

Midwifery RESEARCH REVIEW™

Making Education Easy

Issue 29 – 2022

In this issue:

- Impact of mobile app-based perinatal interventions on parents' well-being
- Teleclinics for the management of diabetes in pregnancy during COVID-19
- Effect of sleep duration on pregnancy and perinatal outcomes
- Impact of physical activity and sedentary behaviour before and during pregnancy
- PCOS and risk of adverse obstetric outcomes
- Long-term risk of type 2 diabetes in women with a history of GDM
- The impact of birth trauma witnessed by maternity health professionals
- Healthcare professionals' experiences with vulnerable families
- Association of GDM with cardiovascular and cerebrovascular disease
- Factors influencing appropriate use of interventions for preterm birth management

Abbreviations used in this issue

BMI = body mass index
COVID-19 = coronavirus disease 2019
GDM = gestational diabetes mellitus
HbA1c = glycated haemoglobin
LGA = large for gestational age
OGTT = oral glucose tolerance test
PCOS = polycystic ovary syndrome
PTSD = post-traumatic stress disorder
SGA = small for gestational age

Kia ora tātou and welcome to Midwifery Research Review.

In this issue, we focus on wellbeing in times of pandemic and look at some of the initiatives developed as a means of adapting healthcare delivery during unprecedented times of uncertainty. We also look at the impact of sleep duration on pregnancy outcomes, physical exercise and pregnancy wellbeing, how PCOS affects pregnancy and how to navigate these risks. We look at lifestyle and dietary interventions for preventing risk for type 2 diabetes mellitus after GDM, mitigating the experience of birth trauma and PTSD in health professionals, and what can be done to ensure vulnerable mothers and families can be supported into successful parenthood.

Ngā manaakitanga,

Rachel Taylor

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Effectiveness of mobile application-based perinatal interventions in improving parenting outcomes

Authors: Chua JYX & Shorey S

Summary: This systematic review examined the effects of app-based interventions on psychosocial well-being in parents during the perinatal period. A search of PubMed, Embase, CINAHL, PsycINFO, Web of Science, Scopus, and ProQuest Thesis and Dissertations identified 12 studies that were suitable for inclusion. Analysis of the data showed that mobile app-based interventions were feasible and had a positive impact on parents' overall well-being during the perinatal period.

Comment: Given the challenges of enforced isolation experienced during the COVID worldwide pandemic, alternative solutions for healthcare support and provision were a necessary adjustment for both healthcare providers and consumers alike. Furthermore, the increase in rates of depression amongst many groups, including new parents, meant that these alternative solutions also needed to be able to mitigate the stresses arising from social isolation and lack of face-to-face support groups. This study aimed to assess the efficacy of mobile phone apps during the COVID crisis in improving the psychosocial well-being of parents as well as parent-child bonding outcomes. While a relatively small number of studies (12) were included in the review, in general, mobile apps that included educational resources for perinatal and newborn care, support services from associated healthcare professionals and peer support options, were found to improve overall parental well-being and were cost effective and well accepted. Future research and funding for such alternatives is warranted and there has certainly been a rapid move towards integration of the virtual reality medium in education (including midwifery) following the sustained lockdowns experienced over the past few years. Longitudinal studies examining the longer-term benefits/ effects of virtual reality as a viable alternative are also required and should not replace the inherent value of social contact and interaction as an innately human condition.

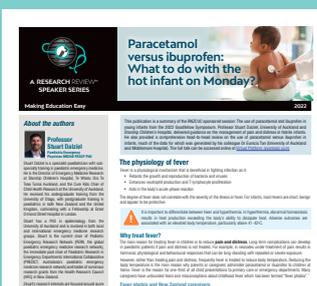
Reference: *Midwifery* 2022;114:103457

[Abstract](#)

GOODFELLOW SPEAKER SERIES: Paracetamol versus ibuprofen - What to do with the hot infant on Monday?

