SingHealth

STUDY PROTOCOL

PROTOCOL TITLE:
Integrating Smart Ring Wearable Technology in Pregnancy Health Monitoring (I-SMART)

PROTOCOL NUMBER:
2.0

PROTOCOL VERSION: 3.0
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PRINCIPAL INVESTIGATOR:
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Nil

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PROTOCOL SIGNATURE PAGE

Protocol Title: Integrating Smart Ring Wearable Technology in Pregnancy Health Monitoring (I-SMART)

Protocol Number: 2.0

Protocol Version/ Date: 3.0 / 28th June 2024

Sponsor Name: NA

Study Site: KK Women's and Children's Hospital

Declaration of Investigator

I confirm that I have read the above-mentioned protocol and its attachments. I agree to conduct the described study in compliance with all stipulations of the protocol, regulations and ICH E6 Guideline for Good Clinical Practice (GCP).

Principal Investigator:	Kok Hian Tan,
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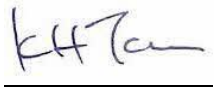
Principal Investigator Signature:	
Date:	28th June 2024

Signed copies of this signature page are stored in the study file and in the respective study site's investigator file.

1. BACKGROUND AND RATIONALE

Rapid technical advancements in integrating wearable sensors and smart digital devices (i.e., smartphones) could extend the capabilities of clinical health care to improve early detection of pregnancy complications, as well as assist with clinical monitoring, and management of pregnancy health outside of traditional care settings.

Physical activity (PA) and sleep are well-established factors for pregnancy complications. There has been sufficient evidence in the recent years to say that sleep and physical activity during pregnancy impacts both maternal and child health outcomes. The Growing UP in Singapore Towards healthy Outcomes (GUSTO) study has shown that poor maternal sleep quality and inadequate nocturnal sleep duration increases the risk of gestational diabetes mellitus (GDM) in Singaporean women (Cai et al., 2017). Maternal short sleep duration has also been associated with increased pre-term birth rates (Warland, Dorrian, Morrison, & O'Brien, 2018). The health benefits of physical activity for women during pregnancy are also well documented, from lowering the risk of developing GDM when combined with a good diet quality (Shepherd et al., 2017), lowering the risk of prenatal depression, reducing excessive gestational weight gain (Haakstad & Bo, 2011), lower risk of pre-term birth (Takami et al., 2018) and better sleep (Yang et al., 2020). In combination, both poor sleep quality and the lack of physical activity had been shown to be associated with a higher risk of depression during pregnancy (van Lee et al., 2020).

In the past decade, wearable biosensors have received tremendous attention in the healthcare industry settings which attempts to apply physical signals such as heart rate, blood pressure, skin temperature, respiratory rate and body motion to extract clinically relevant information (Chan, Esteve, Fourniols, Escriba, & Campo, 2012), (Maijala, Kinnunen, Koskimaki, Jamsa, & Kangas, 2019; Moshe et al., 2021). And smartphone devices coupled with wearable devices are able to provide a continuous stream of data related to an individual's health. This moment-by-moment quantification of the individual-level human phenotype in situ using data from personal digital devices is referred to as "digital phenotyping" (Wisniewski, Henson, & Torous, 2019). Wearable sensor and other smart technologies may play an important part in the early detection of adverse pregnancy-related health events along with motivating improvement in patient and provider interactions for effective pregnancy health management.

The use of wearable sensors like the Oura ring can potentially be used to offer remote, unobtrusive personalized care, encourage preventive care and provide the necessary context for self-help based just-in-time adaptive interventions (feedback loops utilizing digital phenotyping data to trigger in-app interventions). Studies on Oura rings and health outcomes are scarce, and currently there is no available data of the use of the commercially available Oura ring together with smart digital devices (i.e., smart phone) for tracking pregnancy health in women. Our study aims to be the first to generate preliminary pilot data to support it's use in this specific group of women.

2. HYPOTHESIS AND OBJECTIVES

Specific aims and hypothesis:

Aim 1: Assess the acceptability, interest, levels of comfort and potential concerns with the use of the Oura Ring together with smart digital devices during pregnancy.

Hypothesis 1: We hypothesize that patients will respond favourably to the use of wearable to monitor their health during pregnancy.

Aim 2: Asses the association between maternal characteristics (age, pre-pregnancy BMI, pregnancy weight gain, prenatal anxiety and depression scores, prenatal sleep quality scores, maternal pregnancy, delivery and birth outcomes) with data collected from the Oura Ring such as step count, energy expenditure, sleep quality, sleep duration, sleep onset latency, wake after sleep onset, time in bed and heart rate variability in

the second trimester of pregnancy.

Hypothesis 2: We hypothesize that specific maternal characteristics will be associated to outcomes of better or poorer sleep (duration and quality), sleep markers (sleep onset latency, wake after sleep onset, time in bed and heart rate variability) as well as higher or lower physical activity markers (energy expenditure, and step count).

