

iPREM Pilot Trial
Supplementary Material Ver 1.0
27.04.2023

Effect of viral transmission mitigation measures on the incidence of preterm birth in high-risk pregnant women: protocol for a pilot, feasibility randomised trial

Shivadharshini Sridhar^{1,2}, Ben W Mol^{1,2}, Ryan Hodges^{1,2}, Kirsten R Palmer^{1,2}, Suresh Sundram^{3,4}, Rodolfo Carvalho Pacagnella⁵, Renato T Souza⁵, Francisco Barbosa-Junior⁶, David Mackin⁷, Joanne Said^{7,8}, *Daniel L Rolnik^{1,2}, *Atul Malhotra^{9,10,11}

*Equal contribution

1. Department of Obstetrics and Gynaecology, Monash Medical Centre, Melbourne, Australia
2. Department of Obstetrics and Gynaecology, Monash University, Melbourne, Australia
3. Department of Psychiatry, School of Clinical Sciences, Monash University, Melbourne, Australia
4. Mental Health Program, Monash Health, Melbourne, Australia
5. Department of Obstetrics and Gynaecology, University of Campinas, Campinas, Brazil
6. Department of Social Medicine, Ribeirão Preto Medical School, University of São Paulo, Ribeirão Preto, Brazil
7. Department of Maternal Fetal Medicine, Joan Kirner Women's & Children's, Sunshine Hospital, Western Health, Melbourne, Australia
8. Department of Obstetrics and Gynaecology, The University of Melbourne, Melbourne, Australia
9. Department of Paediatrics, Monash University, Melbourne, Australia
10. Monash Newborn, Monash Children's Hospital, Melbourne, Australia
11. The Ritchie Centre, Hudson Institute of Medical Research, Melbourne, Australia

SUPPLEMENTARY MATERIAL

iPREM Pilot Trial
Supplementary Material Ver 1.0
27.04.2023

PARTICIPANT INFORMATION AND CONSENT FORM (MASTER)

Title	Randomised controlled trial investigating the effect of viral transmission mitigation measures on the incidence of preterm birth in high-risk pregnant women
Short Title	iPREM (Pilot)
Project Sponsor	Monash Health
Principal Investigator(s)	Professor Ben Mol
Associate Investigator(s)	Dr A/Prof Daniel Rolnik A/Prof Atul Malhotra Dr Shivadharshini Sridhar

Part 1 What does the participation involve?

1 Introduction

We are inviting you to take part in this research project because you are currently pregnant and have previously given birth to a preterm baby (i.e. a baby born between 22 and 34 weeks of gestation). Your information was obtained from our medical records system. This research project is investigating the feasibility and safety of an intervention in pregnancy that may decrease the risk of preterm birth.

This participant information and consent form will explain the purpose of our project and what it will involve as clearly as possible so that you can be fully informed before you decide whether you would like to take part.

Please take your time to read through this statement carefully. If you have any questions or concerns, please do not hesitate to contact our researcher via email or phone. Before deciding whether you would like to participate, you may want to talk about it with a family member or a medical professional.

Participation in this research project is voluntary and if you decide you do not wish to take part, you do not have to. You will still receive the best possible care regardless of whether you are involved with our study.

iPREM Pilot Trial
Supplementary Material Ver 1.0
27.04.2023

If you do decide to take part, you will need to sign the consent section. By signing this, you are telling us that:

- You understand everything you have read in this statement
- You consent to your participation in this project
- You consent to the use of your personal and health information as described

You will be given a copy of this participant information and consent form to keep.

2 What is the purpose of this research?

Preterm birth (i.e. when a baby is born too early) occurs in around 9% of all deliveries in Australia and can be associated with significant medical consequences for babies. During the COVID-19 pandemic, we, and many other groups around the world have observed that women who have been pregnant during lockdown have experienced a decreased rate of preterm birth. At Monash Health, a 30% decrease in women giving birth before 34 weeks of gestation was observed and this effect was stronger in women who had a previous preterm birth. We believe that this phenomenon may have to do with changes in the way we lived during lockdowns - physical distancing, changes in physical activity, work from home and possibly improved hygiene.

