THE UNIVERSITY OF SYDNEY

Reproduction and Perinatal Centre

Report 2021-2023

Message from the Centre Director

I am pleased to present a report of the activity of the Reproduction and Perinatal Centre (RPC), coinciding with our formal launch on the 28th of August 2023. It celebrates many of the achievements of the Centre between 2021 and 2023 whilst establishing a strong foundation for ongoing and future endeavors. The RPC builds on the vision of my predecessor Professor Brian Trudinger recognising the continuum that exists in the determinants of optimal outcomes of fertility, reproduction and pregnancy, and acknowledging the critical importance of optimal preconception health for best pregnancy and long-term maternal and child health outcomes. Bringing this vision to life whilst appreciating the enormity of expertise and interest within Sydney Medical School (SMS) and Faculty of Medicine and Health (FMH) provides a once in a lifetime opportunity to establish a Centre that is responsive to the many limitations that exist in the understanding of current determinants of adverse fertility and pregnancy outcomes.

RPC is focused on two vertical streams in Reproduction, Endocrinology and Infertility (REI) and Maternal Fetal Medicine (MFM). It brings together expertise and key researchers from all three precincts of the University of Sydney with cross cutting domains in Population Health, Discovery Science, Research Translation and Global Health. Clinical nodes of interest include preconception health, cardiometabolic disease, fetal growth and perinatal outcomes, and birth. Moving forward we will develop nodes in perinatal mental health and infectious diseases recognising the immediate need to address current challenges in reproductive and perinatal health.

This report is only a sample of the outstanding work of our principal investigators, the 38 reported projects and 260 publications between 2021 and 2023 is a testament of this. We have forged ahead with unparalleled support, guidance and governance from the RPC executive team and leadership from SMS, FMH and the Office of the DVCR. To all for which there are many, I thank you.

There have been other key achievements. In 2023, Sydney Health Partners (SHP) a leading advanced research translational centre in New South Wales established a Clinical Academic Group (CAG) in Reproduction, Maternal and Newborn Health. This provides a real conduit to rapidly translate and capacity build creating meaningful changes to clinical practice and policy. Together with my co-lead Professor Adrienne Gordon and the leadership of the CAG we are grateful to SHP for the opportunity that this presents. RPC is focused on developing interdisciplinary futures research leaders and I am pleased that our first PhD midwifery student Sarah Melov will submit her thesis this year. This cements the links between RPC and Western Sydney LHD bringing real change to outcomes for the population of Western Sydney and beyond. Further SMS key academic appointments to clinical schools such as Nepean provides opportunity for collaborative and impactful research programs. In RPC we look forward to the recent appointment of our lead in REI.

Looking to the future we will continue to develop collaborative research programs with other established research centres such as Sydney Infectious Disease Institute, Sydney Vietnam Institute and Westmead Applied Research Centre. These links together with existing and emerging collaborations with global NGO agencies such as PMNCH, UNDP and WHO Vietnam, and FIGO provides the real opportunity for influencing better outcomes for mother and child globally.

Thank you again to all within the Centre for your tireless commitment, my predecessor Professor Brian Trudinger for his vision and the leadership of FMH and SMS, Professors Robyn Ward and Cheryl Jones and their teams for their ongoing support. I look forward to our launch and the year ahead.

Dharmintra Pasupathy
Director, Reproduction and Perinatal Centre
Professor of Maternal Fetal Medicine, Westmead Clinical School

Contents

RPC Executive

Professor Dharmintra Pasupathy
Director Reproduction and Perinatal Centre

Professor Tim Usherwood
Emeritus Professor of General Practice

Professor Nadia Badawi, AM
Macquarie Group Foundation Professor and Chair of Cerebral Palsy

Professor Kirsten Black
Professor of Obstetrics, Gynaecology and Neonatology

Professor Ng Wah Cheung
Director Department of Diabetes and Endocrinology, Westmead Hospital

Professor Adrienne Gordon
Senior Staff Specialist Neonatologist, Royal Prince Alfred Hospital

Professor Richard Lindley
Deputy Head of School, Sydney Medical School

Professor Natasha Nassar
Financial Markets Foundation for Children Chair in Translational Childhood Medicine

Associate Professor Tanya Nippita
Associate Professor of Obstetrics, Gynaecology and Neonatology

Dr Justin McNab
Senior Lecturer, School of Health Sciences

Ms Sarah Melov
CMC in Midwifery Research, Westmead Hospital

RPC Team

Principal Investigators

Professor Kirsten Black

Professor Black completed her PhD from the London School of Hygiene and Tropical Medicine examining access to emergency contraception in South London. She undertook sub-speciality training in sexual and reproductive health and is one of few Australians who hold a Fellowship of the Faculty of Sexual and Reproductive Healthcare, RCOG. She is CI on a NHMRC Centre for Research Excellence for Women Reproductive Health in Primary Care that focuses on improving access to contraception and abortion, an associate editor of BMJ Sexual and Reproductive Health, chair of RANZCOG's Sexual and Reproductive Health Committee and member of RANZCOG's Women's Health Committee.

Professor Ng Wah Cheung

Professor Cheung is the Director of Diabetes & Endocrinology at Westmead Hospital. He has previously served as President of the Australian Diabetes Society, a board member of Diabetes Australia, a council member of the Australasian Diabetes in Pregnancy Society, and as a member of the editorial board of Diabetes Care. He is currently co-chair of the NSW Endocrine Network. His research relates to diabetes in pregnancy, covering gestational diabetes, type 1 and type 2 diabetes in pregnancy, and post-pregnancy care of women with gestational diabetes to prevent the future development of diabetes.

Associate Professor Brad de Vries

Associate Professor de Vries is Head of Obstetrics at Royal Prince Alfred Hospital, NHMRC Future Fellow at the Clinical Trials Centre, the University of Sydney and a management group member for the Sydney Institute for Women, Children and their Families. He completed a Master of Medicine in Clinical Epidemiology and three research degrees including a PhD thesis on the prediction and prevention of caesarean section. He is experienced in the design and conduct of clinical observational studies and randomised controlled trials and has a special interest in caring for women in labour.

Professor Adrienne Gordon

Professor Gordon is a Neonatologist at RPA Centre for Newborn Care and Clinical Professor of Neonatology. She is passionate about the public health impact of a healthy start to life and preventing adverse pregnancy outcome especially stillbirth. She leads the PreBabe Trial which aims to determine whether weight loss prior to pregnancy for women with overweight or obesity can improve pregnancy and newborn outcomes. She is CI on the NHMRC Stillbirth Centre of Research Excellence and President-elect of Perinatal Society of Australia and New Zealand. She has strong links with National parent led organisations - including Stillbirth and Preterm Birth Advocacy Groups both and is Deputy Chair of the National RedNose scientific advisory group.

Dr Justin McNab

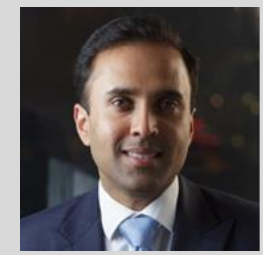
Dr McNab is an experienced researcher and teacher, now a Senior Lecturer in the Discipline of Behavioural and Social Sciences in Health, School of Health Sciences. Dr McNab is a generalist social scientist, implementation scientist and qualitative specialist. His research experience has involved working on large- and small-scale evaluation and implementation science projects across a wide range of health issues and contexts including reproductive, maternal and newborn health but previously encompassing aged care/older people, integration and coordination of services for people with multiple chronic illnesses, also working with diverse and marginalised population.

Emeritus Professor Jonathan Morris, AM

Professor Morris is a Professor of Obstetrics and Gynaecology, University of Sydney and a Senior Maternal Fetal Medicine Subspecialist at Royal North Shore Hospital. He was awarded the Award of the Member of the Order of Australia (AM, 2013) recognising his service to maternal and infant health as a clinician, educator, patient advocate and researcher. He is currently working with NSW Clinical Excellence Commission, implementing MatIQ, a user-friendly platform for clinicians and hospitals to visualise near real-time maternal and newborn outcomes and safety data across NSW.

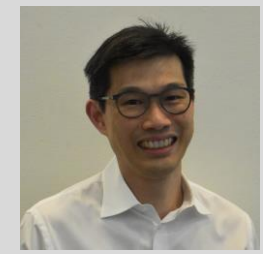
Associate Professor Tanya Nippita

Associate Professor Nippita is a Senior Staff Specialist Obstetrician and Gynaecologist, Head of Obstetrics at Royal North Shore Hospital, Board member of the Perinatal Society of Australia and New Zealand, and Sydney Health Partner representative of the National Women's Health Research Translation Network. Her research interests include variations in obstetric interventions, obstetric decision-making, improving care for women with gestational diabetes, evaluation of NSW Health policy and a particular focus in implementation research.



Professor Dharmintra Pasupathy

Professor Pasupathy is the Inaugural Director of the Reproduction and Perinatal Centre. He is also Professor of Maternal Fetal Medicine and Co-lead of the Specialty of Obstetrics, Gynaecology and Neonatology. Prior to 2020 he was Reader and Consultant in Maternal Fetal Medicine at Guy's and St Thomas' Hospital, King's College London and the first obstetric lead of the National Maternity and Perinatal Audit, the largest maternity quality improvement program in the UK. He is a Perinatal Epidemiologist with a keen interest in improved characterization of pregnancy risk and contribution of health services on perinatal risk. He is the co-lead of the Clinical Academic Group of Reproduction, Maternal and Newborn Health, Sydney Health Partners.



Associate Professor Sean Seeho

Associate Professor Seeho is lead of specialty of Obstetrics, Gynaecology and Neonatology. His research interests focus on improving maternal and infant health. He is a member of the NHMRC Centre of Research Excellence in Stillbirth's executive and steering committees and co-chairs of its education committee. He is the current chair of Stillbirth Foundation Australia. A/Prof Seeho is an associate editor of the Australian and New Zealand Journal of Obstetrics and Gynaecology. He is a member of the Asthma in Pregnancy Toolkit reference group.

Associate Professor Siranda Torvaldsen

Associate Professor Torvaldsen is a well-established public health researcher, is passionate about epidemiology and has three post-graduate epidemiology qualifications, including the Master of Applied Epidemiology. She has over 28 years' epidemiology experience, loves teaching/supervising students and ECRs, and has taught in many epidemiology and biostatistics courses. Previous positions include Epidemiologist in the COVID-19 Public Health Response Branch (NSW Health), Senior Lecturer and DrPH Program Director (UNSW), Research Fellow and NHMRC Postdoctoral Fellow (University of Sydney) and epidemiologist (National Centre for Immunisation Research and Surveillance).

Professor Karen Walker

Professor Walker is a Neonatal Clinical Nurse Consultant at Royal Prince Alfred Hospital. She is the President of the Council of International Neonatal Nurses, past president of the Australian College of Neonatal Nurses and co-founder of the Alliance of Global Neonatal Nurses. She is the Vice Chair of the Knowledge and Evidence Working Group, for the WHO Partnership for Maternal Newborn and Adolescent health (PMNCH), where she co-leads the Maternal, Newborn and Child Health stream. She represents neonatal nursing on many global committees and has both national and international research collaborations. She is also a committee member of the international parent organisation, the Global Alliance for Newborn Care (GLANCE).

Early and Mid-Career Researchers

Jackson Harrison
Ibinabo Ibiebele
Sharon McCracken
Shrujna Patel
Jillian Patterson
Deborah Randall

Higher Degree by Research Students

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Edwina Dorney
Vanessa El-Archi
Amelia Fernandes
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Farah Hashmani
Yusif Jakub
Kelly McNamara
Sarah Melov
Abigail Mulundano
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Preconception Health

Project 1: Optimisation of Healthy Conception Tool

Principal Investigators: Professor Kirsten Black
Co-Investigators: Dorney E, Your Fertility, Robinson Research Institute
RPC Research Stream: Translational Health
Funding Support: Australian Government Department of Health
Progress: In progress

Lay Summary

Preconception care aims to optimise the physical and psychological health of women prior to conception. This project evaluated an existing online preconception health self-assessment tool, The Healthy Conception Tool, developed by Your Fertility, a Commonwealth funded fertility health promotion program. We undertook a range of studies to understand the consumer experience of using this online tool to improve its use and application.

Scientific Summary

This project evaluated an existing online preconception health self-assessment tool, The Healthy Conception Tool, developed by Your Fertility, a Commonwealth funded fertility health promotion program. We undertook a range of studies to understand the consumer experience of using this online tool to improve its use and application.

As an online tool, the Healthy Conception tool has the potential to improve the health of targeted populations that experience health inequities, such as those from rural and remote backgrounds and can be further tailored to other priority populations.

In this project we set out to optimise the health conception tool. We conducted in depth qualitative interviews, user experience testing and discrete choice experiments (DCE) to gain a detailed understanding of women's perceptions about the usefulness of the tool and ways to improve its acceptability, engagement and impact. Based on the findings, the tool was revised and optimised and will be then disseminated nationally through the extensive networks developed through the NHMRC Centre of Research Excellence in Women's Sexual and Reproductive Health in Primary Care (SPHERE), and through a health promotion campaign with Your Fertility.

Progress

We are finalising the optimisation of the tool and have developed a preconception health video to assist with raising awareness of preconception health in general and of the tool specifically.

Output

Updated healthy conception tool, a preconception health video.

Project 2: Pre-pregnancy predictors of hypertensive disorders in pregnancy and adverse obstetric outcomes: a retrospective review of risk factors including Indigenous status

Principal Investigators: Dr T Karmakar V, Sarah J Melov, Associate Professor Vincent Lee
Co-Investigators: Elhindi J, Alahakoon TI, Sinka V
RPC Research Stream: Population Health
Progress: In progress

Lay Summary

Aboriginal and Torres Strait Islander health is of national concern. Improving pregnancy care relies on accurate health information. This project aims to work with key local Aboriginal and Torres Strait Islander groups to work towards improving our understanding of our local Aboriginal and Torres Strait Islander population pregnancy care needs and to achieve a goal

for ‘’Closing the Gap” by working towards improving health outcomes for Aboriginal babies and mothers.

In previous research high blood pressure concerns in pregnancy has been identified as impacting Aboriginal and Torres Strait Islander communities disproportionately but has not been assessed in our health district. High blood pressure concerns including a condition known as preeclampsia, is the reason for around 10% of maternal deaths in Australia. Developing high blood pressure concerns in pregnancy has also been linked to poor long-term outcomes for mothers and babies.

In this research historical pregnancy and birth information relating to births that occurred in the Western Sydney Local Health District (WSLHD) from 1 January 2007 to 31 December 2021 will be assessed to see if there is a relationship between known risk factors for high blood pressure concerns in pregnancy and poor outcomes for mothers or babies. This will help us determine how often high blood pressure concerns occur in pregnancies in WSLHD, if being of Aboriginal and Torres Strait Islander background is a risk factor for developing blood pressure concerns in pregnancy and will also help us compare the pregnancy outcomes of Aboriginal and Torres Strait Islander and non-Aboriginal and Torres Strait Islander women. The researchers will be using the results of this research to co-design with local Aboriginal and Torres Strait Islander maternity care groups and WSLHD Aboriginal health unit to identify areas to improve maternity care and further research.

Scientific Summary

Hypertensive disorder is a leading cause of maternal mortality. Of the hypertensive disorders in pregnancy, pre-eclampsia is one of the most common multisystem disorders of pregnancy characterised by new onset hypertension after 20 weeks of gestation, marked by with or without proteinuria, maternal organ dysfunction or uteroplacental dysfunction and remains a principal cause of maternal and fetal mortality and morbidity. There is also evidence that preeclampsia predisposes women to long term consequences, e.g. chronic kidney disease and cardiovascular disorders, chronic hypertension and neurological complications. Consequently, there are more adverse fetal outcomes compared to normotensive mothers, including an increased risk of preterm birth (PTB), intrauterine growth restriction (IUGR), low birth weight associated with neonatal unit admission and increased future cardiovascular risk.

There have been a few studies in Australia to identify the risk factors of hypertensive disorders in pregnancy among Aboriginal women and therefore, this project will help to calculate the incidence and the risk factors within WSHLD between January 1st 2007–Dec 31st, 2019. The data will compare the results among Aboriginal and non-Aboriginal women and will show us the gap between these two groups. Hence, this project will focus on if Aboriginal status plays an independent role or not.

The objectives of this study are to:

- Determine incidence and risk factors of hypertensive disorders in pregnancies of women in Western Sydney Local Health District.
- Determine if Aboriginal and Torres Strait Islander (First Nation) status is an independent risk factor for preeclampsia.
- Determine the outcomes of pregnancies including congenital anomalies in Aboriginal and Torres Strait Island women and compare these to the background population.

The study will enhance our knowledge base about risk of hypertensive disorders in pregnancy and will demonstrate various risk factors and their prevalence among Aboriginal and non-Aboriginal women. The researchers will be using the results of this research to co-design with local Aboriginal and Torres Strait Islander maternity care groups to identify areas to improve maternity care and further research.

Progress

Key Aboriginal and Torres Strait Island stakeholders have been engaged including the Aboriginal Senior Advisory Leadership Team for Western Sydney Local Health District. We have completed the Aboriginal Health Impact statement and subsequently the gained WSLHD

HREC approval, AHMRC Aboriginal HREC approval. As of March 2023, all data has been collected and analysis in progress.

Project 3: Identification of at-risk groups for low use of folic acid in early pregnancy among a high-migrant population

Principal Investigators: Sarah J Melov
Co-Investigators: Tang H, Elhindi J, Blumenthal C, Pasupathy D
RPC Research Stream: Population Health
Progress: In progress

Lay Summary

Inadequate folic acid (FA) supplementation before conception and in the first few weeks of pregnancy is associated with poor pregnancy outcomes including congenital anomalies in babies, in particular neural tube defects such as spina bifida. The evidence on the importance of FA to the health outcomes of babies is so strong that many governments worldwide have implemented programs to ensure a basic level of FA is in our everyday diet through breads-making flour FA supplementation. In addition, governments support health messaging on the importance of taking FA when planning pregnancy. However, there is little data on actual use of FA in those planning pregnancy in Australia.

International research has found that low use of FA supplements has been related to unplanned pregnancies, low education, low socioeconomic background, recent migration, and being of a non-Caucasian background. Because our local health district has a high migrant population who may not receive the English language public heath messaging, we were concerned that there may be many women who are not taking FA as recommended in our health district.

Our research therefore looked at whether the supplementation of FA pre-pregnancy or early pregnancy is different in the population born in Australia versus the population born overseas. We also hoped to identify factors that were related to low use of FA in pregnancy.

Scientific Summary

Maternal nutrition during the periconceptional period and early pregnancy has a significant impact on fetal development with poor maternal nutrition associated with negative consequences including congenital anomalies. One of the most common types of congenital anomalies is neural tube defects (NTDs) occurring between the third and fourth weeks after conception, with studies showing that NTDs can be prevented with adequate maternal intake of the B vitamin folate. It can be difficult to obtain the recommended amount of naturally occurring folate through food sources alone and the recommendation is for anyone planning pregnancy to take a FA supplement.

Despite the importance of FA supplementation for pregnancy, there remains a wide variation in the health messaging by healthcare providers and inconsistent patient uptake of prenatal FA, whether as a standalone supplement or as part of a multivitamin containing FA. Internationally, low FA supplementation rates have been associated with unplanned pregnancies, low socio-economic background, low education status, recent migration, and ethnicity, particularly being of a non-Caucasian background.

The applicability of international findings to the Australian population is important to establish as nearly 30% of Australia's population is born overseas. Australia's migrant profile is also different from that of other countries. Our research therefore aimed to examine the use of FA supplements among a high-migrant population in Australia that potentially has not received adequate public health messages regarding the importance of FA in pregnancy.

We analysed data routinely collected as part of the first antenatal visit of a pregnancy on women who booked for their pregnancy between 1st January 2018 to 31st July 2022 within WSLHD and whose pregnancies lasted ≥20 weeks gestation. There were 48,158 women who met inclusion

criteria over the study period. Overall, 18,927 women (39.4%) reported no FA supplements at the booking visit.

Results showed that the odds of women born overseas taking FA supplements were 24% higher than women born in Australia. Women were less likely to be taking FA as parity increased, and as maternal age decreased. Diabetes is an independent risk factor for NTDs. It was therefore reassuring to observe that women with pre-existing type 1 or type 2 diabetes were more likely to be taking FA as compared to the women who do not have pre-existing diabetes. Interestingly, the planning of pregnancy was not significantly related to FA supplementation behaviour.

Progress
Results were presented at the 2023 Perinatal Society of Australia and New Zealand (PSANZ) Annual Congress. The manuscript is in draft for planned publication.

Output
Presentations:

- Tang H, Elhindi J, Blumenthal C, Pasupathy D, Melov SJ. Identification of at-risk groups for low use of folic acid in early pregnancy among a high-migrant population. PSANZ 2023 Annual Congress, March 2023.

