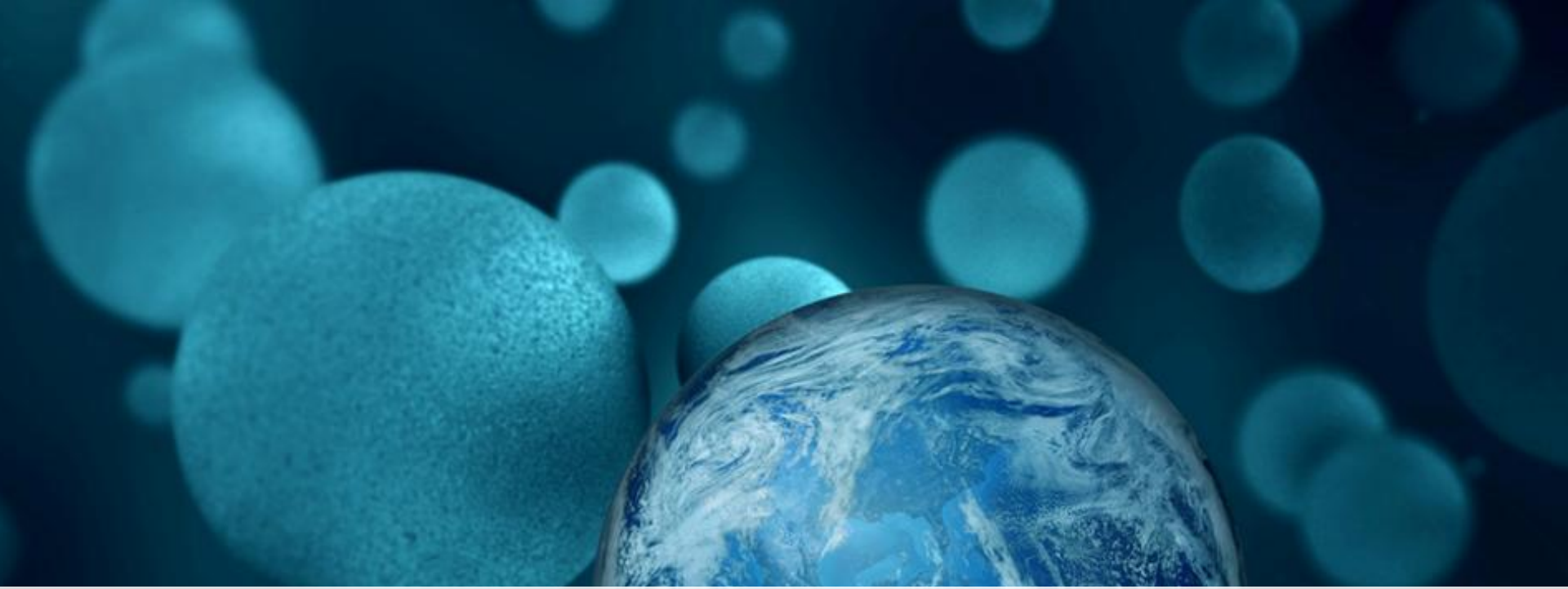
