# 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

FEBRUARY 2022

# Welcome

**Welcome to the first edition of ON TRACK News for 2022**

Kia ora, welcome back to ON TRACK news. We hope you have all enjoyed some relaxation over the holiday season. This month, we feature the C*STEROID Trial. We look at the OPTIMIST-A Trial in Update Your Practice and summarise findings from a large cohort study looking into long-term outcomes on children whose mothers received metformin in pregnancy.

## LATEST NEWS

### Positions vacant—join our National Executive Committee

Our **National Executive Committee (NEC)** works in an advisory capacity to guide and support the Network through its activities. With the start of this new year and a refresh of our strategic plan, we seek new members to join the Committee. If you are interested and committed to improving health and wellbeing for all mothers and babies across Aotearoa New Zealand, we would love to hear from you. We are particularly keen to hear from Māori and Pacific peoples and emerging researchers. If you would like to learn more about becoming a member of the ON TRACK Network NEC, please contact us at **ontracknetwork@auckland.ac.nz**.

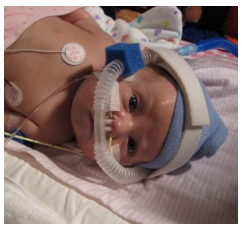
### The New Zealand Registry of COVID-19 in Pregnancy

The registry is for all women in New Zealand who have COVID-19 during or within six weeks of pregnancy. It will help us understand the impact of COVID-19 on pregnancy in New Zealand. Any health practitioner or individual can submit a notification to the registry. So far, the registry has received 56 reports, and the team are keen to support all cases being notified, including historical cases.

The registry website www.liggins.auckland.ac.nz/covid19 provides information and links to a women's information sheet and the notification system. For any queries, please contact the team at covid19@auckland.ac.nz or 021 0831 4824.

## IN THIS EDITION

### Minimally Invasive Surfactant Therapy



In this month's Update Your Practice we look at the **OPTIMIST-A Trial**. Read more on **page 2.**

### Metformin in pregnancy

A large cohort study investigating long-term outcomes on children whose mothers received **metformin in pregnancy** has been published. Read more on **page 3**.

### The C*STEROID Trial

This month's featured trial is **C*STEROID**: Corticosteroids before planned caesarean section from $35^{+0}$ to $39^{+6}$ weeks of pregnancy. Read more on **page 4.**

**SAVE THE DATE**

RANZCOG Symposium 2022 Hybrid meeting (virtual/Melbourne) 28 Feb-1 Mar 2022 https://ranzcog.edu.au

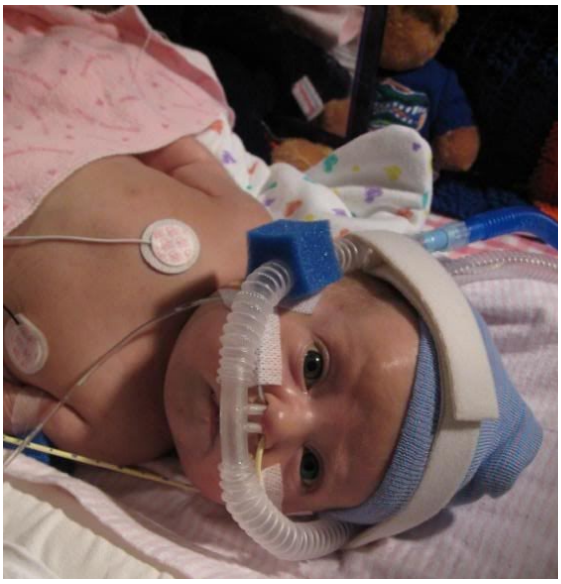
The PSANZ 2022 Congress Adelaide 15-18 May 2022 www.psanz.com.au/

Paediatric Society NZ 73rd Annual Scientific Meeting 2022 New Plymouth 1-3 Nov 2022 www.psnzconference.org.nz

10th Biennial Joan Donley Midwifery Research Forum Tauranga 18 Nov 2022 www.midwife.org.nz

# UPDATE YOUR PRACTICE: Effect of minimally invasive surfactant therapy versus sham treatment on death or bronchopulmonary dysplasia in preterm infants with respiratory distress syndrome – The OPTIMIST-A Randomised Controlled Trial

https://jamanetwork.com/journals/jama/fullarticle/2787253



**BACKGROUND** Preterm infants with respiratory distress syndrome (RDS) are often supported with their breathing using continuous positive airway pressure (CPAP) as recommended in published evidence-based guidelines. Compared with intubation and ventilation, CPAP reduces the risk of a preterm chronic lung disease or bronchopulmonary dysplasia (BPD). For infants with RDS on CPAP, surfactant can be given during spontaneous breathing using a fine trans-glottic catheter (minimally invasive surfactant therapy or MIST). However, in extremely preterm infants the efficacy and safety of MIST compared with the conventional administration of surfactant by endotracheal tube (intubation) followed by ventilation is uncertain.