The purpose of this study is to investigate whether it is feasible to conduct an intervention in pregnancy that mimics the COVID-19 lockdowns and observe if there is an associated decrease in the rate of preterm birth in women who have previously experienced a preterm birth. Once we can establish feasibility and safety of this intervention, larger studies may be conducted to further establish whether these measures actually decrease preterm birth rates.

This research has been initiated by a research team led by Professor Ben Mol. This team, alongside the associate investigators listed above have experience looking after pregnant women and premature babies.

3 Who is organising and funding the research?

This research project is being conducted and led by Professor Ben Mol and his research team.

4 What does participation in this research involve?

If we determine that you are eligible to participate and you choose to take part in this study, you will be required to sign the consent form below.

iPREM Pilot Trial
Supplementary Material Ver 1.0
27.04.2023

We are inviting 100 women to take part in this study. 50 women will be randomly assigned to the 'control' group and undergo standard pregnancy care with no changes. 50 women will be randomised to the 'intervention' group, where they will be asked to comply with a pregnancy intervention that mimics the lockdown measures implemented in Melbourne to prevent the transmission of COVID-19.

If you are part of the pregnancy intervention group, you will be asked to try and comply with the following measures to the best of your ability for the duration of the study:

- Refrain from attending social gatherings and maintain 1.5m distance between yourself and another individual when outside your home
- Try to wear a face mask or covering whenever you leave your home
- Try to perform hand hygiene prior to touching your nose or mouth
- Try to remain in your home unless you must leave for study/work, for essential services, to seek, safety purposes (e.g you do not feel safe in your home) or give care or to do outdoor exercise
- Try to remain at home between the hours of 9pm-5am unless you must leave for work/study, safety purposes or to seek/give care
- Avoid having visitors to your home unless they are an intimate partner
- Try not to travel beyond 5km from your place of residence

We understand that there may be certain circumstances that mean you cannot follow through with all the above recommendations, for example, important events that you must attend such as a wedding or funeral. You are of course free to attend at your discretion, we just ask that wherever you can, please try to follow the recommendations as much as possible. For instance, if you attend a wedding, consider following at least some of the recommendations such as wearing a facemask and performing hand hygiene.

The study will begin 2 weeks before the gestation at which you gave birth to your previous preterm baby (i.e. if you gave birth at 32 weeks, the study would begin at 30 weeks gestation of your current pregnancy). However, if your previous preterm baby was born at 33+6 weeks gestation, the study will begin at 30+6 weeks gestation of this pregnancy so that you are in the study for at least 3 weeks. It will be conducted for 6 weeks (i.e. 2 weeks before and 4 weeks after the gestational age of your previous preterm birth), until 34 weeks gestation or until birth – whichever comes first.

You will be asked to complete a 5-10 minute fortnightly surveys over the course of the study about your work, household contacts, physical activity, hygiene practices, mood and quality of life. You will also be asked to wear a device on your wrist (figure 1), similar to a watch, that will record physical activity, temperature, light and sleep for the duration of your time in the study.

iPREM Pilot Trial
Supplementary Material Ver 1.0
27.04.2023



Figure 1. Actigraphy device.

You will not be paid to take part in this research project and there will be no additional costs to you associated with your participation.

5 Do I have to take part in this research project?

Participation in this trial is entirely voluntary and if you do not wish to take part you are in no way obligated to. If you decide to take part and then change your mind, you are free to withdraw at any stage – you can easily do this by contacting the researcher via email or phone and informing them of your wish to withdraw.

If you do decide to take part, you will be given a copy of this patient information consent form to sign and a copy to keep.

Your decision to take part, or not take part in this study will not affect your relationship with your doctors, midwives, or the health service, and will not impact the care that you are given.