Impact
Discussions have begun with the NSW Ministry of Health, Centre of Population Health Medical Advisor to have available the research findings to support a program being planned to better target messaging on the importance of FA to at-risk groups.

Project 4: Implementation of the London Measure of unplanned pregnancy

Principal Investigators: Professor Kirsten Black
Co-Investigators: Dorney E, Cheney K, Pelosi M
RPC Research Stream: Translational Health
Progress: Complete

Lay Summary
The London Measure of Unplanned Pregnancy measures how well pregnancies are planned.

Scientific Summary
The London Measure of Unplanned Pregnancy (LMUP) is a psychometrically validated measure of the degree of intention of a current or recent pregnancy that captures behaviour around the time of conception. It has been validated in a range of settings and can be used to evaluate family planning or preconception care programs. In the Sydney Local Health District, we introduced the LMUP scale into the maternity booking visit. We employed univariable and multivariable analyses to examine the first 13 months of data on the LMUP extracted from the electronic maternity database in relation to selected maternal demographic and obstetric variables. The LMUP was completed in 2385 women and 70.6% (1684) had a planned pregnancy on the scale. No preconception health actions prior to pregnancy were taken by over half of the sample. Older women were more likely to plan their pregnancies, particularly those in their 30s compared to younger women. Women in the highest socio-economic quintiles were one and a half times more likely to plan their pregnancies compared to those in the lowest. As parity increased, pregnancy planning reduced. Those presenting for their fifth or more birth were far less likely to report the pregnancy as planned compared to nulliparous women.

Output
Planned presentation to international midwifery congress, RANZCOG ASM.

Impact
Manuscript in preparation for publication.

Cardiometabolic Health in Pregnancy

Project 1: The association of previous pregnancy breastfeeding and subsequent pregnancy glucose tolerance

Principal Investigators: Sarah J Melov, Professor Dharmintra Pasupathy
Co-Investigators: Elhindi J, White L, McNab J, Lee V, Donnolley K, Alahakoon TI, Padmanaban S, Cheung NW
RPC Research Stream: Translational Health
Funding Support: Westmead Hospital Charitable Trust Nursing and Midwifery Higher Degree Grant
Progress: In progress

Lay Summary

The length of time a woman breastfeeds for and how often a woman breastfeeds, known as the "intensity" of breastfeeding, has previously been shown to reduce a woman's risk for a wide range of health conditions. In Western Sydney Local Health District (WSLHD), we introduced a measure called the Breastfeeding Length Intensity Scoring System (BLISS) which helps to routinely assess breastfeeding duration and intensity for a woman's previous breastfeeding experience. The BLISS check also provides an opportunity to identify women who have had a history of breastfeeding difficulties and provide breastfeeding support. The high BLISS score reflects optimal intensity breastfeeding.

Previous pilot research undertaken by the investigators of this research, has shown that increased length and intensity of breastfeeding in women who have previously developed diabetes in pregnancy (GDM) is linked to potentially lower diabetes risk in the next pregnancy. However, it is not known what the impact of increased length and intensity of breastfeeding has on the general maternity population.

Using information on women who booked to birth at hospitals within WSLHD over the period March 2019 to October 2022, we set out to identify what factors were associated with optimal breastfeeding and if optimal breastfeeding improved blood sugar levels in the next pregnancy.

We found that:

- Women who migrated to Australia were more likely to breastfeed for over 6 months, but the longer the time the women had resided in Australia, the less likely that was to occur.
- There were six factors linked to both breastfeeding for less than 6 months and lower intensity of breastfeeding they included were having a baby before 37 weeks, smoking and having a history of mental health issues.
- Higher intensity of breastfeeding reduced the chance of an abnormal fasting blood sugar level in a later pregnancy. Duration of breastfeeding did not influence blood sugar levels detected at the GDM test in later pregnancies.

The study confirms that breastfeeding intensely after a birth has positive impacts on a woman's subsequent pregnancies.

Scientific Summary

High intensity breastfeeding (HIBF), and total lifetime duration of breastfeeding (BF) can improve future cardiometabolic risk profile. In a pilot study we have demonstrated that HIBF as measured by BLISS score in women with previous GDM was associated with subsequent pregnancy lower mean oral glucose tolerance test (OGTT). Its association in an unselected population is unknown.

The aim of this study was therefore to:

- Identify factors associated with HIBF/greater length of BF.
- Determine the association between BF intensity (BLISS)/length of BF and:
    - Diagnosis of GDM in subsequent pregnancy.

- OGTT fasting, 1-hour, 2-hour result in a subsequent pregnancy.

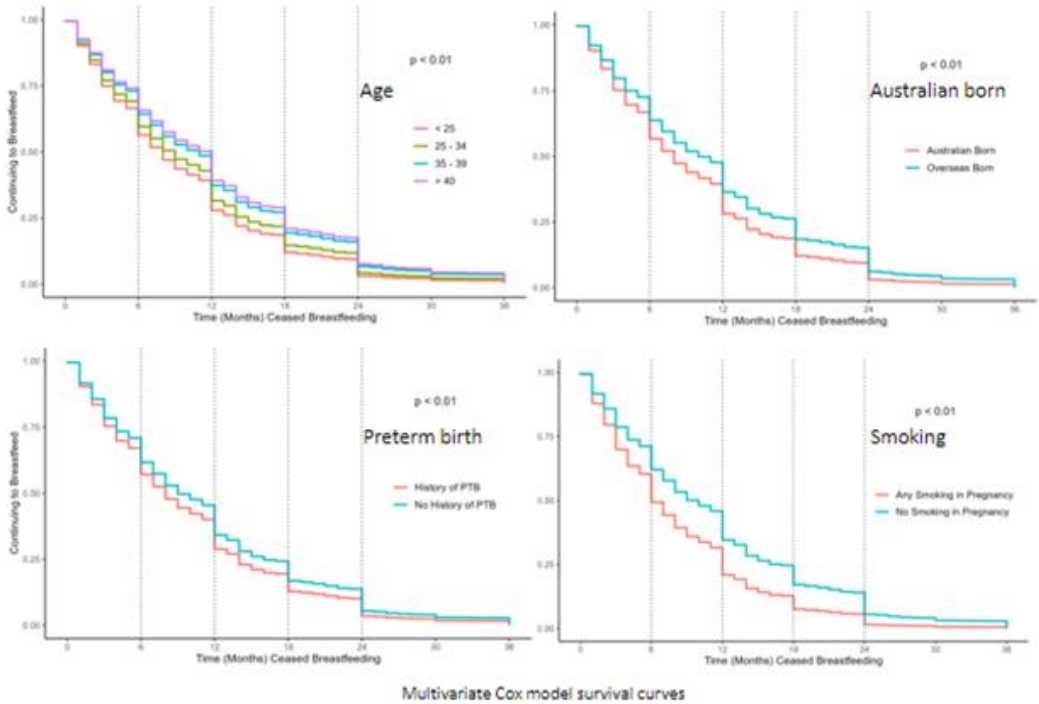
This was a retrospective cohort study of routinely collected data from multiparous women booked at WSLHD Hospitals, NSW over the study period of 1 March 2020 – 31 October 2022. Participants were included if their OGTT result was available, and if they had singleton current and previous pregnancies. We excluded women who had a history of Type 1 or 2 diabetes. Intensity of breastfeeding was measured by the Breastfeeding Length Intensity Scoring System (BLISS). HIBF is a BLISS score of 19-25/25 reflecting optimal first three months postpartum breastfeeding. Analysis was stratified by high risk for GDM defined as per ADIPS criteria. Multivariate logistic models were adjusted for statistically and clinically relevant covariates.

We found that:

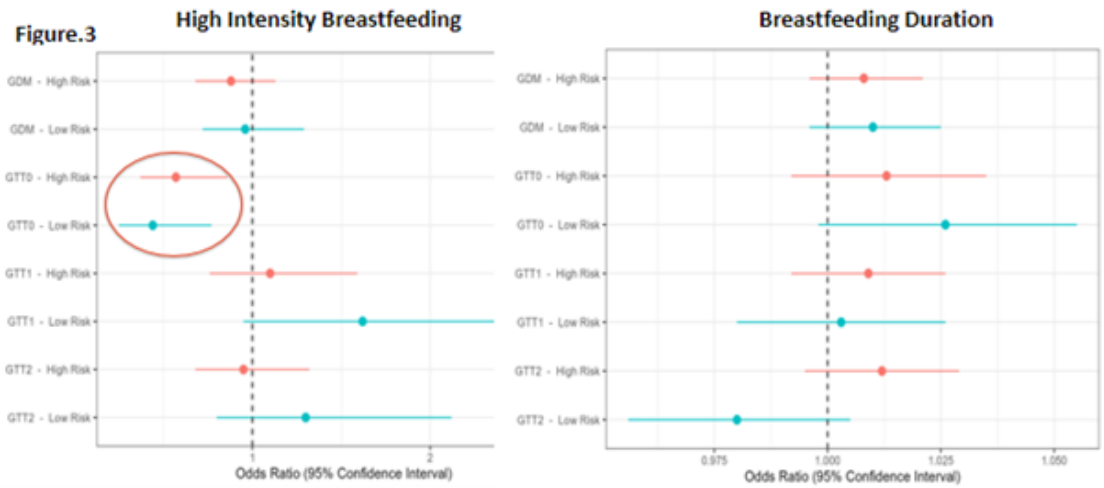
- In the cohort of 5,374 participants 18.3% (n=981) were diagnosed with GDM (IADPSG).
- There were 75.8% (n=4,074) of women who had a history of HIBF.
- HIBF reduced the risk of an abnormal fasting OGTT in a subsequent pregnancy (aOR 0.53; 95% CI 0.38-0.73). No influence was observed with BF duration on other OGTT parameters or GDM diagnosis.
- Women who migrated to Australia were more likely to breastfeed for over 6 months, but the longer the time the women had resided in Australia, the less likely that was to occur.
- Women who self-identified as Middle Eastern ethnicity had no influence on HIBF but they were less likely to breastfeed after 6 months (aOR 0.79, 95% CI 0.66-0.94).
- Characteristics associated with both BF less than the recommended 6 months and BF at a lower intensity were caesarean section birth, preterm birth, Aboriginal/Torres Strait Islander ethnicity, smoking, BMI ≥30, and a history of mental health issues.
- Differences in duration of BF were observed for different groups (Figure 1).

Protecting, promoting and supporting breastfeeding is important for all women but this novel study identifies the importance of mostly or exclusively BF to improve metabolic response in a subsequent pregnancy.

Figure: Survival curves predicting postpartum duration of breastfeeding



Multivariate Cox model survival curves



Progress

- Manuscript in preparation.

Output

Awards:

- Melov SJ. New Investigator Award. PSANZ: Perinatal Society of Australia and New Zealand 2023.

Presentations:

- Melov SJ, White L, Elhindi J, McNab J, Lee V, Donnolley K, Alahakoon TI, Padmanaban S, Cheung NW, Pasupathy D. The Association of Previous Pregnancy High Intensity Breastfeeding and Subsequent Pregnancy Glucose Tolerance. PSANZ: Perinatal Society of Australia and New Zealand 2023.
- Melov SJ, White L, Elhindi J, McNab J, Lee V, Donnolley K, Alahakoon TI, Padmanaban S, Cheung W, Pasupathy D; The Association of Previous Pregnancy High Intensity Breastfeeding and Subsequent Pregnancy Glycaemic Control. Hunter Valley NSW ACM 2023.

Project 2: Antenatal corticosteroids for women with gestational diabetes

Principal Investigators: Ibinabo Ibiebele
Co-Investigators: Glastras S, Randall D, Weir T, Gallimore F, Morris JM, Nippita T
RPC Research Stream: Population Health
Funding Support: NHMRC Ideas Grant (GNT1186572)
Progress: In progress

Lay Summary

Research studies show that antenatal corticosteroids are effective in reducing breathing problems in newborn babies who are born premature up to 34 weeks gestation. But there are few studies that have examined what happens to the mother and baby when the mother has diabetes and antenatal corticosteroids are given slightly later in pregnancy from 35 weeks gestation. This study used de-identified hospital records to follow up women who gave birth at 35 weeks gestation or later at a large public hospital in Sydney between September 2016 and March 2021. Based on whether they had diabetes or received antenatal steroids, they were grouped as: 1) had diabetes and received steroids, 2) had diabetes and did not receive steroids, and 3) did not have diabetes and did not receive steroids. There were no differences in

outcomes for mothers and their babies between women who had diabetes and received steroids compared to women who had diabetes and did not receive steroids. Women who had diabetes and received steroids were more likely to have their babies admitted to special care nursery or intensive care, and their babies were more likely to have low blood sugars compared to women who received steroids but did not have diabetes. The study results show little benefit of antenatal corticosteroids and suggests that clinicians may need to reconsider giving corticosteroids during the late preterm gestations.

Scientific Summary

Studies have shown that antenatal corticosteroids confer benefit if administered prior to birth in preterm uncomplicated pregnancies up to 34 weeks gestation. Women with diabetes are often excluded from such studies and few studies have assessed maternal and neonatal outcomes among women with diabetes who receive antenatal corticosteroids prior to a late preterm birth. The aim of this study was to determine whether antenatal corticosteroids are associated with adverse maternal and neonatal outcomes among women with diabetes who birthed at 35^{+0} weeks gestation or more.

This cohort study included women who gave birth at $\geq 35^{+0}$ weeks in a tertiary public hospital in Sydney, New South Wales between September 2016 and March 2021. Women were assigned to the following groups: 1) had diabetes and received steroids, 2) had diabetes and did not receive steroids, and 3) did not have diabetes and received steroids. Routinely collected de-identified sociodemographic, medical, obstetric and birth data from the eMaternity clinical database were used. Adjusted relative risks (aRR) for maternal and neonatal outcomes were estimated using Modified Poisson regression with robust error variances.

The study population included 5,067 women [Group 1 = 205, Group 2 = 4,028, Group 3 = 834]. Regardless of diabetes status, women who received corticosteroids were more likely to have hypertension, multiple births, receive hospital-based medical care and give birth by caesarean section. No differences were found in maternal and neonatal outcomes for women who had diabetes and received steroids compared to those who had diabetes and did not receive steroids. Infants born to women with diabetes who received corticosteroids had higher risk of neonatal hypoglycaemia (aRR 1.61, 95% CI 1.28-2.02) and a higher risk of admission to special care nursery or neonatal intensive care (aRR 1.18, 95% CI 1.02-1.38) compared to infants born to women without diabetes who received corticosteroids.

These results indicate that there is limited benefit of antenatal corticosteroid use in late preterm gestations and highlights the need to reconsider its use. Also, further investigation into the potential longer-term harms is needed.

Progress

A manuscript is in preparation for publication.

Output

Presentations:

- Ibiebele I, Glastras S, Randall D, Weir T, Gallimore F, Morris JM, Nippita TA. Should we give antenatal corticosteroids to women with diabetes prior to late preterm delivery? Perinatal Society of Australia and New Zealand (PSANZ) 2023 Annual Congress.

Project 3: Geographic variation in burden of Gestational Diabetes Mellitus in NSW

Principal Investigators: Deborah Randall, Associate Professor Tanya Nippita
Co-Investigators: Ibiebele I, Glastras S, Weir T, Torvaldsen S, Gallimore F, Morris J
RPC Research Stream: Population Health
Funding Support: NHMRC Ideas Grant
Progress: In progress

Lay Summary

The incidence of gestational diabetes mellitus (GDM) in Australia has tripled in the last 20 years. Consequently, over 40,000 pregnancies are now diagnosed as 'higher risk' each year in Australia. Research has shown that neighbourhood of residence can influence prevalence of chronic disease, including diabetes, through shared social, environmental and healthcare access factors. Our study aims to determine if there is variation in incidence of gestational diabetes by area of residence in New South Wales (NSW), Australia, and investigate what person- and area-level factors may contribute to the variation. We are planning to do this through examining rates of gestational diabetes by geographic area in NSW, and determining which factors, such as the average age of the mothers or the socio-economic status of the area, can help 'explain' the higher or lower rates.

Scientific Summary

The incidence of gestational diabetes mellitus (GDM) in Australia has tripled in the last 20 years. Consequently, over 40,000 pregnancies are now diagnosed as 'higher risk' each year in Australia. Research has shown that neighbourhood of residence can influence prevalence of chronic disease, including diabetes, through shared social, environmental and healthcare access factors. Our study aims to quantify the variation in incidence of gestational diabetes by area of residence in New South Wales (NSW), Australia, and investigate what characteristics of the pregnancy and of the area are associated with this variation.

Our study includes data for all pregnancies in NSW from 2016-2020, including antenatal information, birth factors and outcomes, and hospital admissions. Each birth has been geocoded to a statistical local area 2 (SA2), a standard geographic unit used by the Australian Bureau of Statistics to represent a community that interacts together socially and economically, and ranges from 3,000 to 25,000 people. The study uses multilevel modelling of pregnancies within areas to assess geographic variation in gestational diabetes, and then includes pregnancy- and area-level factors in the model to determine the association of these factors with the incidence of gestational diabetes. Pregnancy and person-level factors include age of mother at the birth, body mass index, and ethnicity/country of birth, while area-level factors include area socio-economic status, rurality, and health care accessibility.

Outputs of the study will include interactive maps showing areas in NSW with high and low incidence of gestational diabetes, as well as caterpillar plots that will rank areas by incidence. The multilevel modelling analysis will quantify how much of the variation in gestational diabetes incidence can be attributed to the area that a person lives, and how much is attributed to pregnancy and personal characteristics, providing direction for where to target programs and resources to reduce the incidence of gestational diabetes in NSW.

Progress

The SUGARED data has been linked and most of the data has been provided to the research team. The main perinatal, hospital, emergency and deaths data has been cleaned. An analysis dataset has been prepared and initial multilevel models of gestational diabetes incidence have been run.

Project 4: Hospital variation in management and outcomes for Gestational Diabetes Mellitus in NSW

Principal Investigators: Deborah Randall, Associate Professor Tanya Nippita
Co-Investigators: Ibiebele I, Glastras S, Weir T, Torvaldsen S, Gallimore F, Morris J
RPC Research Stream: Population Health
Funding Support: NHMRC Ideas Grant
Progress: In progress

Lay Summary

The incidence of gestational diabetes mellitus (GDM) in Australia has tripled in the last 20 years. Consequently, over 40,000 pregnancies are now diagnosed as 'higher risk' each year in Australia. Through the use of population-level data on all pregnancies in NSW Australia from 2016 to 2020, our study aims to examine variation in management of pregnancies with gestational diabetes by hospital, and variation in birth outcomes for these same pregnancies. By linking obstetric management, such as planning births earlier than 40 weeks' gestation, with outcomes, we will be able to determine which practices are associated with better or worse outcomes, and whether there is unwarranted variation in management that could be contributing to low value care.

Scientific Summary

GDM incidence in Australia has tripled from 5.2% in 2000–01 to 16.1% in 2017–18, partly due to changes in maternal age, obesity and ethnicity, but mostly due to altered diagnostic criteria identifying a greater proportion of women with GDM. Over 40,000 pregnancies are now classified annually as 'higher risk' in Australia, increasing antenatal surveillance, and obstetric intervention, often in the form of delivery earlier than 39 weeks gestation. Though some women with severe or poorly controlled GDM have higher perinatal risks, many women require minor lifestyle changes, if any, and have very good perinatal outcomes. There is a great deal of variation in treatment and management of gestational diabetes across different clinical teams/hospitals in NSW, such as varying adoption of early diagnosis guidelines and diagnostic criteria, varying glycaemic targets and medication thresholds, and differences in obstetric management practices. Using modelling, we will aim to determine how much variation there is in birthing practices and outcomes for pregnancies with gestational diabetes, and how obstetric management decisions impact on outcomes.

Multilevel modelling takes the hierarchical structure of patients within hospitals into account, quantifying the degree that outcome variation is due to patient characteristics or hospitals. To make meaningful comparisons between hospitals, we will adjust for different levels of risk in pregnant women in each hospital using information from the routine datasets (e.g., maternal and pregnancy characteristics). Then, unexplained hospital variation in obstetric management and outcomes of pregnancies with GDM will be identified and quantified with the variance partitioning coefficient and, for logistic regression models, the median odds ratio. The multilevel analyses with single outcomes will be extended to multivariate multilevel models to test association between obstetric management practices, such as early planned births, and health outcomes.

Progress

The SUGARED data has been linked and most of the data has been provided to the research team. The main perinatal, hospital, emergency and deaths data has been cleaned. An analysis dataset has been prepared, ready for the analysis to commence.

