mm to cover the whole vessel

Angle of insonation: less than 30º

Peak systolic velocity: more than 60 cm/s

Mean PI: average PI (left + right / 2)




Plasencia et al. UOG 2007

# Prediction of PE

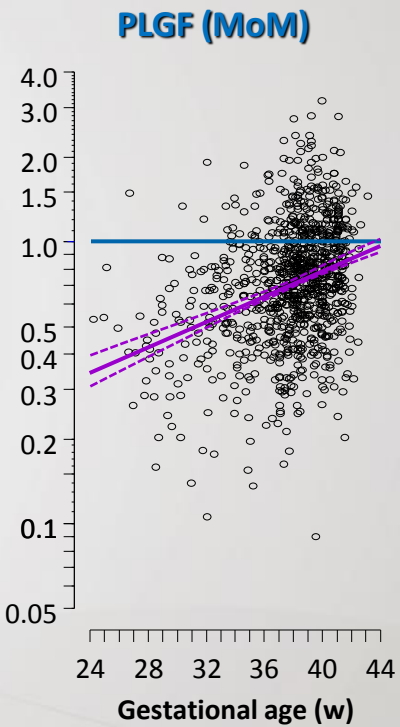
## Angiogenic factors

sVEGFR-1

PlGF

Anti-angiogenesis

Pro-angiogenesis

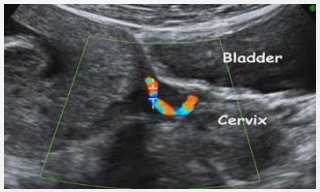


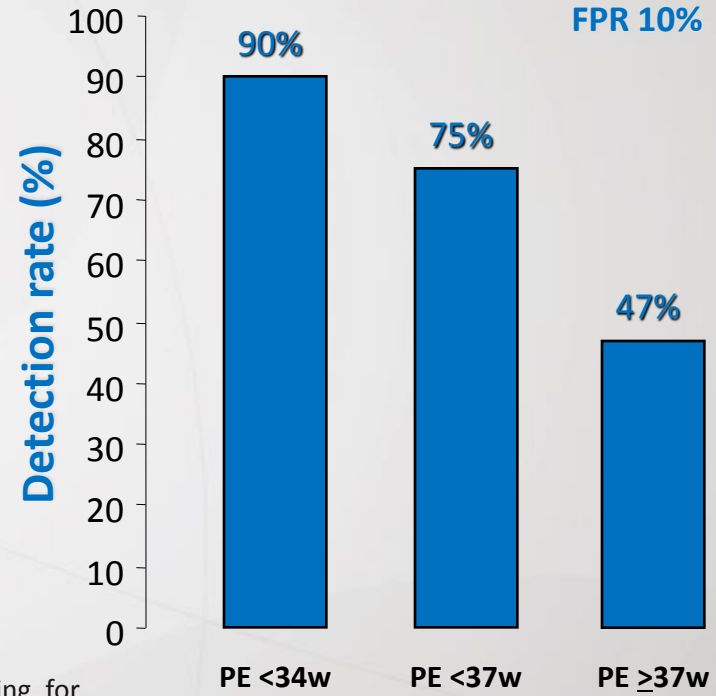
# Prediction of PE

## 1st trimester combined test

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




History, MAP, UT PI, PLGF

AJOG American Journal of Obstetrics & Gynecology

O' Gorman et al. Competing risks model in screening for preeclampsia by maternal factors and biomarkers at 11-13 weeks. Am J Obstet Gynecol 2016; 214: 103

# Prediction of PE

## NICE +ve but FMF -ve

| | High risk factors | Moderate-risk factors |
|---|---|---|
| NICE +ve / FMF +ve | 8.7 (6.8-10.9) | 4.8 (3.3-6.6) |
| NICE +ve / FMF -ve | **0.65** (0.2-1.7) | **0.42** (0.2-0.9) |
| RR (95% CI) | 0.08 (0.03-0.2) | 0.09 (0.04-0.2) |

34,573 singleton pregnancies at 11-13 w: preterm-PE 239 (0.7%)

**In ACOG or NICE +ve women that are FMF -ve the risk of preterm-PE is reduced to within or below background levels**

ULTRASOUND in Obstetrics & Gynecology

Poon et al. ASPRE trial: incidence of preterm preeclampsia in patients fulfilling ACOG and NICE criteria according to risk by the FMF algorithm. Ultrasound Obstet Gynecol. 2018; doi: 10.1002/uog.19019.