6 What are the alternatives to participation?

You do not have to take part in this study to receive treatment at this hospital. Your routine pregnancy care will not change or be impacted if you decide not to take part.

7 What are the possible benefits of taking part?

iPREM Pilot Trial
Supplementary Material Ver 1.0
27.04.2023

This research may provide us with further insight into prevention of preterm birth and could play an integral role in changing future clinical practice. We are conducting this study to mainly check whether such a pregnancy intervention is feasible and safe, and we are not yet sure if/which aspect of lockdown measures impact preterm birth rates. As such, there may be no clear benefit for your pregnancy from your participation.

Given the COVID-19 pandemic is still ongoing, a potential benefit for anyone who is in the intervention group of the study is that they may be less likely to contract the virus given they will be adhering to established viral mitigation measures, that is, restrictions to travel/social distancing/physical contact and recommendations regarding hygiene/face coverings known to prevent transmission.

8 What are the possible risks and disadvantages of taking part?

We anticipate that the main risks associated with participating in this study are feelings of social isolation and perhaps decreased social support in those who are a part of the pregnancy intervention group. You may also find that the additional restrictive measures imposed may make it more difficult to perform your routine tasks, for example, you may have to shop online as opposed to in store for non-essential items. If you are asked to restrict your activities and minimise your social contacts, your partner and/or other household contacts may feel burdened with additional responsibilities such as increased chores or tasks associated with looking after your other children.

In this event, please inform a member of the research team and we will guide you in accessing the appropriate services such as seeing your GP, counselling services and/or speaking with organisation such as Lifeline (13 11 14). You are welcome to contact the researchers at any time via email or phone to discuss this further and you can withdraw from the study at any stage. You will not incur any risk if you choose to withdraw.

9 What if new information arises during this research project?

There are times where during a research project, new information may become available about the condition we are investigating. If this was to occur, the researcher will inform you about it and discuss whether you would like to continue to take part in the study. If you decided that you would still like to be a part of the study, we may ask you to sign an updated consent form.

If we discover new information that leads us to believe that it would be in your best interests to withdraw from the study, the researcher will discuss the reasons with you.

10 What if I withdraw from this research project?

iPREM Pilot Trial
Supplementary Material Ver 1.0
27.04.2023

You can withdraw from the study at any stage. If you decide to withdraw, please let a member of the research team know via email or phone. We will discuss the reason for withdrawal with you so we can determine if there are any specific health risks or requirements linked to withdrawing.

11 Could this research project be stopped unexpectedly?

This study could be stopped unexpectedly for several reasons. For example, if we found that there were unacceptable adverse effects or new information became available regarding the effect of lockdown measures on the rate of preterm birth.

12 What happens when the research project ends?

Once the study finishes, our team will analyse the results. If you would like to be informed of the results, please let us know and we can email you a copy. Your privacy will be protected as we will only be reporting the whole group's results, which means there is no way your individual results could be traced to you.

Part 2 How is the research project being conducted?

13 What will happen to information about me?

By signing this consent form, you are consenting for authorized members of our research team to collect, store and use relevant personal information for this study. Your information may be collected from our medical records, the actigraphy device worn on your wrist and surveys that you will have completed over the duration of the study. Any information we collect with relation to this project that could identify you will be kept confidential to protect your privacy, on a secure, password protected computer system at the relevant health service. Only authorised members of the research team will have access to this information, and it will only be used for the purpose of research. This information can only be disclosed with your permission or if required to do so by law.

We anticipate that the results of this study will be published in a peer-reviewed journal and presented at various forums such as medical conferences when appropriate. Information will only be presented in a de-identified manner, which means you will not be identified, unless you give us permission. As per Monash Health research policy, we will store your information for 15 years. After this period, we may dispose of all the information in a safe and secure manner such as shredding paper records and permanently deleting any electronic records.

