## Trials on preeclampsia

<table>
<thead>
<tr>
<th>Treatment of pre-eclampsia (MAGPIE trial)*</th>
<th>Countries</th>
<th>Women</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary prevention of preeclampsia (calcium)</td>
<td>6</td>
<td>8500</td>
<td>On going</td>
</tr>
<tr>
<td>Primary prevention of preeclampsia (antioxidants)</td>
<td>4</td>
<td>4040</td>
<td>Early implementation phase</td>
</tr>
<tr>
<td>Secondary prevention of preeclampsia (treatment of hypertension)</td>
<td>4</td>
<td>1600</td>
<td>In preparation</td>
</tr>
<tr>
<td>TOTAL</td>
<td></td>
<td>24281</td>
<td></td>
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</table>
Calcium supplementation in low calcium intake women for the prevention of preeclampsia

- Hypothesis: calcium supplementation reduces the risk of preeclampsia (Calcium deficiency is associated with vasoconstriction)
- Intervention: 1500 mg/day from 20 weeks
- Outcome of interest: preeclampsia,
- Rationale: evidence from observational and randomized clinical trial
- Settings: 7 centres in 6 countries
- Population: 8500 nulliparous women
Effect of calcium supplementation to low calcium intake pregnant women on maternal calcium metabolism (sub-study)

• Hypothesis: calcium supplementation will result in less alterations of calcium related metabolites possibly associated to vasoconstriction
• Intervention: 1500 mg/day from 20 weeks
• Outcome of interest: levels of calcium metabolites in plasma and urine
• Rationale: identify mechanisms of calcium effect on preeclampsia, clarify pathophysiology
• Settings: 1 centre (Peru)
• Population: 200 nulliparosus women
Effect of calcium supplementation to low calcium intake pregnant women on placental hemodynamic and fetal growth (sub-study)

• Hypothesis: calcium supplementation will result in better fetal growth, bone development and uteroplacental circulation

• Intervention: 1500 mg/day from 20 weeks

• Outcome of interest: growth of fetal anatomical parameters, Doppler velocitometry of uterine and umbilical arteries

• Rationale: identify mechanisms of calcium effect on preeclampsia, clarify pathophysiology

• Settings: 4 centres: Argentina, Egypt, India (2)

• Population: 600 nulliparous women
Vitamin C and E supplementation in pregnancy for the prevention of preeclampsia
(In collaboration with St. Thomas Hospital, London)

- **Hypothesis**: Antioxidant supplementation to pregnant women at increased risk of preeclampsia reduces the risk of preeclampsia
- **Intervention**: 1000 mg of vitamin C and 400IU of vitamin E from the second trimester
- **Outcome of interest**: preeclampsia
- **Rationale**: oxidative stress may be a cause of preeclampsia
- **Settings**: 4 centres (India, Peru, Vietnam, England)
- **Population**: 4044 nulliparous women
Labetalol for the treatment of de-novo mild to moderate hypertension during pregnancy

• Hypothesis: Treatment of mild to moderate hypertension reduces the risk of preeclampsia

• Intervention: treating pregnant women with de-novo mild to moderate hypertension with the anti-hypertensive agent labetalol (from 300 to 1200 mg/day)

• Outcome of interest: proteinuria (preeclampsia)

• Rationale: Treatment of mild to moderate hypertension has been proposed as a strategy to prolong pregnancy and improve maternal and perinatal outcomes, but data supporting this intervention are scarce
INADEQUATE CALCIUM INTAKE

- Decreased extracellular ionized calcium
  - Increased production of PTH
    - Increased intracellular calcium
      - Tissue damage
        - Kidney
        - Placenta
      - Decreased synthesis of CGRP
        - Decreased Vit D synthesis
        - Decreased PTHrP synthesis
    - Decreased urinary calcium excretion
  - Decreased calcium intestinal absorption