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| January 2019 Edition 28 | Neonatal | The ELFIN Trial: Enteral lactoferrin supplementation for very preterm infants: a randomised placebo-controlled trial https://doi.org/10.1016/S0140-6736(18)32221-9 | Enteral supplementation with bovine lactoferrin does not reduce the risk of late onset infection in very preterm infants. These data do not support its routine use to prevent late-onset infection and associated morbidity or mortality in very preterm infants. |
| February 2019 Edition 29 | Preterm birth | Association of Fetal Growth Restriction with Neurocognitive Function After Repeated Antenatal Betamethasone Treatment vs Placebo. Secondary Analysis of the ACTORDS Randomized Clinical Trial https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2723407 | Health care professionals should use up to three repeat doses of antenatal corticosteroids when there is ongoing risk of preterm birth, regardless of FGR, in view of the associated neonatal benefits and absence of later adverse effects |
| April 2019 Edition 31 | Miscarriage & preterm birth | Levothyroxine in women with thyroid peroxidase antibodies before conception https://www.nejm.org/doi/full/10.1056/NEJMoa1812537 | Given the size and generalisability of the TABLET trial, the results indicate thyroxine does not prevent adverse outcomes in euthyroid women with antibodies, and that thyroxine therefore should not be routinely prescribed to these women. |
| May 2019 Edition 32 | Obstetrics | Placental growth factor testing to assess women with suspected pre-eclampsia: a multicentre, pragmatic, stepped-wedge cluster-randomised controlled trial https://www.thelancet.com/action/showPdf?pii=S0140-6736%2818%2933212-4 | The results of this trial support the adoption of routine PIGF testing in women with suspected pre-eclampsia and the test is set to become widely available across the UK. We need to consider the applicability of this testing in the New Zealand context. It looks like a great test to 'rule in' and 'rule out' preeclampsia providing opportunity to target our resources (such as in-patient care) to those who will benefit most and reduce unnecessary interventions for those that won't (a bit like fetal fibronectin testing women symptomatic of preterm labour). |
| June 2019 Edition 33 | Obstetrics | Prophylactic antibiotics in the prevention of infection after operative vaginal delivery (ANODE): a multi-centre randomised controlled trial https://www.thelancet.com/action/showPdf?pii=S0140-6736%2819%2930773-1 | Given the importance of antibiotic stewardship where evidence of the benefit of antibiotic use has been lacking, current WHO and national guidelines explicitly state that routine antibiotic prophylaxis is not recommended for women undergoing operative vaginal birth. This is the case for New Zealand guidance for instrumental vaginal birth published by RANZCOG (current version March 2016). This guidance references a Cochrane Review published in 2004, which summarises that evidence to support antibiotic prophylaxis in this indication is lacking. Findings of the |

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| | | | ANODE trial have changed this and it is now time to reconsider our practice. |
| July 2019 Edition 34 | Neonatal | High-flow nasal cannulae Use in Non-Tertiary centres for Early Respiratory distress: The HUNTER Trial https://www.nejm.org/doi/full/10.1056/NEJMoa1812077 | What do these results mean for practice: The results suggest CPAP is superior to nasal high-flow therapy. However, there may be a role for nasal high-flow therapy dependent upon the circumstances of the patient. |
| August 2019 Edition 35 | Neonatal | Antimicrobial-impregnated central venous catheters for prevention of neonatal bloodstream infection. The PREVAIL Trial https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(19)30114-2/fulltext | These results mean antimicrobial-impregnated CVCs offer no benefit and so should not be used. The PREVAIL trial is the largest trial to date of this intervention for this population. The trial is of high methodological quality and power due to its coordinated approach with 18 units involved. Although no evidence of benefit was found, the trial has addressed the need for a large RCT. The results of this trial are important as they contradict findings for the same intervention in older children and adults, supporting standardised evidence-based care and informing future research for antimicrobial-impregnated CVC specifically in neonates |
| September 2019 Edition 36 | Obstetrics | Ursodeoxycholic acid versus placebo in women with intrahepatic cholestasis of pregnancy (PITCHES): a randomised controlled trial https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)31270-X/fulltext | PITCHES was five times larger than any previous trial of this intervention and nearly three times larger than all previous trials combined. An updated systematic review and metaanalysis, including PITCHES, conducted by the Cochrane Pregnancy and Childbirth Group (December 2018) found that UDCA does not reduce the incidence of stillbirth, spontaneous preterm birth, or neonatal unit admission. Ursodeoxycholic acid does not have any significant clinical benefit when used routinely for treatment of women with intrahepatic cholestasis of pregnancy. It is time to reconsider its use for this condition. |
| October 2019 Edition 37 | Obstetrics | Planned early delivery or expectant management for late preterm pre-eclampsia (PHOENIX): a randomised controlled trial https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)31963-4/fulltext | The PHOENIX trial with its sample size of 899 women is considerably larger than previous trials included in the Cochrane systematic review that considered the same gestational age window. Previous trial results have not led to significant clinical practice change as there was uncertainty over the trade-off between maternal benefit and perinatal |