Project 5: Exploring the Relationship between Metabolic Dysfunction-Associated Fatty Liver Disease and Gestational Diabetes Mellitus

Principal Investigators: Dr TY Chai, Professor NW Cheung
Co-Investigators: George J, Pasupathy D
RPC Research Stream: Discovery Science, Translational Health
Funding Support: Diabetes Australia Research Program Grant 2021
Progress: Completed

Lay Summary

Gestational diabetes mellitus (GDM) affects about 15% of pregnant women in Australia and is associated with adverse pregnancy outcomes as well as a high risk of type 2 diabetes in the long-term. Metabolic dysfunction-associated fatty liver disease (MAFLD, formerly known as non-alcoholic fatty liver disease) is also a common disorder affecting some 5.5 million Australians. MAFLD is a potential precursor to liver cirrhosis, and in itself is also associated with adverse pregnancy outcomes.

There have been limited studies examining the relationship between GDM and MAFLD in pregnancy, though it is known that a relationship possibly exists. Our study has further explored the relationship between MAFLD and GDM and determined the significance of a finding of MAFLD being more prevalent in women with GDM and that MAFLD identified in early-to-mid pregnancy is associated with the development of GDM. Our study also examined the biochemical markers of insulin resistance and inflammation in both MAFLD and GDM to help further facilitate our understanding of the likely common pathophysiology of the 2 conditions. We found that pregnant women with MAFLD and GDM were more insulin resistant. In the end, our study has provided further information to be utilized in clinical care, particularly in terms of risk stratification of GDM during pregnancy, as well as the need for more intensive lifestyle management both during and after pregnancy to prevent cardiometabolic complications, such as type 2 diabetes, from happening.

Scientific Summary

The three main aims of our study were to:

- To determine the prevalence of MAFLD in a cross–sectional multiethnic cohort of pregnant women with GDM.
- To determine the clinical value of detecting MAFLD during pregnancy in women at risk of GDM.
- To whether serum biomarkers differ between pregnant women with both MAFLD & GDM compared to those without either (Control group) and those with MAFLD or GDM alone.

The study was conducted from the multiethnic antenatal clinic at Westmead Hospital between March 2019 to September 2021. A cross-sectional study was firstly performed to determine the prevalence of MAFLD in pregnant women with GDM. A single FibroScan® assessment was performed between 24 – 32 weeks of gestation in a cross-sectional population of GDM-only women. Study participants were asked to fast for at least 2.5 hrs prior to the scan. The controlled attenuation parameter, or CAP, was used to quantify hepatic steatosis, with a cut-off score greater than or equal to 233.5dB/m signifying the presence of MAFLD. Out of a total of 352 women included in the study, based on FibroScan® assessment, 38% had MAFLD, with 21% having mild steatosis, 13% had moderate steatosis and 5% had severe steatosis, as based on CAP scores.

A prospective longitudinal cohort study was used to determine whether the detection of MAFLD via FibroScan® in early–to–mid pregnancy is associated with the development GDM and also determining whether serum biomarkers differed in pregnant women without, with both or one of either MAFLD and GDM. Out of a total of 328 women, based on FibroScan® assessment, around 41.2% had MAFLD whilst 26.4% were diagnosed with GDM. A higher rate of GDM were identified in those women with MAFLD compared to those without (36.3% vs. 19.7%, p<0.01).

A stepwise increase in GDM risk occurred with higher MAFLD severity, even after adjustment for age, ethnicity, body mass index, prior history of GDM and family history of diabetes (adjusted odds ratio (OR) for moderate–to–severe hepatic steatosis 3.43, 95% CI 1.58–7.46, p<0.01).

From our prospective longitudinal study, 120 women had fasting blood collected between 24-28 weeks' gestation to determine serum levels of tumour necrosis factor alpha (TNF-α), interleukin 6 (IL-6), fibroblast growth factor 21 (FGF-21), high molecular weight adiponectin (HMW-APN), glucose and insulin. HOMA-IR was calculated with the following equation: (fasting glucose x fasting insulin)/22.5. Four groups of *Control* (no GDM/MAFLD), *MAFLD only*, *GDM only*, *MAFLD & GDM* were formed. Biomarkers were analysed by general linear models after log transformation, adjusted for maternal risk factors of age, body mass index, ethnicity and nulliparity. Of 120 women, 47 were *Control*, 37 *MAFLD only*, 14 *GDM only* and 22 *MAFLD & GDM*. Compared to the *Control* group, *MAFLD & GDM* women had 1.8–fold higher HOMA-IR (95% CI 1.44-2.56; p<0.01); *GDM only* women had 1.3-fold higher HOMA-IR (95% CI 1.05-1.71; p=0.02) and *MAFLD only* women had 1.3-fold higher HOMA-IR (95% CI 1.09-1.62; p<0.01). Only *MAFLD & GDM* women had significantly elevated IL–6 levels when compared to those in *Control* (1.8-fold higher; 95% CI 1.04-3.10; p=0.04), although when using MAFLD only or GDM only as the reference group, no significant differences in IL–6 levels occurred in women from the *MAFLD & GDM* group in comparison to either the *MAFLD only* or *GDM only* groups in the adjusted models. No significant differences in TNF–α, FGF–21 or HMW–APN occurred between groups. Significantly elevated HOMA-IR levels in pregnant women with MAFLD & GDM suggests a more insulin resistant phenotype.

Output

Presentations:

- Chai TY, Byth K, George J, Pasupathy D and Cheung NW. Elevated HOMA-IR and IL-6 in pregnant women with metabolic dysfunction–associated fatty liver disease and gestational diabetes mellitus.
  American Diabetes Association 83rd Scientific Sessions, San Diego, USA, Jun 2023.
- Chai TY, Deng D, George J, Pasupathy D and Cheung NW. The prevalence of metabolic dysfunction– associated fatty liver disease and its association with adverse pregnancy outcomes in women with gestational diabetes mellitus.
  Australasian Diabetes Congress, Virtual, Aug 2021.
- Chai TY, Deng D, Byth K, George J, Pasupathy D and Cheung NW. Metabolic dysfunction–associated fatty liver disease detected via FibroScan® in early–to–mid pregnancy is associated with the development of gestational diabetes mellitus. Australasian Diabetes Congress, Brisbane, Aug 2022.
- Chai TY, Deng D, Byth K, George J, Pasupathy D and Cheung NW. Serial FibroScan® Controlled Attenuation Parameter (CAP) scores were improved in pregnant women treated for gestational diabetes mellitus.
  International Association of the Diabetes and Pregnancy Study Groups Meeting, Sydney, Nov 2022.

Publications:

- Chai TY, Byth K, George J, Pasupathy D, Cheung NW. Elevated Hepatic Steatosis Index is Associated with the Development of Adverse Maternal, but Not Adverse Neonatal, Outcomes: A Retrospective Cohort Study. Int J Womens Health. 2023 Apr 13;15:589-598.
- Chai TY, Deng D, Byth K, George J, Pasupathy D, Cheung NW. The prevalence of metabolic dysfunction-associated fatty liver disease and its association on adverse pregnancy outcomes in women with gestational diabetes mellitus. Diabetes Res Clin Pract. 2022 Sep;191:110038.
- Chai TYL, Rajaratnam RM, Deng D, George J, Pasupathy D, Cheung NW. The prevalence of gestational diabetes mellitus in women diagnosed with non-alcoholic fatty liver disease during pregnancy: A systematic review and meta-analysis. J Diabetes Complications. 2021 Sep;35(9):107991.

Impact

Our research findings have demonstrated that clinically, there appears to be a synergistic adverse effect of having both MAFLD and GDM. In particularly, the presence of MAFLD appears to magnify the adverse metabolic consequences of GDM, such as worsening the degree of insulin resistance and increasing the need for earlier management with insulin therapy. Translationally, our research findings could be considered in the ongoing debate of identifying and managing early diagnosis of GDM, where the presence of MAFLD in the first trimester of pregnancy could be considered as a possible risk factor/stratification method used to screen for early diagnosis of GDM.

Nevertheless, our research findings further support the importance and need for a life-course approach, particularly emphasizing the importance of ongoing lifestyle interventions, towards managing GDM and being proactive in preventing the cardiometabolic consequences inherent in the two intertwining conditions of MAFLD and GDM.

Future Work

To determine if the early detection of MAFLD in reproductive aged females could be used as a parameter to allow for early screening for GDM and whether this is beneficial in preventing adverse maternal or neonatal outcomes compared to those women without any MAFLD.

Project 6: Pregnancy outcomes in women with gestational diabetes mellitus by models of care: a retrospective cohort study

Principal Investigators: Dr Jackson Harrison, Professor Dharmintra Pasupathy
Co-Investigators: Melov S, Kirby A, Athyde N, Boghossian A, Cheung NW, Inglis E, Padmanadhan S, Hook M
RPC Research Stream: Translational Health
Progress: Complete

Lay Summary

Gestational diabetes (GDM) affects up to 15% of women during pregnancy in Australia. Women with GDM in pregnancy are at higher risk of pregnancy complications. These women require close monitoring of blood sugar levels and the growth of their babies to inform the care received during pregnancy which include lifestyle and dietary advice. Health care services adopt different approaches to caring for women with GDM. In some instances, all women with GDM are seen in dedicated Diabetes antenatal clinics independent of severity whilst in some hospitals only women requiring medication are seen in these dedicated clinics. Women with GDM often requiring only dietary modification is seen in routine antenatal services. We studied the influence of health service provision on pregnancy outcomes in women with GDM. We compared outcomes for both mother and babies in women who attended dedicated Diabetes antenatal clinics compared to those who continued in other routine antenatal clinics.

Women allocated to non-dedicated Diabetes clinics may have been expected to have lower rates of complications of pregnancy given the milder forms of GDM, most not requiring treatment. Our findings would suggest that these women had comparable higher risk of adverse outcomes to women attending dedicated diabetes antenatal clinics with more severe GDM.

These findings have important implications for the design of health care services for women with GDM. Given women who previously may have been considered lower-risk have comparable outcomes to those considered higher-risk, current methods of risk stratification appear to be somewhat limited. As a result, further research is needed to assign care for women with GDM.

Scientific Summary

The aim of our retrospective cohort study was to compare the maternal and neonatal outcomes of women with GDM to the background population, stratifying for the model of antenatal care they received. The study was undertaken using data from Westmead Hospital, a large tertiary referral centre in Sydney, Australia. Data was collated from the electronic medical records

system from 01/01/2018 – 30/11/2020. Births <24 weeks, multiple gestations and women with pre-existing diabetes were excluded from inclusion in the study. Once data was obtained from medical records, women were classified according to GDM status, and the clinic they last attended prior to delivery. Strata for models of care included routine antenatal care and dedicated GDM obstetric clinics. Outcomes of interest included; hypertensive disorders of pregnancy (HDP), pre-term birth (PTB), induction of labour (IOL), operative delivery, small for gestational age (SGA), large for gestational age (LGA), post-partum haemorrhage (PPH), obstetric anal sphincter injury (OASIS), neonatal hypoglycaemia, neonatal hypothermia, neonatal respiratory distress, neonatal intensive care unit (NICU) admission.

The rate of GDM in our study population was 16.3%. Of these women, 34.7% were managed in dedicated GDM clinics. Women with GDM had higher rates of adverse outcomes across several domains. Women with GDM attending non-dedicated clinics had increased rates of HDP Adj OR 1.6, 95%CI 1.2-2.0), PTB (Adj OR 1.7, 95% CI 1.4-2.0), OASIS (Adj OR 1.4, 95% CI 1.0-2.0), similar odds of induction (Adj OR 1.0, 95% CI 0.9-1.2) compared to non-GDM women. These increased risks were not seen in women with GDM attending dedicated GDM clinics. Our findings suggest that women with GDM receiving care in lower risk clinics had similar or higher rates of adverse outcomes to those in dedicated clinics. In order to minimise the risk to women and babies, pathways of care need to be similar for all women with GDM.

Output

Awards:

- Early Career Researcher Award. Perinatal Society of Australia and New Zealand Annual Scientific Meeting 2022.

Presentations:

- Harrison J, Melov S, Kirby A, Dunn M, Wearne N, Athayde N, Boghossian A, Cheung W, Inglis E, Pasupathy D - Models of care and outcomes for women with GDM: A retrospective cohort study.
  Perinatal Society of Australia and New Zealand Annual Scientific Meeting 2022.

Publications:

- Harrison J, Melov S, Kirby AC, Athayde N, Boghossian A, Cheung W, Inglis E, Maravar K, Padmanabhan S, Luig M, Hook M, Pasupathy D. Pregnancy outcomes in women with gestational diabetes mellitus by models of care: a retrospective cohort study. BMJ Open. 2022 Sep 26;12(9):e065063.

Impact

Novel finding on the impact of clinical care provision on outcomes for women with GDM. Serving as the foundation for further research in the area, including development of risk stratification tools and improved health service provision. The work has recently been published and contributes to a growing body of literature exploring methods for improving outcomes for women with GDM, a growing issue for women in Australia and globally.

Future Work

Development of a risk stratification tool to better determine need for dedicated clinic referral in early pregnancy.

Project 7: Improving maternal & PeRinatal Outcomes aMongst wOmen with and without obesity – a personalised and acceptable approach of risk assessment and stratification using social, clinical, nutritional and physical activity data (PROMOTE Pilot Study)

Principal Investigators: Professor Dharmintra Pasupathy
Co-Investigators: Lucewicz A, Rhou YJJ, Melov S, Flood V, Cheung NW, Smith B, McNab J, Heads J, Ryan J, McLean M
RPC Research Stream: Discovery Science
Funding Support: RPC
Progress: In progress

Lay Summary

Obesity and gestational diabetes (GDM) are associated with both short-term and long-term adverse outcomes for both mothers and their children. However, interventions targeting obesity and other risk factors for GDM have not shown promising benefits on important pregnancy outcomes. This study aims to evaluate combinations of metabolic risk factors to help identify subgroups of pregnant women at greatest risk to target future interventions, utilising predominantly non-invasive and/or routinely collected data.

Scientific Summary

Obesity and gestational diabetes (GDM) are associated with short-term and long-term adverse maternal and offspring outcomes, as outlined the table below.

Table 1: Risks associated with obesity and gestational diabetes

Short term		Long term	
Maternal	**Offspring**	**Maternal**	**Offspring**
• Hypertensive disorders, including pre-eclampsia • Birth trauma • Caesarean delivery	• Large for gestational age • Shoulder dystocia • Hypoglycaemia • Polycythaemia • Jaundice	• Recurrence of GDM in future pregnancies • Diabetes throughout life • Cardiovascular events • Hypertension	• Diabetes • Insulin resistance • Obesity • Circulatory disease

Previous randomised controlled trials evaluating the impact of dietary and lifestyle interventions have not demonstrated meaningful impact on important outcomes, such as perinatal morbidity associated with obesity and GDM or long-term implications for the mother and offspring. However, it is increasingly recognised that women with cardiometabolic risk factors are not at a uniformly increased risk, and this heterogeneity may have contributed to the disappointing results of previous clinical trials. Further research is needed to evaluate the interplay of metabolic risk factors in women in early pregnancy to identify subgroups at greatest risk. This will facilitate improved risk stratification and development of targeted interventions.

This study is a prospective cohort study of women recruited at <16 weeks' gestation, aiming to identify combinations of risk factors for obesity and GDM-related maternal and perinatal adverse outcomes. It involves collection of validated survey data on dietary, physical activity, nutritional and psychosocial parameters in early pregnancy as well as routinely-collected antenatal data, and optional collection of maternal +/- venous cord biomarkers.

Progress

Following initial ethics approval, policies and procedures were put in place in 2022 to commence recruitment, survey and biomarker collection and biobanking. The study commenced recruitment in 2022 and to date >350 women have been recruited with approximately 190 women birthed. Preliminary analysis will commence following further recruitment.

Project 8: Association Between Length Of Residence Lived In Australia And Perinatal Outcomes Amongst Migrant Women

Principal Investigators: Sarah J Melov
Co-Investigators: Quian H, Elhindi J, Talla G, Byrnes O, Nippita T, Zachariah D, Simmons M, de Vroome M, Gilroy G, Pasupathy D
RPC Research Stream: Population Health
Progress: In progress

Lay Summary

A large proportion percentage oof people who live in Australia are migrants. They contribute significantly to the Australian economy and to the development of Australian society and culture. Evidence suggests that migrants are affected by poorer health outcomes than people born in Australia and they are also under-represented in health research. While ethnicity and country of birth has previously been found to be related to a person's health, there has also been some evidence to suggest that the number of years migrants have lived in their host country may also affect how healthy a migrant is. Our research aims to assess whether, for first generation migrants, there is a relationship between the length of time lived in Australia and gestational diabetes. A secondary goal is to assess whether, for first generation migrants, there is a relationship between the length of time lived in Australia and other pregnancy outcomes including a mother's weight when they first book in for their pregnancy or medical issues arising in pregnancy.

Scientific Summary

Australia is recognised globally as one of the most multicultural societies. In 2020, 37.9% of women who gave birth in NSW were born overseas. Migrants are increasingly likely to be highly educated and more likely to work full time compared to the Australian-born population, with migrants making up 19% of the Australian workforce. Subsequently, migrants make a substantial contribution to Australia's economy, social and cultural development. Health inequalities disproportionately affect migrants and remain under-represented in research.

Migrant women have higher prevalence of gestational diabetes than women in their host country, and when disaggregated by country of origin, Asian women have the highest risk of developing gestational diabetes. Gestational diabetes is associated with adverse pregnancy outcomes including increased odds of caesarean section, preterm delivery, large for gestational age baby, neonatal respiratory distress and neonatal intensive care unit admission. Whilst ethnicity and country of origin is an identified risk factor for gestational diabetes, there is a growing body of literature that demonstrates additional risk of developing metabolic syndrome (including gestational diabetes and obesity) amongst certain ethnicities post migration to a foreign host country. This supports the notion that time since migration influences the risk of developing gestational diabetes with country of origin being an important effect modifier. Utilising existing routinely collected data may provide insight into the complexities of acculturation and perinatal health outcomes for migrant women.

The primary aim of our study is to investigate the association between length of residence in Australia and gestational diabetes in first generation migrants. The secondary aim is to investigate the association between length of residence in Australia and important perinatal characteristics and outcomes in first generation migrants. This project will provide valuable information to potentially guide targeted programs to improve care for migrant women and their families.

This is a multisite interdisciplinary project involving Western Sydney Local Health District (WSLHD), Nepean Blue Mountains Health District (NBMLHD), Northern Sydney Local Health District (NSLHD) and collaborating with Central Coast Local Health District (CCLHD), encompassing 35% of the birthing population in NSW with differing diversity of overseas born women from varying socioeconomic cohorts.

Progress

The study has received ethical approval.

Fetal Growth, Development and Perinatal Outcomes

Project 1: Trends in early gestation stillbirth and neonatal death in New South Wales, 2002-2019

Principal Investigators: Ibinabo Ibiebele
Co-Investigators: Parry M, Torvaldsen S, Nippita TA, Bowen J, Morris JM
RPC Research Stream: Population Health
Funding Support: Stillbirth Foundation Australia / Stillbirth Centre of Research Excellence grant; Prevention Research Support Program, New South Wales Ministry of Health
Progress: Complete

Lay Summary

There has been little research to understand trends in early gestation stillbirths and neonatal deaths, that is, deaths where the baby was born between 20-27 weeks gestation, even though early stillbirths make up more than 65% of stillbirths in Australia. This study examined recent trends in early (20-27 weeks) stillbirths and neonatal deaths in NSW, after excluding pregnancy terminations. The study examined birth, hospital and death information for all female NSW residents who had a birth of at least 20 weeks gestation between 2002 and 2019. Pregnancy terminations were excluded. The study found decreasing rates of early gestation stillbirths and neonatal deaths overall and among singletons. However, there were no trends for twin stillbirths across gestational age groups.

Scientific Summary

There has been a scarcity of research directed at understanding trends in early gestation stillbirths and neonatal deaths, that is, perinatal deaths occurring at 20-27 weeks gestation. This is despite early stillbirths accounting for more than 65% of stillbirths in Australia. The aim of this study was to investigate recent temporal trends in early gestation stillbirths and neonatal deaths after excluding terminations of pregnancy in New South Wales (NSW), Australia.

This population cohort study involved all female NSW residents with at least one birth ≥20 weeks gestation between January 2002 and December 2019. Linked pregnancy and birth, hospital and death data were used. Births following an induced pregnancy termination were identified using hospital data and excluded from the study population. Gestational-age specific stillbirth rates were calculated using the 'fetus-at-risk' approach and gestational-age specific neonatal death rates were calculated using the 'births-based' approach. Evidence of linear trends in the calculated stillbirth and neonatal death rates for all, singleton and twin births were investigated using linear regression models.

