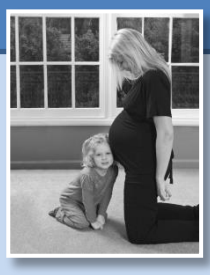
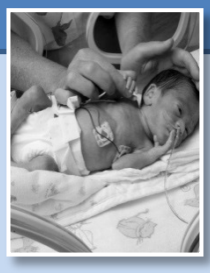
The ON TRACK Network

April 2017

Newsletter Edition 9



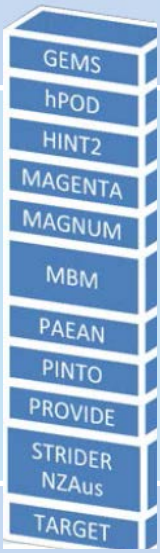



What's in this issue?

Welcome to the April edition of the ON TRACK Network newsletter

ON TRACK News

This month we welcome **Peter Melville** to the role of Network Administrator. He brings extensive clinical experience as a midwife at Royal Prince Alfred Hospital, Sydney, as well as research experience in clinical trials and completing a Master of International Public Health at the University of Sydney.



The ON TRACK Trial Development Workshop

Last month we told you a little bit about this inaugural ON TRACK workshop which took place over two days in February with 64 participants from around NZ. Expert facilitators guided discussions and contributed to the development of seven research projects. We thought we would profile these concepts for you over the next few months – you may be keen just to hear what research is being developed or may want to get more closely involved.

PINTO: Pre-diabetes in pregnancy, can early intervention improve outcomes? Dr Ruth Hughes from Canterbury DHB is the lead investigator of this proposed trial. This trial aims to assess women with HbA1c levels in the pre-diabetes range early in pregnancy and determine whether early blood glucose monitoring and initiating treatment for hyperglycaemia to maintain blood glucose levels within pregnancy targets compared with lifestyle advice and routine gestational diabetes screening at 24-28 weeks' gestation can improve pregnancy health outcomes.

The team have recently completed the PINTO feasibility study, which identified a number of issues indicating that a change to the methodology was required for any future definitive trial. The OTN Workshop provided an ideal opportunity to develop the study protocol with significant improvements to the trial design including a stepped wedge cluster randomisation design and extending the gestation of eligibility. The primary outcome measure was changed to caesarean section rate. It is estimated that a definitive trial will need to run across at least 10 sites in New Zealand over a period of 2-3 years.

The next step in development is to conduct a 12 month national observational study. This will ascertain the current rates of proposed outcome measures at each site, specifically in women with HbA1c levels in the pre-diabetes range at booking. These data are necessary for the power analysis calculations required for a stepped wedge cluster randomisation design. Ethical approval has been granted to collect laboratory records for women with HbA1c in the pre-diabetes range at booking. Support from the OTN in linking in with practitioners and decision support teams to extract national clinical outcome data that can then be linked with the laboratory data will be invaluable. **Contact: Ruth.Hughes@cdhb.health.nz**

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The ON TRACK Network

Antenatal corticosteroids prior to planned CS delivery from 35+0 weeks; a randomised controlled trial assessing the effects on respiratory morbidity and glycaemic control. Investigators from the University of Auckland joined with other interested clinicians and researchers to develop this proposal. Current guidelines vary in the advice given for corticosteroid use prior to planned CS delivery. There is potential for short term neonatal respiratory benefit, but use may also lead to short term harm (neonatal hypoglycaemia) and there is very limited evidence suggesting possible longer term harm by school age.

Taking time to work through the proposal at the OTN Workshop resulted in significant adjustments to the proposed primary outcome and now two primary outcomes are planned; one measuring short term benefit (NICU admission with respiratory distress with ≥4 hours of respiratory support) and the second, measuring short term harm (failure of primary treatment of hypoglycaemia as per NZ hypoglycaemia guidelines). There will not be sufficient time or funding within a project grant to explore longer term outcomes but the study will be designed to establish a cohort with sufficient power to assess long term benefit and/or harm. *A priori* a long term primary outcome was set; difference in IQ at school age as a continuous variable (5-7 years) with other measures of neurodevelopmental outcome and cardiovascular and respiratory health also included.

