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

Welcome

Welcome to the November edition of ON TRACK News

Kia ora, this month in Update Your Practice, we look at the TOTAL Trials investigating prenatal surgery in fetuses with congenital diaphragmatic hernia. We also look at a Ministry of Health hosted social media campaign for COVID vaccination and pregnancy. Let us know if you have any feed-back or wish to share your maternal and perinatal clinical trials news.

LATEST NEWS

ON TRACK Network Trial Development Workshop 2022 POSTPONED

The 2022 ON TRACK Network Trial Development Workshop planned for February has been postponed.

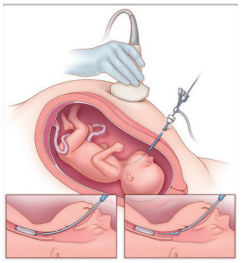
COVID has had significant impact on all areas of our lives including planning for future great clinical trials!

We remain committed to working with the investigators that submitted trial concepts and will deliver targeted workshops to meet their specific needs a little later in the year (likely to be April/May). We will let you know once the date and format have been confirmed. If the topic is of interest to you, you may well want to come along and contribute, as well as learn about trial development processes.

We also aim to host a forum to bring people together to plan how we can develop clinical trial ideas identified from the ON TRACK Network Research Prioritisation Project. More details to come in the new year.

IN THIS EDITION

Prophylactic antibiotics and incomplete abortion - We look at a recent systematic review **page 3**.



Update Your Practice - Does key-hole surgery on the fetus improve out-comes for pulmonary hypoplasia? **page 2**.

COVID vaccination and pregnancy - Find out about an 'Ask the experts' social media livestream on **page 4**.

Scan for the ON TRACK website

Update Your Practice: Tracheal Occlusion To Accelerate Lung growth (TOTAL Trials)

DOI: 10.1056/NEJMoa2027030; DOI: 10.1056/NEJMoa2026983

In this month's Update Your Practice, we look at two trials conducted in parallel to investigate percutaneous fetoscopic endoluminal tracheal occlusion (FETO) to treat pulmonary hypoplasia in the fetus. These trials involved many sites across a number of countries and would not have been possible without global collaboration as they focus on a highly specialised area of medicine.

Background Congenital diaphragmatic hernia (CDH) is a birth defect consisting of a hole in the diaphragm that affects approximately 1/2500 babies. Organs positioned below the diaphragm can ascend into the chest, compressing the developing lungs, leading to impaired lung development in the fetus. The condition can be diagnosed in the prenatal period and classified as severe, moderate, or mild, with expected postnatal survival of approximately 20%, 55%, and 85%, respectively. Perinatal death and morbidity are caused mainly by pulmonary hypoplasia and pulmonary hypertension.

A therapeutic approach to CDH is percutaneous FETO; keyhole surgery performed by a fetal medicine specialist where a small balloon is inserted into the windpipe of the fetus, just above where the lungs branch. The balloon is subsequently removed usually at around 34 weeks of pregnancy. Experimental data suggest the tracheal occlusion reduces pulmonary hypoplasia as trapped lung fluid stimulates stretch receptors and induces airway proliferation.

The TOTAL Trials were global multicentre, randomised, open-label, parallel-group clinical trials investigating FETO versus expectant management as a therapeutic intervention for complications of CDH in the fetus.

TOTAL Moderate: Women with a singleton pregnancy and fetus diagnosed with a moderate CDH assigned in a 1:1 ratio to FETO at 30-32 weeks of gestation or expectant care.

Recruitment: 12 FETO centres and 46 neonatal units globally. October 2008 to May 2019.

Primary outcomes: infant survival to discharge from a neonatal intensive care unit (NICU) and survival without oxygen supplementation at six months of age.

Findings: 62/98 (63%) infants in the FETO group and 49/98 (50%) in the expectant care group survived to discharge (relative risk, 1.27; 95% confidence interval [CI], 0.99 to 1.63; two-sided P=0.06).