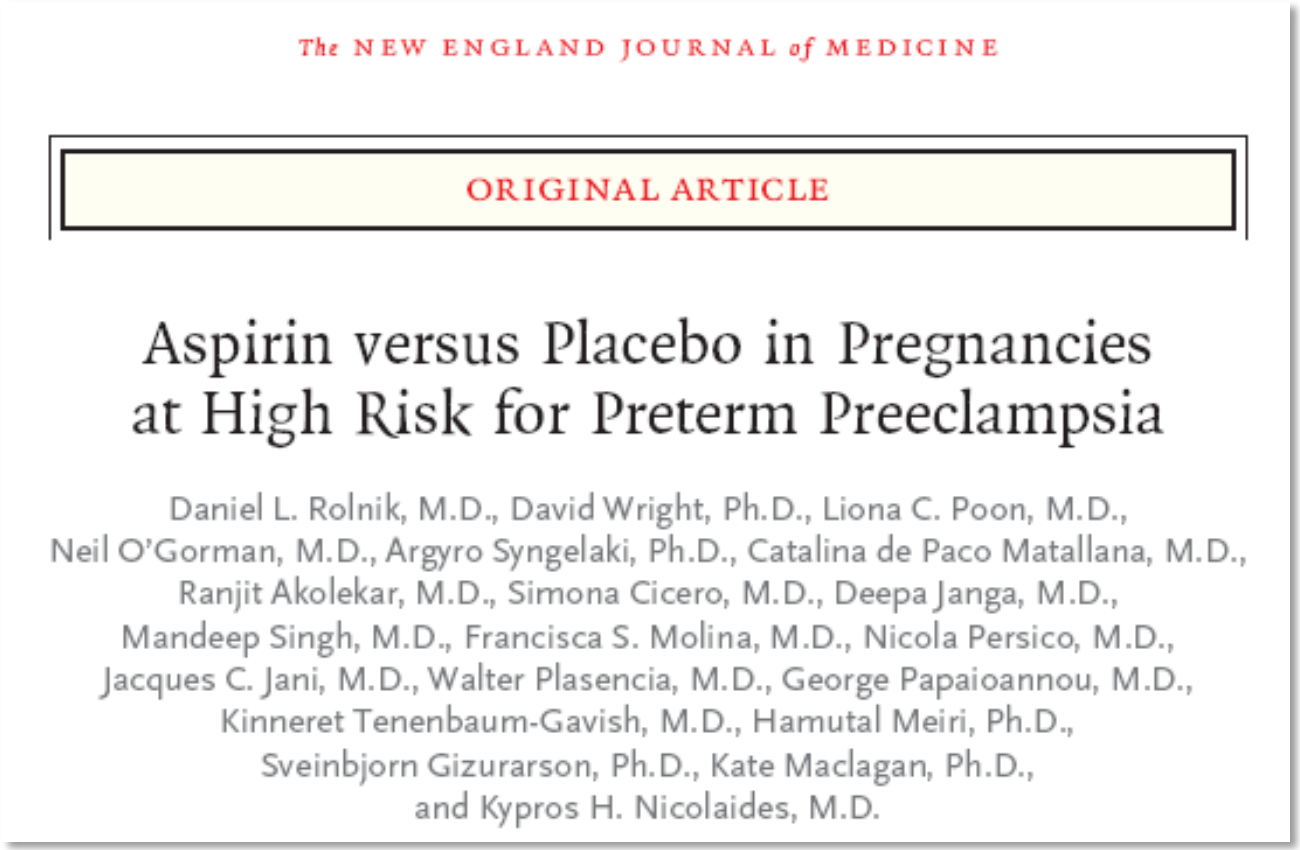