**DESIGN** **The OPTIMIST-A Trial (cOllaborative Paired Trials Investigating Minimally Invasive Surfactant Therapy) investigated if in extremely preterm infants (25 to 28 weeks) with RDS (Fi02 ≥0.3) on CPAP at <6 hours after birth, MIST compared with no MIST (sham) would reduce the incidence of the composite outcome of death or BPD or its components.** Infants in both groups were continued on CPAP and intubated if requiring FiO2 of 0.45 or greater (or by clinician discretion when requiring FiO2 >0.40) or if there was severe or recurrent apnoea or persistent respiratory acidosis.

**RESULTS** Four hundred and eighty-five preterm infants were randomised between December 2011 and March 2020 across 33 tertiary neonatal intensive care units worldwide, including New Zealand.

Death or BPD occurred in 105/241 (43.6%) infants in the MIST group and 121/244 (49.6%) in the sham group (RD -6.3%, 95% CI -14.2%, 1.6%). The rate of death before 36 weeks' postmenstrual age did not differ significantly between groups (24 [10.0%] MIST versus 19 [7.8%] sham), but the rate of BPD in survivors to 36 weeks' postmenstrual age was lower in the MIST compared with sham group (81/217 [37.3%] versus 102/225 [45.3%], RD -7.8%, 95% CI -14.9%, -0.7%). MIST was associated with other secondary benefits, including reduced risk of pneumothorax requiring drainage, intubation within 72 hours of birth, home oxygen, patent ductus arteriosus and duration of respiratory support. Serious adverse events were similar between groups (10.3% versus 11.1%).

| | **No./total (%)** | | | | |
|---|---|---|---|---|---|
| | MIST group | Sham group | Risk Difference % (95%CI) | Relative Risk (95% CI) | P value |
| Death or BPD | 105/241 (43.6) | 121/244 (49.6) | -6.3 (-14.2 to 1.6) | 0.87 (0.74 to 1.03) | .10 |
| Death prior to 36 weeks' postmenstrual age | 24/241 (10.0) | 19/244 (7.8) | 2.1 (-3.6 to 7.8) | 1.27 (0.63 to 2.57) | .51 |
| BPD in survivors to 36 weeks' postmenstrual age | 81/217 (37.3) | 102/225 (45.3) | -7.8 (-14.9 to -0.7) | 0.83 (0.70 to 0.98) | .03 |

**INTERPRETATION** Among extremely preterm infants on CPAP with RDS and Fi02 ≥0.30 at <6 hours after birth, MIST compared with no MIST and expectant management did not reduce the composite outcome of death or BPD. However, MIST was feasible, safe and associated with other clinical benefits.

**WHAT DO THESE RESULTS MEAN FOR NEW ZEALAND PRACTICE?** MIST can be considered for extremely preterm infants (25 to 28 weeks) being managed on CPAP who have an Fi02 ≥0.30 shortly after birth.

## Metformin in pregnancy: large cohort study published

https://drc.bmj.com/content/10/1/e002363.long

Three to four-thousand women in New Zealand are diagnosed with gestational diabetes (GDM) each year, usually by routine screening at 26-28 weeks gestation. Lifestyle changes can help manage GDM, but metformin and/or insulin are often also needed.

Metformin has been shown in clinical studies to be safe during pregnancy. The Metformin in Gestational diabetes (MiG) trial, led by New Zealand researchers, was published in 2008 after recruiting 751 women in Auckland and Adelaide. Women with GDM were randomly assigned to treatment with metformin or insulin. The trial found metformin is not associated with increased perinatal complications compared with insulin treatment.

Although perinatal outcomes concerning the use of metformin during pregnancy are encouraging, unlike insulin, metformin can cross the placenta making it more important to understand metformin's potential long-term effects on the fetus. Data on the association between metformin exposure during pregnancy and long-term adverse outcomes in children has been limited. The MiG TOFU study followed up children of mothers who participated in the MiG trial at two years of age. Body composition was measured in 154 and 164 children whose mothers were treated with metformin and insulin, respectively. The investigators found that although children exposed to metformin had larger subcutaneous fat measures, overall body fat was the same as those whose mothers were treated with insulin alone.

This recently published cohort study provides the largest non-randomised data set of long-term outcomes in infants of pregnancies exposed to metformin. The data represents 10,129 children with maternal exposure to metformin, insulin or both born in Finland between 2004 and 2016. Primary outcomes were long-term offspring obesity, hypoglycemia, hyperglycemia, diabetes, hypertension, polycystic ovary syndrome, and motor–social development challenges. The study found antenatal exposure to metformin and combination treatment of metformin and insulin was not associated with long-term increased risk of obesity, hypoglycemia, hyperglycemia, diabetes, or challenges in motor-social development compared with insulin alone. Despite not representing rigorous clinical trials data, this study further supports the use of metformin during pregnancy.