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Goodfellow Symposium paediatric
analgesia talk by Professor Stuart Dalziel

Professor Dalziel discussed the use of paracetamol and ibuprofen, delivering guidance on the management of pain and distress in febrile infants. He also provided a comprehensive head-to-head review on the use of paracetamol versus ibuprofen in infants.



Teleclinics for the management of diabetes in pregnancy during COVID-19 – maternal satisfaction and pregnancy outcomes

Authors: Shashikumar A et al.

Summary: During lockdown for COVID-19, the diabetes in pregnancy (DiP) service at Counties Manukau Health (CMH) switched from face-to-face appointments to teleclinics. This study examined the satisfaction of pregnant women with the teleclinics and compared clinical outcomes and attendance for those receiving care through teleclinics versus standard care. 35 women who attended a teleclinic completed a standardised questionnaire (37% response rate), and 89% of them scored the clinic highly for satisfaction and future use. No differences in clinical outcomes were seen between women who attended a teleclinic compared with those who attended an actual clinic in the previous year.

Comment: DiP rates are increasing exponentially in Aotearoa/NZ, particularly amongst Pacific, Indian and Māori women, for whom access to antenatal care is often inequitable and difficult to attend. During COVID-19 lockdowns in Auckland from 2020 on, the DiP service in CMH South Auckland had to cancel many face-to-face appointments and offer remote teleclinics as an option instead. This study aimed to assess the satisfaction of pregnant women with DiP attending remote teleclinic appointments and compare clinical outcomes and attendance rates alongside outcomes for those women who received standard face-to-face care in both pre-lockdown and lockdown conditions. Women attending teleclinics were asked to undertake a standardised questionnaire while a separate, retrospective study of clinical outcomes, and the number of appointments scheduled/attended were compared between all DiP patients who were scheduled an appointment during lockdown, as well as those who were scheduled appointments in the previous year. Although only 37% of participants who attended the teleclinics completed the survey, 89% scored the clinic highly for satisfaction and future use, meaning there is scope for further investigation into how this model could be better adapted to suit specific cultural and demographic needs as a viable alternative to face-to-face appointments, given the likelihood of future pandemics and the difficulties experienced by many women in accessing healthcare services, be it due to transportation issues or lack of services in particularly rural and poorer sectors. Additionally, space within our hospital services is at a premium, meaning teleclinics may need to become the default model of care in certain instances, so future insights of how remote services can be improved to reflect the needs of our most vulnerable populations are valuable.

Reference: NZ Med J 2022;135(1562):63-77

[Abstract](#)

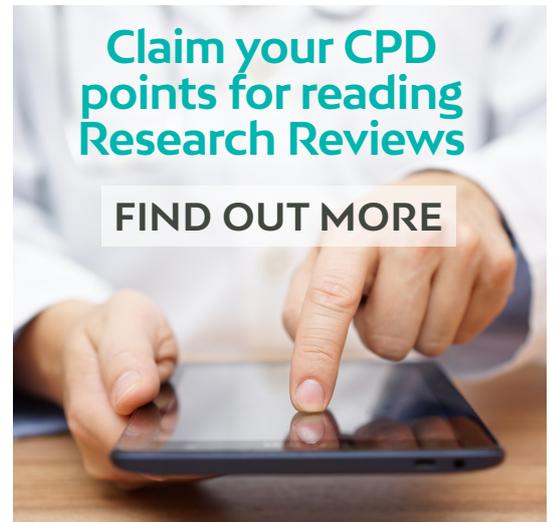
Independent commentary by Rachel Taylor



Rachel is currently employed as a Clinical Midwifery Coach at Waikato Women's Hospital and is embarking on her PhD journey with a focus interest on the relationship between poverty, environmental factors, and the incidence of preeclampsia in Aotearoa/New Zealand. Prior to rejoining the midwifery team at Waikato, Rachel was employed as a Senior Lecturer of Midwifery at Wintec in Hamilton. She has been Co-Director of NZ Action on Preeclampsia since 2019, working alongside her fabulous colleagues, Dr Joyce Cowan and Lou McInnes.