# Prevention of PE

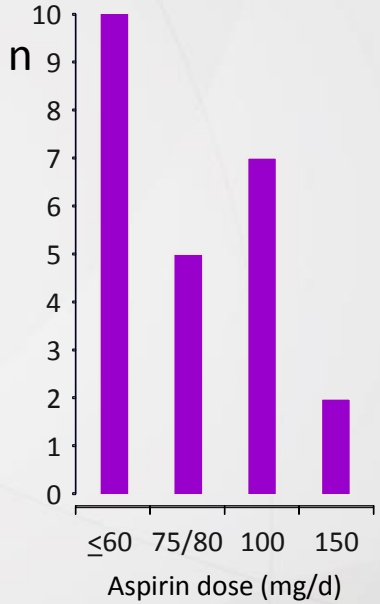
## Low-dose aspirin: background

**Antiplatelet agents for prevention of pre-eclampsia: a meta-analysis of individual patient data**

Askie et al. Lancet 2007; 369: 1791

- Meta-analysis of individual patient data from 32,217 women in 31 RCTs (24 ASA RCTs)

- RR for PE: 0.90 (95% CI 0.84-0.97)
- RR for birth <34 w: 0.90 (95% CI 0.83-0.98)



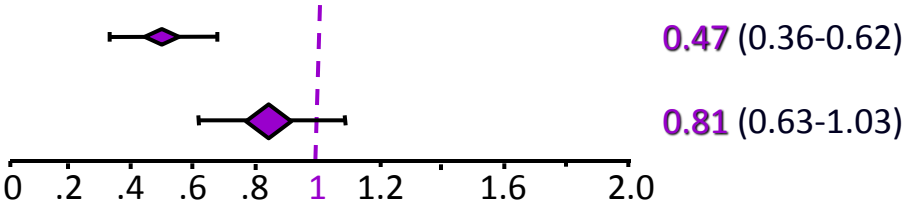


**15 different definitions of PE**

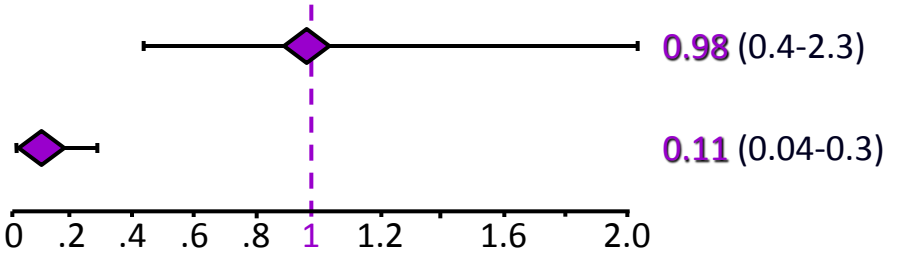
# Prevention of PE

## Low-dose aspirin: background

### Gestation at start of aspirin




### In the group with aspirin at <16 w




Bujold et al., 2010; Roberge et al., 2012; 2013

# ASPRE: Prevention of preterm PE

## Study design

| | | |
|---|---|---|
| **DOSE:** | **150 mg / day** | **Aspirin resistance: 30% at 81mg and 5% at 160 mg**<br>Caron et al: J Obstet Gynaecol Can 2009;31:1022-7 |
| **START:** | **11-13 weeks** | |
| **FINISH:** | **36 weeks** | **Avoid potential hemorrhage for neonate** |
| **TIME:** | **Bed time** | **RCT aspirin 100 mg vs placebo morning, afternoon, night**<br>**Aspirin at night: lower incidence of PE, FGR, PTB or IUD**<br>Ayala DE, Ucieda R, Hermida RC: Chronobiol Int 2013; 30:260-279 |
| **OUTCOME:** | | **Preterm PE** |
| **STUDY POPULATION:** | | **High-risk group defined by FMF algorithm** |

