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

ON TRACK

Welcome to our July ON TRACK Network newsletter

Kia ora. Welcome to the July edition of ON TRACK news. This month we provide an update from the ON TRACK Network Trial Development Workshop, we feature the MAVRIC trial in update your practice, celebrate the OBLIGE trial achieving significant recruitment milestones, and provide the latest New Zealand maternal and perinatal clinical trials news.

The ON TRACK Network Research Prioritisation Project

It is not too late to have your say about research most urgently needed to improve health and healthcare for mothers and babies in Aotearoa.

We have had an amazing response to the collection of knowledge gaps for the ON TRACK Network **Research Prioritisation Project**. If you haven't already contributed your thoughts, there is still opportunity to have your say and help shape New Zealand's research agenda for better health of mothers and babies. You could also win one out of ten $25 prezzie card vouchers. To find out more about the project visit our website: https://ontrack.perinatalsociety.org.nz/research-prioritisation/.

Clara (midwife and PhD student) and Jody (project manager) are keen to talk to anyone interested by **phone/video call interview**. To participate in an interview please contact Clara by email **c.mossinger@auckland.ac.nz** or phone on **022 4311 988** to arrange a time convenient for you.

The integrity of our final ranked research priorities rely on getting the right knowledge gaps at the start.

Trial Development Workshop 2020: Concept update - The NeoGluCO Study

Dr Chris McKinlay (front-centre) & Professor Lex Doyle (second from left) who facilitated the group that selected Chris's concept to help develop during workshop breakout sessions

Dr Chris McKinlay, neonatologist at Counties Manukau Health and Senior Lecturer at the Liggins Institute, was one of the Concept Lead Investigators at the 2020 ON TRACK Network Trial Development Workshop that took place in February.

Chris and his team considered their concept titled '*Neonatal Glucose Care Optimisation (NeoGluCO) Study-II. A phase 3, two-arm, parallel, double blind, placebo-controlled trial of early oral diazoxide therapy for severe or recurrent neonatal hypoglycaemia*'. The trial has the aim of identifying a simple, low cost oral treatment that can be used for early second line treatment in severe or recurrent neonatal hypoglycaemia.

Chris tells us the workshop was excellent for refining the trial protocol and that following discussions during the workshop, he now intends to use the Network's Forum for Women & Whānau to talk with parents about what the trial outcome priorities should be. With consumer representatives in attendance, the workshop provided a great opportunity for all teams presenting trial concepts to learn more about the importance and value of engaging consumers in the design of clinical trials, and how the Network can play a part in connecting researchers and those that will ultimately benefit from the research.

We look forward to seeing how these discussions progress when the NeoGluCO trial team reach out to hear from those interested in collaborating via our Forum's Facebook page (@ontracknetwork).

In the meantime NeoGluCO Study-I, an earlier (phase 2) trial of the NeoGluCO intervention which aims to recruit 74 babies, opened to recruitment at Counties Manukau in May this year and has already randomised 8 babies with recruitment opening shortly at Auckland City Hospital.

Outpatient Balloon vs. Inpatient Gel

Oblige

A multicentre randomised controlled trial for induction of labour

There was recent cause for celebration at Waikato Hospital with 100 women now recruited into the OBLIGE trial at their site.

Reaching this local milestone would not be possible without all the women who agree to take part in the trial and so it was only right that Courtney Collins, the 100th participant at Waikato, join the celebration with the team.

Pictured from left to right: Hayley Rae, Sarah Bennett, Claire Carpenter, and Courtney Collins; (kneeling) Celeste Pon, Nerida Titchiner, Jessica Jordan and Anna Turkington; (standing) Sarah Power, Shyralee Parker and Gina Chaney.

About OBLIGE Most women in New Zealand have induction of labour (IOL) using prostaglandin gel, which can sometimes cause contractions and therefore requires hospitalisation for heart rate monitoring. An alternative method for IOL is using a balloon catheter where contractions are less likely and monitoring is not usually required. Outpatient balloon IOL has the potential to give women more choice and improve satisfaction, and to save on health care costs, while maintaining safe outcomes for mothers and babies. Trials are needed to determine the safety and effectiveness of outpatient IOL with balloon catheter and the OBLIGE trial is one of the largest trials of IOL ever undertaken.

The objective of the OBLIGE trial is to **demonstrate the clinical effectiveness, safety and cost effectiveness for mothers and babies who are allowed to go home after commencing IOL with balloon, versus remaining in hospital after commencing IOL with prostaglandin gel**. The trial's primary outcome is rate of caesarean section birth. A total of 1,552 women will be recruited to OBLIGE in which half of the women will be assigned to prostaglandin gel and stay in hospital, and the other half will be assigned to receive the balloon and go home for the first 18-24 hours.

