ON TRACK News

ON TRACK NETWORK
BETTER HEALTH FOR MOTHERS AND BABIES
Te Awhi Rito

TOGETHER WE CAN ACHIEVE BETTER HEALTH FOR MOTHERS AND BABIES

JULY 2021

Welcome

Welcome to the July edition of ON TRACK News

Kia ora, this month, we take a look at the IMox trial in Update Your Practice and present an opportunity to get involved with a study investigating the management of postpartum anaemia. If you have any feedback or would like to share any of your maternal and perinatal clinical trials news, let us know.

LATEST TRIALS NEWS

The PLUSS Trial has passed the halfway mark!

The team at Counties Manukau had the honour of enrolling the 530th infant into the PLUSS trial, passing the halfway mark to the total 1060 recruits. PLUSS investigates if surfactant and budesonide given via the trachea compared with surfactant alone increases survival free of bronchopulmonary dysplasia. Well done to everyone involved who has helped reach this important milestone. If you would like to learn more about the trial, contact: Pluss@thewomens.org.au

CALL FOR ABSTRACTS

PSNZ PERINATAL SOCIETY NEW ZEALAND.

The **Perinatal Society New Zealand** Annual Scientific meeting will be held in Wellington on 23/24 November 2021. Abstract submissions on clinical and preclinical studies are welcome from midwives, sonographers, nurses, students, and doctors, from all levels of training. Work in progress submissions are also welcome. Deadline 30th Sept 2021. Further details: **https://perinatalsociety.org.nz/**

SAVE THE DATE

IMPACT PSANZ Seminar Series -Virtual 30 July 2021 3-5pm https://zoom.us/webinar/register/WN_FSLimV2_SZeYcc1pc-Z9gA

New Zealand Medical Sciences Congress - Queenstown - 1-2 Sept 2021 - www.queenstownresearchweek.org

Paediatric Society NZ 72nd Annual Scientific Meeting 2021 - Rotorua - 2-5 Nov 2021 - www.psnzconference.org.nz

New Zealand College of Midwives 16th Biennial National Conference - Christchurch - 5-6 Nov 2021 - https://www.midwife.org.nz

Perinatal Society NZ Annual Scientific Meeting 2021 - Wellington - 23-24 Nov 2021 https://perinatalsociety.org.nz/event/psnz-annual-scientific-meeting-2021/

The PSANZ 2022 Congress - Adelaide - 27-30 Mar 2022 www.psanz.com.au/

IN THIS EDITION

Update Your Practice

In this month's Update Your Practice, we feature the IMox trial investigating uterotonic agents in the treatment of postpartum haemorrhage. Read more on **page 3**

Postpartum Anaemia Research

Get involved in research aiming to improve the care and outcomes for women with severe postpartum anaemia. Learn more on **page 2**

Educational Site Visit - Hawkes Bay

A/Prof Jane Alsweiler was joined by Dr Michelle Wise and Billie Bradford for our latest Educational Site Visit. Read more on **page 4**

ON TRACK Network Trial Development Workshop The 6th ON TRACK Network Trial Development Workshop will take place in Auckland on **Thurs & Fri 24/25 February 2022**. Registrations will open soon, but for now it's TIME TO SAVE THE DATE.

Severe postpartum anaemia in Aotearoa, New Zealand

How can we improve the management of clinically stable women with severe postpartum anaemia?

Severe postpartum anaemia is a common problem, although the true prevalence in Aotearoa is currently unreported. Postpartum anaemia is associated with increased morbidity and mortality and impacts the quality of life of new mothers affecting recovery from birth, energy levels, mood, breastfeeding, and maternal-infant bonding. **Esther Caljé (pictured), a senior midwife from Christchurch, is leading research to improve the care and outcomes for women with severe postpartum anaemia.**

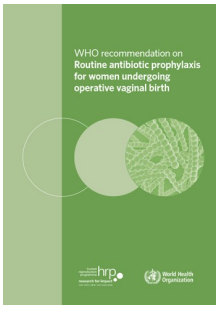
Esther originally brought an idea for a clinical trial exploring treatments of severe postpartum anaemia to the ON TRACK Network Trial Development Workshop in 2019. Consequently, she has secured herself several supervisors and a Health Research Council Clinical Training Fellowship. She is now into her second year of a Ph.D. to undertake the research to prepare for a high-quality multicentre trial in Aotearoa New Zealand.

As little is known about women's, clinicians', and other stakeholders' views of severe postpartum anaemia and its management, Esther is undertaking a series of interviews to learn more about current opinion and practice. She is also keen to hear what people think about a potential randomised trial of blood transfusion versus intravenous iron across multiple sites.

The interviews are just one component of her Ph.D. studies. She has just completed an observational study of rates of postpartum anaemia and current practice at Counties Manukau, Waikato, and Canterbury DHBs and is undertaking a systematic review of studies assessing the use of blood transfusion and intravenous iron to treat severe postpartum anaemia. Once these studies are complete, Esther will consider a pilot trial and feasibility study as she works towards the FIT (Fatigue after Infusion or Transfusion) Trial. More to come from Esther in the future for sure!