There was evidence of declining trends in early gestation stillbirth and neonatal death rates. Among early gestation births, stillbirth rates decreased from 1.9 and 0.9/1,000 fetuses-at-risk (FAR) in 2002 to 1.6 and 0.7/1,000 FAR in 2019 among 20-23 and 24-27 week births, respectively. Among early gestation live births, neonatal death rates declined from 940 and 315/1,000 live births in 2002 to 925 and 189/1,000 live births in 2019 among 20-23 and 24-27 week births, respectively. Declining trends in stillbirth and neonatal death rates across all age groups were observed among singletons, except for 37-38 week stillbirths. Across gestational age groups, no temporal trends were found for stillbirths among twins, although there were decreasing rates of neonatal death among 20-23 week twins.

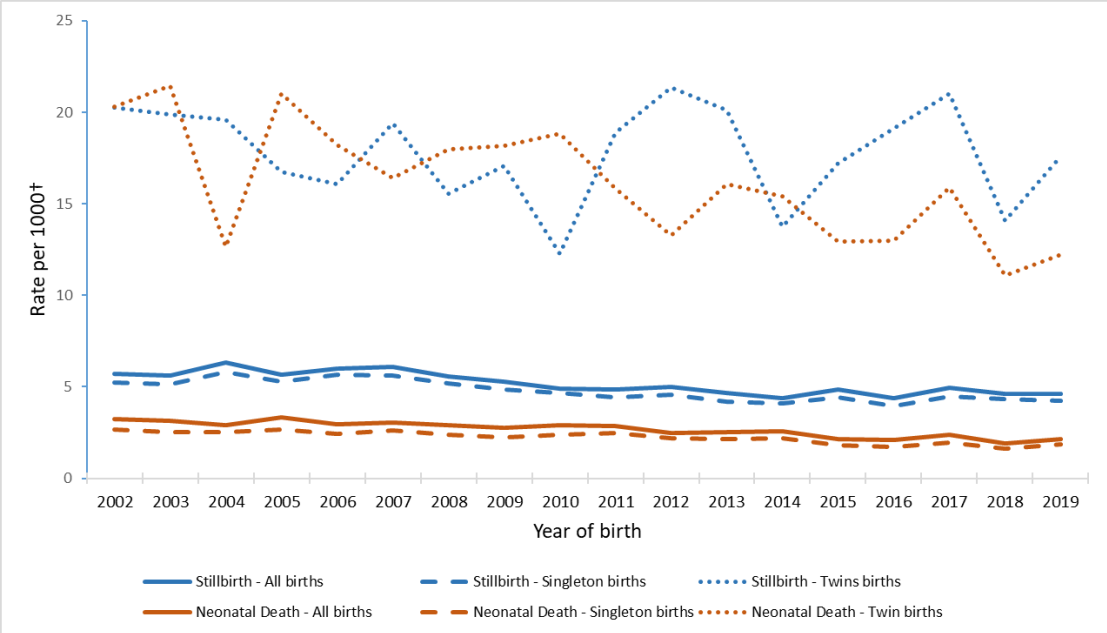


Figure: Overall rates of stillbirth and neonatal death (≥20 weeks gestation) by population group, New South Wales, 2002-2019. †Stillbirth rates are expressed per 1,000 fetuses-at-risk and neonatal death rates are expressed per 1,000 live births

Early gestation stillbirth and neonatal death rates have declined in recent decades in New South Wales but more work is needed to reduce early and late gestation stillbirth rates among twins.

Output

Presentations:

- Parry M, Torvaldsen S, Nippita TA, Bowen J, Morris JM, Ibiebele I. Trends in early gestation stillbirths and neonatal deaths in New South Wales, Australia 2002-2016. International Stillbirth Alliance (ISA) -International Society for the Study and Prevention of Perinatal and Infant Death (ISPID) 2021 Digital Conference Incorporating the Australian National Stillbirth Forum – Driving change in Stillbirth, SIDS and Infant Death [Online], November 11-13, 2021.

Publications:

- Parry M, Torvaldsen S, Nippita TA, Bowen J, Morris JM, Ibiebele I. Trends in early gestation stillbirths and neonatal deaths in New South Wales, Australia 2002-2019. Aust N Z J Obstet Gynaecol. 2023 Apr 16.

Future Work

Further studies are planned to examine risk factors for, and birth outcomes in the next pregnancy following an early gestation stillbirth or neonatal death.

Project 2: Risk factors for early stillbirth

Principal Investigators: Ibinabo Ibiebele
Co-Investigators: Parry M, Torvaldsen S, Nippita TA, Bowen J, Morris JM
RPC Research Stream: Population Health
Funding Support: Stillbirth Foundation Australia / Stillbirth Centre of Research Excellence grant; Prevention Research Support Program, New South Wales Ministry of Health
Progress: In progress

Lay Summary

Despite early stillbirths (<28 weeks gestation) comprising more than 65% of stillbirths in Australia, there has received little attention. This study aimed to determine which maternal and pregnancy characteristics are associated with increased risk of having an early stillbirth. The linked pregnancy, hospital and death records for all women who had a singleton birth of at least 20 weeks gestation in New South Wales (NSW) during 2016 to 2019 were examined. A total of 345,209 births were examined. The factors associated with increased risk of having an early stillbirth included: maternal age, maternal region of birth, socioeconomic disadvantage, smoking, body mass index >30kg/m^2, history of diabetes or hypertension prior to pregnancy, having no previous pregnancies, previous cervical surgery, having a previous small-for-gestational age baby and having a previous stillbirth. This study identified several characteristics that can be used to identify women at increased risk of having an early stillbirth.

Scientific Summary

Despite early stillbirth (fetal death occurring <28 weeks gestation) accounting for more than two-thirds of reported stillbirths in Australia, these deaths have received little consideration. The aim of this study was to determine what maternal and pregnancy factors are associated with increased risk of having an early stillbirth.

This cohort study involved all female New South Wales residents who had at least one singleton birth ≥20 weeks gestation between January 2016 and December 2019. Linked routinely collected birth, hospital and mortality data which had been probabilistically linked at the individual-level were used. Induced pregnancy terminations were identified using hospital data and excluded from the study. Stillbirth classified as early (<28 weeks gestation) or late (≥28 weeks gestation) was the outcome of interest. Associations between stillbirth and various maternal demographic, medical and obstetric factors were estimated using Modified Poisson regression models with robust error variances. Adjusted relative risks (aRR) and 95% confidence intervals for early stillbirth relative to no stillbirth are presented.

Among 345,209 births, 698 (0.2%) were early stillbirths and 749 (0.2%) were late stillbirths. Factors associated with increased risk of early stillbirth included: maternal age (<20, ≥35 years), maternal region of birth [Sub-Saharan Africa (aRR 1.79, 95% CI 1.10-2.90), South Asia (aRR 1.34, 95% CI 1.04-1.72)], socio-economic disadvantage (aRR 1.33, 95% CI 1.04-1.72), smoking (aRR 1.70, 95% CI 1.37-2.12), body mass index >30kg/m^2 (aRR 1.26, 95% CI 1.02-1.54), pre-existing hypertension (aRR 2.42, 95% CI 1.67-3.52), pre-existing diabetes (aRR 1.85, 95% CI 1.21-2.84), primiparity (aRR 1.41, 95% CI 1.19-1.68), previous cervical surgery (aRR 1.47, 95% CI 1.10-1.97), having a previous small-for-gestational age infant (aRR 1.46, 95% CI 1.14-1.88) and having a previous stillbirth (aRR 3.18, 95% CI 1.94-5.22).

This study found potentially modifiable risk factors, maternal characteristics, medical and obstetric factors that can be used to identify women at increased risk of early stillbirth. These results highlight the need for continued efforts to:

- Address potentially modifiable risk factors for stillbirth
- Optimise pre-pregnancy maternal health, and
- Provide appropriate care for women at increased risk of stillbirth

Progress

A manuscript is in preparation for publication.

Output

Presentations:

- Ibiebele I. Early stillbirth: trends, risk factors and subsequent pregnancy outcomes. Reproduction and Perinatal Centre (RPC) Research Meeting, Westmead Hospital, May 2, 2023 (Invited presentation).
- Ibiebele I, Parry M, Torvaldsen S, Nippita TA, Bowen J, Morris JM. Risk factors for early gestation stillbirth in New South Wales, Australia.
- Perinatal Society of Australia and New Zealand (PSANZ) 2023 Annual Congress.
- Ibiebele I. Stillbirth CRE/Stillbirth Foundation Early Career Researcher Update. ISA-ISPID 2021 Digital Conference Incorporating the National Stillbirth Forum – Driving change in Stillbirth, SIDS and Infant Death [Online], November 11-13, 2021. (Invited Plenary).

Project 3: Evaluation of the Growth Assessment Protocol (GAP) for antenatal detection of small for gestational age: The DESiGN cluster randomised trial

Principal Investigators: Matias C Vieira, Professor Dharmintra Pasupathy
Co-Investigators: Relph S, Elstad M, Coker B, Moitt N, Delaney L, Winsloe C, Healey A, Coxon K, Alagna A, Briley A, Johnson M, Page LM, Peebles D, Shennan A, Thilaganathan B, Marlow N, McCowan L, Lees C, Lawlor DA, Khalil A, Sandall J, Copas A, DESiGN Collaborative Group
RPC Research Stream: Translational Health
Funding Support: Guy's & St Thomas' Charity, Stillbirth and Neonatal Death Charity (SANDS), Tommy's Charity.
Progress: Complete

Lay Summary

A baby who is small compared to others born at the same time is known as SGA (small-for-gestational-age). SGA babies are more likely to suffer complications during pregnancy and birth but also after birth and longer term in later life. By detecting SGA babies during pregnancy, it is thought that we may be able to prevent some of these babies dying before they are born (stillbirth). There are many ways of defining and detecting which babies are SGA during pregnancy. In the UK and other countries, many hospitals either use a system called GAP (Growth Assessment Protocol) or standard care. GAP provides a customised, or personalised, chart for each woman, and includes a package of care that includes training of staff, the use of protocols and individualised assessment of the pregnant woman, auditing of outcomes and performance measures. Standard care differs mainly in that the charts and standards are generic, based on the UK population rather than the individual. This trial compared GAP to standardised care in the detection of SGA babies and did not find any difference in the detection of SGA babies during pregnancy between the two.

Scientific Summary

There is a strong international drive to reduce the number of preventable stillbirths. One method is through the detection and appropriate management of babies who are small-for-gestational age. The Growth Assessment Protocol (GAP), developed by the Perinatal Institute, is a complex intervention that includes the risk assessments, customised charts, protocols, training of clinical staff, audit and benchmarking of performance. Our aim was to compare the effectiveness of GAP compared to standard care in the detection of SGA.

This was a pragmatic, superiority, 2-arm, parallel group, open, cluster randomised control trial (RCT) including women who gave birth after 24+0 weeks' of gestation between November 2016 to February 2019. Multiple pregnancies and pregnancies affected by fetal abnormalities were excluded. This was the first RCT to compare GAP to standard care. Data were obtained from routinely collected electronic hospital records and divided into three time periods: pre-randomisation and outcome period (last 6 months of the study) as well as the period between the two ('washout'). SGA detection, the primary outcome, was defined antenatally as an estimated fetal weight <10th centile using customised or Hadlock centiles. SGA was similarly confirmed at birth by both customised and population centiles. Secondary outcomes included

maternal as well as neonatal outcomes. A 2-stage cluster–summary approach was used for the analysis. Of the 7 clusters randomised to the intervention arm, two made no attempt to implement the intervention (GAP) and therefore were excluded in a modified intention to treat (mITT) analysis. 11,096 births were exposed to the intervention (5 clusters) and 13,810 to standard care (6 clusters) during the outcome period. During this time, the characteristics of the mothers in each arm were similar, apart from a lower proportion of women of white ethnicity (56.2% vs 62.7%) and in the least deprived quintile (7.5% vs 16.5%) in the invention arm. The antenatal detection of SGA was 25.9% vs 27.7% in the intervention and standard care arms respectively (adjusted difference 2.2%, 95% confidence interval −6.4% to 10.7%; p = 0.62). The full ITT was also reported and findings were consistent. In terms of the intervention, 88.7% of women were reached overall, but this was variable between clusters. We observed no difference in antenatal detection of SGA when GAP was compared to standard care. The variability in the extent of and commitment to GAP implementation highlight the need to incorporate standardised measures of this into future studies.

Output

Presentations:

- Screening for Fetal Growth Restriction and DESiGN.
  British Maternal Fetal Medicine Society Annual Congress, November 2022.
- Screening for fetal growth anomalies - insights from the DESiGN Trial.
  RANZCOG NZ Annual Scientific Meeting, August 2022.
- The DESiGN Trial - Evaluation of the Growth Assessment Protocol (GAP) for antenatal detection of small for gestational age.
  19th Fetal Medicine Foundation Congress, Crete, June 2022.
  RCOG International Congress, London, June 2022.

Publications:

- Vieira MC, Relph S, Muruet-Gutierrez W, Elstad M, Coker B, Moitt N, Delaney L, Winsloe C, Healey A, Coxon K, Alagna A, Briley A, Johnson M, Page LM, Peebles D, Shennan A, Thilaganathan B, Marlow N, McCowan L, Lees C, Lawlor DA, Khalil A, Sandall J, Copas A, Pasupathy D; DESiGN Collaborative Group. Evaluation of the Growth Assessment Protocol (GAP) for antenatal detection of small for gestational age: The DESiGN cluster randomised trial. PLoS Med. 2022 Jun 21;19(6):e1004004.
- Vieira MC, Relph S, Copas A, Healey A, Coxon K, Alagna A, Briley A, Johnson M, Lawlor DA, Lees C, Marlow N, McCowan L, Page L, Peebles D, Shennan A, Thilaganathan B, Khalil A, Sandall J, Pasupathy D; DESiGN Collaborative Group. The DESiGN trial (DEtection of Small for Gestational age Neonate), evaluating the effect of the Growth Assessment Protocol (GAP): study protocol for a randomised controlled trial. Trials. 2019 Mar 4;20(1):154.
- Relph S, Elstad M, Coker B, Vieira MC, Moitt N, Gutierrez WM, Khalil A, Sandall J, Copas A, Lawlor DA, Pasupathy D; DESIGN Trial team. Using electronic patient records to assess the effect of a complex antenatal intervention in a cluster randomised controlled trial-data management experience from the DESiGN Trial team. Trials. 2021 Mar 8;22(1):195.

Impact

This study has been cited 11 times at the time of writing. It has the potential to inform future guidelines and implementation of strategies to improve the detection of the small-for-gestational age fetus.

Future Work

Several planned secondary analyses of the DESiGN trial have been completed and others are on-going. It was recommended in the publication that any future studies of GAP *"assess implementation using standardised outcomes (fidelity, reach and dose) in order to determine the generalisability of our findings, identify the barriers to implementation, and hence better inform policy for improving perinatal outcome."*

Project 4: Improving antenatal detection of small-for-gestational-age fetus: economic and process evaluations from the DESiGN cluster randomised trial

Principal Investigators: Sophie Relph, Kirstie Coxon, Andrew Healey, Professor Jane Sandall, Professor Dharmintra Pasupathy
Co-Investigators: Vieira MC, Copas A, Alagna A, Delaney L, Melaugh A, Briley A, Johnson M, Lawlor DA, Lees C, Marlow N, McCowan L, McMicking J, Page L, Peebles D, Shennan A, Thilaganathan B, Khalil A, DESiGN Collaborative Group
RPC Research Stream: Translational Health
Funding Support: Guy's & St Thomas' Charity, Stillbirth and Neonatal Death Charity (SANDS), Tommy's Charity
Progress: Complete

Lay Summary

Different approaches exist in caring for women during pregnancy, in particular relating to those strategies used to enhance the detection and management of a baby who is small for its gestational age (SGA). One strategy is known as the Growth Assessment Protocol (GAP), which involves the training of staff, an individualised approach to monitoring babies during a pregnancy and audits among other elements of care. It is important to understand the implications of introducing such strategies, such as the costs of caring for a patient during and after a pregnancy and the ease and effectiveness of introducing such a strategy. We recognise that any findings and conclusions drawn are influenced by the in assumptions made (such as the cost of each element of care) and also the time frame of the study (for example, longer term health implications of having a small baby were not taken into account). We found GAP was generally acceptable to staff tasked with implementing the protocol, however hospital sites implemented the changes to differing levels. Differences in leadership and resources were found to have an impact on the feasibility of changes. However based on our analysis the economic case for GAP was weak.

Scientific Summary

Over half of all stillbirths in developed countries occur in small-for-gestational-age (SGA) babies, therefore improving SGA detection is one of the keys to antenatal ultrasound surveillance. The Growth Assessment Protocol is a complex intervention aimed at improving the rate of SGA detection. It is a package of care that includes training of staff, individualised or customised screening of patients amongst other elements. Understanding the acceptability, feasibility surrounding its implementation as well as costs around such interventions is vital when different protocols of care are introduced into a healthcare setting. Through a systematic review of the literature, we gained an insight into the unit costing of each element of antenatal, intrapartum and postpartum care. Whilst this highlighted the need for a standardised cost perspective to enable healthcare strategies and protocols to be compared, it also provided a foundation for an economic evaluation of GAP. We found that, compared to standard care, the introduction of GAP would increase costs on average. The benefit of GAP would be found in the increased detection of SGA and improvement of perinatal outcomes, however the DESiGN trial did not find significant differences in the detection of SGA with GAP compared to standard care. Therefore overall, the economic evaluation did not support GAP implementation in the context of detection of SGA.

A further study was performed to evaluate the process of GAP implementation through interviews with 28 lead clinicians and 27 frontline healthcare professionals. Whilst the protocol was deemed acceptable to staff on the whole, concerns were raised about the implications for resource allocation and beliefs varied about its overall value as an intervention. GAP advises a face-to-face training target of >75% of staff, but only one site managed to reach the target and used e-learning methods in order to do so. Whilst reach (the number of women found to have the customised charts) was found to be high (median 94%), the dose (women monitored for SGA as recommended by GAP) was low (median 31%) in the implementing sites. Human factors in leadership are likely to be at play when effective implementation is desired and resource allocation is key, which we now better understand.

Output

Presentations

- Relph S, Coxon K, Vieira M, Pasupathy D, Sandall J on behalf of the DESiGN Collaborative Group. Effect of the Growth Assessment Protocol on the DEtection of the Small for GestatioNal age fetus: Process evaluation from the DESiGN cluster randomised trial.
  BMFMS Annual Conference, Birmingham, Nov 2022.
- Relph S, Vieira M, Pasupathy D, Healey A on behalf of the DESiGN Collaborative Group. Improving antenatal detection of the small for gestational age fetus: reporting the DESiGN trial economic evaluation of the Growth Assessment Protocol.
  BMFMS Annual Conference, Birmingham, Nov 2022.

Publications

- Relph S, Vieira MC, Copas A, Coxon K, Alagna A, Briley A, Johnson M, Page L, Peebles D, Shennan A, Thilaganathan B, Marlow N, Lees C, Lawlor DA, Khalil A, Sandall J, Pasupathy D, Healey A; DESiGN Trial Team. Improving antenatal detection of small-for-gestational-age fetus: economic evaluation of Growth Assessment Protocol. Ultrasound Obstet Gynecol. 2022 Nov;60(5):620-631.
- Relph S, Coxon K, Vieira MC, Copas A, Healey A, Alagna A, Briley A, Johnson M, Lawlor DA, Lees C, Marlow N, McCowan L, McMicking J, Page L, Peebles D, Shennan A, Thilaganathan B, Khalil A, Pasupathy D, Sandall J; DESiGN Collaborative Group. Effect of the Growth Assessment Protocol on the DEtection of Small for GestatioNal age fetus: process evaluation from the DESiGN cluster randomised trial. Implement Sci. 2022 Sep 5;17(1):60.

Impact

This study has the potential to inform future guidelines and implementation of strategies to improve the detection of the small-for-gestational age fetus.

Project 5: Characteristics and perinatal outcomes associated with antenatally unidentified small-for-gestational age fetuses: prospective cohort study nested within DESiGN randomised control trial

Principal Investigators: Sophie Relph, Chivon Winsloe, Professor Dharmintra Pasupathy
Co-Investigators: J Elhindi, M C Vieira, A Copas, A Alagna, L Page, C Winsloe, A Shennan, A Briley, M Johnson, C Lees, D A Lawlor, J Sandall, A Khalil, on behalf of the DESiGN Trial Team and DESiGN Trial team
RPC Research Stream: Population Health
Funding Support: Guy's & St Thomas' Charity, Stillbirth and Neonatal Death Charity (SANDS), Tommy's Charity
Progress: In progress

Lay Summary

A baby who is born small for its gestational age is known as SGA and this is associated with more adverse outcomes during pregnancy, at birth as well as later in life. Ultrasound scans can detect some of these babies during pregnancy, but we need to improve the number of babies we detect before birth in order to improve the outcomes of these SGA babies. In order to do this, we tried to better understand the mothers whose babies are in fact small, yet who are not detected before they are born. Undetected SGA babies were more common in mothers who would not ordinarily have required extra ultrasound scans in pregnancy. They were also more common in babies who were head down at birth and in mothers who were overweight. Undetected SGA babies tended to be small, but not as small as those who were detected. We are also gathering data to obtain a better understanding about whether these undetected babies experience more serious complications, such as stillbirth or severe complications at birth.

