Effect of folic acid supplementation in pregnancy on pre-eclampsia – Folic Acid Clinical Trial (FACT)

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Background
FACT is an international, multi-centre, double-blind, placebo-controlled trial of 3,656 women, sponsored by the Ottawa Hospital Research Institute (OHRI) and funded by the Canadian Institutes of Health (CIHR). The Women’s and Children’s Health Network (WCHN) Adelaide is the Australian lead site.

Introduction
Observational studies suggest that folic acid supplementation during pregnancy reduces the risk of pre-eclampsia (PE). No randomised trial has been conducted to demonstrate the effect of folic acid supplementation on PE.

Objectives
FACT aims to determine efficacy of a PE prevention strategy using high dose folic acid supplementation from early pregnancy until delivery in women at high risk of developing PE.

Methods
Subjects
Pregnant women between 8⁰ and 16⁶ weeks gestation, aged ≥18 years, taking ≤1.1mg of folic acid supplementation with at least one of the following risk factors for PE
- Pre-existing hypertension,
- Pre-pregnancy diabetes,
- Twin pregnancy,
- History of PE,
- BMI ≥35kg/m²

Primary Outcome
PE, defined as diastolic hypertension ≥90mmHg on two occasions ≥4 hours apart with de novo proteinuria in women greater than 20 weeks gestation.

Or
HELLP (Haemolysis, Elevated Liver Enzymes, Low Platelets) syndrome
- Haemolysis
- Serum LDH ≥600U/L
- Serum AST ≥70U/L
- Platelets <100 x10⁹/L

Or
Superimposed PE, defined as history of pre-existing hypertension with new proteinuria.

Proteinuria is defined as:
- Urinary protein ≥300mg/24 hour, OR
- ≥2+ protein dipstick, OR
- Random protein-creatinine ratio ≥30mg protein/mmol creatinine.
**Results**
As of September 19th, 565 participants (531 Canadian, 30 Australian and 4 Argentinean participants) have been randomised (Figure 1). Recruitment will begin in autumn 2013 in Jamaica and in spring 2014 in the UK and Holland, and is expected to end June 2015.

Figure 1. Projected and actual recruitment for FACT (to August 31st, 2013)

**Conclusions**
Results from FACT will provide a definitive answer to whether folic acid supplementation can prevent PE.