At 6 months of age, 53/98 (54%) of infants in the FETO group and 43/98 (44%) in the expectant care group were alive without oxygen supplementation (relative risk, 1.23; 95% CI, 0.93 to 1.65).

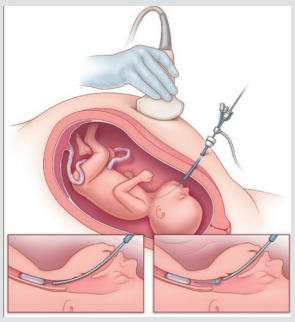
Preterm, pre-labour rupture of membranes was higher in the FETO group than in the expectant care group (44% vs. 12%; relative risk, 3.79; 95% CI, 2.13 to 6.91), as was the incidence of preterm birth (64% vs. 22%, respectively; relative risk, 2.86; 95% CI, 1.94 to 4.34).

TOTAL Severe: Women with a singleton pregnancy and fetus diagnosed with a severe CDH assigned in a 1:1 ratio to FETO at 27-29 weeks of gestation or expectant care.

Recruitment: 10 FETO centres and 26 neonatal units globally. February 2011 to March 2020.

Primary outcome: infant survival to discharge from the neonatal intensive care unit.

Findings: 16/40 (40%) infants in the FETO group and 6/40 (15%) in the expectant care group survived to discharge (relative risk, 2.67; 95% confidence interval [CI], 1.22 to 6.11; two-sided P=0.009). Survival to 6 months of age was identical to the survival to discharge (relative risk, 2.67; 95% CI, 1.22 to 6.11).



Preterm, pre-labour rupture of membranes was higher in the FETO group than in the expectant care group (47% vs. 11%; relative risk, 4.51; 95% CI, 1.83 to 11.9), as was the incidence of preterm birth (75% vs. 29%; relative risk, 2.59; 95% CI, 1.59 to 4.52).

Interpretation: There was no significant benefit regarding survival to discharge or the need for oxygen supplementation at six months of FETO performed at 30 to 32 weeks gestation over expectant care for fetuses with moderate pulmonary hypoplasia. However, FETO performed at 27 to 29 weeks of gestation for infants with severe pulmonary hypoplasia resulted in a significant benefit over expectant care regarding survival to discharge. This benefit was sustained at six months of age.

What do these results mean for New Zealand practice? FETO is a procedure producing significant benefit for the most severe CDH but it is also associated with risk. It should only be performed by highly skilled and trained fetal medicine specialists in centres with the appropriate facilities. The only Australasian hospital to have participated in the TOTAL trials was the Mater Hospital in Brisbane. The team there includes two fetal medicine specialists trained in FETO insertion and deflation, both of whom spent time overseas to develop their skill. It seems unlikely that New Zealand will have sufficient cases of CDH to justify the intense training required to gain sufficient skill to offer FETO as a service. However, New Zealand already has a relationship with the Mater Hospital for the antenatal surgical repair of myelomeningocele (open spina bifida) and so it may be possible that we will be able to offer FETO as an option for antenatal treatment of severe CDH in the future.

Prophylactic antibiotics for preventing genital tract infection in women undergoing surgical procedures for incomplete abortion doi/10.1111/1471-0528.16637

Incomplete abortion affects one-fifth of all pregnancies. Removal of retained tissues by surgical procedures such as curettage or vacuum aspiration is often necessary but poses the risk of genital tract infection (GTI) and as such prophylactic antibiotics are often administered. However, evidence as to the effectiveness of this practice is conflicting.

A Cochrane review published in 2012* including evidence from 19 randomised controlled trials (RCTs) concluded antibiotic prophylaxis is effective in preventing post-abortion GTI. However, the review combined placebo and non-placebo (active intervention) comparisons, making the effect of the antibiotic prophylaxis challenging to determine. Also, since its publication, nine new RCTs have been published. The authors of the Cochrane review also highlighted a gap in knowledge about the efficacy of antibiotic prophylaxis in women in low- and middle-income countries.