# Prevention of PE

## Aspirin: platelet aggregation

**Aim**

To compare the effects of different doses of aspirin on platelet aggregation and $PGI_2$ production by vessel wall after ischaemia.

**Methods**

- 25 young healthy volunteers
- Subjects were allotted to the various dosage groups of aspirin (2, 2.5, 3.5, 5, 8 and 10 mg/Kg).
- $PGI_2$ production and platelet aggregation were investigated before and after aspirin administration.

**Results**

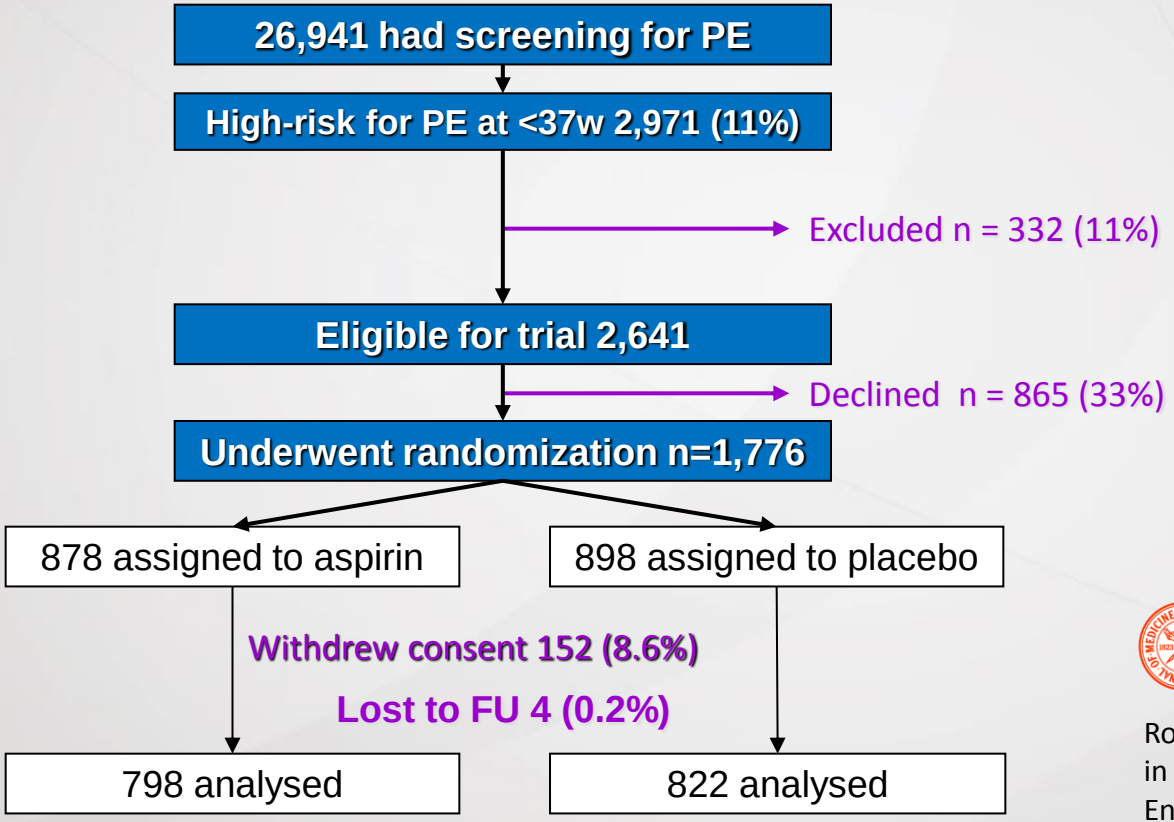
- A dose of 2.5 mg/Kg reduced platelet aggregation by 25-35%.
- The inhibition of platelet aggregation was almost at maximum 2h after administration of 3.5 mg/Kg of aspirin. Further increase in the dose (5, 8 and 10 mg/Kg) only provoked a slight increase in inhibition, which was not proportional to the increase in dose.
- $PGI_2$ production induced by ischaemia was affected by aspirin only at doses higher than 2.5mg/kg.