Scientific Summary

In this prospective cohort study, pregnancies in the baseline and control arm of the DESiGN trial were included if singleton, non-anomalous babies had been found to be SGA at birth. Of the 15,784 SGA babies included, it was found that over three-quarters (78.7%) were not detected antenatally. Undetected SGA was defined as a fetus without a scan or one with an estimated fetal weight ≥10% centile on their last scan in pregnancy, yet weighing <10% centile at birth. We found that mothers of undetected SGA babies were less likely to have had an indication for serial ultrasound scans in pregnancy, and were also more likely to have BMI 25.0-29.9kg/m2. Undetected SGA babies were more likely to be of a cephalic presentation at birth and although they were small, they were not as small as those who had been detected. We highlighted the importance of addressing how best to screen for SGA in low-risk pregnancies, as well as the continued importance at term of screening accuracy. The perinatal outcomes relating to undetected SGA are also important to understand. We found an increased risk of stillbirth but lower rates of neonatal morbidity in undetected SGA babies.

Progress

Findings from analysis on characteristics associated with undetected SGA has been published. The findings from screening characteristics and outcomes have been presented and manuscript is in preparation.

Output

Presentations:

- Pasupathy D. (2022) Screening for fetal growth restriction and DESiGN. (Invited presentation). BMFMS Annual Conference, Birmingham, Nov 2022.
- Relph S, Pasupathy D on behalf of the DESiGN Trial Team Characteristics associated with undetected SGA: secondary analysis of the DESiGN Cohort. BMFMS Annual Conference, Birmingham, Nov 2022.

Publications:

- Relph S, Vieira MC, Copas A, Alagna A, Page L, Winsloe C, Shennan A, Briley A, Johnson M, Lees C, Lawlor DA, Sandall J, Khalil A, Pasupathy D; DESiGN Trial Team and DESiGN Collaborative Group. Characteristics associated with antenatally unidentified small-for-gestational-age fetuses: prospective cohort study nested within DESiGN randomized controlled trial. Ultrasound Obstet Gynecol. 2023 Mar;61(3):356-366.

Project 6: Differences in factors associated with preterm and term stillbirth: a secondary cohort analysis of the DESiGN Trial

Principal Investigators: Chivon Winsloe, Professor Dharmintra Pasupathy
Co-Investigators: Elhindi J, Vieira MC, Relph S, Arcus C, Alagna A, Briley A, Johnson M, Page LM, Shennan A, Thilaganathan B, Marlow N, Lees C, Lawlor DA, Khalil A, Sandall J, Copas A, on behalf of the DESiGN Trial team
RPC Research Stream: Population Health
Funding Support: Guy's & St Thomas' Charity, Stillbirth and Neonatal Death Charity (SANDS), Tommy's Charity
Progress: In progress

Lay Summary

Stillbirth is when a baby is born from 24 weeks' of pregnancy onwards but showing no signs of life. By analysing data from a large study of over 200,000 women, we found differences between the mothers who suffer preterm stillbirths (occurring between 24 to 37 weeks' gestation) and term stillbirths (occurring from 37 weeks' onwards). Understanding these differences can help to know what to look out for in pregnant women so that we can monitor them more closely and prevent this devastating complication from happening.

Scientific Summary

This was a secondary cohort analysis of the DESiGN trial, including singleton, non-anomalous pregnancies in England. Those without a reported birth outcome or those without a known gestational age at birth were excluded from this analysis. We included 195,344 pregnancies, including 667 stillbirths (3.4 per 1000 births). We performed multiple logistic regression and interaction tests of maternal and pregnancy characteristics to investigate differences between preterm and term stillbirths. 'Preterm' was defined as births occurring <37+0 weeks' and 'term' as 37+0 to 42+6 weeks' of gestation. Significant interactions were observed for most of the exposures explored, demonstrating differences between the mothers experiencing preterm stillbirth and those experiencing stillbirth at term. The different associations between stillbirth occurring preterm and term identified have the potential to contribute towards timely surveillance and interventions to further mitigate the risk of stillbirth.

Progress

Analysis complete, abstract presented, manuscript submitted for publication.

Output

Presentation:

- Winslow C, Elhindi J, Copas A, Pasupathy D on behalf of the DESiGN Collaborative Group. Differences in risk factors for stillbirth between preterm and term births – a secondary analysis of the DESiGN Trial (Fetal medicine prize presentation). BMFMS Annual Conference, Birmingham, Nov 2022.

Project 7: Antenatal detection of large-for-gestational-age fetuses following implementation of the Growth Assessment Protocol: secondary analysis of a randomised control trial

Principal Investigators: Sophie Relph, Professor Dharmintra Pasupathy
Co-Investigators: M C Vieira, Copas, A Alagna, L Page, C Winslow, A Shennan, A Briley, M Johnson, C Lees, D A Lawlor, J Sandall, A Khalil, on behalf of the DESiGN Trial Team
RPC Research Stream: Population Health
Funding Support: Guy's & St Thomas' Charity, Stillbirth and Neonatal Death Charity (SANDS), Tommy's Charity
Progress: Completed

Lay Summary

The Growth Assessment Protocol (GAP) was developed by the Perinatal Institute in the UK to improve detection of small babies (as defined by smaller than 10% of babies at the same gestational age) during pregnancy so as to better isolate those who were at risk of stillbirth. The DESiGN trial evaluated the impact and performance of GAP and was published in 2022. Staff involved in the implementation of GAP during the trial raised concerns that the program inadvertently increased detection of large babies ('large' as defined as bigger than 90% of babies at the same gestational age) which, in the absence of clear management guidelines, created uncertainty amongst practitioners, and anxiety amongst patients. Hence, a secondary analysis of the DESiGN trial was conducted to challenge whether or not this was true and whether or not there was a change in the rate of associated maternal and fetal complications. The analysis compared the performance of GAP with standard clinical care to detect large babies born after 36 weeks gestation and associated clinical events for the mother (such as bleeding, anal sphincter injury, analgesic use, type of labour, mode of birth) and baby (admission to the nursery, birth weight, resuscitation requirements and others). The analysis found that there were no differences in the detection of large babies and no difference in the rate of associated clinical events between GAP and standard care. The study highlights the need for further research on how to better screen for and manage large babies.

Scientific Summary

The Growth Assessment Protocol (GAP) was developed by the Perinatal Institute in the UK to improve detection of the small for gestational age fetus (SGA) with a view towards improved stillbirth prevention. The DESiGN trial published by Viera and Pasupathy in 2022 was the first

cluster randomised trial to evaluate the impact of GAP on antenatal detection of SGA. A secondary analysis of the DESiGN data was performed to address concerns raised by staff members who implemented GAP during DESiGN that it inadvertently increased detection of the large-for-gestational-age-fetus (LGA) which, in the absence of clear evidenced based guidelines, created patient distress and a clinical management dilemma. This study compares the impact of GAP to standard on the detection of LGA infants and associated complications.

The analysis spanned 11 DESiGN sites. LGA was defined as estimated fetal weight > 90% after 34 weeks on both population and customised charts and born with a birth weight > 90% after 36 weeks gestation) and associated secondary maternal and neonatal outcomes.

Of the 80,856 women who participated in the DESiGN trial, 5.3% were LGA by both customised and population charts. Importantly, there was no difference in the rate of detection of LGA between GAP and standard care (GAP 38.0% vs standard care 48.0%; adjusted effect size −4.9%; 95% CI −20.5, 10.7; p =0.54) (Table 2). There was also no difference in rate of false positive results, secondary outcomes or the utilisation of ultrasound.

Output

Presentations:

- Relph S, Vieira M, Copas A, Pasupathy D on behalf of the DESiGN Collaborative Group. Antenatal detection of the large for gestational age fetus following implementation of the Growth Assessment Protocol: secondary analysis of a randomised control trial.
  BMFMS Annual Conference, Birmingham, Nov 2022.

Publications:

- Relph S, Vieira MC, Copas A, Winsloe C, Coxon K, Alagna A, Briley A, Johnson M, Page L, Peebles D, Shennan A, Thilaganathan B, Marlow N, Lees C, Lawlor DA, Khalil A, Sandall J, Pasupathy D; DESiGN trial team. Antenatal detection of large-for-gestational-age fetuses following implementation of the Growth Assessment Protocol: secondary analysis of a randomised control trial. BJOG. 2023 Mar 30.

Impact

This study has the potential to inform future guidelines and implementation of strategies to improve the detection of fetal growth anomalies.

Project 8: Maternal and neonatal outcomes in the pregnancy subsequent to an early stillbirth

Principal Investigators: Ibinabo Ibiebele
Co-Investigators: Torvaldsen S, Bowen J, Morris JM, Nippita TA
RPC Research Stream: Population Health
Funding Support: Stillbirth Foundation Australia / Stillbirth Centre of Research Excellence grant; Prevention Research Support Program, New South Wales Ministry of Health
Progress: In progress

Lay Summary

There is conflicting information about what happens to women and infants in the pregnancy after an early stillbirth, which makes it difficult for doctors counselling future parents planning a pregnancy. This study examined the risk of having an adverse outcome for the mother and baby in the next pregnancy after an early stillbirth. Linked birth, hospital and death data for all women who had two consecutive singleton births in NSW during 2007-2019 were examined after pregnancy terminations were excluded. The study included 337,312 women and 674,624 pregnancies (index and subsequent pregnancies for each woman). Having an early stillbirth was associated with increased risk of pregnancy hypertension, antepartum haemorrhage, maternal morbidity, preterm birth, small-for-gestational age, neonatal morbidity and stillbirth in the subsequent pregnancy.

Scientific Summary

Contradictory evidence about pregnancy outcomes for the next pregnancy after an early stillbirth makes counselling prospective parents about future pregnancies difficult. Of particular concern is the risk of stillbirth recurrence, with studies showing risks ranging from no increased risk to 10-fold increased risk. This study aimed to determine the risk of maternal and neonatal adverse outcomes in the next pregnancy following an early stillbirth.

The study population included all women residing in New South Wales who had at least two consecutive singleton births of at least 20 weeks gestation between January 2007 and December 2019. Linked routinely collected birth, hospital and mortality data were used. Pregnancy terminations were identified in the hospital data and excluded from the study. The study exposures were early (<28 weeks) and late (≥28 weeks) stillbirth in the index pregnancy. Maternal and neonatal outcomes examined in the subsequent pregnancy included pregnancy hypertension, antepartum haemorrhage (APH), preterm birth, small-for-gestational age (SGA), neonatal morbidity and stillbirth. Modified Poisson regression models with robust error variances were used to estimate adjusted relative risks (aRRs) and their 95% confidence intervals. Results for early stillbirth as an exposure are presented.

A total of 337,312 women and their 674,624 (337,312 index and 337,312 subsequent) pregnancies were included in the study. Among the index pregnancies, there were 971 (0.3%) early and 1,228 (0.4%) late stillbirths. Women with an early or late stillbirth in the index pregnancy were more likely to be aged 35 years or older, smoke, have pre-existing medical conditions (diabetes, hypertension and other chronic), use assisted reproductive technology in the 12 months prior to the subsequent birth and have previous uterine surgery. Having an index pregnancy early stillbirth was associated with increased risk of pregnancy hypertension (aRR 1.85, 95% CI 1.56-2.19), APH (aRR 2.18, 95% CI 1.68-2.84), maternal morbidity (aRR 2.29, 95% CI 1.72-3.05), preterm birth [spontaneous (aRR 4.06, 95% CI 3.41-4.84), planned (aRR 4.00, 95% CI 3.34-4.78)], SGA (aRR 1.62, 95% CI 1.36-1.92), neonatal morbidity (aRR 2.46, 95% CI 2.12-2.86) and stillbirth (aRR 4.78, 95% CI 3.05-7.48).

Women with a previous early stillbirth represent a higher risk obstetric group. While there is significantly increased risk of recurrent stillbirth and other adverse outcomes, reassuringly most women did have a favourable outcome.

Progress

A manuscript is in preparation for publication.

Output

Presentations:

- Ibiebele I, Torvaldsen S, Bowen J, Morris JM, Nippita TA. Maternal and neonatal outcomes in the pregnancy following an early stillbirth.
  Perinatal Society of Australia and New Zealand (PSANZ) 2023 Annual Congress.
- Ibiebele I. Stillbirth CRE/Stillbirth Foundation Early Career Researcher Update.
  ISA-ISPID 2021 Digital Conference Incorporating the National Stillbirth Forum – Driving change in Stillbirth, SIDS and Infant Death [Online], November 11-13, 2021. (Invited Plenary).

Infectious Diseases in Pregnancy

Project 1: Indirect effects of the COVID-19 pandemic on risk of gestational diabetes and factors contributing to increased risk

Principal Investigators: Dr Yoon Ji Jina Rhou, Professor Dharmintra Pasupathy
Co-Investigators: Elhindi J, Melov S, Cheung NW
RPC research stream: Population Health
Funding Support: RTP Scholarship
Progress: Complete

Lay Summary

The COVID-19 pandemic has been associated with adverse pregnancy outcomes in international studies, including potential effects on the risk of gestational diabetes (GDM). The contributors to these adverse effects remain unclear. Our local population consists of a high migrant, multiethnic population that experienced particularly strict COVID-19 pandemic-related restrictions in the second year of the pandemic. Evaluation of our cohort at different stages of the pandemic offers a valuable opportunity to determine effects on a multiethnic population and the potential mediators of these effects.

Scientific Summary

COVID-19 has been associated with adverse maternal and perinatal outcomes, including an increased risk of gestational diabetes (GDM). Direct effects of COVID-19 have been proposed, but indirect consequences of pandemics and pandemic-mitigating restrictions have been increasingly recognised. Although studies have evaluated these associations, there is scarce data for multiethnic populations, as well as populations subject to varying stringency of restrictions. There is also limited research attempting to determine the causes of these observed associations.

This study is a retrospective, multicentre cohort study of pregnancies in the Western Sydney Local Health District pre-COVID-19, first year post-COVID-19 (low prevalence, lower stringency restrictions) and second year post-COVID-19 (high prevalence, higher stringency restrictions), evaluating the primary outcome of GDM. Baseline maternal data and detailed gestational weight gain data were assessed to determine potential mediators of the observed association between pandemic periods and GDM. The study comprised analyses of 28,207 pregnancies meeting the inclusion criteria. It demonstrated a progressive increased risk of GDM with pandemic exposure (21.2% pre-COVID-19 vs 22.9% during first year of COVID-19 vs 24.8% during second year of COVID-19; p<0.001). There were progressive changes in baseline maternal characteristics including traditional GDM risk factors such as increasing maternal age, pre-pregnancy BMI and changes in ethnic profile, and in proportion with excessive gestational weight gain (64.3% vs 66.0% vs 66.6%; p=0.009). These changes in maternal characteristics contributed to the increase in GDM, but COVID-19 Year 2 remained independently associated with GDM on multivariate analysis (see table), suggesting that there were also unmeasured mediating factors during the second year of the pandemic.

Table: Unadjusted and adjusted odds ratios for the risk of gestational diabetes

Characteristic	Univariate OR (95% CI)	P-value	Multivariate OR (95% CI)	P-value
Exposure period				
Pre-COVID-19	Reference			
COVID-19 Year 1	1.11 (1.02, 1.21)	0.02	1.05 (0.96, 1.15)	0.33
COVID-19 Year2	1.34 (1.23, 1.46)	<0.001	1.17 (1.06, 1.28)	0.01
Gestational weight gain (kg/week)	1.07 (0.95, 1.21)	0.3	1.31 (1.15, 1.49)	<0.001
Maternal age				
<20 years	0.34 (0.20, 0.56)	<0.001	0.39 (0.23, 0.66)	<0.001
20-24.9 years	0.49 (0.41, 0.59)	<0.001	0.54 (0.44, 0.65)	<0.001
25-34.9 years	Reference			
35-39.9 years	1.64 (1.52, 1.78)	<0.001	1.57 (1.44, 1.71)	<0.001
40 years and over	1.96 (1.66, 2.32)	<0.001	1.92 (1.59, 2.31)	<0.001

Characteristic	Univariate OR (95% CI)	P-value	Multivariate OR (95% CI)	P-value
BMI category				
Underweight	0.79 (0.64, 0.97)	0.03	0.84 (0.68, 1.05)	0.12
Healthy weight	Reference			
Overweight	1.59 (1.46, 1.72)	<0.001	1.61 (1.48, 1.76)	<0.001
Obese	1.86 (1.70, 2.05)	<0.001	2.10 (1.89, 2.33)	<0.001
Ethnicity				
Caucasian	Reference			
South Asian	2.27 (2.02, 2.55)	<0.001	2.24 (1.98, 2.53)	<0.001
Middle Eastern	1.54 (1.36, 1.73)	<0.001	1.50 (1.32, 1.70)	<0.001
East/Southeast Asian	1.95 (1.70, 2.23)	<0.001	2.14 (1.85, 2.47)	<0.001
Aboriginal and Torres Strait Islander	1.42 (1.04, 1.94)	0.03	1.47 (1.05, 2.05)	0.03
Prior GDM	6.25 (5.54, 7.06)	<0.001	6.05 (5.28, 6.92)	<0.001

Output

Awards:

- Rhou YJ. Australasian Diabetes Congress 2022 Paul Lee Best Oral Clinical Presentation Prize.
- Rhou YJ. Endocrine Society Outstanding Abstract Prize, ENDO 2023

Presentations:

- Rhou YJ, Elhindi J, Melov SJ, Cheung NW, Pasupathy D. Effect of low and high prevalence COVID-19 on obesity, gestational weight gain and risk of gestational diabetes (Prize presentation).
  Australasian Diabetes Congress, Brisbane, Aug 2022.
- Rhou YJ, Elhindi J, Melov SJ, Cheung NW, Pasupathy D. Indirect effects of COVID-19 on the risk of gestational diabetes and factors mediating increased risk (Prize presentation).
  ENDO Annual Meeting, Chicago, Jun 2023.

Publications:

- Rhou YJJ, Elhindi J, Melov SJ, Cheung NW, Pasupathy D; Western Sydney COVID-19 Pregnancy Study Group. Indirect effects of the COVID-19 pandemic on risk of gestational diabetes and factors contributing to increased risk in a multiethnic population: a retrospective cohort study. BMC Pregnancy Childbirth. 2023 May 12;23(1):341.

Impact

The study has increased our understanding of the potential impact of current and future pandemics on the risk of gestational diabetes, highlighting the importance of public health measures to identify and limit the impact of pandemics on GDM and associated morbidity.

Project 2: Covid-19 vaccine acceptance among pregnant women and the reasons for hesitancy: A multi-centre cross-sectional survey

Principal Investigators: Monica Rikard-Bell, Dr Kerrie Wiley, Professor Dharmintra Pasupathy
Co-Investigators: Elhindi J, Lam J, Seeho S, Black K, Melov S, Jenkins G, McNab
RPC Research Stream: Translational Health
Progress: Complete

Lay Summary

In response to the COVID-19 pandemic, national guidance advised the vaccination of women who were pregnant**.** It was recognised that there were hesitation in the general population to the acceptance of vaccination for many reasons including the concerns on the side effects of vaccination. It was also recognised that these concerns may also extend to women who were pregnant. The aim of our study was to assess COVID-19 vaccine acceptance and reasons for hesitancy in the pregnant population at two tertiary hospitals in Sydney which reflect two distinct diverse populations, during the COVID-19 pandemic of 2021. Our hope was that the findings of the study could potentially inform future policies on vaccinations for COVID-19 in pregnancy.

An online survey was developed and modified for the pregnant population. The survey was then administered to pregnant women in the antenatal clinics of Royal North Shore Hospital (RNSH) and Westmead Hospital. Two hundred and eighty-seven women were surveyed and revealed that COVID-19 vaccination rates in the pregnant population were lower than the general population and rates between the two hospitals differed with Westmead patients having lower vaccination rates than RNSH. The findings demonstrated that trust and confidence in vaccine safety appear to be the significant drivers of the difference in vaccination rates observed in both sites. We observed a high level of trust in health care providers across both sites and at that stage of the pandemic access to the vaccine did not seem to be a barrier to vaccination. Therefore, concluding that a multi-faceted and locally specific approach is needed to increase vaccination uptake with an emphasis on safety and benefits for mother and baby.