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| | | | harm. Although the PHOENIX trial provides further evidence of maternal benefit with planned delivery the potential for neonatal harm of planned delivery has not been excluded. Hopefully the PHOENIX trial will be able to follow these offspring and explore late effects of planned earlier birth versus expectant management. |
| November 2019 Edition 38 | Preterm birth | Maternal intramuscular dexamethasone versus betamethasone before preterm birth (ASTEROID): a multicentre randomised controlled trial https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(19)30292-5/fulltext | The A*STEROID Trial is the first large trial to report on the comparative effects of dexamethasone and betamethasone on infant morbidity and mortality, long-term childhood health, and maternal outcomes. Survival free of neurosensory disability in children at age 2 years after in-utero exposure was similar for dexamethasone and betamethasone. Findings from the A*STEROID Trial provide reassurance that both dexamethasone and betamethasone have similar effects on neonatal health and neurodevelopmental outcome into early childhood. The A*STEROID findings support current guideline recommendations that either drug can be used for women at risk of preterm birth. The unexpected but potentially clinically important differences of reduced risk of caesarean birth and fewer children being hypertensive at two years of age when exposed to dexamethasone compared to betamethasone needs later assessment as to the impact and clinical relevance. Confirmation in different populations is warranted. |
| December 2019 Edition 39 | Neonatal | Association of umbilical cord milking versus delayed umbilical cord clamping with death or severe intraventricular haemorrhage among preterm infants https://jamanetwork.com/journals/jama/fullarticle/2755614 | Delayed cord clamping reduces mortality in preterm babies and should be the standard of care. This trial, despite its early termination, suggests umbilical cord milking in preterm infants is not beneficial, and may be harmful. A recent Cochrane Review has been undertaken but the numbers in the review were very small and there were many gaps in the data. Further studies of umbilical cord milking in preterm infants will be needed including longer term follow up in infants in this trial. In the meantime, umbilical cord milking should be avoided in preterm infants. |
| February 2020 Edition 40 | Obstetrics | Induction of labour at 41 weeks versus expectant management until 42 weeks (INDEX): multicentre, randomised non-inferiority trial | Results of these three trials should be interpreted with some caution because of their heterogeneity. We would expect that IOL will reduce the risk of stillbirth but this may be at the expense of other perinatal |