3. EXPECTED RIKS AND BENEFITS

Possible expected risks

The smart ring is a commercially available device which has been shown to be minimally invasive and has a low irritability when worn. Below is some basic safety information for the participants to take note of when using the smart ring:

1) To be cautious that the ring or any other product worn at the same time does not get caught on fixed structures or heavy objects.

2) Finger size can vary depending on the time of the day, and sometimes it may be difficult to remove the ring from the finger. In case the ring should get stuck:

- Cold water and gentle soap should be used to wet finger before slowly twist the ring to remove it.
- Hand should be help up above heart until the blood pressure gets lower before attempting to remove the ring.

3) To avoid wearing the ring when strength training, carrying heavy objects made of metal, ceramics or stone, or wearing the ring next to other rings or objects which are made of metal, ceramics or stone, like diamond. The smart ring may get scratches or it can scratch softer metal jewellery made of e.g. gold or silver. Keep the ring away from children. Do not leave the ring exposed to heat, such as in a vehicle or in the sun. Do not puncture the ring or its battery.

4) There is only the risk of damaging the battery of the ring due to overheating if the device is left on the charger for greater than one week. This smart ring only takes 20-80 minutes to fully charge – users will receive a push notification on their mobile app to indicate that is ring is fully charged, and there will be a Led light on the charger that will stop pulsing once the ring is fully charger.

5) The smart ring emits minimal electric and magnetic fields (EMFs) and allows the Airplane mode to be enabled to limit contact even further. The Bluetooth of the smart ring is only active during a small portion of the day- well below 1%. The Bluetooth signal and advertising are turned off when you're inactive or sleeping. The limit for SAR (Specific Absorption Rate) for the smart ring is 2.0W/kg for head and body. The smart ring's SAR level is 0.0003 W/kg. For context, all cell phones sold in the United States tends to have SAR level at or below 1.6W/kg.

6) The device and its battery is also water proof. The ring can also be used in water (up to 50m deep) and in sauna, but it is not to be left off-finger in hot spaces. There shouldn't be a risk for electrocution because this product has been certified to be water-resistant up to 100 meters. This means participants can bathe, swim, dive, wash dishes and do anything with the ring that involves water without having to remove it.

Potential benefits

As a commercial product the smart ring gave the participants health-related information such as summary of your sleep and physical activity. The feedback provided to the participants via the phone application may encourage positive changes in your physical activity engagement and sleep habits.

The indirect benefits will be to use this preliminary data from this pilot study to better understand the feasibility and acceptability of using the smart ring the track women's health during pregnancy in a remote and unobtrusive way and to study how commercial wearables such as the smart ring might be used in the future to augment routine prenatal care in a clinical setting.

As for incentives, SGD50 will be provided as part of transport reimbursement.

4. STUDY POPULATION

4.1. List the number and nature of subjects to be enrolled.

This is a single-arm, observational and hospital-based study. A total of 200 pregnant women will be recruited with consent form completion after meeting our inclusion criteria.

4.2. Criteria for Recruitment and Recruitment Process

Pregnant women attending KKH for antenatal consultation. The participant information sheet will be handed out at this point. Only the women who meet the inclusion criteria will be eligible for the study and will be given the consent form to sign.

4.3. Inclusion Criteria

1. From the first to third trimester of pregnancy (4-39 weeks of gestational age)
2. Mobile phone's operating system supported by the smart ring application.
3. Above 21 years to 45 years

4.4. Exclusion Criteria

4. Can't read or speak English
5. Below or above gestational age limit
6. Limited mobility
7. Diagnosed with severe unstable mental conditions
8. Diagnosed with severe chronic disorders
9. Mobile device not compatible with smart ring

5. STUDY DESIGN AND PROCEDURES/METHODOLOGY

This will be a single-arm observational study. A total of 200 women will be recruited from the first trimester of pregnancy onwards (4 weeks of gestational age). The women recruited will be those who were attending KKH for antenatal consultation during their pregnancy. Pregnant women who meet our inclusion criteria will be recruited by our clinical research coordinators, and will be given a sufficient amount of time to consider their participation in this study. The participant information sheet will be given to the participant at this point and women who are interested in participating in the study will be given the consent form to sign at the clinic itself.

The 200 women who meet the inclusion criteria will be given a smart ring to wear for up to delivery (7-14 days wear-time per trimester) (Figure 1). During the duration of the smart ring wear, data such as the ones listed in Figure 1 will be collected. All participants recruited into the study will be given a wearable smart ring which they are required to wear on their freely selected finger. As a commercial product, the smart ring gave the participants health-related information such as summary of their sleep and physical activity. The ring can also be used in water (up to 50m deep) and in sauna, but it is not to be left off-finger in hot spaces. Lifting heavy weights while wearing the ring is not recommended, and this is to avoid damaging the ring because heavy weights might scratch the surface of the ring. However, the sensor doesn't need to be power on due to its automation which means that the smart ring is automatically in the "ON" mode once it is worn on any finger, it does not need to be turned on or off. The entire smart ring is water proof. The participant

who wears such device is free to take a shower or swim with it anytime.