Would you like to talk to Esther? She is inviting clinicians who regularly provide maternity care for women with postpartum anaemia to take part in the interviews. If you would be willing to share your thoughts and experience, she would love to hear from you. For more information contact: esther.calje@auckland.ac.nz

GUIDELINE UPDATE: Routine antibiotic prophylaxis for women undergoing operative vaginal birth



The **World Health Organisation (WHO)** has published updated recommendations on preventing and treating maternal peripartum infections after operative vaginal birth (forceps and ventouse birth). The recommendations have been informed by new evidence from clinical trials.

Two clinical trials, including the ANODE trial, formed the basis of the updated WHO recommendation. We featured the ANODE trial in 'Update Your Practice' last year after its publication in the Lancet. The trial investigated whether antibiotic prophylaxis with intravenous amoxicillin and clavulanic acid (Augmentin) versus placebo prevented maternal infection after operative vaginal birth. It showed a benefit of a single dose of antibiotic.

Previous WHO recommendations stated that routine antibiotic prophylaxis was not recommended for women undergoing operative vaginal birth due to a lack of evidence to support benefit and amid concerns about inappropriate antibiotic use hampering the global effort to prevent and reduce antimicrobial resistance. New Zealand guidance for instrumental vaginal birth published by RANZCOG (version March 2016) reflected the WHO guidance.

Findings of the ANODE trial highlighted it was time to reconsider practice and these latest WHO recommendations now support this; WHO recommends routine antibiotic prophylaxis for women undergoing operative vaginal birth.

The combination, dose and class of antibiotic, mode of administration, and views and perspectives of women regarding the use of antibiotics for operative vaginal birth have been highlighted in the WHO update as areas for future research.

For full details:

WHO recommendation on Routine antibiotic prophylaxis for women undergoing operative vaginal birth
https://apps.who.int/iris/bitstream/handle/10665/341862/9789240027992-eng.pdf

UPDATE YOUR PRACTICE: Intramuscular oxytocin versus Syntometrine® versus carbetocin for prevention of primary postpartum haemorrhage after vaginal birth (The IMox Study) https://doi.org/10.1111/1471-0528.16622

Background: Oxytocin, Syntometrine® (oxytocin and ergometrine), and carbetocin (a long acting analogue of oxytocin) are uterotonic agents used to treat postpartum haemorrhage (PPH) caused by uterine atony after childbirth. Each agent has its benefits and drawbacks; for example, Syntometrine® requires cold storage, whereas carbetocin is heat-stable but can be more expensive. Studies have compared the drugs and different routes of administration; however, no clinical trial has directly compared intramuscular (IM) Syntometrine® and carbetocin for prevention of PPH after vaginal birth and included quality of life outcomes. IMox compared oxytocin, Syntometrine®, and carbetocin for the prevention of PPH after vaginal delivery.

Methods: A randomised controlled, double-blind trial at six UK hospitals to determine if: i) IM carbetocin is as effective as IM Syntometrine® ii) IM carbetocin is more effective than IM oxytocin iii) IM Syntometrine® is more effective than IM oxytocin. Women were eligible if they were ≥ 18 years with a spontaneous or assisted vaginal birth of a singleton baby ≥ 24 weeks gestation. Women were randomised to one of three groups: oxytocin, Syntometrine®, or carbetocin. A single intramuscular injection of the allocated identical-looking uterotonic was administered after clamping the umbilical cord before delivery of the placenta. **The primary outcome measure was the proportion of women receiving additional uterotonics after administration of the study drug**. Secondary outcomes included blood loss, adverse effects, and participant-reported quality of life, including mother's ability to bond with and care for her baby in the first two hours after birth.

Results: A total of 5,929 women were recruited and randomised between February 2015 and August 2018. 5,717 received study drug and were included in the analysis (oxytocin n=1,894; Syntometrine® n=1,914 and carbetocin n=1,909).

368 (19.5%) of women in the oxytocin arm, 298 (15.6%) in the Syntometrine® arm, and 364 (19.1%) in the carbetocin arm received additional uterotonics.
Women receiving carbetocin were more likely to receive additional uterotonics than those receiving Syntometrine® (OR 1.28, 95% CI 1.08–1.51, P = 0.004); women receiving Syntometrine® were less likely to receive additional uterotonics than those receiving oxytocin (OR 0.75, 95% CI 0.65–0.91, P = 0.002).

Use of Syntometrine® reduced non-drug PPH treatments compared with oxytocin (OR 0.64, 95% CI 0.42–0.97) but not carbetocin (P = 0.64). Rates of PPH and blood transfusion were not different between all groups. Syntometrine® was associated with an increase in maternal adverse effects and reduced the mother's ability to bond with her baby in the first two hours of life.