**Average weight 50 Kg = 175 mg/day**

Masotti et al, Lancet, 1979

# ASPRE: Prevention of preterm PE

## Screening, randomization, follow-up



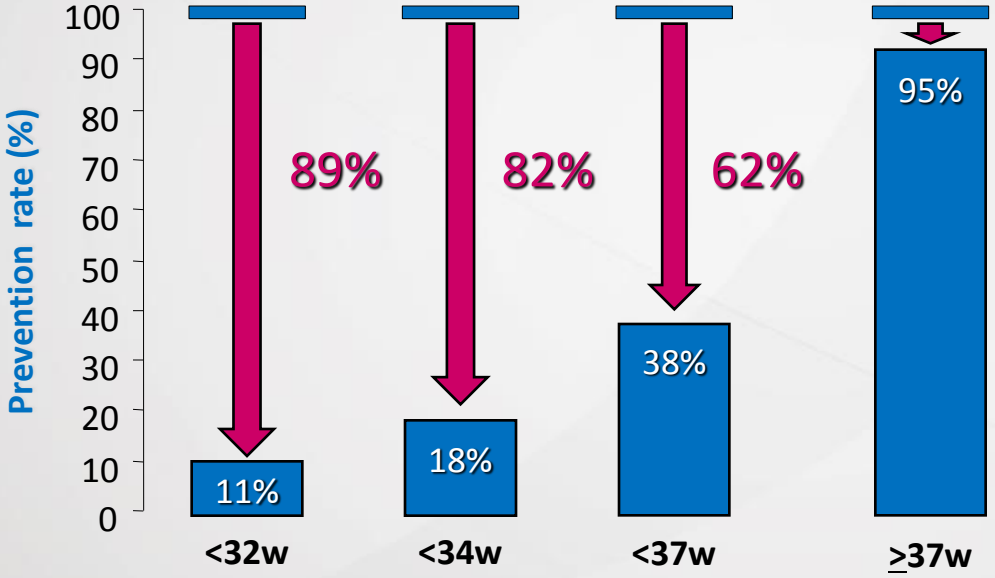

| | |
|---|---|
| 253 | Receiving aspirin |
| 47 | Hypersensitivity to aspirin |
| 17 | Peptic ulcer, bleeding disorders |
| 10 | Participation in another drug trial |
| 2 | Miscarriage before randomization |
| 3 | Termination before randomization |

The NEW ENGLAND JOURNAL of MEDICINE

Rolnik DL, Wright D, Poon L, et al. Aspirin versus placebo in pregnancies at high risk of preterm preeclampsia. N Engl J Med 2017;377:613-22.