ThermoFisher SCIENTIFIC

Literature comment ASPRE study: Rolnik et al; New England Journal of Medicine; 2017

Dr. Kathrin Matischak; Global Product Manager PNS
May 16, 2017

Rolnik et al; 2017



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Aspirin versus Placebo in Pregnancies at High Risk for Preterm Preeclampsia

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- Authors involved in the Study are from
  - UK ,Hong Kong, Spain, Italy, Belgium, Greece, Israel , Iceland
- Publication is open access
  - http://www.nejm.org/doi/pdf/10.1056/NEJMoa1704559

Rolnik et al; 2017

- PubMed abstract

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Aspirin versus Placebo in Pregnancies at High Risk for Preterm Preeclampsia.

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Abstract

Background:Preterm preeclampsia is an important cause of maternal and perinatal death and complications. It is uncertain whether the intake of low-dose aspirin during pregnancy reduces the risk of preterm preeclampsia. Methods:In this multicenter, double-blind, placebo-controlled trial, we randomly assigned 1776 women with singleton pregnancies who were at high risk for preterm preeclampsia to receive aspirin, at a dose of 150 mg per day, or placebo from 11 to 14 weeks of gestation until 36 weeks of gestation. The primary outcome was delivery with preeclampsia before 37 weeks of gestation. The analysis was performed according to the intention-to-treat principle. Results:A total of 152 women withdrew consent during the trial, and 4 were lost to follow up, which left 798 participants in the aspirin group and 822 in the placebo group. Preterm preeclampsia occurred in 13 participants (1.6%) in the aspirin group, as compared with 35 (4.3%) in the placebo group (odds ratio in the aspirin group, 0.38; 95% confidence interval, 0.20 to 0.74; P=0.004). Results were materially unchanged in a sensitivity analysis that took into account participants who had withdrawn or were lost to follow-up. Adherence was good, with a reported intake of 85% or more of the required number of tablets in 79.9% of the participants. There were no significant between-group differences in the incidence of neonatal adverse outcomes or other adverse events. Conclusions:Treatment with low-dose aspirin in women at high risk for preterm preeclampsia resulted in a lower incidence of this diagnosis than placebo. (Funded by the European Union Seventh Framework Program and the Fetal Medicine Foundation; EudraCT number, 2013-003778-29 ; Current Controlled Trials number, ISRCTN13633058 .).

Rolnik et al; 2017

- Goal of the study
  - To show if low-dose Aspirin can reduce the risk of preterm preeclampsia*
- Study design
  - Multicenter, double-blind, placebo-controlled trial
  - Study sites: 13 maternity hospitals in UK, Spain, Italy, Belgium, Greece, Israel
  - 1776 women with singleton pregnancy at high risk (>1 in 100) for preterm preeclampsia (identified after first trimester combined screening in weeks 11+0-13+6)
  - Randomization at 1:1 ratio (Aspirin vs Placebo)
- Administration of low-dose Aspirin or Placebo
  - 150 mg/day at bedtime
  - Start intake after screening test (wks11-14) until week 36 or onset of labor or early delivery

* preterm preeclampsia: onset of preeclampsia before 37 weeks of gestation

Rolnik et al; 2017

- Primary outcome measure
  - Delivery with preeclampsia before 37 weeks of gestation
- Secondary outcome measures
  - Adverse outcomes < 34 weeks OR < 37 weeks OR > 37 weeks
  - Stillbirth, neonatal death, neonatal complications and low birth weight
- Study population
  - 26 941 women with singleton pregnancies were screened
  - 2971 (11%) were identified at high risk, 2641 were found to be eligible
  - 1776 agreed to participate in trial and underwent randomization
    - 878 received low dose aspirin; 898 received placebo
    - No significant differences between aspirin and placebo group with regard to baseline characteristics

Rolnik et al; 2017

- Results: Primary outcome (Delivery with preeclampsia before 37 weeks of gestation)
  - Aspirin arm: Preterm PE occurred in 1,6%
  - Placebo arm: Preterm PE occurred in 4,3%

Statistically significant
P=0.004

Table 2. Outcomes According to Trial Group.

Outcome	Aspirin Group (N=798)	Placebo Group (N=822)	Odds Ratio (95% or 99% CI)*
Primary outcome: preterm preeclampsia at <37 wk of gestation — no. (%)	13 (1.6)	35 (4.3)	0.38 (0.20–0.74)

Rolnik et al; 2017

- Results: Secondary outcome (Adverse outcomes other than preeclampsia)
  - There was a observed reduction of adverse outcomes in the aspirin group
  - This was not statistically significant
  - Note: the trial was NOT powered for medication on adverse outcome
- Adherence (Compliance)
  - 79.9% of patients took >85% of medication

Table 2. Outcomes According to Trial Group.