The current paper's authors conducted a systematic review and meta-analysis of up-to-date evidence on the effect of prophylactic antibiotics compared with placebo in women undergoing surgical procedures for incomplete abortion.

Sixteen thousand one hundred seventy-eight women who participated in 24 RCTs published between 1975 and 2019 were included. Pooled estimates showed the risk of GTI following surgical procedures after incomplete abortion was significantly lower among those who had prophylactic antibiotics (relative risk [RR] = 0.72; 95% CI 0.58–0.90; I2 = 49%). There was no significant effect of antibiotics in women in low- and middle-income countries (three studies, 3,579 participants, RR = 0.90; 95% CI 0.50–1.62; I2 = 63%), but it was clinically and statistically significant among women high-income countries (21 studies, 12 599 participants, RR = 0.67; 95% CI 0.53–0.84; I2 = 44%).

A **relative risk reduction of 33% was associated with prophylactic antibiotic use among women in high-income countries**, with the quality of evidence assessed to be high. The authors noted this has important implications for clinical practice, as current guidelines on the use of prophylactic antibiotics provide conflicting recommendations. **They concluded antibiotic prophylaxis is beneficial in reducing post-abortion GTI among women undergoing surgical procedures for incomplete abortion.** However, more studies are needed from low- and middle-income countries.

* doi: 10.1002/14651858.CD005217.pub2

COVID-19 and pregnancy: encouraging vaccination

As the delta variant of COVID-19 continues to spread, there is growing concern about the number of pregnant women not yet fully vaccinated against COVID-19 in Aotearoa New Zealand.

Risks of COVID-19 during pregnancy to both mother and baby are becoming more evident. We now know pregnant women who contract COVID-19 are more likely to be admitted to an intensive care unit. Their babies are five times more likely to be born premature and require admission to a neonatal intensive care unit (Ministry of Health NZ). Meanwhile, growing data supports the safety of the COVID-19 vaccine during pregnancy and its protection to babies in utero.

Key messages on the risks of COVID-19 during pregnancy and the protection offered by vaccination are being communicated via mainstream media, social media, and healthcare agencies, providers and practitioners. Despite this, the pregnant population remains very vulnerable to COVID-19, with the vaccination uptake being slow.

To support your discussions with pregnant women and their whānau concerning COVID-19 vaccination, there are several online resources with the New Zealand Ministry of Health, New Zealand College of Midwives, and RANZCOG all having dedicated COVID-19 pages on their respective websites.

One of the latest resources made available by the Ministry of Health is a recording of an 'Ask an expert' live stream that you can signpost women to. This was a social media live stream moderated by new mum and host of TV3's The Project, Kanoa Lloyd. **Experts from across Aotearoa New Zealand, joined Kanoa to discuss the importance and safety of vaccination during pregnancy. You can access the video to view and to share** on the Ministry of Health website and YouTube: https://youtu.be/xTdjudZzWHI

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	246
DIAMOND	DIfferent Approaches to MOderate & later preterm Nutrition	488
FIIX Trial	The Fertility, IVF and Intrauterine Insemination trial in couples with uneXplained infertility	351
NeoGluco	Neonatal Glucose Care Optimisation Study (I)	53
OBLIGE	Comparing two methods of starting an induction of labour in pregnant women (balloon at home versus hormone gel in hopsital)	1087
PIPPA	Paracetamol and Ibuprofen in Primary Prevention of Asthma	2612
PLUSS	Preventing Chronic Lund Disease in Extremely Preterm Infants Using Surfactant + Steroid	142
PROTECT	IV pentoxifylline as adjunct therapy to improve long-term disability in preterm infants	64
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 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 target for women with gestational diabetes: the randomised trial	

SAVE THE DATE

RANZCOG Symposium 2022 - *New Perspectives*
Melbourne 28 Feb-1 Mar 2022 Virtual/physical hybrid meeting
https://ranzcog.edu.au

PSANZ 2022 Annual Congress
Adelaide 15-18 May 2022 Physical meeting with digital pass available (although 'better together')
www.psanz2022.com.au