The ON TRACK Network

September 2018 Edition 25




ON TRACK NETWORK
BETTER HEALTH FOR MOTHERS AND BABIES

Welcome to the September edition of the ON TRACK Network newsletter

ON TRACK News

Outpatient Balloon vs. Inpatient Gel
oblige

- Recruitment numbers for the **OBLIGE Trial** are rising. Auckland City Hospital have hit the 100th participant mark this month, congratulations, keep on recruiting!
- IMPACT Meeting, Sydney Nov 1/2. Enhancing Clinical Trial Activity. See over for details.
- ON TRACK Network 3rd Concept Development Workshop. Open for submissions of research ideas SOON.

PLUS+S

The PLUSS Trial: Preventing Lung Disease Using Surfactant and Steroid

Most babies born before 28 weeks have very immature lungs and require respiratory support. At least half of these babies will go on to develop bronchopulmonary dysplasia (BPD) or chronic lung disease and will have an ongoing need for oxygen or respiratory support for many weeks or months. BPD is associated with increased infant mortality, chest infections and wheezing illnesses in childhood and beyond, and adverse neurodevelopmental outcomes. Despite the advances that have been made in neonatal care rates of BPD remain unchanged and preventative therapies are urgently required.

Systemic (enteral/intravenous) steroids are effective at preventing BPD due to their anti-inflammatory effects, but are not suitable for routine use because of significant short and long-term harm to growth and development. Alternatively, providing steroids directly to the lungs may be a promising mechanism for maximising the steroid effect in the lung while minimising systemic uptake and adverse effects.

The aim of the PLUS+S Trial is to determine whether intratracheal budesonide given with surfactant will increase survival free of BPD in extremely preterm infants. Participants will be randomised to either **budesonide plus surfactant** or **surfactant alone.**

In the PLUS+S Trial the steroid budesonide is given in combination with surfactant. Delivering budesonide in this way distributes the medication throughout the distal airway where it is taken up into epithelial cells, resulting in prolonged local action. Only a very small percentage enters the systemic circulation and this does not appear to enter the neonatal brain. Emerging evidence suggests that along with an anti-inflammatory effect budesonide may also promote lung maturation in a manner similar to antenatal steroids.

PLUS+S will recruit 1060 infants.

Middlemore Hospital and four Australian centres are recruiting, Auckland City Hospital is about to start.

The PLUS+S team are looking for additional NZ sites.

Dr Chris McKinlay, NZ Lead Investigator, Phone: 0274725099 mail: c.mckinlay@auckland.ac.nz OR pluss@auckland.ac.nz

Inclusion criteria:

- **23^{+0} – 27^{+6} weeks & <48 hours of age with prospective, written, informed consent**
- **Receiving a) mechanical ventilation via ET tube or b) non-invasive respiratory support AND decision made to treat with surfactant (1st or 2nd dose)**

Exclusion criteria :

- **Prior treatment with corticosteroid for lung disease**
- **Infant is considered non-viable, not for NICU admission**
- **Known or suspected major congenital anomaly likely to affect respiratory status**
- **Infant likely to be transferred to a non-participating NICU within 24 hours of birth**

The ON TRACK Network

Multicentre Trials currently recruiting in NZ

DIAMOND | GEMS | HINT2 | hPOD | MBM | OBLIGE | PAEAN | PIPPA Tamariki | PLUSS | PROVIDE

Update Your Practice

The Folic Acid Clinical Trial (FACT)

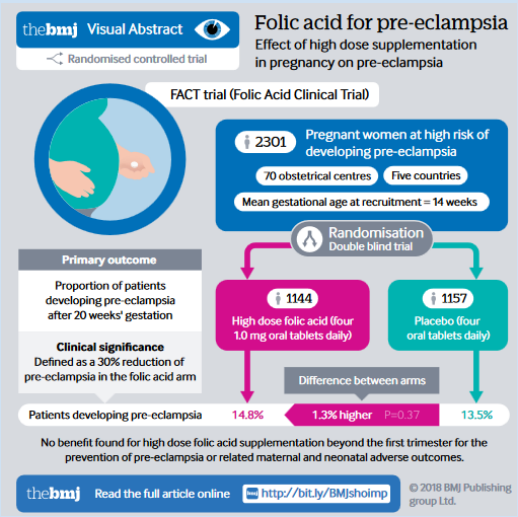
Wen et al *BMJ* 2018;362:k3478
http://dx.doi.org/10.1136/bmj.k3478

Recommendation for the use of folic acid 400-800mcg (0.4-0.8mg) daily is well recognised as the standard of care for women planning pregnancy and during the first trimester (up to 12 weeks). This is based on high quality evidence demonstrating a reduction in the incidence of neural tube defects.

Multiple epidemiological and biological studies have suggested that on-going folic acid supplementation through the second and third trimesters is associated with a reduction in the incidence of preeclampsia. To date this has not been confirmed in large randomised placebo controlled trials.

The FACT trial was a randomised, double blinded, placebo-controlled trial conducted in 70 high-risk obstetric centres in Canada, Argentina, Australia, Jamaica, and the UK. Women at high risk for pre-eclampsia (due to pre-existing hypertension, pre-pregnancy diabetes (type 1 or 2), twin pregnancy, preeclampsia in a previous pregnancy and BMI ≥35 kg/m) were invited to participate and commencement treatment from 8 to 16 weeks gestation. They were randomised to receive either 4.0 mg (high dose) folic acid or placebo until delivery. The trial's primary outcome was the incidence of preeclampsia. ISRCTN23781770/ NCT01355159.

Results: 6499 pregnant women were screened and 2464 were enrolled; 1228 were randomised to receive folic acid and 1236 placebo. Primary outcome data were available for 2301 women.



Pre-eclampsia occurred in 169/1144 (14.8%) women in the folic acid group and 156/1157 (13.5%) in the placebo group (RR 1.10, 95% CI 0.90 to 1.34; p=0.37). There were no differences between groups for any other adverse maternal or neonatal outcomes including severe preeclampsia, placental abruption, intrauterine growth restriction and or preterm delivery.

What does this mean in practice: high dose folic acid use after the first trimester does not prevent preeclampsia in women at high risk. **This finding does not alter advice that women should use daily folic acid 400-800mcg (0.4-0.8mg) when planning pregnancy and during the first trimester (up to 12 weeks) for the prevention of neural tube defects.** However, we should be more cautious about recommending on-going use of folic acid (high or low dose) as there is currently no proven benefit (no doubt the subject of research trials to come!).

Dates for your diaries

The 3rd ON TRACK Concept Development Workshop, Auckland 21st and 22nd Feb 2019
Whether you would like to present a trial concept or join in with developing research ideas, we hope you will book this into your diary. More details to come from us in the coming months.

PSANZ IMPACT Network 1st and 2nd November 2018 *Enhancing Clinical Trials Activity Across the IMPACT Network*. For more details go to https://impact.psanz.com.au/

PSNZ Annual Scientific Meeting, Wellington 29th and 30th Nov 2018 *Joining the Dots: Journey from Antenatal through to Neonatal Care.* For more details go to https://perinatalsociety.org.nz/

ACTA Summit, Sydney 29th and 30th Nov 2018. *Building a self-improving health care system*
For more details go to http://www.clinicaltrialsalliance.org.au

PSANZ Annual Congress 17th to 20th March 2019 *Surfing the Waves of Evidence*.
For more details go to http://psanz2019.com.au/

PSANZ IMPACT Pre-congress Meeting 16th and 17th March 2019 *Preterm Birth*

ontracknetwork@auckland.ac.nz http://ontrack.perinatal.org.nz/