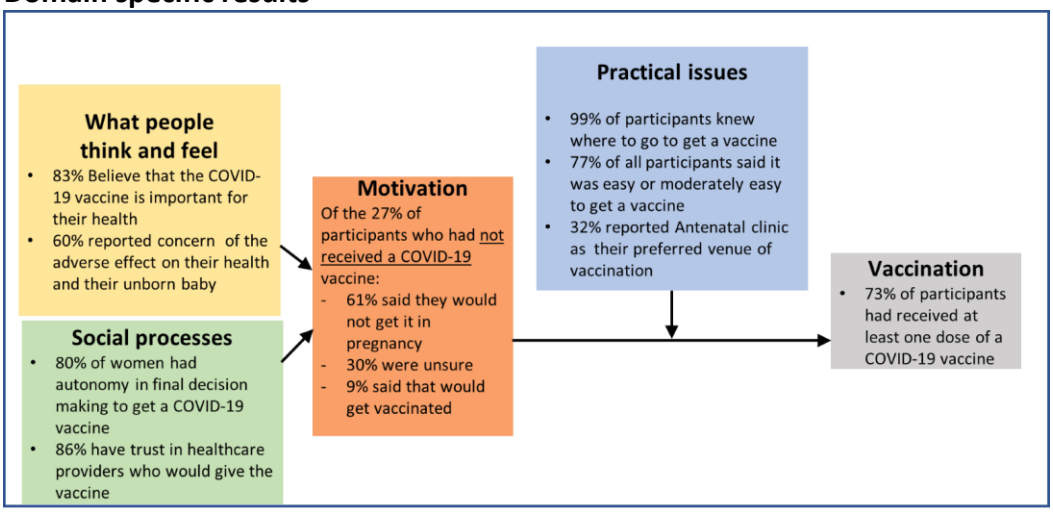
Scientific Summary

On 9 June 2021, ATAGI and RANZCOG recommended that pregnant women receive Comirnaty (Pfizer) messenger RNA vaccine at any stage of pregnancy. The initial uptake of COVID-19 vaccination was limited by multiple factors including concerns of the potential side effect of the vaccination. These concerns also extended to women who were pregnant and their health care providers. Reports confirming these concerns were largely surveys and data from a general population. There were limited evidence from Australia on vaccine hesistancy between women who were pregnant from two health districts with distinct sociodemographic profiles. This multi-centre study aimed to assess vaccine acceptance, reasons for hesitancy and determine if differences exist between health districts, to inform future policy strategies for COVID-19 vaccination in pregnancy.

An online survey was developed based on the World Health Organisation Behavioural and Social Drivers survey and modified for the pregnant population, then administered to a sample population of pregnant women attending two metropolitan hospitals (Westmead and Royal North Shore Hospital (RNSH)) in NSW between 15 September 2021 and 22 October 2021. The recruitment period of the survey coincided with the outbreak of the delta variant of COVID-19 in NSW.

287 pregnant women were surveyed comprising of 198 (69%) from Westmead and 66 (23%) from RNSH. Demographically, the respondents were largely similar between both sites except those respondents from Westmead were generally more socioeconomically disadvantaged, had more previous children, were less likely to be born in Australia and less likely to speak English at home. Lower levels of household income has previously been shown to be associated with increased likelihood of COVID-19 vaccine hesitancy and more difficulty in understanding government messaging around COVID-19, which may to some extent explain the comparatively lower levels of vaccination in the Westmead sample.

Domain specific results



Up to 60% of women were concerned of the adverse effect of vaccine on their health and that of their unborn baby, with higher rates at Westmead. However, two thirds agreed that getting a COVID-19 vaccine was very important for their health. Demonstrating that women in general valued COVID-19 vaccination, however they were hesitant in pregnancy due to concern for their baby's health and safety of the vaccine. More than 80% of women felt they had the final say on whether or not to get the COVID-19 vaccine and we observed there was a high level of trust in the health care providers across both sites. Provider recommendation has been found to be strongly associated with uptake of other recommended vaccines uptake during pregnancy.

Vaccine acceptance does not seem to be affected by access to vaccination in this sample. Almost all participants knew where to go to get a COVID-19 vaccine, suggesting that public health messaging and media was prominent and effective at that stage of the pandemic response.

Vaccination rates in the pregnant population are lower than the general population and hesitancy in pregnancy is important to address for the health of women and their babies. Our findings have demonstrated that trust and confidence in vaccine safety appear to be a significant driver of the difference in vaccination rates observed in both sites. We have demonstrated that level of concern varies between populations therefore strategies to optimize vaccination rates will be most effective if they are tailored to be site specific.

Output

Presentations:

- Rikard-Bell M, Elhindi J, Lam J, Seeho S, Black K, Melov S, Jenkins G, McNab J, Wiley K, Pasupathy D. Covid-19 Vaccine acceptance among pregnant women and the reasons for hesitancy. A multi-centre cross-sectional survey.
  E-Poster presentation. RANZCOG Symposium 2022.
  Perinatal Society of Austalia and New Zealand (PSANZ) Annual Conference 2022.

Publications:

- Rikard-Bell M, Elhindi J, Lam J, Seeho S, Black K, Melov S, Jenkins G, McNab J, Wiley K, Pasupathy D. COVID-19 vaccine acceptance among pregnant women and the reasons for hesitancy: A multi-centre cross-sectional survey. Aust N Z J Obstet Gynaecol. 2023 Jun;63(3):335-343.

Impact

This study helped raise awareness of the numbers of women who had received the COVID-19 vaccination during that time of the pandemic. For those women who were unvaccinated the study helped understand the motivations and reasons for their hesitancy. This information assisted healthcare providers in their conversations with women in antenatal clinics and healthcare providers were able to emphasise safety and benefits for the fetus in regard to COVID-19 vaccination, which was found to be the most significant contributor to hesitancy.

Future Work

Permission has been requested to use the modified survey for ongoing research projects within the pregnant population.

Project 3: Investigating service delivery and perinatal outcomes during the low prevalence first year of COVID-19 in a multiethnic Australian population: a cohort study

Principal Investigators: SJ Melov, Professor Dharmintra Pasupathy
Co-Investigators: Elhindi J, McNab J, McGee TM, Lee VW, Cheung NW, Chua SC, Alahakoon TI
RPC Research Stream: Population Health
Funding Support: Grant Westmead Charitable Trust
Progress: Complete

Lay Summary

COVID-19 led to great changes in medical and maternity care around the world. There has been little research on the effect these changes had on a culturally diverse population who experienced low levels of COVID-19 community transmission, a relatively short lockdown period but huge changes in the way society functioned, such as increased ability to work from home, the use of telehealth and visiting restrictions at hospitals, and in the birth unit. Therefore, the aim of this research was to look at how responses to the pandemic affected the pregnancy and birth outcomes for mothers and babies in a large multiethnic Australian population and discover possible reasons for both positive and negative results of the maternity care provided during the pandemic.

We analysed historical information that was normally collected on women having pregnancy care in the Western Sydney Local Health District (WSLHD) relating to the period 1 January 2018 to 31 January 2020. Comparisons were made between the outcomes of births that happened in the 2 years before the COVID-19 pandemic and the outcomes of births that happened in the first year of the COVID-19 pandemic when there was very few cases in the local community.

In the first year of the COVID-19 pandemic, there were no changes in the number of labours that were induced, a 25% rise in births by caesarean section birth. During the entire COVID-19 period, there was: no change in planned preterm births. The chances of the following were reduced by: 15% for unplanned preterm births, 10% having a baby of smaller than expected weight and 15% for fully breastfeeding for women when going home from the hospital.

Our research found that despite low levels of COVID-19 community transmission, the pandemic affected the outcomes of pregnancies in both positive and negative ways.

Scientific Summary

This retrospective cohort study was undertaken to investigate the impact of the COVID- 19 pandemic on perinatal outcomes in an Australian high migrant and low COVID- 19 prevalent population to identify if COVID- 19 driven health service changes and societal influences impact obstetric and perinatal outcomes.

Using routinely collected data in the WSLHD, we compared birth outcomes greater than or equal to 20 weeks of gestation in the 2 years prior to the COVID-19 pandemic to the first year of the COVID-19 pandemic. The study period is defined as pre-COVID-19: 1 January 2018–31 January 2020 to the first twelve months of the COVID-19 pandemic 1 February 2020–31st January 2021. There were a total of 632 cases recorded of COVID-19 in the WSLHD for the study period.

Considerable preventative measures were implemented in the region including access to telehealth, ability to work from home, restrictions in healthcare settings such as mask wearing and health-screening questions on entry to all hospitals. Community activities returned to near normal by July 2020 in NSW, however international and state borders continued to be disrupted with ongoing outbreaks emerging. Restrictions to visitors and other COVID-19 risk mitigation policies remained present for the maternity services throughout the study period. COVID-19 vaccinations were not available in Australia during the study period.

During the first year of COVID- 19, there was no change for induction of labour (adjusted OR, aOR 0.97; 95% CI 0.92 to 1.02, p=0.26) and a 25% increase in the odds of birth by caesarean section (aOR 1.25; 95% CI 1.19 to 1.32, p<0.001). During the COVID- 19 period, we found no change in iatrogenic preterm births (aOR 0.94; 95% CI 0.80 to 1.09) but a 15% reduction in the odds of a spontaneous preterm birth (aOR 0.85; 95% CI 0.75 to 0.97, p=0.02) and a 10% reduction in SGA infants at birth (aOR 0.90; 95% CI 0.82 to 0.99, p=0.02). Composite adverse neonatal outcomes were marginally higher (aOR 1.08; 95% CI 1.00 to 1.15, p=0.04) and full breastfeeding rates at hospital discharge reduced (aOR 0.85; 95% CI 0.80 to 0.90, p<0.001).

Table Odds ratio for maternal and neonatal pregnancy outcomes during the first year of COVID-19 compared to the previous two years in an Australian metropolitan health district
COVID = 1st February 2020 – Jan 31st 2021(n=10 381) Pre-COVID = 1st January 2018 – 31st January 2020 (n=23 722)

Outcome	Sample Size	Unadj. OR	P	Model 1 OR	P	Model 2 OR	P
Induction of labour	34,082	0.90 (0.86,0.94)	<0.001	0.97 (0.92,1.02)	0.26	-	-
Caesarean birth	34,063	1.14 (1.09,1.20)	<0.001	1.23 (1.17,1.30)	<0.001	1.25 (1.19,1.32)	<0.001
Preterm birth	34,080	0.86 (0.79,0.94)	0.00	0.91 (0.83,0.99)	0.03	0.88 (0.80,0.97)	0.01
Spontaneous preterm birth	34,080	0.76 (0.67,0.85)	<0.001	0.88 (0.77,0.99)	0.04	0.85 (0.75,0.97)	0.02
Small for gestational age at birth	33,880	0.88 (0.81,0.96)	0.01	0.90 (0.82,0.99)	0.02	-	-
Composite adverse neonatal outcome	33,632	1.03 (0.97,1.09)	0.38	1.08 (1.00,1.15)	0.04	-	-
Full breastfeeding at hospital discharge	31,113	0.86 (0.81,0.90)	<0.001	0.85 (0.81,0.90)	<0.001	0.85 (0.80,0.90)	<0.001

Composite adverse neonatal includes any: stillbirth, admission to NICU, Apgar score under 7 at 5 minutes, or newborn resuscitation with intubation.
Variables adjusted for in each model:
Model 1: Includes maternal age, Socioeconomic status SEIFA disadvantage quintile, gestational age, parity, ethnicity, BMI (numeric), smoking status, mental health status and model of pregnancy care variable.
For preterm birth outcome the models are not adjusted for gestational age.
Model 2: Includes Model 1 covariates and additional covariates - caesarean birth: birthweight and induction of labour; Preterm birth: composite maternal complications variable (gestational diabetes or hypertensive disorders of pregnancy); Breastfeeding: birthweight, mode of delivery, length of stay <24 hours and gestational age/preterm.

Output

Publications:

- Melov, S. J., Elhindi, J., McGee, T. M., Lee, V. W., Cheung, N. W., Chua, S. C., McNab, J., Alahakoon, T. I., & Pasupathy, D. (2022). Investigating service delivery and perinatal outcomes during the low prevalence first year of COVID-19 in a multiethnic Australian population: a cohort study. BMJ Open, 2022 Jul 12;12(7):e062409. PMID: 35820747; PMCID: PMC9277027. https://doi.org/10.1136/bmjopen-2022-062409.

Presentations:

- Melov SJ, Elhindi J, McGee T, Lee V, Cheung NW, McNab J, Alahakoon TI, Pasupathy D. Investigating Perinatal Outcomes During the Low Prevalence First Year of COVID-19 in a Multiethnic Australian Population.

PSANZ: Perinatal Society of Australia and New Zealand, 2022 Adelaide May 16-18.

Impact
This research has provided evidence for the need to improve breastfeeding support for women. A new antenatal lactation clinic has been established.

Future Work
Review breastfeeding outcomes after two years of new lactation support.

Project 4: Exploring the COVID-19 pandemic experience of maternity clinicians in a high migrant population and low COVID-19 prevalence country: A qualitative study

Principal Investigators: Sarah Melov
Co-Investigators: Galas N, Swain J, Alahakoon TI, Lee V, Cheung NW, McGee T, Pasupathy D, McNab J
RPC Research stream: Translational Health
Funding Support: Westmead Hospital Charitable Trust
Progress: Complete

Lay Summary
COVID-19 led to many changes in medical and maternity care around the world. Even though Australia initially did not have many cases of COVID-19 as compared to many other countries around the world, the community and maternity care was affected. COVID-19 was also more common in areas with a higher proportion of migrants. Migrants also often commonly plan for their relative to visit from overseas to help during a pregnancy and after birth. This was no longer possible due to COVID-19 international travel restrictions.

This research, which collected data through individual interviews with maternity staff who work in an area with a large proportion of migrants, was designed to understand the impact of COVID-19 on:

- the experiences of patients
- the services provided; and
- their own personal experiences.

We found the following three main themes in the responses:

1. Travel restrictions during the COVID-19 pandemic led to a loss in the ability to get support from extended family.
2. Maternity care services during COVID-19 were negatively affected as staff were less able to provide care in a way that supported the choices of patients.
3. There were also many challenges and difficulties for staff working through the pandemic.

Scientific Summary
This qualitative study was designed to investigate the experiences of maternity clinicians working in a high-migrant population on the impact that COVID-19 during a low prevalence time-period. Data were collected using semi-structured in-depth interview with 14 maternity care clinicians in Western Sydney Local Health District during a four-week period over November to December 2020, with data analysis undertaken using a reflexive thematic approach.

A key theme in the data was ‘COVID-19 related travel restrictions result in loss of valued family support for migrant families’. However, partners were often ‘stepping-up’ into the role of missing overseas relatives. The main theme in clinical care was a shift in healthcare delivery away from optimising patient care to a focus on preservation and safety of health staff.

1.	**Clinicians' perceptions of patient experience**
	Main theme
	COVID-19 related travel restrictions result in loss of valued family support for migrant families
	Sub-themes
	Birth and cultural differences: "…they're just by themselves, as opposed to an Aussie couple…"
	The cultural practice of postpartum extended in-house support from overseas
	Loss of support and impact on clinical care
	Changing support from partners: "…the fathers themselves actually did step up"
	Mental health impact of loss of support: "Big time struggling because she's sort of just very isolated"
	Missing out on important life events in the pregnancy journey "…husbands are missing the births of their babies"
	The hospital is not a safe place to be "… we're a big tertiary hospital, and we're the COVID central"
2.	**Maternity care service delivery during COVID-19**
	Main theme
	For the greater good, loss of efficient women-centred care: "it was just a matter of plugging the holes when you could identify them"
	Sub-theme
	Doing your own thing: "This doesn't feel right ..."
3.	**Clinicians' personal experience during COVID-19**
	Main theme
	Challenges and difficulties in difficult times- "you just dealt with it";"… and we came straight off the bushfires"
	Sub-themes
	Guilt- "can I keep everyone safe?"; "…that was the fear. Taking it home and then … them not surviving it."
	Self-care: new activities and work facilitating connection with people

Clinicians were of the view migrant women were deeply affected by the loss of traditional support. However, the benefit may be the potential for greater gender equity and bonding opportunities for partners. Conflict with professional beneficence principles and values may result in bending rules when a disconnect exists between relaxed community health orders and restrictive hospital protocols during different phases of a pandemic.

This research adds to the literature that migrant women require individualised culturally safe care because of the ongoing impact of loss of support during the COVID-19 pandemic.

Main themes and sub-themes. Exploring the COVID-19 pandemic experience of maternity clinicians in a high migrant population and low COVID-19 prevalence country: a qualitative study.

Output

Publications:

- Melov SJ, Galas N, Swain J, Alahakoon TI, Lee V, Cheung NW, McGee T, Pasupathy D, & McNab J. Exploring the COVID-19 pandemic experience of maternity clinicians in a high migrant population and low COVID-19 prevalence country: A qualitative study. Women and Birth. 2022 Sep;35(5):493-502. doi: 10.1016/j.wombi.2021.10.011.

Impact

The study may assist in future planning and optimising service delivery that ensure that women-centred care is optimised as soon as possible in changing conditions.

Project 5: Women's experience of perinatal support in a high migrant Australian population during the COVID-19 pandemic: a mixed methods study

Principal Investigators: Sarah Melov
Co-Investigators: Galas N, Swain J, Alahakoon TI, Lee V, Cheung NW, McGee T, Pasupathy D, McNab J
RPC Research Stream: Translational Health
Funding Support: Westmead Hospital Charitable Trust Nursing and Midwifery Higher Degree Grant
Progress: Complete

Lay Summary

COVID-19 dramatically affected society and maternity care in Australia despite low cases in the community of COVID-19 as compared to many other countries around the world in the first year of the pandemic. In Australia the borders were closed to international travellers for two years, affecting people socially as well as economically. It is known that good support from friends and family can help decrease stress and improve health. COVID-19 reduced the ability of people to source this support, particularly for migrants who make up around 30% of the Australian population.

We undertook a study to look at women's experiences of social support during their pregnancy and in the postnatal period during the COVID-19 pandemic by interviewing and surveying women who live Western Sydney, Australia over the period October 2020 to April 2021.

The following main themes were found in the responses:

1. There was a significant disruption and loss of support during pregnancy for all women however during the postnatal period Australian born women felt more supported compared to migrant women who had ongoing feelings of loss.
2. Migrant women appreciated their partners filling the care-roles for what would have traditionally been done by their extended families also providing opportunity for family bonding.
3. All women were high users of virtual support during the pandemic.

Scientific Summary

High quality social support can be a buffer against stress and improve health. As a COVID-19 risk mitigation measure, Australia closed its international borders for two years with significant social and economic disruption, including impacting approximately 30% of the Australian population who are migrants.

A mixed methods study was undertaken to explore women's experience of peripartum social support during the COVID-19 pandemic. Data were collected with semi-structured interviews and surveys in the high-migrant (58%) maternity population of Western Sydney, Australia over the period October 2020 to April 2021 during a very low-prevalence period of COVID-19 disease.

A total of 40 interviews were conducted antenatally (22 interviews) and postnatally (18 interviews) with 14 migrant and 10 Australian-born women. Themes included 'Significant disruption and loss of peripartum support during the COVID-19 pandemic and ongoing impact for migrant women'; 'Husbands/partners filling the support gap' and 'Holding on by a virtual thread'. Half of all women felt unsupported during the antenatal period, this dissipated for only the Australian-born women postnatally. Migrant women expressed gratitude partners were stepping into traditional roles and duties of their absent mothers and mothers-in-law and appreciated the opportunity for family bonding and contribution of partners to domestic work.

High quality social support leads to improved health outcomes and clinicians need to facilitate support for women in their care, particularly vulnerable populations. Loss of overseas social support for migrant families during the pandemic is ongoing but has revealed some benefits

including greater gender equity for unpaid domestic work and childcare in the immediate postpartum period.

Clinicians should be aware of ongoing disruption to support for migrant women and the impact on health. Care providers should be mindful of assumptions and changing gender roles regarding domestic work for migrant families. Clinicians should consider leveraging the high use of virtual support for family counselling and education.

Output

Presentations:

- Melov SJ, Galas N, Swain J, Alahakoon TI, Lee V, Cheung NW, McGee T, Pasupathy D, McNab J. Women's experience of perinatal support in a high migrant Australian population during the COVID-19 pandemic.
  Australian College of Midwives NSW State Conference, Orange, 17-18 June 2022 (Invited speaker).
- Melov SJ, Galas N, Swain J, Alahakoon TI, Lee V, Cheung NW, McGee T, Pasupathy D, McNab J. Women's experience of perinatal support in a high migrant Australian population during the COVID-19 pandemic.
  33rd ICM Triennial Congress, Bali, Indonesia, 11-13 June 2023.