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Investigating causal relations between sleep duration and risks of adverse pregnancy and perinatal outcomes

Authors: Yang Q et al.

Summary: This study used Mendelian randomisation (MR) and multivariable regression to examine the effects of sleep duration on the risk of adverse pregnancy and perinatal outcomes. Data were analysed from various cohort studies: UK Biobank (n=176,897), FinnGen (n=123,579), Avon Longitudinal Study of Parents and Children (n=6826), Born in Bradford (n=2940) and Norwegian Mother, Father and Child Cohort Study (n=14,584). 78 previously identified genetic variants were used as instruments for sleep duration. Using UK Biobank data, MR showed that sleep duration at 30 weeks' gestation had nonlinear effects on stillbirth, perinatal depression and low offspring birthweight. Shorter and longer duration increased stillbirth and low offspring birthweight; shorter duration increased perinatal depression.

Comment: This Mendelian linear and nonlinear randomisation analysis of data from more than 300,000 parents and children sought to examine the relationship between sleep quality in pregnancy and risk for adverse outcomes including stillbirth, miscarriage, GDM, hypertensive disorders of pregnancy, perinatal depression, preterm birth and neonatal birthweight, specifically LGA or SGA. 78 previously identified genetic variants were used as instruments for determining maternal sleep quality and duration at 30 weeks' gestation. From the UK Biobank data (n=176,897), MR provided evidence of nonlinear effects of sleep duration on stillbirth, perinatal depression and low offspring birthweight. While shorter and longer sleep duration increased risk for stillbirth and SGA/intrauterine growth retardation, perinatal depression was associated with shorter duration alone. However, risks of all outcomes were higher in women reporting <5 and ≥10 h/day sleep when compared with those reporting 8–9 h/day. Nonlinear models fitted the data better than linear models for most outcomes, except for GDM. While larger studies with more cases are needed to detect potential nonlinear effects of sleep duration on hypertensive disorders of pregnancy, preterm birth and high offspring birthweight, this study is nonetheless significant in its findings of impact of sleep quality/duration in pregnancy and poor outcomes for both mothers and babies. While the study did not consider sleep positioning in pregnancy as a potential influence, 2019 research from the University of Auckland led by Professor Lesley McCowan and Dr Robin Cronin analysed more than 800 late pregnancy stillbirth cases, revealing a 2.5–6-fold increase in the risk of late stillbirth if women sleep on their backs from the third trimester of pregnancy (Cronin et al., 2019). Additionally, it would be interesting to align this with the effects of shift work and sleep interruption and adverse pregnancy outcomes, given known links between shift work and increases in serum cortisol and associated risk for hypertensive disorders, diabetes, placental malperfusion and depression.

Reference: *BMC Med* 2022;20:295

[Abstract](#)



**Te Tatau o te Whare Kahu
Midwifery Council**

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Approval number: 2021CME005E

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Research Review publications are intended for New Zealand health professionals.

Patterns of physical activity and sedentary behavior before and during pregnancy and cardiometabolic outcomes

Authors: Wallace MK et al.

Summary: This secondary analysis of 2 cohort studies investigated whether physical activity and sedentary behaviour before and during pregnancy are related to gestational weight gain, blood pressure, or blood glucose during pregnancy. 131 pregnant women aged 18–45 years self-reported physical activity and sedentary behaviour pre-pregnancy and in each trimester using validated questionnaires. Physical activity was lower in each trimester compared with pre-pregnancy, and sedentary behaviour was higher in each trimester. Multivariable regression analysis showed that higher pre-pregnancy physical activity was associated with higher systolic blood pressure (SBP) in the first trimester (p=0.02) and greater weight gain in the third trimester (p=0.02). Increasing sedentary behaviour was also associated with greater weight gain in the third trimester (p=0.03).