Outcome	Aspirin Group (N=798)	Placebo Group (N=822)	Odds Ratio (95% or 99% CI)*
Secondary outcomes according to gestational age			
Adverse outcomes at <34 wk of gestation			
Any — no. (%)	32 (4.0)	53 (6.4)	0.62 (0.34–1.14)
Preeclampsia — no. (%)	3 (0.4)	15 (1.8)	0.18 (0.03–1.03)
Gestational hypertension — no. (%)	2 (0.3)	2 (0.2)	1.02 (0.08–13.49)
Small-for-gestational-age status without preeclampsia — no./total no. (%)†	7/785 (0.9)	14/807 (1.7)	0.53 (0.16–1.77)
Miscarriage or stillbirth without preeclampsia — no. (%)	14 (1.8)	19 (2.3)	0.78 (0.31–1.95)
Abruption without preeclampsia — no. (%)	1 (0.1)	3 (0.4)	0.36 (0.02–7.14)
Spontaneous delivery without preeclampsia — no. (%)	12 (1.5)	12 (1.5)	1.07 (0.37–3.10)
Adverse outcomes at <37 wk of gestation			
Any — no. (%)	79 (9.9)	116 (14.1)	0.69 (0.46–1.03)
Gestational hypertension — no. (%)	8 (1.0)	7 (0.9)	1.19 (0.31–4.56)
Small-for-gestational-age status without preeclampsia — no./total no. (%)†	17/785 (2.2)	18/807 (2.2)	1.01 (0.42–2.46)
Miscarriage or stillbirth without preeclampsia — no. (%)	14 (1.8)	19 (2.3)	0.78 (0.31–1.95)
Abruption without preeclampsia — no. (%)	2 (0.3)	4 (0.5)	0.52 (0.06–4.91)
Spontaneous delivery without preeclampsia — no. (%)	40 (5.0)	49 (6.0)	0.83 (0.47–1.47)
Adverse outcomes at ≥37 wk of gestation			
Any — no. (%)	178 (22.3)	171 (20.8)	1.12 (0.82–1.54)
Preeclampsia — no. (%)	53 (6.6)	59 (7.2)	0.95 (0.57–1.57)
Gestational hypertension — no. (%)	72 (9.0)	62 (7.5)	1.24 (0.78–1.98)
Small-for-gestational-age status without preeclampsia — no./total no. (%)†	54/785 (6.9)	56/807 (6.9)	1.00 (0.60–1.66)
Stillbirth without preeclampsia — no. (%)	2 (0.3)	2 (0.2)	1.01 (0.08–13.40)
Abruption without preeclampsia — no. (%)	2 (0.3)	2 (0.2)	1.05 (0.08–13.92)