Published:

- Sarah J. Melov, Nelma Galas, Julie Swain, Thushari I. Alahakoon, Vincent Lee, N Wah Cheung, Therese McGee, Dharmintra Pasupathy, Justin McNab. Women's experience of perinatal support in a high migrant Australian population during the COVID-19 pandemic: a mixed methods study. BMC Pregnancy Childbirth 23, 429 2023.

Impact

Provide understanding of the migrant experience and potential drivers for long-term impact of the COVID-19 pandemic.

Project 6: Sexually Transmitted Infections: prevalence and clinical outcomes amongst pregnant women in Western Sydney Project

Principal Investigators: Dr Irene Ju, Professor Dharmintra Pasupathy
Co-Investigators: Elhindi J, Hook M, Melov SJ, Shawleshwarkar S, Zablotska I
RPC Research Stream: Population Health
Progress: In progress

Lay Summary

There has been an alarming increase in the incidence of sexually transmitted infections (STIs) in women of reproductive age in Australia within the last decade. Recorded cases of syphilis in particular have more than tripled in Australia, despite a reduction in testing numbers. These infections in pregnancy are associated with poor outcomes for the mother and baby, including stillbirth, miscarriage, neonatal blindness and congenital syphilis. The aim of this study was to identify prevalence and clinical outcomes of STIs in pregnancy in Western Sydney over the last ten years. This study included 112,853 women who were booked in for pregnancy care at Westmead, Auburn and Blacktown Hospitals between January 2012 and December 2022. STIs in pregnancy were associated with women who were younger than 25, had a BMI greater than 30, and women who smoked, consumed alcohol and used illicit drugs. Stillbirth was significantly associated with STIs in pregnancy.

Scientific Summary

STIs in pregnancy are associated with an increased risk of adverse outcomes including miscarriage, stillbirth, prematurity and low birth weight. In Sydney between 2015-2020, there has been a 223% increase in reported incidences syphilis infection in women of reproductive age, with chlamydia and gonorrhea also increasing. In this preliminary analysis, we report the prevalence, characteristics and clinical outcomes of women with STIs in pregnancy in the Western Sydney Local Health District (WSLHD) over the last ten years.

This was a retrospective cohort study of all pregnant women booked for antenatal care at Westmead, Auburn and Blacktown Hospitals between January 2012 and December 2022. Characteristics and outcomes associated with past or current STI (chlamydia, gonorrhea, HIV and syphilis) are reported using multivariable analysis adjusting for relevant confounders.

There were 112,853 births between 2012-2022 and 527 women (0.47%) who tested positive for an STI during this time period. The recorded incidence of previous chlamydia, gonorrhea and syphilis infections have increased over the last ten years ($p<0.05$). Women with STIs in pregnancy were more likely below age 24 (<20 adjusted OR aOR 7.26 95% CI 5.14-10.26, 20-24 aOR 3.13, 95% CI 2.50-3.91), had a BMI >30 (aOR 1.67, 95%CI 1.34-2.08), smokers (aOR 2.17, 95% CI 1.68-2.80) and consumed alcohol (aOR 3.14, 95% CI 1.96-5.03) and illicit drugs (aOR 2.49, 95% CI 1.63-3.79). Following adjustment, STI in pregnancy was associated with stillbirth (aOR 2.29 95% CI 1.01-5.19). STIs did not have a significant impact on preterm birth (aOR 1.15, 95% CI 0.85-1.57), admission to NICU (aOR 1.03, 95% CI 0.80-1.32) or small for gestational age (SGA- aOR 0.97, 95% CI 0.75-1.24).

There were sociodemographic factors associated with recorded incidences of STI in pregnancy. While STIs in pregnancy did not have an impact on preterm birth, NICU admission and SGA in our cohort, there was a significant association with stillbirth. Future research should investigate factors contributing to stillbirth, as well as the possibility of increasing the scope of screening for STIs in pregnancy for high risk groups.

Progress
A manuscript is in preparation for publication.

Output
Presentations:

- Ju, I. Sexually Transmitted Infections: prevalence and clinical outcomes amongst pregnant women in Western Sydney. Western Sydney Obstetrics and Gynaecology Research Meeting, Westmead Hospital, April 18, 2023 (Oral Prize Presentation).

Project 7: A systematic review of interventions aimed at improving antenatal screening rates for syphilis, HIV and hepatitis B in low- and middle-income countries

Principal Investigators: Dr Jackson Harrison, Dr Manisha Yapa
Co-Investigators: Pasupathy D
RPC research stream: Translational Health
Progress: In progress

Lay Summary
Syphilis, HIV and hepatitis B are infectious diseases cause considerable morbidity and mortality for those living in settings with limited access to healthcare. These conditions share similar patterns of distribution and transmission and can be cured or controlled if diagnosed early. Of particular importance is the transmission from mother-to-child (vertical transmission) during pregnancy or delivery. The World Health Organisation has called for nations to work toward ‘triple-elimintation’, that is, elimination of the mother-to-child transmission (MTCT) of syphilis, HIV and hepatitis B across the world. For many living in high-income countries these conditions are rare and scarcely a concern during pregnancy, but for those living in low- and middle-income countries (LMICs) where disease burden is highest, there remain significant barriers to triple elimination.

Diagnosis of women attending antenatal clinic appointments who are suffering from syphilis, HIV or hepatitis B is a key step in achieving triple elimination. This systematic review examines a wide range of interventions aimed at increasing screening rates in the antenatal period in LMICs. The aim is for the review to highlight effective intervention approaches, whether they be community or clinic based, focused at a local or more broad level, to inform policy formulation

aimed at achieving triple elimination. The effectiveness, feasibility and scalability of effective interventions will be explored, and important gaps in the literature will be identified. Key literature databases will be systematically searched and an academic paper suitable for peer-reviewed publication will be produced.

Scientific Summary

A systematic review of the literature will be conducted with the aim to identify the impact of interventions to improve rates of screening for syphilis, HIV, and hepatitis B in pregnancy in low- and middle-income countries (LMICs). This is in the context of the World Health Organisation's call for 'triple-elimination' of mother-to-child-transmission (MTCT) of syphilis, HIV, and hepatitis B. These three diseases constitute a considerable proportion of the burden of neonatal disease worldwide every year, and have proven and cost-effective means of diagnosis and treatment. Syphilis, HIV, and hepatitis B share a common means of transmission in MTCT, and epidemiological features, disproportionately impacting those in LMICs.

Our search will include the Medline, Embase and Econlit databases. A search strategy will be developed and adapted for each database, covering relevant terminology specific to the aim of our study. Results will be deduplicated and screened for inclusion first by title, then by abstract and body. Included studies will have data extracted and synthesised to formulate our finalised systematic review. The review will examine a wide range of potential interventions across various contexts, from local health centres, to community based interventions, to public health and policy approaches. Our aim is that our review can highlight the most effective interventions aimed at achieving triple-elimination for the purpose of program and policy formulation.

Progress

The project is currently in the data collection phase. We have performed an initial literature search and are currently working through identifying suitable studies for inclusion in our review and extracting the relevant data for synthesis.

Birth

Project 1: Variations in Preterm Birth Across Sydney

Principal Investigators: Dr Vanessa El-Achi, Professor Dharmintra Pasupathy
Co-Investigators: Gordon A, de Vries B, Nippita T, Morris J, Black K, Melov S, McNab J, Elhindi J, Walker K, Muscat D
RPC Research Stream: Population Health
Funding Support: RTP Scholarship, Sydney Health Partners
Progress: In progress

Lay Summary

Preterm birth (PTB) is a common complication of pregnancy, affecting about 1 in 12 pregnancies in Australia. PTB has important implications for the mother and baby in terms of short and long-term outcomes. While PTB is sometimes spontaneous, other times PTB is necessary due to deteriorating health of the mother or the baby during pregnancy. Therefore, it is important that health services optimise guidance of pregnancy care and management to reduce preventable PTB whilst not compromising outcomes for mothers and babies. This project will examine the frequency, causes and variations of PTB across Western Sydney, Northern Sydney and Sydney Local Health Districts (LHDs).

Scientific Summary

Preterm birth (PTB) is defined as birth before 37 completed weeks of pregnancy and complicates 7-9% of pregnancies in Australia and NSW. PTB is the leading cause of perinatal mortality and morbidity (e.g admission to intensive care, cerebral palsy, learning difficulties and chronic lung disease). This translates into major personal, emotional and financial costs for the family and healthcare system i.e. the annual cost of PTB in Australia is $1.4 billion. Rates of PTB vary according to the three main categories - spontaneous PTB with intact membranes (sPTB), preterm prelabour rupture of membranes (PPROM) or medically-initiated PTB due to maternal or fetal complications. Some PTBs are medically-indicated and delivery should proceed if required, however, if delivery could be delayed safely, the prevalence of PTB and the huge economic cost could be reduced. Aughey et al found 53% of PTBs were iatrogenic (medically-indicated), with some differences observed in risk factors (e.g BMI) compared to sPTB and that there is significant variation underpinning iatrogenic (medically-indicated) PTB.

The aim of this study is to assess the rates and factors associated with PTB and the variations in the categories of PTB across gestational age and model of care across Western Sydney, Northern Sydney and Sydney LHDs.

This information will result in strategies being incorporated into guidelines and provide better education for doctors and midwives, resulting in fewer PTBs, and better overall health of women and their children.

Progress

Ethics approval has been received across the three LHDs to allow data collection to begin.

Project 2: Outcomes Following Induction of Labour in Women with Gestational Diabetes – Does Gestational Age Make a Difference?

Principal Investigators: Vu A, Professor Dharmintra Pasupathy
Co-Investigators: Elhindi J, Harrison J, Melov SJ, Athayde N, Maravar K, Cheung NW, Padmanabhan S, Inglis E
RPC Research Stream: Population Health
Progress: Complete

Lay Summary

Gestational diabetes mellitus (GDM) affects 14% of pregnant women in Australian pregnancies and induction of labour (IOL) is frequently offered to minimise complications of late pregnancy. At present there is limited evidence to inform the exact timing of birth in women with GDM. We compared outcomes for both the mother and the baby following in IOL in women with and without GDM for each week of pregnancy between 37-42 weeks. We found that IOL was more common in GDM women and in most gestational windows the effect on outcomes did not depend on GDM status. Our findings may suggest that the lowest rates of adverse outcomes associated with IOL is at 38-39+6 weeks.

Scientific Summary

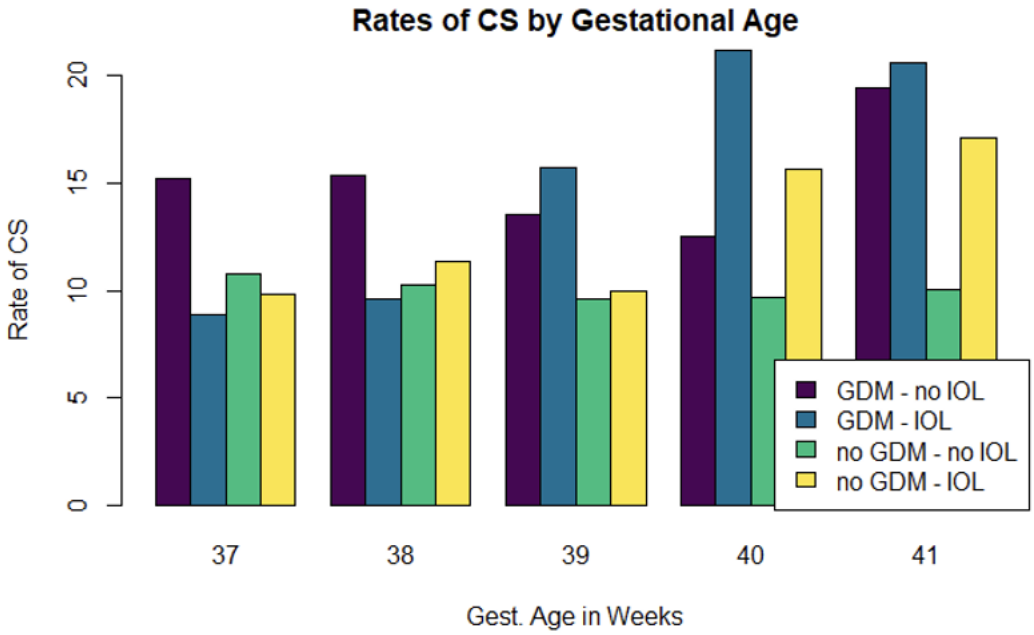
GDM is an increasingly common complication of pregnancy as rates of women diagnosed in Australia tripled from 5% to 15% from 2001 – 2017. This is reason for concern as we know GDM is associated with worsening maternal and neonatal outcomes. The complications associated with GDM can develop throughout pregnancy but especially at term. For the woman, this includes caesarean delivery, operative vaginal birth and pre-eclampsia. Complications for the fetus might include macrosomia, shoulder dystocia, hypoglycaemia, jaundice and stillbirth.

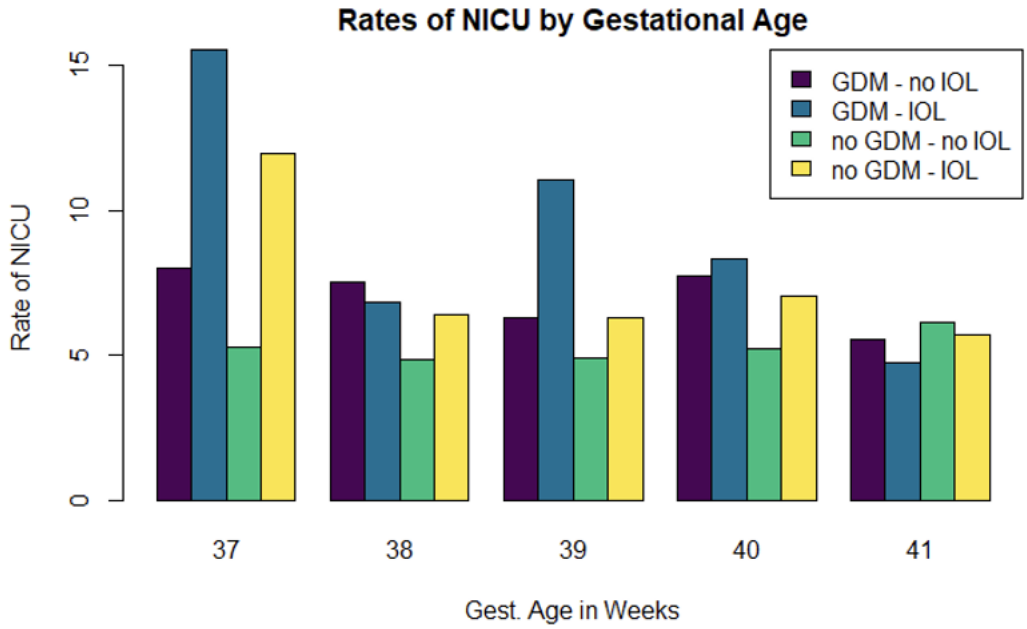
Induction of labour (IOL) is an intervention that can be considered indicated when the balance of risk in continuation of the pregnancy shifts away from the risk associated with early delivery. Because of the potential to do more harm, many find the increasing frequency of IOL needing to be justified. Australian data reflects an international trend showing a 32% increase in IOL from 2007 to 2017. Given that many of the poor outcomes associated with GDM can potentially be mitigated with early delivery it stands to reason that IOL is often recommended for these women. There is no uniformity in Australian national guidelines on when women with GDM should be delivered. It is common practice for women with GDM requiring treatment with insulin to be offered an IOL between 38 and 40 weeks and for women with GDM controlled by diet between 40 and 41 weeks. However, many call into question this strategy citing concerns about both its effectiveness in reducing the poor outcomes associated with GDM and the potential harm done by intervening through an IOL.

The aim of this analysis was to examine the effect of IOL versus spontaneous labour on various maternal and neonatal outcomes in women with GDM and those without, stratified by gestational age in a population from a single site using one uniform protocol of diagnosis.

We compared maternal and neonatal outcomes in IOL stratified by GDM and gestational age at term (37-42 weeks). Our cohort included women from 1st January 2018 to 30th June 2021 with singleton, non-anomalous, term births excluding pre-existing diabetes and pre-labour caesarean sections (CS). Induction at each gestational week was compared to expectant management for that week and all births in subsequent weeks.

There were 12488 women included, 14.3% with GDM. IOL rate was higher in GDM (50.0% vs 37.2%; $p<0.05$). IOL was associated with higher risk of PPH (10% vs 6.6%; $p<0.001$), CS (13.2% vs 10.1%; $p<0.001$) and admissions to NICU (7.4% vs 5.0%; $p<0.001$). The higher rate of CS amongst IOL was only observed >40 weeks gestation. For these outcomes the effect of IOL did not differ by GDM at each GA at term (int $p>0.05$). However, at 38 weeks IOL was protective against CS in women with GDM (p interaction 0.02). The effect of IOL on NICU admissions were highest prior to 38 weeks (aOR 2.3, 95% CI 1.7-3.2).





Output

Presentations:

- Vu A, Elhindi J, Harrison J, Melov SJ, Athayde N, Dr Kavita Maravar, Cheung NW, Padmanabhan S, Inglis E, Smet E, Pasupathy D. Outcomes Following Induction of Labour in Women with Gestational Diabetes – Does Gestational Age Make a Difference?
  RANZCOG Symposium 2022, February 28 – March 1, 2022.
- Vu A, Elhindi J, Harrison J, Melov SJ, Athayde N, Dr Kavita Maravar, Cheung NW, Padmanabhan S, Inglis E, Smet E, Pasupathy D. Outcomes Following Induction of Labour in Women with Gestational Diabetes – Does Gestational Age Make a Difference?
  Perinatal Society of Australia and New Zealand (PSANZ) 2022 Annual Congress.

Impact
IOL was more common in GDM women and in most gestational windows the effect on outcomes did not depend on GDM status. Our findings may suggest that the lowest rates of adverse outcomes associated with IOL is at 38-39+6 weeks.

Future Work
We are acquiring ethics approval to extend the study to a multicentre study in collaboration with Westmead Hospital, Royal Prince Alfred Hospital and Royal North Shore Hospital. This study is also adopted as one of the projects to assess variation in practice for these women across the partners of the Clinical Academic Group in Reproductive, Maternal and Newborn Health of Sydney Health Partners.

Project 3: The EASE-OUT Trial: (EASing oxytocin in Early labour: OUTcomes for mothers and Babies)

Principal Investigators: Krisanaleela A, Associate Professor Brad de Vries
Co-Investigators: Phipps H, Pakzadian S, Bruce B, Dempsey E, Barton K, Eggins R, Tarnow-Mordi W
RPC Research Stream: Translational Health
Funding Support: Sydney Institute for Women, Children and their Families, NHMRC Clinical Trials Centre
Progress: In progress

Lay Summary
Induction of labour is an increasingly common practice in maternity care. Although it is not associated with an increase in the overall rate of caesarean section, there is potential that it may influence the rate of caesarean section because of fetal distress. The purpose of this pilot trial is to assess the potential of a larger trial of a reduced dose of medication used during induction compared to current standard care.

Scientific Summary
Induction of labour prevents overall emergency caesarean section but not caesarean section for fetal distress. Ceasing oxytocin in active labour reduces uterine over-stimulation and fetal distress, but this does not always translate to fewer caesarean sections - due to poor compliance and the frequent need to restart oxytocin. The aim of this study is to determine the efficacy of reducing oxytocin in the active phase of induced labours for improving outcomes for mothers and babies. Among women with oxytocin induction of labour, halving the rate of oxytocin infusion will prevent emergency caesarean section overall and caesarean section for fetal distress compared with infusion using standard protocols.

The purpose of this feasibility trial with a sample size of 50 women in each arm of the trial is to assess potential for a larger trial. This blinded randomized controlled trial of oxytocin infusion using local (NSW Health) protocols will be compared with a protocol of halving the dose of oxytocin in the active phase of labour (intervention). Women with oxytocin IOL in active labour (≥4cm cervical dilatation) with ≥3 regular uterine contractions every 10 minutes and intending vaginal birth will be randomized to the trial. The main outcome is feasibility including: barriers encountered to recruitment, the mean total oxytocin dose per participant (to assess if the two treatment allocations result in a meaningful difference in the received dose of oxytocin), number of potential participants assessed for eligibility, number of potential participants who agree to participate, number of participants randomised and final oxytocin infusion rates.

Progress
Ethics approval at two sites has been obtained (RPA Hospital and Canterbury Hospital) Trial registration: ACTRN12622001342707.

This project is supported by the Clinical Trials Centre, University of Sydney and Sydney Institute for Women, Children and their Families.