Information regarding your participation in this trial will be recorded in your health record.

iPREM Pilot Trial
Supplementary Material Ver 1.0
27.04.2023

As per Australian and/or Victorian privacy and other relevant laws, you have the right to request access to the information the research team collects and stores. You also have the right to request that any information you disagree with be rectified. If you would like to take part in our study and would like access to the information we collect, please feel free to contact a member of the research team (their details are at the end of this document).

14 Complaints and Compensation

If you suffer from a medical condition or complication because of this trial, please contact a member of the research team immediately so that we can assist in arranging the appropriate medical treatment. Any treatment you require should be free of charge if you are a Medicare card holder and attend an Australian public hospital as a public patient.

15 Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by Monash Health HREC.

This project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2018)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

16 Further information and who to contact

The person you may need to contact will depend on the nature of your query.

If you want any further information concerning this project or if you develop any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact the principal study doctor as below:

Principal Study Doctor

Name	A/Prof Daniel Rolnik
Position	Consultant Obstetrician and Gynaecologist, Monash Health
Telephone	0452 105 585
Email	daniel.rolnik@monash.edu

iPREM Pilot Trial
Supplementary Material Ver 1.0
27.04.2023

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

Reviewing HREC name	Monash Health Human Research Ethics Committee
HREC Executive Officer	HREC Executive Officer
Telephone	03 9594 4611
Email	Research@monashhealth.org

iPREM Pilot Trial
Supplementary Material Ver 1.0
27.04.2023

Consent Form

Title	Randomised controlled trial investigating the effect of viral transmission mitigation measures on the incidence of preterm birth in high-risk pregnant women
Short Title	Viral mitigation measures and preterm birth
Project Sponsor	Monash Health
Principal Investigators	Professor Ben Mol
Associate Investigators	A/Prof Daniel Rolnik, A/Prof Atul Malhotra, Dr Shivadharshini Sridhar

Declaration by Participant

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the research described in the project.

I give permission for my doctors, other health professionals, hospitals, or laboratories outside this hospital to release information to Monash Health concerning my health for the purposes of this project. I understand that such information will remain confidential.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to my participation in this research project as described and understand that I am free to withdraw them at any time during the research project without affecting my future health care.

I understand that I will be given a signed copy of this document to keep.

Participant's Name (please print): _____
Participant's Signature: _____ Date _____

iPREM Pilot Trial
Supplementary Material Ver 1.0
27.04.2023

Name of Witness*
to participant's signature (please print)

Signature: _____ Date: _____

* Witness is not to be the investigator, a member of the study team or their delegate. In the event that an interpreter is used, the interpreter may not act as a witness to the consent process. Witness must be 18 years or older.

Declaration by Study Doctor

I have given a verbal explanation of the research project; its procedures and risks and I believe that the participant has understood that explanation.

Name of Study Doctor
(please print):

Signature: _____ Date: _____

Note: All parties signing the consent section must date their own signature.

iPREM Pilot Trial
Supplementary Material Ver 1.0
27.04.2023

FORTNIGHTLY PARTICIPANT SURVEY

1. On average, how often did you wear a face covering when outside your home in a week?
 - a. Never
 - b. Sometimes (specify which type)
 - c. Most of the time (specify which type)
 - d. Always (specify which type)
2. On average, how often were you within 1.5m distance of another person who is not a household contact in a week?
 - a. Never
 - b. Sometimes
 - c. Most of the time
 - d. Always
3. On average, how often did you perform hand hygiene prior to touching your nose/mouth in a week?
 - a. Never
 - b. Sometime
 - c. Most of the time
 - d. Always
4. On average, how many times did you leave your house for activities that are not considered 'essential' in a week? Essential activities include shopping for essentials, to work/study, to give/seek care or for outside exercises.
 - a. 0-5 times
 - b. 5-10 times
 - c. 10-20 times
 - d. > 20 times
5. On average, how often did you travel beyond 5km of your place of residence in a week?
 - a. 0-5 times
 - b. 5-10 times
 - c. 10-15 times
 - d. >15 times
6. On average, how often did you leave your home between the hours of 9pm-5am for non-essential purposes in a week? Essential activities include for work/study or to seek/give care.
 - a. 0-5 times
 - b. 5-10 times
 - c. 10-15 times
 - d. >15 times
7. On average, how many visitors did you have to your home in a week, excluding an intimate partner?
 - a. 0-2
 - b. 2-4
 - c. 4-6
 - d. >6