# ASPRE: Prevention of preterm PE

## Results: effect on rate of PE

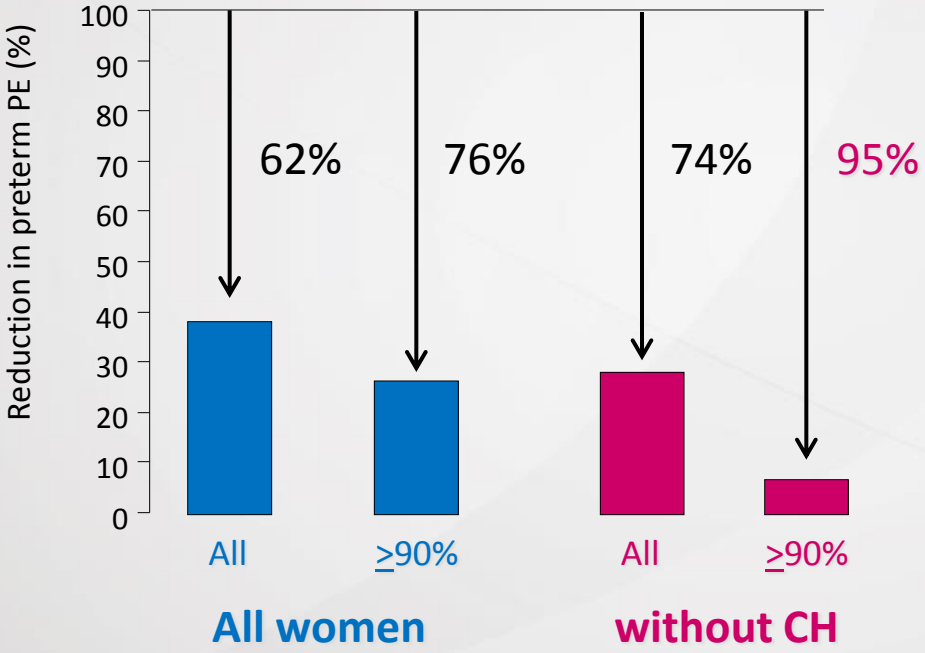



The NEW ENGLAND JOURNAL of MEDICINE

Rolnik DL, Wright D, Poon L, et al. Aspirin versus placebo in pregnancies at high risk of preterm preeclampsia. N Engl J Med 2017;377:613-22.

# ASPRE: Prevention of preterm PE

## Results: effect of maternal factors




Poon et al. ASPRE trial: effect of aspirin in prevention of preterm preeclampsia in subgroups of women according to their characteristics and medical and obstetrical history. Am J Obstet Gynecol 2017; 217: 585.e1-585.e5.

