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 2022

Welcome

Welcome to the September edition of ON TRACK News for 2022

Kia ora, welcome to ON TRACK News for September, our spring edition. This months publication is briming with insights to update your practice all from NZ led clinical trials. We hope you enjoy reading our newsletter and share a copy with your colleagues in your tea room, kia tutaki ano tatou.

LATEST NEWS

There are lots of publications of clinical trials that have been supported by the ON TRACK Network emerging at the moment. It is Awesome to see the GEMS, LATTE Dosage and TARGET trials and the C*STEROID feasibility study being published.

You can read the media release for the GEMS Trial here and this newsletter will cover two of the four studies more closely.

November is shaping up to be an **epic month for conferences.** Check out our Save the Date box at the bottom of this page for further details and links. A special mention for **Perinatal Society of New Zealand** who are hosting their annual meeting early November in person, after 3 years online, isn't great to get to get some normality back in our lives, a great time to reconnect!

I would like to welcome in Spring with this cheerful little lamb, nothing says spring in New Zealand quite like a baby lamb and daffodils!

IN THIS EDITION

Read up on how the GEMS Trial team discovered lower-glycaemic criteria is needed for Gestational Diabetes screening

Read more on Page 2

LATTE Dosage Trial have published and confirmed their findings for effective caffeine citrate use for preterm infants, to prevent intermittent hypoxaemia.

Read more on Page 3

FEATURE TRIAL: The **LATTE Trial** what next?

Read more on Page 4

SAVE THE DATE

AusBiotech Conference **Perth** 26-28 October, www.clinicaltrialsalliance.org.au
Home Birth Aotearoa Hui and Conference 2022 **Waikato** 29th 30th October, www.whba.org.nz
Paediatric Society NZ 73rd Annual Scientific Meeting 2022 **New Plymouth**, 1-3 November, www.psnzconference.org.nz
ACTA Annual Scientific Meeting 2022 **Adelaide**, 7-8 November, www.clinicaltrialsalliance.org.au
Perinatal Society New Zealand meeting **Auckland,** 10-11 November, www.perinatalsociety.org.nz
Australian Perinatal Epidemiology Update (APEU) **Melbourne** 14-15th November, www.mercyperinatal.com
10th Biennial Joan Donley Midwifery Research Forum **Tauranga,** 18 November, www.midwife.org.nz
The Carosika Project, Taonga Tuku Iho. Project Event & Hui **Auckland**, 8-9 December, AUT South Campus, TBA details

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UPDATE YOUR PRACTICE: Lower versus Higher Glycaemic Criteria for Diagnosis of Gestational Diabetes - GEMS Trial

Crowther CA. et al. DOI: 10.1056/NEJMoa2204091

Gestational Diabetes Mellitus Study of Detection Thresholds

Background

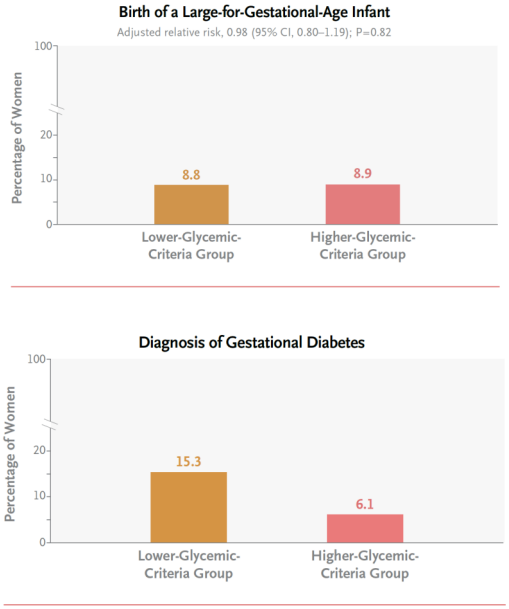
Gestational Diabetes Mellitus (GDM) is a major worldwide health issue that can cause short term and lifelong problems for both mother and her infant. Treatment of GDM with nutritional therapy, blood glucose monitoring and pharmacological treatment when needed improves mothers' and infants' health. What has been unclear is what blood glucose threshold to use for the diagnosis, so this varies globally. Many organisations, including the Ministry of Health (MOH) in New Zealand, have recommended randomised trials are warranted that assess different diagnostic glycaemic thresholds .

The Gestational Diabetes Mellitus Trial of Diagnostic Detection Thresholds (GEMS) aimed to assess whether detection and treatment of gestational diabetes using lower-glycaemic criteria, recommended by the International Association of Diabetes in Pregnancy Study Groups, compared with higher-glycaemic criteria currently recommended by the MOH and used in New Zealand, would lead to lower perinatal morbidity without higher maternal health-related risk. An additional objective was to determine differences in the use of health services between the two trial groups.