Comment: This analysis of 2 prospective cohort studies in 2 antenatal research centres in the US sought to assess how physical activity and sedentary behaviour may change from pre-pregnancy to pregnancy, and if pre-pregnancy and pregnancy physical activity and sedentary behaviour are related to outcomes such as gestational weight gain, hypertension and blood glucose levels across pregnancy. 131 pregnant women from 18–45 years of age, of any BMI but with no pre-existing medical conditions or medications were asked to self-report both physical activity and sedentary behaviour prior to pregnancy and during each trimester of pregnancy using validated questionnaires. Blood pressure and blood glucose readings and weights were obtained from participant clinic visits and/or via electronic medical records. Multivariable regression examined associations between pre-pregnancy, trimester-specific, and changes in physical activity and sedentary behaviour with weight gain and blood pressure outcomes in each trimester, and blood glucose in the second trimester only, in line with timing of the OGTT. Compared to pre-pregnancy, physical activity was lower in each subsequent trimester, and sedentary behaviour conversely higher. Furthermore, while increasing physical activity from pre-pregnancy levels was associated with lower first trimester SBP, unexpectedly, higher pre-pregnancy physical activity was associated with both higher SBP in the first trimester and higher weight gain in the third trimester. Higher and increasing sedentary behaviour was also associated with greater weight gain in the third trimester. However, the study did not comment on one of its primary aims, which was to evaluate blood glucose levels, specifically in the second trimester, although one could reasonably argue that the link between maternal obesity and risk for GDM is already well proven. There are undisputed benefits to the incorporation of moderate exercise in pregnancy but there is also known risk in over-exercise as well as links between low pre-pregnancy BMI and risk for SGA. Future studies within a NZ context would be beneficial to ascertain which kinds of exercise are best suited for pregnancy and when is the best time to implement these to enhance pregnancy outcomes and prevent risk for hypertension and excessive weight gain. Additionally, what impact did COVID isolation have on women being able to exercise during their pregnancies and, if so, did this have any bearing on pregnancy outcomes?

Reference: *Midwifery* 2022;114:103452

[Abstract](#)

10TH BIENNIAL
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Polycystic ovary syndrome and risk of adverse obstetric outcomes: A retrospective population-based matched cohort study in England

Authors: Subramanian A et al.

Summary: This population-based cohort study evaluated the risk of various obstetric outcomes in women with PCOS. 27,586 deliveries with maternal PCOS were matched for age to 110,344 deliveries without PCOS. Fully adjusted logistic regression models showed that maternal PCOS was associated with an increased risk of preterm birth (adjusted odds ratio [aOR] 1.11, 95% CI 1.06–1.17), emergency caesarean (aOR 1.10, 95% CI 1.05–1.15), elective caesarean (aOR 1.07, 95% CI 1.03–1.12) and instrumental vaginal delivery (aOR 1.04, 95% CI 1.00–1.09). However, maternal PCOS was not associated with low birthweight, high birthweight or stillbirth.

Comment: PCOS is the most common endocrine disorder among young women. While incidence is difficult to accurately determine due to previously high rates of misdiagnosis, the condition is reported to affect 5–10% of women of reproductive age. NZ studies report a similar proportion of women with PCOS although ultrasound findings of polycystic ovaries are considerably more common, being found in 21% of randomly selected NZ women (Farquhar et al., 2008). Long-term health risks for women with PCOS include GDM and type 2 diabetes mellitus, hypertension and cardiovascular disease, infertility, endometrial hyperplasia and cancer, while more recent studies have linked PCOS with obstructive sleep apnoea, irrespective of BMI. While obesity contributes to these risks, not all women with PCOS are obese and it is widely accepted that insulin resistance is largely responsible for many of the long-term health consequences. This particular study aimed to assess the risk of obstetric outcomes among a population-based representative cohort of women with PCOS compared to an age-matched cohort of women without PCOS. 27,586 births from mothers with PCOS were considered alongside 110,344 births in women without PCOS. Findings were then adjusted for age, ethnicity, deprivation, blood glucose disorders, hypertension, thyroid disorders, number of babies and pre-pregnancy BMI. Maternal PCOS was found to be associated with risk for preterm birth, emergency and elective caesarean as well as instrumental birth. For support with information regarding pregnancy and PCOS, the [Women's Health Action Group Aotearoa](#) has free, evidence-based information and links with the latest research to guide midwives caring for women with PCOS.