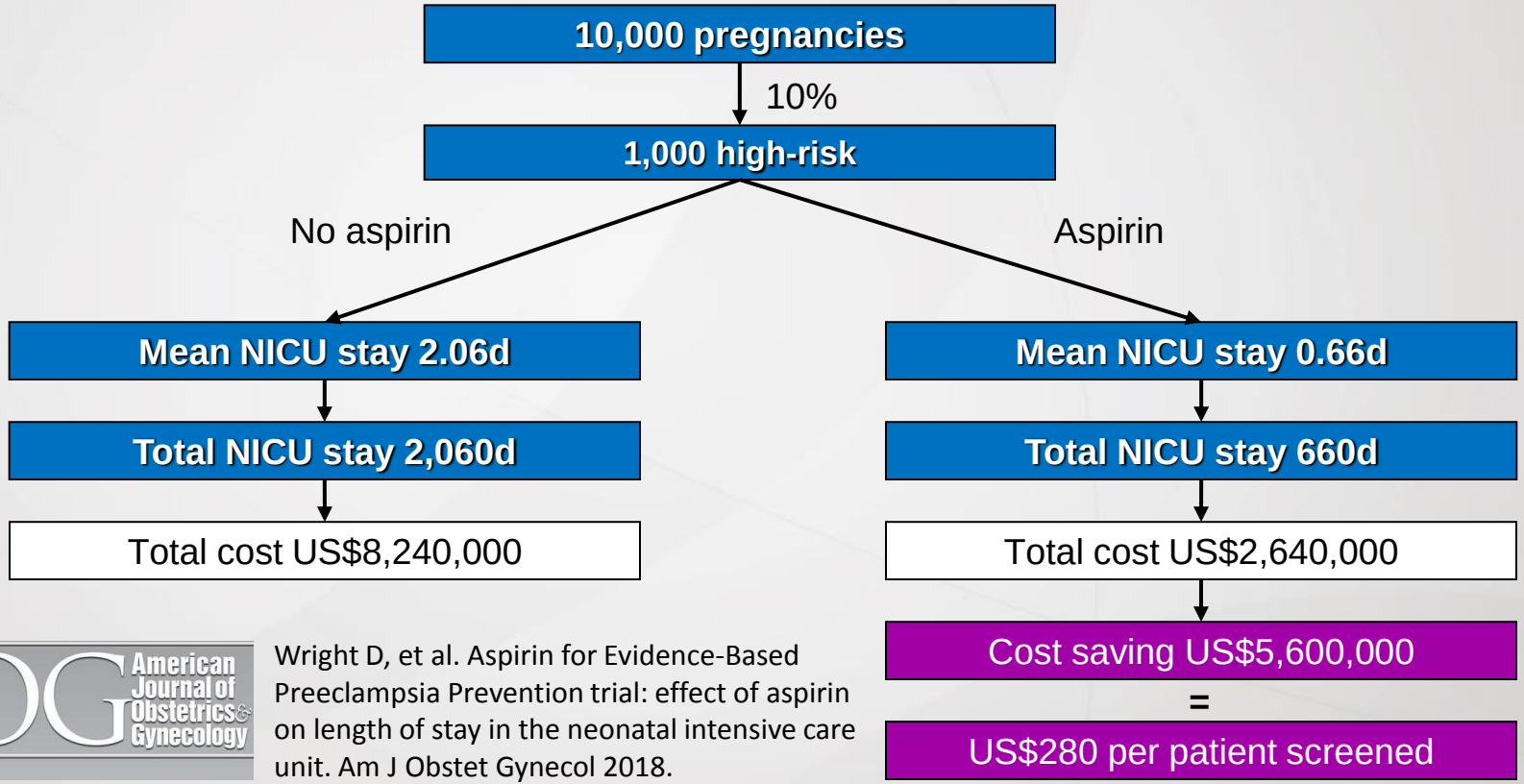
# ASPRE: Prevention of preterm PE

## Results: NICU length of stay

| Outcome measure | Aspirin | Placebo | |
|---|---|---|---|
| **Length of stay in NICU (d)** | | | **Diff in means (95% CI)** |
| Study population: admission | N=49 | N=54 | |
| Mean (SD) | **11.1 (23.4)** | **31.4 (53.0)** | **20.3 (7.0-38.6)** |
| Study population: all cases in the trial | N=798 | N=822 | |
| Mean (SD) | **0.66 (6.3)** | **2.06 (15.5)** | **1.40 (0.45-2.81)** |
| **No. of babies in NICU** | | | OR (95% CI) |
| Study population: livebirths | N=777 | N=794 | |
| **Number by GA at birth** | | | |
| Any, n (%) | **48 (6.2)** | **54 (6.8)** | **0.94 (0.63-1.42)** |
| PE | 2 (0.3) | 18. (2.3) | 0.11 (0.02-0.50) |
| No PE | 46 (5.9) | 36 (4.5) | 1.38 (0.88-2.15) |
| <32w, n (%) | **9 (1.2)** | **23 (2.9)** | **0.42 (0.19-0.93)** |
| PE | 0 | 7 (0.9) | 0.00 (0.00-0.56) |
| No PE | 9 (1.2) | 16 (2.0) | 0.59 (0.26-1.36) |
| **Length of stay (d)** | **531** | **1696** | |

# ASPRE: Prevention of preterm PE

## Results: potential cost saving




Wright D, et al. Aspirin for Evidence-Based Preeclampsia Prevention trial: effect of aspirin on length of stay in the neonatal intensive care unit. Am J Obstet Gynecol 2018.

# ASPRE: Prevention of preterm PE

## Conclusions

**Aspirin:**

- at a dose of 150 mg per night from 12 to 36 weeks' gestation reduces the rate of PE <37 w by 62% and PE <34w by 82%
- does not reduce preterm PE in women with CH
- in women without CH the risk of preterm PE is reduced by 95%
- reduces the length of stay in NICU and associated cost by about 70% in pregnancies at high-risk of PE

*Thank you*