Design

The trial was conducted at ADHB and Counties Manukau Health, in Auckland. Women with a singleton pregnancy having a 75-g oral glucose-tolerance test (OGTT) at 24 to 32 weeks' gestation, with consent, were randomised to the lower glycaemic-criteria (fasting plasma glucose level of ≥5.1 mmol/L, a 1-hour level of ≥10.0 mmol/L, or a 2-hour level of ≥8.5 mmol/L) or the higher glycaemic-criteria (fasting plasma glucose level of ≥5.5 mmol/L, or a 2-hour level of (≥9.0 mmol/L).

Results



A total of 4061 women were randomised into the study and baseline characteristics were similar, between the groups. As expected, gestational diabetes was diagnosed more frequently in the lower-glycaemic-criteria group (15.3%) than in the higher glycaemic-criteria group (6.1%); a two and a half times increase.

Overall, for the **primary outcome** of large for-gestational-age infant, the risk was similar between groups, 8.8% in the lower-glycaemic-criteria group and 8.9% in the higher-glycaemic-criteria group. Infants born to mothers in the lower-glycaemic-criteria group were more likely to be treated for hypoglycaemia and the women were more likely to have labour induced, receive pharmaceutical treatment for glycaemic control, and use more health services compared with women in the higher-glycaemic-criteria group.

These overall findings were strongly influenced by the subgroup analysis that reported findings for the 9.2% of women with milder GDM for whom GDM was diagnosed and treated if randomised to the lower-criteria group and not diagnosed if assigned to the higher-criteria group. Here, birth of a large for-gestational-age infant was reduced in the lower-criteria versus the higher-criteria group (6.2% versus 18.0%) as was the risk of a serious infant outcome, that included shoulder dystocia, (0.5% versus 3.9%). For the women, pre-eclampsia was less common in the lower-criteria group compared with the higher-criteria group (0.5% versus 5.6%). As in the whole trial cohort, neonatal hypoglycaemia was detected and treated more frequently in the lower-criteria group, women were more likely to have an induction, use pharmaceutical treatment for glycaemic control, and health service utilisation was increased compared to the higher-criteria group. **Conclusion:** Overall, use of the lower glycaemic-criteria for diagnosis of GDM compared with the higher-glycaemic criteria increased the proportion of women diagnosed with gestational diabetes, did not reduce perinatal morbidity and increased the use of health services. However for the women with milder gestational diabetes there were health benefits for them and their infants from detection and treatment. Follow-up of the women and their children will be important to assess any later benefits and harms.

What does this mean for New Zealand practice? *The GEMS trial provides high-quality local Aotearoa data to help inform future practice. The national diabetes in pregnancy guideline group will now be able to review this evidence and consider what the best approach will be. We look forward to hearing about their recommendations.*

Caffeine to prevent intermittent hypoxaemia in late preterm infants: randomised controlled dosage trial – Latte Dosage Trial

Latte Dosage Trial
Caffeine for the prevention of intermittent hypoxaemia in late preterm babies

Oliphant EA. et al. doi:10.1136/archdischild-2022-324010

Hypoxaemia is associated with negative effects on cognition and neurodevelopmental outcomes in preterm infants, with episodes of intermittent hypoxaemia (IH) more prevalent in late preterm infants (34^{+0} – 36^{+6}) than term-born. The rate of IH peaks at two weeks' postnatal age, before reducing to near birth levels at term corrected age. Caffeine is effective for the prevention and treatment of apnoea of prematurity and IH in very preterm infants, reducing the incidence of chronic lung disease, cerebral palsy and cognitive delay. Caffeine elimination is extremely slow in preterm infants increasing with gestational age requiring larger doses as they age to maintain therapeutic dose. In very preterm infants' caffeine is usually tolerated but can reduce weight gain and infants can develop tachycardia and feed intolerance. This study's aim was to establish the most effective and best tolerated dose of caffeine to reduce IH in late preterm infants.

Method

Participating infants were randomised to one of four daily doses of caffeine (5, 10, 15 or 20 mg/kg/day of caffeine citrate) or placebo (water) within 72 hours of birth until full-term equivalent age 40 weeks. The primary outcome was the rate of IH two weeks after randomisation.

Results

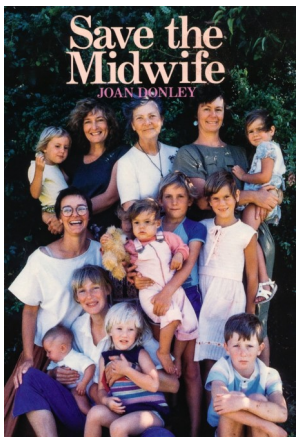
There were 132 infants randomised in the trial, with a mean gestational age of 35 weeks. **Primary outcome** Caffeine citrate at 10 or 20 mg/kg/day reduced the mean rate of IH by 61% and 67%, respectively, with no effect of the 5 or 15 mg/kg/day doses. The rate of IH was significantly reduced for infants allocated to any dose of caffeine overall compared to the placebo. **Secondary outcomes** The 10 and 20mg/kg/day dose groups had significantly higher mean SpO2 and the 15mg/kg/day group had higher mean heart rate. All groups spent significantly more time with tachycardia (heart rate > 180 beats per min) at 2 weeks which persisted to term equivalent age. Caffeine did not have any adverse effects on sleep, gastro-oesophageal reflux or feeding. There was no difference in weight gain between the groups, but there was a reduction in length z score in the 20 mg/kg/day group.