Reference: *BMC Med* 2022;20(1):298

[Abstract](#)

Modifiable risk factors and long term risk of type 2 diabetes among individuals with a history of gestational diabetes mellitus

Authors: Yang J et al.

Summary: This analysis of the Nurses' Health Study II investigated the impact of 5 modifiable risk factors (BMI, diet, exercise, alcohol consumption, and smoking) on long-term risk of type 2 diabetes mellitus (T2DM) in women with a history of GDM. 924 out of 4275 (21.6%) women with a history of GDM developed T2DM during a median 27.9 years of follow-up. Women who had optimal levels of all 5 modifiable risk factors had >90% lower risk of developing T2DM during follow up than women without optimal levels. Hazard ratios for T2DM in women with optimal levels of 1, 2, 3, 4 or 5 factors compared with none were 0.94 (95% CI 0.59–1.49), 0.61 (95% CI 0.38–0.96), 0.32 (95% CI 0.20–0.51), 0.15 (95% CI 0.09–0.26), and 0.08 (95% CI 0.03–0.23), respectively ($p_{\text{trend}} < 0.001$).

Comment: This study sought to evaluate both individual and combined associations of 5 modifiable risk factors with ensuing risk for T2DM among 4275 women with a history of GDM between 1991 and 2009. The study additionally aimed to assess whether these risks differed according to obesity and/or genetic predisposition to T2DM. Modifiable risk factors assessed included BMI, diet, exercise, smoking and alcohol consumption. Genetic susceptibility for type 2 diabetes was characterised by a genetic risk score based on 59 single nucleotide polymorphisms associated with T2DM in a subset of 1372 participants. Of the participants, 924 or 21.6% of women went on to develop T2DM. Compared with women who had a high BMI (overweight or obese), a poor diet, sedentary lifestyle and smoked and/or consumed alcohol in pregnancy, those who had optimal levels of all 5 factors had a greater than 90% lower risk of developing T2DM. Furthermore, even those women with genetic predisposition for T2DM were incrementally less likely to develop the disorder if all 5 modifiable factors were optimised, meaning lifestyle and dietary factors were more important than having a normal BMI alone. This study shows how good nutrition, moderate exercise, and avoidance of recreational drugs in pregnancy can balance out obesity and genetic associations with later-onset diabetes. Education and health initiatives such as removing regressive taxation on healthy foods and ensuring equitable access to high quality pregnancy and midwifery care should therefore be prioritised.

Reference: *BMJ* 2022;378:e070312

[Abstract](#)

The perceived impact of birth trauma witnessed by maternity health professionals

Authors: Uddin N et al.

Summary: This systematic review investigated the impact of birth trauma on maternity health professionals. A search of CINAHL, MEDLINE, PsychARTICLES, PsychINFO and PsychTESTS databases identified 18 studies involving a total of 8630 midwives, nurses and obstetricians that were suitable for inclusion. Between 45% and 96.9% of the maternity health professionals had witnessed a traumatic birth event. The prevalence of secondary traumatic stress (STS) ranged from 12.6–38.7% and the prevalence of PTSD ranged from 3.1–46%. The maternity health professionals reported both positive and negative effects associated with witnessing traumatic birth events.