A submission to the HRC for a project grant will be made this year and next steps identified in preparation for this include; a survey to women undergoing planned CS to assess their views on such a clinical trial; a practitioner survey to assess current attitudes to the use of corticosteroids prior to planned CS and attitudes to involvement in a trial, an audit of current practice at 3 NZ sites, development of the research team, review of relevant data and seeking further statistical advice. The practitioner survey and request for expressions of interested recruiting sites will be circulated to all Site Network Leaders via the OTN within the next month. **Please complete and return to help us plan a truly collaborative trial that answers this important clinical question.** **Contact: Dr Katie Groom k.groom@auckland.ac.nz**

Upcoming Events

There will be another OTN Trial Development Workshop early in 2018 but if have a trial idea you would like to develop soon the **PSANZ IMPACT Network** have a meeting in Sydney in August. Submission deadline 5th May so get in quick!

https://impact.psanz.com.au/meetings-and-events/impact-network-workshops/

PSNZ 37th Annual Scientific Meeting
14th June Te Papa, Wellington

Several members of the OTN National Exec Committee will be at the meeting – we hope to see you there!

https://www.perinatal.org.nz/event/37th-annual-scientific-meeting/

Update Your Practice

Preeclampsia & IUGR remain two of the major causes of maternal & perinatal morbidity & mortality. Aspirin (& calcium for preeclampsia) from <20 weeks are known to reduce the risk of recurrence of these diseases. However, the effect size is only modest. This RCT led by NZ investigators explores the potential of a LMWH in addition to aspirin (& calcium) for the prevention of preeclampsia & IUGR.

Enoxaparin for the prevention of preeclampsi and intrauterine growth restriction in women with a history: a randomized trial

The EPPI Trial

Katie M. Groom, MBBS, PhD, FRANZCOG, CMFM; Lesley M. McCowan, MB ChB, MD, FRANZCOG, CMFM; Laura K. Mackay, BSc; Arier C. Lee, PhD; Joanne M. Said, MBBS, PhD, FRANZCOG, CMFM; Stefan C. Kane, MBBS, FRANZCOG; Susan P. Walker, MBBS, MD, FRANZCOG, CMFM; Thijs E. van Mens, MD, MBA Natalie J. Hannan, PhD; Stephen Tong, MBBS, PhD, FRANZCOG; Larry W. Chamley, PhD; Peter R. Stone, MB ChB, MD, FRANZCOG, CMFM; Claire McLintock, MB ChB, FRACP; the Enoxaparin for

Objective: To assess the effectiveness of enoxaparin in addition to high risk care for prevention of preeclampsia and small for gestational age (SGA) pregnancy in women with a prior history of these conditions.

Study design: This was an open label randomised controlled trial in 5 tertiary care centers in three countries. Women with a viable singleton pregnancy were invited to participate between $>6^{+0}$ and $<16^{+0}$ weeks if deemed to be at high risk of preeclampsia and/or SGA based on their obstetric history. Eligible participants were randomly assigned to standard high risk care or standard high risk care plus enoxaparin 40mg (4000 IU) by subcutaneous injection daily from recruitment until 36^{+0} weeks.

Results: 149 participants were included. The addition of enoxaparin had no effect on the rate of preeclampsia and/or SGA <5th birthweight centile ; enoxaparin 18/72 (25%) vs no enoxaparin 17/77 (22.1%), (OR 1.19, 95%CI 0.53-2.64).

Am J Obstet Gynecol. 2017 Mar;216(3):296.e1-296.e14.

What does this mean? The results of the EPPI trial are consistent with other similar multicentre trials including those published in a recent Lancet IPD analysis. Enoxaparin should not be offered as a preventative therapy for women at high risk.

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