Women with a live singleton cephalic presentation planning IOL at 37 weeks' gestation or more are potentially eligible for the trial. The total number of women recruited to date across sites (**Auckland, Waikato, Tauranga, Wellington, Waitemata, Hawkes Bay, Hutt Valley, Taranaki, Dunedin, Whakatane**) is 800. For further details contact the Principal Investigator: Michelle Wise (m.wise@auckland.ac.nz) or, visit the trial website: www.oblige.auckland.ac.nz

C*STEROID

C*STEROID Trial awarded HRC Funding

Congratulations to Associate Professor Katie Groom and her team who have been awarded $1.43 million by the Health Research Council of New Zealand to lead the C*STEROID Trial. The C*STEROID trial was first considered at the 2017 Trial Development Workshop. The trial concerns the potential benefits (neonatal respiratory) and/or harms (neonatal hypoglycaemia) of corticosteroid use before planned caesarean section (CS) at late preterm and term gestations.

Through the Trial Development Workshop process it was established that a very large trial would be needed and that a feasibility study would strengthen the planning and funding of such a large trial. The C*STEROID Feasibility Study led by investigators from the Liggins Institute and funded by Cure Kids, Lottery Health, the Hugo Charitable Trust and the University of Auckland, closed recruitment at Auckland City, Tauranga and Waikato Hospitals in March this year. Results will be available soon.

The **main C*STEROID Trial funded by the HRC will open later this year and is planned to take place in at least 14 hospitals across New Zealand.** 2,548 mothers and babies will be recruited into the trial. Associate Professor Groom says "this will be a national effort to answer an important question. Findings aim to be definitive and will inform clinical practice in New Zealand and across the world."

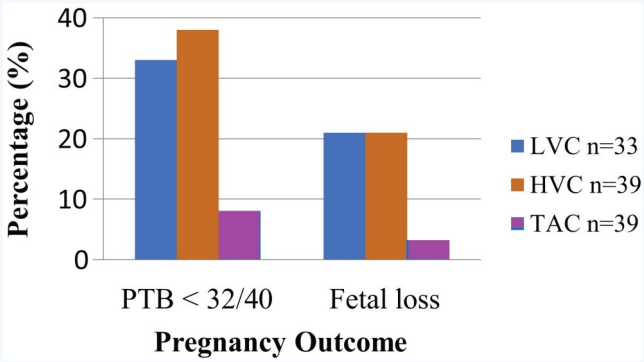
For further information about the C*STEROID trial email **csteroid@auckland.ac.nz.** Further information is also available at: **www.liggins.auckland.ac.nz/csteroid**

Update your practice: MAVRIC: a multicentre randomised controlled trial of transabdominal versus transvaginal cervical cerclage

Shennan et al Am J Obstet Gynecol 2020;222:261.e1-9.

Background: Cervical cerclage (a suture around the cervix) is used as a treatment for women at risk of spontaneous preterm birth. It is generally reserved for women with recurrent second trimester loss or early preterm birth. For the majority, a transvaginal cervical cerclage (TVCC) is effective, however, a few will continue to experience pregnancy loss, despite this treatment even when dissection of vaginal tissue is undertaken to place the TVCC in a higher position. For these women transabdominal cervical cerclage (TACC) should be considered. TACC requires a laparotomy (or if placed pre-pregnancy a laparoscopy may be used) for placement by an experienced surgeon and delivery by caesarean section. It is reserved for the most high-risk women and limited evidence from observational studies supports its use for the prevention of preterm birth in this group of women. The MAVRIC trial is the only randomised trial to compare if it's effective against both a standard TVCC and a high TVCC (hTVCC).

Methods: A multicentre randomised controlled trial in which women were assigned (1:1:1) to receive TACC, hTVCC, or TVCC either before conception or at <14 weeks of gestation. Women were eligible for inclusion if they had a history of spontaneous birth at 14-28 weeks despite a TVCC. The primary outcome was birth at <32 weeks. Choice of cerclage technique used for each TACC, hTVCC, or TVCC was at the treating clinician's discretion. Vaginal cervical cerclage was inserted at <16 weeks under regional anaesthesia and removed at 37 weeks, or earlier if preterm labour occurred. hTVCC involved mobilisation of the bladder from the anterior cervix to allow higher placement (usually requiring regional anaesthesia for removal). TACC was placed preconception or at <14 weeks of gestation as an open procedure under regional or general anaesthesia. Women with TACC were scheduled for elective caesarean delivery at 38–39 weeks gestation with retention of the TACC for future pregnancies.