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| | | <p>https://www.bmj.com/content/364/bmj.l344</p> <p>Labor Induction versus Expectant Management in Low-Risk Nulliparous Women (ARRIVE)</p> <p>https://www.nejm.org/doi/10.1056/NEJMoa1800566</p> <p>Induction of labour at 41 weeks versus expectant management and induction of labour at 42 weeks (SWEdish Post-term Induction Study, SWEPIS): multicentre, open label, randomised, superiority trial</p> <p>https://www.bmj.com/content/367/bmj.l6131</p> | <p>morbidity or mortality, and maternal risk. However, none of these trials support that concept but rather other risks appear to be reduced. It therefore seems very reasonable and appropriate to consider IOL by 41 weeks although this should continue to be viewed within context weighing up expected benefits versus possible adverse effects for each mother and baby. It should be noted that in the SWEPIS trial all perinatal deaths occurred in nulliparous women, a finding also seen in other studies where stillbirths were more common in nulliparous than multiparous women. The care of nulliparous women may therefore require particular attention concerning timing of IOL. The numbers in these trials are large but substantially larger trials are needed here to evaluate differences in the context of our own healthcare environment. Future clinical trials could also focus on long term perinatal outcomes following post term IOL.</p> |
| March 2020 Edition 41 | Neonatal | <p>The HypoEXIT Trial: Hypoglycaemia Expectant Monitoring versus Intensive Treatment</p> <p>https://www.nejm.org/doi/full/10.1056/NEJMoa1905593</p> | <p>This is a potentially valuable study, but there are some important details to keep in mind. (1) Babies whose hypoglycaemia was severe (<1.9mmol/l) or early (<3 hours) were excluded, not all measurements were done using an accurate method, and the study was not blinded. (2) Not surprisingly, babies who were not treated until their glucose concentrations were <2.0mmol/l received fewer blood tests and less treatment, including less supplemental feeding and less intravenous glucose, than those treated at our current threshold of 2.6mmol/l, although breastfeeding was not affected. However, it is concerning that those treated at the lower threshold had more frequent, repeated and severe hypoglycaemia. This is important, because there is some evidence that repeated and severe hypoglycaemia is associated with worse developmental outcomes. (3) Neonatal hypoglycaemia does not affect Bayley motor or cognitive scores in pre-school children (doi: 10.1159/000492859) so the study finding that these scores are similar in babies treated at the lower threshold does not provide any reassurance that their more repeated and severe hypoglycaemia will not result in</p> |

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| | | | worse neurodevelopmental outcomes in the future. |
| June 2020 Edition 44 | Neonatal | The effect of lactoferrin supplementation on death or major morbidity in very low birthweight infants (LIFT): a multicentre, double-blind, randomised controlled trial https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(20)30093-6/fulltext | Although lactoferrin supplementation was not shown to reduce death or major morbidity in VLBW babies in LIFT, the meta-analysis did show a significant reduction in late-onset sepsis. Therefore, further research of the potential benefits of lactoferrin supplementation for reducing the risk of late onset sepsis in VLBW babies does warrant further research. Large, collaborative clinical trials will be needed to detect moderate and clinically important effects reliably and to investigate different doses of lactoferrin. |
| July 2020 Edition 45 | Obstetrics | MAVRIC: a multicentre randomised controlled trial of transabdominal versus transvaginal cervical cerclage https://www.ajog.org/article/S0002-9378(19)31206-2/fulltext | Transabdominal cervical cerclage (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 |
| August 2020 Edition 46 | Obstetrics/ midwifery | The ICARIS Trial. Caesarean delivery rates and analgesia effectiveness following injections of sterile water for back pain in labour: A multicentre, randomised placebo-controlled trial https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(20)30191-7/fulltext | Sterile water injections for lower back pain during labour are used in New Zealand, although not frequently. The ICARIS Trial has shown that although this intervention does not reduce the need for CS, it is a safe alternative analgesic. It seems a very valid option for use in units where regional anaesthesia is not available and for women who wish to avoid an epidural. |
| September 2020 Edition 47 | Neonatal | Effects of Liberal versus Restrictive Transfusion Thresholds on Survival and Neurocognitive Outcomes in Extremely Low-Birth-Weight Infants: | ETTNO Trial limitations included loss of follow up of 85 infants (8%), and death/BDP substantially lower than population data indicating sicker infants were not enrolled, which may have impacted outcomes. The trial |

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| | | <p>The ETTNO Randomised Clinical Trial https://pubmed.ncbi.nlm.nih.gov/32780138/</p> | <p>did not stratify infants according to gestational and chronological age and yet it is likely that neonatal haemodynamics are variable in these groups. There were transfusions given outside of protocol guidelines with a net result that the haematocrit difference between groups was only 3%. This was lower than that of the PINT study (5%) which did suggest improved neurodevelopmental outcome in the liberal group. However, the ETTNO trial was large and did study the most vulnerable preterm group and allowed low haematocrit values to be reached in the restrictive group. Although no evidence of benefit was found, there was no harm either and there was a median decrease of one transfusion per infant. The results of this trial support the need for future research to better inform standardised use of RBCT in the treatment of preterm infants. The large USA TOP study is in progress and results awaited. In the meantime, it appears we can be reasonably confident that the trend toward more restrictive transfusion criteria does not appear to be harmful.</p> |