iPREM Pilot Trial
Supplementary Material Ver 1.0
27.04.2023

Sleep, Mood and Quality of Life

1. How many hours of sleep are you getting each night?
 - a. 2-6 hours
 - b. 6-8 hours
 - c. 8-10 hours
 - d. >10 hours
2. How often have you felt sad/low for no good reason?
 - a. Never
 - b. Sometimes
 - c. Most of the time
 - d. All of the time
3. How often have you felt anxious or panicky for no good reason?
 - a. Never
 - b. Sometimes
 - c. Most of the time
 - d. All of the time
4. How often have you looked forward with enjoyment to things?
 - a. Never
 - b. Sometimes
 - c. Most of the time
 - d. All of the time
5. How often have you felt like you were having trouble coping with things?
 - a. Never
 - b. Sometimes
 - c. Most of the time
 - d. All of the time
6. How often have you felt that you have someone with whom you can share your joys, sorrows and anxieties with?
 - a. Never
 - b. Sometimes
 - c. Most of the time
 - d. All of the time
7. How often have you felt that you have someone to count on when you need help?
 - a. Never
 - b. Sometimes
 - c. Most of the time
 - d. All of the time
8. How often have you felt unable to cope with performing your usually day to day activities alongside your pregnancy?
 - a. Never
 - b. Sometimes
 - c. Most of the time
 - d. All of the time
9. How satisfied do you feel with your social life right now?
 - a. No satisfaction
 - b. Some satisfaction
 - c. Mostly satisfaction

iPREM Pilot Trial
Supplementary Material Ver 1.0
27.04.2023

d. Complete satisfaction

Study Experience (For intervention group only, included as part of the final survey)

1. How difficult do you feel it was to comply with the lockdown measures in this study?
 - a. Very difficult
 - b. Mostly difficult
 - c. Neither difficult nor easy
 - d. Mostly easy
 - e. Very easy
2. Which measure was the most difficult to comply with?
 - a. Maintaining 1.5m distance between yourself and another individual
 - b. Wearing a face covering
 - c. Performing hand hygiene prior to touching your nose/mouth
 - d. Remaining within 5km of your residence
 - e. Remaining at home between 9pm-5am, except for essential purposes (work/study or to seek/give care)
 - f. Only leaving home for essential purposes (work or study, to seek/give care or for outside exercise)
 - g. Refraining from having visitors to your home except for an intimate partner
3. How disruptive were these lockdown measures to your day-to-day life?
 - a. Very disruptive
 - b. Mostly disruptive
 - c. Somewhat disruptive
 - d. Not disruptive at all
4. If we could definitively prove that lockdown decreased the risk of preterm birth, do you feel that this is a reasonable set of measures to ask pregnant women to comply with?
 - a. Yes
 - b. No
5. Do you feel that the lockdown measures you were required to comply with put a strain on your partner/friends/family?
 - a. Yes (specify why/how)
 - b. No
6. Was the wrist device you were asked to wear comfortable?
 - a. Yes
 - b. No
7. Did you feel it was reasonable to ask pregnant women to wear the wrist device for the duration of their time in the trial?
 - a. Yes
 - b. No
8. Were there any reasons why you felt you could not wear the device or had to remove it for extended periods of time (e.g more than 3 hours)?
 - a. Yes (please specify when/why)
 - b. No
9. Please feel free to add any other thoughts/comments/concerns about your experience in this study:
 - a.

Page 14 of 8