Rolnik et al; 2017

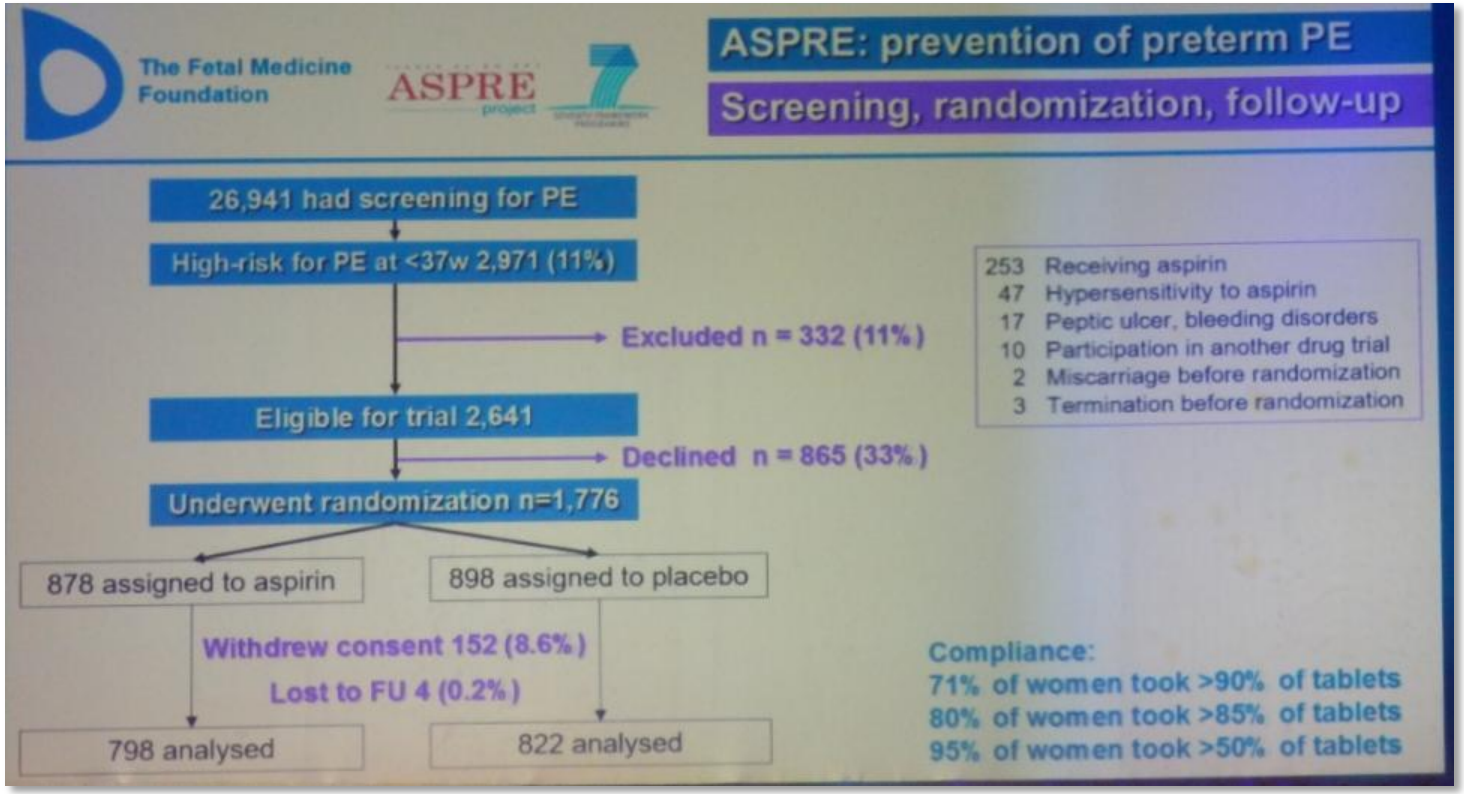
- Conclusion

In conclusion, this randomized trial showed that among women with singleton pregnancies who were identified by means of first-trimester screening as being at high risk for preterm pre-eclampsia, the administration of aspirin at a dose of 150 mg per day from 11 to 14 weeks of gestation until 36 weeks of gestation resulted in a significantly lower incidence of preterm pre-eclampsia than that with placebo.