Project 4: The SLIP-OUT Trial (Satisfaction with Labour Induction using oral Prostaglandins: OUTcomes for women and babies)

Principal Investigators: Associate Professor Brad de Vries
Co-Investigators: Phipps H, Vu A
RPC research stream: Translational Health
Progress: In progress

Lay Summary

The purpose of this study is to assess the use of an oral medication for the induction of labour compared to current standard care. The primary purpose of the study is to assess women's satisfaction with this phase of induction of labour. The study will also evaluate clinical outcomes in both mother and baby.

Scientific Summary

Childbirth can be positive and empowering yet 20 to 48% of women experience birth as traumatic and 2 to 9% develop post-traumatic stress disorder. Despite this, data on preventing birth trauma is sparse. Oral misoprostol, used extensively in Europe for cervical ripening for induction of labour, was TGA approved in December 2022, but is not yet used in Australia. Vaginal prostaglandins and cervical balloons are used, which cause vaginal pain/irritation and emotional distress. In a Network meta-analysis, oral misoprostol ranked highest for preventing CS, but women's experiences and views are unknown.

The aim of this study is to (1) reduce the emotional trauma associated with childbirth; (2) assess oral misoprostol for improving birth experience compared with current invasive methods of cervical ripening. The hypothesis of this study is that among women having cervical ripening for IOL, oral misoprostol will result in greater satisfaction for women compared with local use of vaginal prostaglandins and cervical balloons. This is an open label randomised controlled trial of 2-hourly 25mcg oral misoprostol compared with local protocols for vaginal prostaglandins + cervical balloon catheters. Women having cervical ripening for induction of labour with Bishop Score <7 and no contraindication to oral misoprostol, vaginal prostaglandins or to cervical balloon catheters. The intervention is standard inpatient protocol of oral misoprostol commencing at 25mcg 2-hourly will be compared against Royal Prince Alfred and Canterbury Hospitals in NSW for vaginal prostaglandins and cervical balloon catheters. The outcomes of interest include Primary: (1) Visual analogue scale of maternal satisfaction with cervical ripening process; and (2) Satisfaction with childbirth experience [Childbirth Experience Questionnaire (CEQ)]; Secondary: Combined serious maternal morbidity or mortality; and combined serious perinatal/neonatal morbidity or mortality within 6 weeks of birth. The calculated sample size for this study – 168 (84 in each arm).

Progress

This project is supported by the Clinical Trials Centre, University of Sydney and Sydney Institute for Women, Children and their Families.

Project 5: The Association Between Interpregnancy Interval And Uterine Rupture Among Women With One Previous Caesarean Section

Principal Investigators: Adily P, Associate Professor Brad de Vries
Co-Investigators: Bettison T, Mackie A, Berghella V, Narayan R, Phipps H, Haghighi M, Perren K, Johnson G
RPC research stream: Population Health
Progress: In progress

Lay Summary
Women with a history of caesarean birth in their previous pregnancy is often faced with the decision on choice of mode of birth in their subsequent pregnancy. Midwives and obstetricians are also keen to provide reliable estimates of risk associated with subsequent attempts at vaginal delivery so that informed decisions can be made by women. Often the duration since the previous birth is considered in these consultations. However further more detailed data is required on interpregnancy interval on the risk of complications following previous caesarean birth.

Scientific Summary
The caesarean rate has been increasing globally, one major cause being caesarean section for a previous caesarean section. Previous caesarean section confers a risk of future uterine rupture during labour which can lead to adverse perinatal outcomes including stillbirth, hypoxic ischaemic encephalopathy and neonatal death; and adverse maternal outcomes including massive haemorrhage, intensive care unit admission and hysterectomy. Short interpregnancy interval is a risk factor for uterine rupture but data are very limited.

The aim of this study is to describe rates of uterine rupture and other adverse pregnancy outcomes by interpregnancy interval on a month by month- by-month basis. This is a large population based retrospective cohort study using publicly available data from the Centre for Disease Control in the United States. Data from 2011 to 2021 are available, representing more than 40 million births. Outcomes for those women with one previous livebirth where that birth was by caesarean section who had a trial of labour will be described for women with spontaneous and induced or augmented labours. The primary outcome is uterine rupture. Other outcomes include perinatal death (stillbirth and perinatal death within 28days), low 5 minute Apgar scores, NICU admission, neonatal ventilation, neonatal seizures, maternal blood transfusion, ICU admission and unplanned hysterectomy. Multivariable logistic regression will be performed for uterine rupture on interpregnancy interval, adjusting for maternal age, height, body mass index, hypertension, diabetes in pregnancy, ethnicity, cigarette smoking, and education.

It is anticipated that these data will inform counselling for women with a previous caesarean section who are deciding between elective caesarean section and a trial of vaginal birth.

Progress
This project is supported by the Sydney Institute for Women, Children and their Families.

Project 6: The Association Between Intravenous Fluid Use In Labour And Post-Partum Haemorrhage

Principal Investigators: Bruce B, Associate Professor Brad de Vries
Co-Investigators: Leask J, Shepherd H, Khan S
RPC research stream: Population Health
Progress: In progress

Lay Summary
Women are often prescribed fluids in labour which are administered through an intravenous line. The impact of this additional fluid administration of labour and birth outcomes are unknown. This study aims to address the gap in knowledge that exist.

Scientific Summary
Intravenous fluids are frequently used in labour, often with little evidence to support their use. Intravenous fluid use in labour is poorly documented and there is minimal guidance for clinicians from governing bodies. It is possible that excessive maternal hydration could lead to post-partum haemorrhage through mechanisms such as uterine oedema or dilution of oxytocin concentrations impacting on uterine contractility, or intravascular dilution of clotting factors. The aim of this study is to assess the association between the volume of intravenous fluids in the first and second stages of labour, and primary post- partum haemorrhage. This is a

retrospective observational study of women with a term pregnancy, cephalic presentation, who were planning a vaginal birth at the time they went into labour. The study compares outcomes in women receiving intravenous fluids (examined as both a bivariate and continuous variable) to women with lower volumes or no intravenous fluids in labour. The primary outcome is primary post-partum haemorrhage. Other relevant maternal and perinatal outcomes will be assessed. The primary analysis will be a logistic regression adjusted for potential confounders including birthweight, prolonged ruptured membranes, rapid labour, prolonged labour, epidural analgesia, hypertension in pregnancy, obesity, parity, and use of oxytocin infusion.

Knowledge of the association between intravenous fluid use and post-partum haemorrhage will lead to improved guidance about the use of intravenous fluids in labour.

Progress

This project is part of a PhD being undertaken through the Susan Wakil School of Nursing and Midwifery, University of Sydney.

Project 7: Is Uterine Over-Stimulation Associated With Maternal Age?

Principal Investigators: Boots B, Associate Professor Brad de Vries
Co-Investigators: Hyett J, Phipps H
RPC research stream: Population Health
Progress: In progress

Lay Summary

Higher than normal uterine contractions during the process of induction of labour is a recognized complication and often a result of the medications used. The purpose of this study is to examine the influence of the age of the mother on the rates of over contractions. This study which analysed birth data from more than 2800 women observed that younger women were more likely to experience an increase of uterine contractions more than what is expected. These findings have the potential to inform protocols for induction of labour for women.

Scientific Summary

Induction of labour at term is associated with a small decrease in the risk of caesarean section compared with no planned induction of labour. Emerging evidence suggests that induction of labour has different effects on caesarean section for labour dystocia (decreased) compared with caesarean section for fetal concerns (no difference). The latter may be mediated by excessive uterine contractions due to oxytocin use leading to umbilical cord compression, fetal heart rate abnormalities and fetal hypoxaemia, and was observed to be more prominent in younger women, potentially due to age-related changes in uterine contractility. The aim of this study is to assess the relationship between excessive uterine activity, uterine hyperstimulation (with fetal heart rate changes) and maternal age among women undergoing induction of labour. This is a retrospective observational study of birth outcomes in women with induction of labour at term and no previous caesarean section. The rate of excessive uterine contractions (tachysystole, hypertonus, hyperstimulation), other relevant maternal and perinatal outcomes were compared between women in younger and older age groups.

Our preliminary results of the data from 2876 women, rates of at least one episode of hypertonus or tachysystole were 17.0%, 18.2%, 12.4%, 5.7%, and 4.1% in age groups <25, 25-29, 30-34, 34-39, and 40+ years respectively. The mean number of hyperstimulation events in these age group were 0.52, 0.46, 0.34, 0.18, and 0.09 respectively. In a multivariable poisson regression, age group remained associated with these events (p=0.0002). Maternal height (p=0.003), birthweight (0.004) and parity (p=0.02) were also independently associated with the number of hyperstimulation events. Young maternal age is associated with uterine hyperstimulation among women with induction of labour at term. This is important for developing future induction of labour practices and protocols.

Global Health

Project 1: Trend in the preterm birth rate at a major tertiary maternity hospital in Vietnam

Principal Investigators: Quynh Truc, Ibinabo Ibiebele
Co-Investigators: Seeho S, Nippita T, Morris J
RPC Research Stream: Global Health
Progress: In progress

Lay Summary

Preterm birth is associated with considerable infant morbidity and mortality, particularly in low resource settings. Infants are also at risk of long-term adverse health outcomes. The rate of preterm birth has increased in many countries, including Australia. Data on the rate of preterm birth in Vietnam are lacking. The aim of this study was to determine the rates of preterm birth in a major maternity hospital in Vietnam over a five-year period, and compare the preterm birth rates to those in New South Wales, Australia over the same time period.

Scientific Summary

The study population included all singleton livebirths delivered from 20 weeks' gestation, between January 2015 and December 2019 in Tu Du Hospital, Vietnam, and New South Wales, Australia. Multiple births, stillbirths, pregnancy terminations, births with a gestational age less than 20 weeks, births with missing gestational age, duplicates, and unmatched records were excluded. Preterm birth was defined as birth less than 37 weeks' gestation.

In this study, data were exported from the electronic database in Tu Du hospital and obtained from three data sources in NSW. The NSW Perinatal Data Collection - 'birth data' is a population surveillance system capturing information on all births of at least 20 weeks' gestation or 400 g in public and private hospitals and home births in NSW; the NSW Admitted Patient Data Collection, which is 'hospital data' captured information on all in-patient discharges from public and private hospitals and day procedure units; and information on diagnoses and procedures were coded using the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian modification (ICD10AM) and Australian Classification of Health Interventions (ACHI), respectively. Data on mortality was obtained from the Register of Births Deaths and Marriages – Death Registration ('death data'). Individual-level data were linked using probabilistic methods by the NSW Centre for Health Record Linkage. The study outcome of preterm birth was defined as birth less than 37 weeks' gestation. The study population included 325,026 singleton livebirths from Tu Du Hospital and 464,414 singleton livebirths from NSW. Preterm birth rates were steady in both Tu Du Hospital (11.2% in 2015 to 12.1% in 2019, ptrend=0.081) and NSW (5.8% in 2015 to 5.4% in 2019, ptrend=0.358). There were no significant changes in the distribution of gestational age at birth over the study period for both Tu Du Hospital and NSW.

Progress

Data collection and analyses have been completed. The study is being prepared for submission to a peer-review scientific journal.

Project 2: Neonatal outcomes following preterm birth in Vietnam

Principal Investigators: Quynh Truc, Sean Seeho
Co-Investigators: Ibiebele I, Nippita T, Morris J
RPC Research Stream: Global Health
Progress: In progress

Lay Summary

Preterm birth is associated with significant infant morbidity and mortality, and long-term harm. Ad-verse sequelae associated with preterm birth are particularly increased in babies born extremely preterm. In developed countries, the risk of adverse outcomes for preterm babies is well de-scribed for each week of pregnancy. In lower resource settings such as Vietnam, adverse outcome data for babies born preterm are lacking. The aim of this study was to determine the risk of ad-verse outcomes following preterm birth following a singleton pregnancy in Tu Du Hospital in Ho Chi Minh City, Vietnam. Tu Du Hospital is a large maternity hospital that has more than 60,000 births annually.

Scientific Summary

This retrospective cohort study included all singleton live births between 28- and 36-weeks' gestation at Tu Du hospital between 1 June 2019 and 30 June 2020. The study excluded infants who were stillborn, born following termination of pregnancy, or who had unknown or inaccurate gestational age.

Data were obtained from the maternal and neonatal hospital records, and included maternal demographics, medical and pregnancy conditions, and birth outcomes. All births between 28- and 36-weeks' gestation during the study period were identified through the hospital's electronic database. Medical records were individually reviewed for eligibility and to extract relevant data. Ethics approval for the study was obtained from the ethics committee of Tu Du Hospital with the number 854/QD-BVTD.

5,374 singleton live births between 28-36 weeks' gestation met the inclusion criteria. 2,765 (51.5%) births followed spontaneous onset of labour and 2,616 (48.5%) were planned preterm births. There were 663 infants (12.4%) born between 28-31 weeks' gestation, 824 (15.3%) between 32-33 weeks' gestation, and 3,887 (72.3%) between 34-36 weeks' gestation. Neonatal morbidity rates decreased from 184.5/1000 to 5.4/1000live births between 28-36 weeks. Between 28-33 weeks, >90% neonates had morbidity, with the rate of morbidity decreasing from 34 weeks. The odds of neonatal mortality were not significantly different following labour induction (aOR 1.22; 95% CI 0.72-2.09) or pre-labour caesarean section (aOR 1.04; 95% CI 0.63-1.73) compared with spontaneous labour. The odds of neonatal morbidity were higher among pregnancies following labour induction (aOR 1.53; 95% CI 1.31-1.80) and pre-labour caesarean section (aOR 2.14; 95% CI 1.84-2.50) compared with spontaneous labour.

In conclusion, preterm birth in Vietnam is associated with high rates of mortality and morbidity, particularly prior to 34 weeks' gestation. Planned preterm birth is associated with a greater rate of morbidity.

Progress

Data collection and analyses have been completed. The study is being prepared for submission to a peer-review scientific journal.

Output

Presentations:

- Tran QTT, Nippita TA, Seeho SK, Morris JM, Ibiebele I. Neonatal outcomes following preterm birth in a middle-income Asian country.
  Perinatal Society of Australia and New Zealand (PSANZ) 2022 Annual Congress.

Project 3: Impact of being small for gestational age on the risk of stillbirth according to gestational age in a middle-income country

Principal Investigators: Dr Jackson Harrison, Dr Matias C Vieira, Professor Dharmintra Pasupathy
Co-Investigators: Souza RT, Esteves-Pereira AP, Madeira Domingues RMS, Lopes Moreira ME, Vieira da Cunha Filho E, Seed P, Sandall J, Cecatti JG, do Carmo Leal M, Bastos Dias MA, Copas A
RPC Research Stream: Global Health
Funding Support: MRC Challenge Fund
Progress: In progress

Lay Summary

Over 2.5 million stillbirths occur each year, and of these 98% occur in low- and middle-income countries (LMICs). Stillbirth has a number of risk factors, including foetuses which are small for gestational age (SGA). The risk factors for stillbirth vary between high income (HICs) and LMICs. Most of the research on stillbirth and SGA has occurred in HICs, and there is an urgent need to further investigate causes of stillbirth in LMICs.

Brazil is a middle-income country with a socially and economically diverse society. Brazil's GDP has been increasing steadily since 2000, and rates of stillbirth falling from 11.1/1000 births in 2007, to 10.4/1000 births in 2019. We analysed data from the Brazilian national registry for livebirths and stillbirths to assess the relationship between SGA and stillbirth at various time periods throughout the pregnancy. Our aim was to assess whether the risk of stillbirth attributable to SGA varied throughout the pregnancy.

We assessed over 2.8 million births from the year 2019 in Brazil. Approximately 40% of all stillbirths were classified as SGA, whilst 10% of livebirths were classified as SGA. Using statistical analysis, we found that the risk of stillbirth attributable to SGA was consistent in the pre-term period, with 5.7 – 6.1 times higher odds, and fell after 37 weeks to 3.1 – 4.8 times higher odds. We also found a large proportion of SGA stillbirths (approximately 47%) occurred in the late between 34 and 42 weeks.

Prevention of late term stillbirth may be possible through detection and delivery of the baby before foetal death. Our findings suggest that by focussing on detecting SGA foetuses, they may be able to be delivered before having the poor outcome.

Scientific Summary

Our study aimed to determine the association between SGA and the risk of stillbirth in the Brazilian population, and to assess if the association would be modified by gestational age. Given the vast overrepresentation of LMICs in the global distribution of stillbirths, we hoped that this investigation would be able to inform research on stillbirth prevention in the LMIC setting more broadly.

We undertook a retrospective cohort study using data from publically available Brazilian national registries for livebirths (SINASC) and stillbirths (SIM). Pregnancies with missing data for birthweight, number of foetuses or GA, GA < 24 weeks or GA > 42 weeks, foetal anomalies, or birthweight Z-score > 5 or < -5 were excluded. Summary statistics were calculated for demographic factors. The prospective risk of stillbirth was calculated for SGA and AGA foetuses for six separate strata of GA. Using the Wald test, multivariate logistic regression was used to assess for effect modification of GA strata on the relationship between SGA and stillbirth. The model was adjusted for maternal age, parity and education and generated adjusted odds ratios for stillbirth amongst SGA versus AGA foetuses at various GA.

In total 2 785 609 livebirths and 19 768 stillbirths were included for analysis. Overall the stillbirth rate was 7.1/1000 deliveries. Amongst stillbirths, the proportion with birthweight centiles categorising them as SGA was higher than livebirths (38.0% SGA for stillbirths, 9.6% SGA for livebirths). The multivariate analysis showed all interaction parameters to be significant, suggesting effect modification of SGA on stillbirth across all GA strata. The adjusted effect of

SGA on stillbirth according to gestational age were: 24+0 to 27+6 OR 5.87 (95%CI 5.68 – 6.07), 28+0 to 30+6 OR 6.06 (95%CI 5.85 – 6.28), 31+0 to 33+6 OR 6.01 (95%CI 5.77 – 6.25), 34+0 to 36+6 OR 5.71 (95%CI 5.45 – 5.98), 37+0 to 39+6 OR 4.75 (95%CI 4.46 – 5.06), ≥ 40+0 OR 3.17 (95%CI 2.79 – 3.61).

The effect of SGA on the risk of stillbirth varies with GA, the effect is consistent with decreasing contribution to stillbirth after 37 weeks. However, a large absolute proportion of SGA stillbirths occur closer to term. In considering implications for policy in resource limited settings, this may represent an area where a large proportion of the burden mortality associated with stillbirth lies.

Progress
Statistical analysis and draft manuscript completed. Ongoing editing of manuscript prior to submission for publication.

Project 4: Continuation rates of postpartum Implants and impact on birth spacing at Port Moresby General Hospital

Principal Investigators: Professor Kirsten Black
Co-Investigator: Mola G
RPC Research Stream: Global Health
Funding Support: Philanthropic donation
Progress: In progress

Lay Summary
Our previous research studied the midwife-led immediate postpartum implant program at Port Moresby General Hospital. We found that antenatal education about the contraceptive implant significantly impacted on likelihood of immediate postpartum method uptake. Women who had no prior use of contraception and those with unplanned pregnancies were also more likely to request the implants, suggesting that the midwife led postpartum service is successfully reaching women with a previous unmet need for contraception. spacing. The World Health Organization recommends birth spacing of 24 months as there is evidence that particularly if the interval between one birth and the conception of the next pregnancy is less than 12 months, a range of adverse outcomes perinatal are observed. These include maternal anaemia, preterm delivery small for gestational age, stillbirth and neonatal death. To understand the full benefit of the immediate postpartum implant program it is important to document the continuation rate of implant use up to 12 months postpartum and the impact of implant use on birth spacing.

Scientific Summary
We will undertake a prospective cohort study of 150 women choosing the implant and 150 women choosing user dependent methods and follow them up for 12 months postpartum.

Based on data from PNG and from other studies, the chance of an interpregnancy interval of less than 12 months is currently 35%; that is over one third of women present with a pregnancy within 12 months of a birth. We seek to explore whether a 45% reduction (ie to 20%) is achieved with the implant program by delaying the subsequent pregnancy. We will seek to recruit 160 women who chose the implant and 160 who don't (accounting for a 20% loss to follow up). The initial recruitment will be undertaken by Masters of Obstetrics and Gynaecology students at the Port Moresby General Hospital over a three-month time frame. Follow up will then occur 12 months later.

Progress
The study has recently commenced.

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2023

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Highlights

RPC Across 3 Precincts: Central, Western and Northern

PSANZ Annual Congress
Adelaide, Australia
May 2022

FMF International Congress
Crete, Greece
June 2022

PSANZ Annual Congress
Adelaide, Australia
May 2022

RPC Strategy Day
The University of Sydney
September 2022

IADPSG
Sydney, Australia
November 2022

RPC Christmas Celebrations
Darling Harbour
Sydney, Australia
December 2022

PSANZ Annual Congress
Melbourne, Australia
March 2023

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