Results: 139 women were randomised in nine UK hospitals between January 2008 and September 2014. Of these, 111 women had conceived with known outcome by the completion of the trial four years later and are included in the analysis. 39 women were assigned randomly to TACC, 39 to hTVCC, and 33 to TVCC. All cerclages were placed by consultant grade doctors.

The rate of birth <32 weeks was significantly lower for women who received TACC compared with TVCC (8% [3/39] vs 33% [11/33]; relative risk, 0.23; 95% confidence interval, 0.07-0.76; P=.0157). The number needed to treat to prevent 1 preterm birth was 3.9 (95% confidence interval, 2.32-12.1). There was no difference in preterm birth rates between hTVCC and TVCC (38% [15/39] vs 33% [11/33]; relative risk, 1.15; 95% confidence interval, 0.62-2.16; P=.81). There were no neonatal deaths. Women with TACC had fewer fetal losses (second trimester loss and stillbirth) compared with TVCC (3% [1/39] vs 21% [7/33]; relative risk, 0.12; 95% confidence interval, 0.016-0.93; P=.02). The number needed to treat to prevent 1 fetal loss was 5.3 (95% confidence interval, 2.9-26).

Interpretation: In this population of high-risk women with a previously failed transvaginal cervical cerclage, a TACC is superior to TVCC in the prevention of early preterm birth and improved perinatal survival. hTVCC had no benefit over standard TVCC.

What do these results mean for New Zealand clinical practice and future research? TACC is already offered in some tertiary centres in New Zealand, results of the MAVRIC trial support its ongoing use for the most high-risk women. However, caution should be expressed in extrapolating results to those women who have not been treated with a less invasive transvaginal cervical cerclage. Future use of TACC should remain with specialists with a particular interest in the care of women at high risk of preterm birth and ideally through designated preterm birth clinics. It is unlikely this type of randomised trial will be repeated anywhere in the world due to the very low incidence of women meeting the inclusion criteria and who may be willing to be randomised to different treatments in such circumstances. It is highly commendable that the researchers were able to complete this trial.

New Zealand Trials		New Zealand recruits
DIAMOND	DIfferent Approaches to MOderate & late preterm Nutrition	330
FIIX Trial	The Fertility, IVF and Intrauterine Insemination trial in couples with uneXplained infertility	96
LATTE Dosage	The most effective and best tolerated dose of caffeine to reduce intermittent hypoxaemia	103
Little Eye Drop	Microdrop Administration of Phenylephrine and Cyclopentolate Eye Drops in Neonates	47
NeoGluco	Neonatal Glucose Care Optimisation Study (I)	8
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	800
PAEAN	Preventing Adverse Outcomes of Neonatal Hypoxic Ischaemic Encephalopathy with Erythropoietin	59
PIPPA	Paracetamol and Ibuprofen in Primary Prevention of Asthma	1573
PLUSS	Preventing Chronic Lung Disease in Extremely Preterm Infants Using Surfactant + Steroid	59
PROTECT	IV pentoxifylline as adjunct therapy to improve long-term disability in preterm infants	28
Recruitment completed - follow up to primary outcome ongoing		
C*STEROID Feasibility	C*STEROID Feasibility: Corticosteroids before planned CS form 35^{+0} to 39^{+6} weeks	
ECOBABe	The ECOBABe study (Early Colonisation with Bacteria After Birth)	
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	
STRIDER NZAus Childhood Outcome Study	Sildenafil TheRapy In Dismal prognosis Early onset fetal growth Restriction (2-3 years)	
TARGET Follow up Study	Optimal glycaemic targets for women with gestational diabetes: the randomised trial	

Publications & Grants Have you or colleagues had any **publications** or received any **research grants** in women's and babies' health that relate to clinical trial activity supported by the Network? If so, please share details with us for our next ON TRACK Strategic Research Initiative Fund (SRIF) report. The report provides essential information for our funders. It is also a great opportunity to demonstrate the collective hard work of clinical trials research in New Zealand and can be used to support our sustainability beyond the SRIF funding. Please email details to us: ontracknetwork@auckland.ac.nz

Save the date

Nga Maia National Hui/AGM 2020 - Waikato - 30th Nov-2nd Dec 2020

Society for Maternal Fetal Medicine 41st Annual Pregnancy Meeting 2021 - Las Vegas - 25-30 Jan 2021

PSANZ Annual Congress (2020 postponement) Sydney - 10-13 Feb 2021

RANZCOG 2021 ASM Hobart 14-17 Feb 2021

RANZCOG 2020 NZ Annual Scientific Meeting (2020 postponement) Wellington - 16 - 18 Jun 2021

New Zealand College of Midwives 16th Biennial National Conference - Christchurch - 2-4 Sept 2021

PSNZ 72nd Annual Scientific Meeting 2021 - Rotorua - 2-5 Nov 2021