Comment: Midwives and maternity care providers caring for women may often witness or be involved in traumatic birthing outcomes and the risk of this will no doubt increase in direct correlation to unprecedented workforce shortages and the rising tide of women unable to engage with antenatal care in Aotearoa. This can be associated with ongoing vicarious trauma/STS and PTSD, which may impact carers both emotionally and physically. The aims of this review were therefore to determine the prevalence of STS and PTSD in maternity health professionals, and the impact of witnessing birth trauma on maternity health professionals. A mixed-methods systematic review was carried out by conducting literature searches on CINAHL, MEDLINE, PsychARTICLES, PsychINFO and PsychTESTS databases. A total of 18 studies were included in the review and participants included midwives, maternity nurses and obstetricians aged 18–77 years. 45–96.9% of them had witnessed a traumatic birth event, while 12.6–38.7% cited ongoing STS or vicarious trauma, and 3.1–46% met criteria for diagnosis of PTSD. Being involved with a traumatic birth event has profound and multi-layered emotional and physical responses as well as long-term impacts for maternity care providers. Grief and stress impact directly on their confidence to continue providing care while team and peer support was identified as essential to recovery. Implementation of initiatives such as perinatal bereavement education, team building and support interventions such as Employee Assistance Programme (EAP) counselling, alongside supportive leadership structures are key in providing not only immediate assistance but also in mitigating the long-term effects of sustained trauma. If you or a colleague have borne witness to a traumatic birth event, please do not hesitate to reach out to your professional body and counselling services through EAP and via your local region.

Reference: *Midwifery* 2022;114:103460

[Abstract](#)



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Engaging in partnerships is the key to preserving and creating a trustful collaboration with vulnerable families

Authors: Ejertsen C et al.

Summary: This qualitative study evaluated healthcare professionals' experiences of vulnerable families and their extended stay in the obstetric department at a university hospital in Denmark, and described the collaboration between primary and secondary healthcare sectors for postnatal care. 16 health professionals from an obstetric department and primary healthcare sectors participated in focus group interviews in Feb 2019. The overall finding was that engaging in partnership across sectors and with families can improve postnatal care for vulnerable families.

Comment: Maternal vulnerability, teen pregnancy, poverty and socioeconomic deprivation represent massive challenges to parenthood and remain a critical task for midwives and other health professionals working alongside these women in both the antenatal and postnatal settings. Being born to a vulnerable mother additionally carries risk for long-term childhood behavioural and psychosocial development, including impaired cognitive development, antisocial behaviours and mental health disorders which may continue into adulthood, bearing significant risk for inequity in all facets of life, from employment to the ability to conduct meaningful and rewarding interpersonal relationships with others. This qualitative inductive descriptive design study with focus group participation was conducted at a university hospital in Denmark and sought to explore the perspectives of healthcare professionals caring for vulnerable families during pregnancy and postnatally, to identify potential barriers and challenges as well as introduce opportunities to improve outcomes. The study also aimed to describe the healthcare professionals' experience of vulnerable families and assess the success of primary and secondary collaboration during the postnatal period. 16 health professionals from the hospital's obstetric department and primary healthcare sectors participated in focus group interviews. The overall theme of the study determined that engaging collaboratively across the primary-secondary-tertiary interface was key in improving postnatal care and outcomes for vulnerable families. Given the increase in socioeconomic deprivation and housing crisis in Aotearoa since the onset of COVID, this theme is even more pronounced. It is vital that our new health entity Te Whatu Ora places priority on working alongside vulnerable families and whānau and equips the healthcare and maternity sectors with the resources, funding and staff so desperately required.

Reference: *Midwifery* 2022;114:103440
[Abstract](#)

Association of gestational diabetes mellitus with overall and type specific cardiovascular and cerebrovascular diseases

Authors: Xie W et al.

Summary: This systematic review and meta-analysis quantified the risk of cardiovascular and cerebrovascular diseases and venous thromboembolism (VTE) in women with a history of GDM. A search of PubMed, Embase, and the Cochrane Library identified 15 studies involving 513,324 women with GDM (and >8 million women without GDM) that were suitable for inclusion. Meta-analysis of the data showed that, compared with women without GDM, women with a history of GDM were at increased risk for incident coronary artery disease (risk ratio [RR] 1.40, 95% CI 1.18–1.65), myocardial infarction (RR 1.74, 95% CI 1.37–2.20), heart failure (RR 1.62, 95% CI 1.29–2.05), angina pectoris (RR 2.27, 95% CI 1.79–2.87), cardiovascular procedures (RR 1.87, 95% CI 1.34–2.62), stroke (RR 1.45, 95% CI 1.29–1.63), ischaemic stroke (RR 1.49, 95% CI 1.29–1.71), and VTE (RR 1.28, 95% CI 1.13–1.46).