Conclusion

Caffeine citrate reduces IH in late preterm infants with dose of 10 and 20 mg/kg/day being effective. Side effects include tachycardia and possibly growth. The larger Latte trial will determine if caffeine citrate in late preterm babies improves neurodevelopmental outcomes at 2.5 years corrected age.

What does this mean for New Zealand Practice? *This dosage trial has provided valuable evidence that has supported the development of the Latte Trial. This will be now be rolled out across Aotearoa. See over for more details and have a good think about your site becoming involved!*

JOAN DONLEY MIDWIFERY RESEARCH COLLABORATION



Established in 2001, the Joan Donley Midwifery Research Collaboration (JDMRC) is the evidence arm of the New Zealand College of Midwives (NZCOM) and provides the framework research programme. Joan Donley was a founding member of NZCOM. Every second year JDMRC hosts a 2 day conference recognising her legacy and commitment to evidence-informed practice providing a collaborative space for researchers, midwifery educators, schools, universities and hospitals to get together share their research, and evaluate the effectiveness and appropriateness of midwifery practice and policy.

Where: Tauranga - Trustpower Baypark Stadium

When: 17 & 18 November 2022 . Register: www.midwife.org.nz

PSNZ PERINATAL SOCIETY NEW ZEALAND.
2022 ANNUAL SCIENTIFIC MEETING

The PSNZ Annual meeting will be **in person for the first time in 3 years!** A 2 day meeting will be hosted at the

Fisher and Paykel Clinical Education Centre, Auckland Hospital, 10-11th of November.
Register at:

www.perinatalsociety.org.nz

FEATURE TRIAL

Caffeine to improve neurodevelopmental outcomes in infants born later preterm: The Latte Trial.

It is common for babies to be born late preterm (34^{+0} -36^{+6} weeks gestational age). Late preterm birth is associated with a higher risk of developmental and health problems in later life. Equity is a priority for all aspects of health and wellbeing, including late preterm babies, 20% of whom are Māori. The Latte Trial has been informed by the Latte Dosage Trial (page 3),which suggested the best dose of caffeine citrate to consider when exploring it's effect on intermittent hypoxaemia, and neurodevelopmental impairment, in babies born late preterm.

The aim of the Latte Trial is to determine if prophylactic caffeine citrate treatment, given to babies born late preterm from birth to term equivalent age, improves neurodevelopmental outcomes at 2.5 years' corrected age. This is a Phase III, multi-centre, double blind, randomised controlled trial and has an emphasis on Māori recruitment to assist Mana Whakamārama (equal explanatory power).

Caffeine in very preterm babies

- reduces apnoea of prematurity
- reduces bronchopulmonary dysplasia
- improves neurodevelopmental out come

Inclusion Criteria

- Late preterm babies 34-36^{+6} weeks gestational age.
- Less than 3 days old.
- Who have not been treated with caffeine prior.
- No have any contraindications to caffeine treatment.

The Latte Trial **Primary Outcome** - is the Bayley Scale of Infant Development IV cognitive score at 2.5 years' corrected age. **Secondary outcomes include** Bayley Scale of Infant Development IV motor and language scores, pre-school wheeze, death, anthropometry, health related quality of life, healthcare utilisation.

Recruits - The Latte trial will include **191 babies in each arm (total 382),** allowing for a 20% drop out rate, due to withdrawal or loss to follow up, total of 478 babies will be recruited.

The Latte Trial was recently awarded funding from the Health Research Council of New Zealand.

This trial will provide valuable information on a potential treatment to improve outcomes for late preterm babies.

New Zealand Trials		New Zealand recruits
PROTECT Me	Antenatal melatonin supplementation in fetal growth restriction for fetal neuroprotection	20
C*STEROID	Corticosteroids before planned caesarean section from 35^{+0} to 39^{+6} weeks of pregnancy	371
FIIX Trial	The Fertility, IVF and Intrauterine Insemination trial in couples with unexplained infertility	477
NeoGluco	Neonatal Glucose Care Optimisation Study (I)	66
PIPPA TAMARIKI	Paracetamol and Ibuprofen in Primary Prevention of Asthma	3248
PLUSS	Preventing Chronic Lung Disease in Extremely Preterm Infants Using Surfactant + Steroid	183
PROTECT	IV pentoxifylline as adjunct therapy to improve long-term disability in preterm infants	79

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
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
DIAMOND	Different Approaches to Moderate & later preterm Nutrition

Childhood Outcome Studies	
GEMS Follow up study	Gestational Diabetes Mellitus Trial of Diagnostic Detection Threshold
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