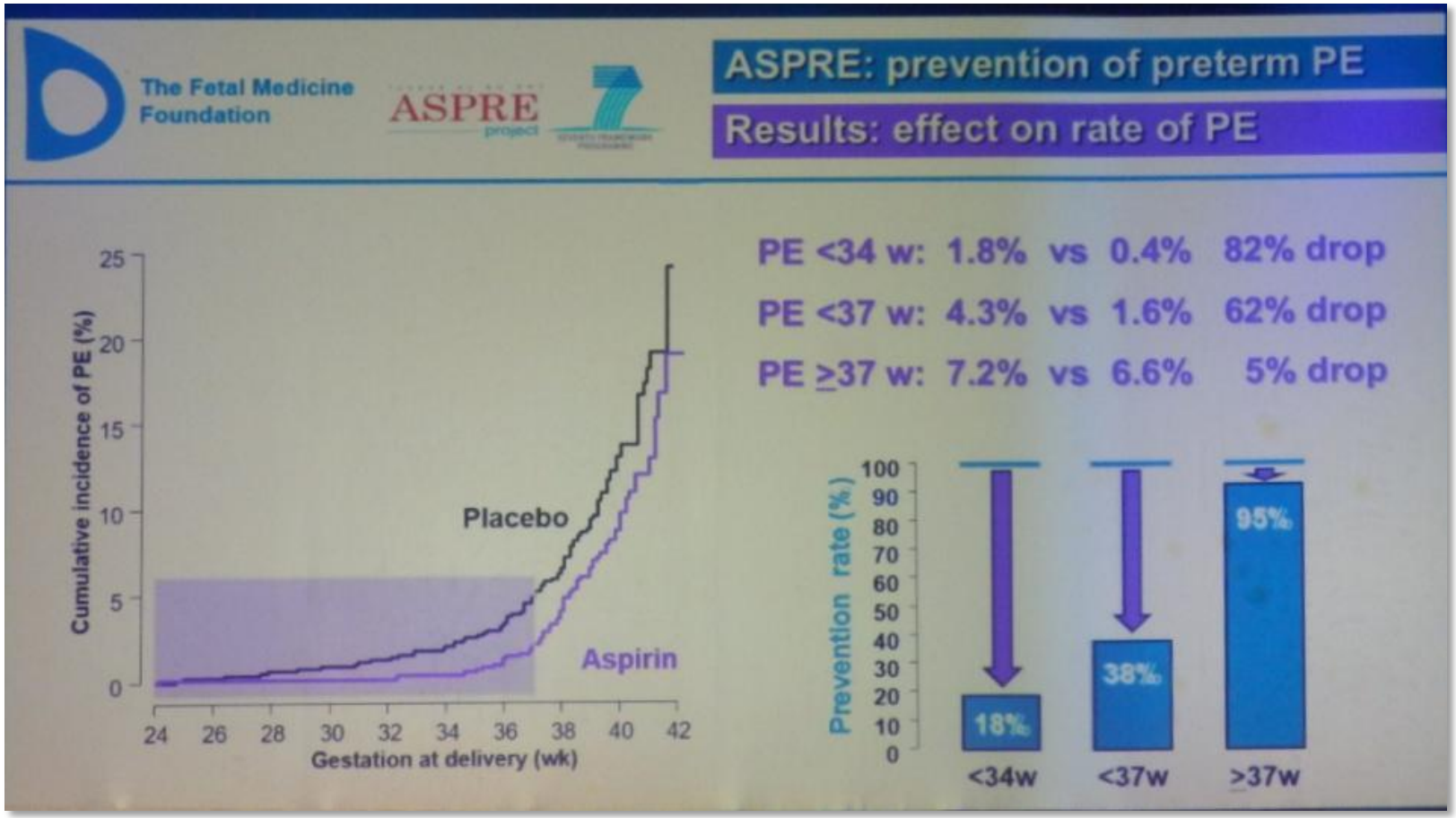
- Please note: Primary goal was to show that intake of low-dose aspirin reduces the risk of preeclampsia
  - When comparing results of aspirin versus placebo group, study results prove a significant reduction of
    - Preeclampsia < 34 wks of 82%
      - 1,8% of patients did develop PE < 34 wks in placebo group
      - 0,4% of patients did develop PE < 34 wks in aspirin group
    - Preeclampsia < 37 wks of 62 %
      - 4,3% of patients did develop PE < 37 wks in placebo group
      - 1,6% of patients did develop PE < 37 wks in aspirin group

Slides Dr. Liona Poon, June 28, 2017 at FMF World Congress

- Patients and compliance data



- Result
  - Significant reduction of preeclampsia in aspirin arm



L. Poon, June 28, 2017 at FMF World Congress

- Conclusion