Interpretation: All three IM uterotonics are equally effective for preventing PPH. IM Syntometrine® was associated with less need for additional uterotonics but more maternal adverse effects compared with oxytocin and carbetocin.

WHAT DO THESE RESULTS MEAN FOR NEW ZEALAND PRACTICE?

RANZCOG guidance recommends the prevention of PPH with uterotonic agents. Still, it does not go as far as to suggest any one agent over another. IMox demonstrated clinical effectiveness of three IM uterotonics was similar; blood loss and need for blood transfusion were the same for each. Syntometrine® may reduce the use of additional uterotonic agents; however, its use results in higher maternal adverse events. Therefore, in complying with RANZCOG guidance managing PPH with pharmacological agents, the adverse effects of Syntometrine® on a mother's birth experience and ability to bond with her baby should be weighed against the benefit of the reduced requirement for additional uterotonics.

C*STEROID Trial awarded a grant to open in Australia

C*STEROID

The Australian government is investing A$180 million in 106 ground-breaking medical research projects to improve the lives of Australians. Projects funded through the government's Medical Research Future Fund (MRFF) International Clinical Trials Collaborative Programme include the ON TRACK Network supported C*STEROID Trial led by A/Professor Katie Groom.

$2.2 million has been awarded to A/Professor Jo Said at the University of Melbourne to lead the international collaboration for C*STEROID in Australia. This randomised placebo-controlled trial to determine the effect of antenatal corticosteroids on newborn health when given before planned caesarean section birth from 35^{+0} to 39^{+6} weeks of pregnancy is already active in New Zealand and continues to roll out across the country.

We look forward to publishing recruitment milestones for C*STEROID, which are about to receive a boost with our colleagues coming on board from across the Tasman. Well done to everyone involved in this fantastic achievement.

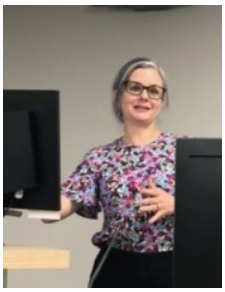
Further information: $180 million in medical research to improve the lives of Australians | Health Portfolio Ministers

EDUCATIONAL SITE VISIT: It was great to meet the teams at Hawkes Bay District Health Board

Our latest Educational Site Visit took place earlier this month at Hawkes Bay DHB. As well as learning about the value of clinical trials and the ON TRACK Network, presentations included:

- Billie Bradford, registered midwife and Senior Lecturer University of Wellington: **Fetal movements: an indicator of fetal wellbeing.**
- Michelle Wise, Senior Lecturer and consultant obstetrician, Auckland City Hospital: **Induction of labour - implementing national guidelines and filling the evidence gaps.**
- Jane Alsweiler, Associate Professor and neonatal paediatrician, Auckland City Hospital: **The prevention and treatment of neonatal hypoglycaemia.**

We are currently planning more visits for later in the year. If you would like to learn more or request a visit for your site, speak with your Site Network Leader or email us directly: ontracknetwork@auckland.ac.nz



Billie Bradford

Michelle Wise

From left: Michelle Wise, Kirsten Gaerty (Site Network Leader) & Jane Alsweiler

New Zealand Trials		New Zealand recruits
Protect Me	Antenatal melatonin supplementation in fetal growth restriction for fetal neuroprotection	6
C*STEROID	Corticosteroids before planned caesarean section from 35^{+0} to 39^{+6} weeks of pregnancy	209
DIAMOND	DIfferent Approaches to MOderate & late preterm Nutrition	450
FIIX Trial	The Fertility, IVF and Intrauterine Insemination trial in couples with uneXplained infertility	298
Little Eye Drop	Phenylephrine and Cyclopentolate Eye Drops in Neonates	128
NeoGluco	Neonatal Glucose Care Optimisation Study (I)	44
OBLIGE	Comparing two methods of starting an induction of labour in pregnant women (balloon at home versus hormone gel in hospital) to assess chance of vaginal birth	1046
PIPPA	Paracetamol and Ibuprofen in Primary Prevention of Asthma	2365
PLUSS	Preventing Chronic Lung Disease in Extremely Preterm Infants Using Surfactant + Steroid	120
PROTECT	IV pentoxifylline as adjunct therapy to improve long-term disability in preterm infants	47

Recruitment completed - follow up to primary outcome and/or data analysis ongoing	
LATTE Dosage	The most effective and best tolerated dose of caffeine to reduce intermittent hypoxaemia
GEMS	Gestational Diabetes Mellitus Trial of Diagnostic Detection Threshold
MAGENTA	Magnesium Sulphate at 30 to 34 weeks' gestational age: Neuroprotection Trial
PROVIDE	Higher IV protein intake for extremely low birthweight babies in the first week after birth on survival free from neurodevelopmental disability at 2 years' corrected age

Childhood outcome studies	
hPOD@2YR Follow-up Study	Hypoglycaemia Prevention in newborns with Oral Dextrose
TARGET Follow up Study	Optimal glycaemic targets for women with gestational diabetes: the randomised trial