Comment: This systematic review and meta-analysis of 15 observational studies reporting on the association between GDM and cardiovascular and cerebrovascular diseases found that, compared with women without GDM, women with GDM had a 45% increased risk for both cardiovascular and cerebrovascular diseases, including myocardial infarction, heart failure, and stroke. Risk for VTE was 28% higher in women with GDM and overall risk could be aligned with factors such as socioeconomic deprivation, smoking, obesity, and other pre-existing comorbidities. Since the introduction of the booking HbA1c as part of our first trimester screening recommendations, detection of GDM has increased in Aotearoa, meaning options for dietary, lifestyle and pharmaceutical interventions and optimal pregnancy management can be introduced in a timely manner and enhance outcomes for both mother and baby, both in the immediate postnatal period and for their future and longer term health.

Reference: *BMJ* 2022;378:e070244
[Abstract](#)

Factors influencing appropriate use of interventions for management of women experiencing preterm birth

Authors: Zahroh RI et al.

Summary: This systematic review evaluated factors affecting the appropriate use of 4 interventions (antenatal corticosteroids, tocolytics, magnesium sulphate, and antibiotics) to improve preterm birth management. A search of MEDLINE, EMBASE, CINAHL, Global Health, and grey literature identified 46 studies from 32 countries that described factors affecting use of antenatal corticosteroids (32 studies), tocolytics (13 studies), magnesium sulphate (9 studies), and antibiotics (5 studies). Barriers to use of the interventions included inaccurate gestational age assessment, inconsistent guidelines, varied knowledge, perceived risks and benefits, confusion around prescribing and administering authority, inadequate stock, inadequate human resources, and inadequate labour and newborn care.

Comment: Globally, preterm birth-related complications are a leading cause of death in neonates and children under the age of 5. And while health outcomes of preterm babies can be dramatically improved with appropriate use of antenatal corticosteroids to promote fetal lung maturity, tocolytics to delay birth, magnesium sulphate for fetal neuroprotection, and antibiotics for preterm pre-labour rupture of membranes, there is inconsistency nationally in Aotearoa in the application of these interventions, which may mean variance in health outcomes for these babies. This mixed-methods systematic review of 46 primary studies from 32 countries across multiple research databases aimed to assess both barriers and facilitators affecting the appropriate use of antenatal corticosteroids, tocolytics, magnesium sulphate, and antibiotics to improve preterm birth management. Barriers to the appropriate use of these 4 interventions included inconsistencies in guidelines and varied knowledge levels amongst practitioners, perceived risks and benefits of the interventions, confusion around prescribing and administering authority, and supply and staffing shortages impacting directly on maternity services ability to provide labour and newborn cares. Women also reported hesitancy in accepting interventions, especially if only learning about them during emergencies. Most of the included studies were from high-income countries (37/46 studies), which may affect the transferability of the findings to low- or middle-income settings. This study's findings highlight the importance of implementing sound and evidence-based national guidelines for the management of preterm birth and labour, to avoid inconsistencies and inequity of outcomes for more vulnerable and at-risk populations. It also reinforces that policy makers need to focus on addressing barriers to inequity and place immediate emphasis on funding maternity services appropriately, which includes staffing. A research project currently underway, *Taonga Tuku Iho: Knowledge Translation for Equity in Preterm Birth Care and Outcomes in Aotearoa*, aims to address these concerns within a NZ context by developing a national guideline for the prevention and management of preterm labour and birth. The guideline is expected to be available within the next few months (following panel review) and we look forward to its findings and recommendations.

Reference: *PLoS Med* 2022;19(8):e1004074
[Abstract](#)

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