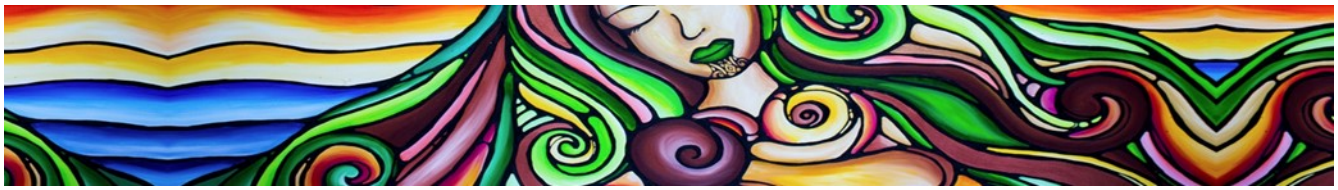
## Additional maternal benefits of breastfeeding

https://www.ahajournals.org/doi/10.1161/JAHA.121.022746

Maternal health benefits of breastfeeding have been widely published. Health benefits commonly reported relate to ovarian and breast cancer and type II diabetes. A systematic review recently published in the Journal of the American Heart Association has now highlighted the **protective effect on mothers of breastfeeding in reducing the risk of cardiovascular disease**. The study combined results from 8 separate studies involving >1 million women in a meta-analysis. Although the data is not from randomised controlled trials, the findings are interesting to note.

The authors found parous women who ever breastfed during their lifetime had a reduced risk for developing cardiovascular disease (CVD), coronary heart disease, stroke, and fatal CVD compared with parous women who never breastfed. There was a relative risk reduction of 11% (95% CI, 5% -17%) for CVD events, 14% (5% -22%) for CHD events, 12% (1% -21%) for stroke events, and 17% (8% -24%) for fatal CVD events.

This study emphasises the importance of facilitating breastfeeding, given the health benefits to both mother and baby. In New Zealand, **Mama Aroha** has created tools designed to enable healthcare providers to empower all mothers to breastfeed. If you have not already checked them out, we suggest you visit their website to learn more: **https://www.mamaaroha.co.nz/**



# The C*STEROID Trial: Corticosteroids before planned caesarean section from $35^{+0}$ to $39^{+6}$ weeks of pregnancy

The **C*STEROID Trial** will involve more than 2,500 pregnant women and their babies across Aotearoa New Zealand and Australia. The trial has been designed **to determine whether giving mothers corticosteroid injections before having a planned caesarean section from $35^{+0}$ to $39^{+6}$ weeks of pregnancy will safely reduce the risk of short-term breathing problems for babies**. The trial funded by the Health Research Council of New Zealand and the Medical Research Future Fund, is the largest trial ever undertaken in this area. It will be the first to explore both the treatment's benefits and potential side effects, specifically neonatal respiratory morbidity and neonatal hypoglycaemia. The trial also aims to assess the impact of corticosteroids during pregnancy on later childhood development.

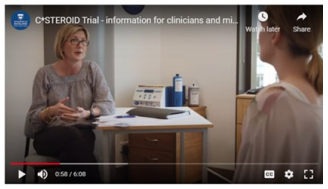
**Co-primary outcomes are incidence of respiratory distress requiring > 60 minutes of respiratory support (neonatal benefit); and incidence of hypoglycaemia (blood glucose level <2.6 mmol/L) prior to primary hospital discharge (neonatal harm).**

C*STEROID opened to recruitment in Auckland in October 2020, and to date, 272 mothers and 290 babies have been recruited. Auckland, Waikato, Christchurch, Tauranga, Northland, and Wellington are active, with Palmerston North, Counties Manukau and Hawkes Bay expected to come on board soon. Sites across Australia are also being set up.

### Inclusion criteria

- Planned CS at 35+0 to 39+6 weeks
- >24 hours & <7 days until planned birth
- Singleton or twin pregnancy with a live fetus

Scan the QR code for more information




Many resources are available to help sites with recruitment, including videos, trial webpages, Facebook page, site folders, banners, posters, information flyers, participant wristbands, magnets, pens, and lanyards – everything needed to remind everyone of this great opportunity to get involved! We recommend you look at the trial videos in the first instance. A video is available for both potential participants and healthcare professionals: https://youtu.be/ai6MFtF1CZA and https://youtu.be/-2MxTKPsg94

| New Zealand Trials | | New Zealand recruits |
|---|---|---|
| **PROTECT Me** | Antenatal melatonin supplementation in fetal growth restriction for fetal neuroprotection | 9 |
| **C*STEROID** | Corticosteroids before planned caesarean section from $35^{+0}$ to $39^{+6}$ weeks of pregnancy | 272 |
| **DIAMOND** | DIfferent Approaches to MOderate & late preterm Nutrition | 516 |
| **FIIX Trial** | The Fertility, IVF and Intrauterine Insemination trial in couples with uneXplained infertility | 384 |
| **NeoGluco** | Neonatal Glucose Care Optimisation Study (I) | 56 |
| **PIPPA TAMARIKI** | Paracetamol and Ibuprofen in Primary Prevention of Asthma | 2778 |
| **PLUSS** | Preventing Chronic Lung Disease in Extremely Preterm Infants Using Surfactant + Steroid | 154 |
| **PROTECT** | IV pentoxifylline as adjunct therapy to improve long-term disability in preterm infants | 66 |

| 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 |