Participants will be asked to download the smart ring application from either the Google Play Store or the Apple App Store to their mobile phones, and create a cloud account. The ring can then be connected to the mobile phone application, via Bluetooth which must be turned on. Participants are able to view their own data provided by the application. Participants will be advised to open the mobile application every morning if they wish to, to upload the data from the ring to the mobile application, so that they may view their latest updates on their physical activity or sleep data collected from the smart ring.

At the end of the study, uploaded data will be automatically transferred via Bluetooth to the study database in the smart ring cloud service. The research coordinators of the study will then extract the data from the smart ring via the cloud. This will be a secured Singapore local cloud for all smart ring users. Only registered users will be able to log onto the cloud and upload their data and view the results subsequently. Without permission of the physicians, research personnel are not allowed to view a patients' data at all. The retention of the data in the cloud service is only during the duration of the smart ring account lifecycle. The personal data will be deleted when the account is no longer active. We will not be using identifiers when registering for the accounts, we will use only the Subjects IDs. All the data in the cloud service will be extracted as a csv file and will be saved into an encrypted hard disk.

At the end of the study, participants will be asked to return the smart ring so that it can be used again for newly recruited participants. The "factory reset" function will be used to remove all existing data in the smart ring before it is given to the next participant for use. The participants will also be asked to uninstall the application. All the smart rings will also be thoroughly sanitized before it is given to a newly recruited participant of the study.

At the recruitment (baseline) visit: Participants signing of the consent form, learning to use the smart ring, completing questionnaires ((Depression, Anxiety and Stress Scale, Pregnancy Physical Activity Questionnaire, and Pittsburgh Sleep Quality Index), and completing the case report form.

Subsequent clinic visits: Participants will be required to attend research clinic visits at every trimester of pregnancy until delivery, and one more time post-delivery. All the research visits will be scheduled to coincide with the research participants routine antenatal clinic visits. At every clinic visit, the participants will need to complete a set of questionnaires (Depression, Anxiety and Stress Scale, Pregnancy physical activity questionnaire, and Pittsburgh Sleep Quality Index), and at post-delivery participants will be required to complete a feedback survey.

Measured During Day
Activity Levels
Calories
Steps
Inactive Times
Naps

Measured During Sleep
Resting Heart Rate
Heart Rate Variability (HRV)
Respiratory Rate
Body Temperature
Light, Deep and REM Sleep
Nighttime Movement
Sleep Timing and Quality

Figure 1: The smart ring (Oura ring) and measurements

6. SAFETY MEASUREMENTS

6.1. Definitions

Serious adverse event (SAE) in relation to human biomedical research, means any untoward medical occurrence as a result of any human biomedical research which:

- results in or contributes to death
- is life-threatening
- requires in-patient hospitalisation or prolongation of existing hospitalisation
- results in or contributes to persistent or significant disability/incapacity or
- results in or contributes to a congenital anomaly/birth defect
- results in such other events as may be prescribed

Adverse event (AE) in relation to human biomedical research means any untoward medical occurrence as a result of any human biomedical research which is NOT serious. Adverse event can be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease possibly/ probably/ definitely associated with the participant in the human biomedical research.

6.2. Collecting, Recording and Reporting of Serious Adverse Events (SAEs) to CIRB

The reporting requirements will be in accordance to the reporting requirements published on CIRB website at the time when the event took place.

Only related SAEs (definitely/ probably/ possibly) will be reported to CIRB. Naturally occurring pregnancy events/complications from obstetric conditions such as (but not limited to) miscarriage, pre-eclampsia, eclampsia, antepartum haemorrhage, premature rupture of membrane will not be reported and recorded as AE/SAE. Related means there is a reasonable possibility that the event may have been caused by participation in the research.

The investigator is responsible for informing CIRB after first knowledge that the case qualifies for reporting. Follow-up information will be actively sought and submitted as it becomes available.

Related AEs will not be reported to CIRB. However, the investigator is responsible to keep record of such AEs cases at the Study Site File.

6.3. Safety Monitoring Plan

Data extracted from the cloud will be deleted when the participants' account is no longer active. Identifiers will not be used when registering for the accounts, but only Subjects IDs. All the data in the cloud service will be extracted as a csv file and will be saved into an encrypted hard disk. The clinical research coordinators will be trained to administer the Participant Consent Form to make sure the participants are aware of all the risks involved when using the smart ring.

6.4. Complaint Handling

All complaints will be recorded by the ground staff and reported to the PI. Also, all participants can contact the PI directly with her contact listed in the consent form. The research PI will look into the issue being complained and try all means to solve it. All complains will be addressed and feedback will be given back to the participant.

7. DATA ANALYSIS

7.1. Data Quality Assurance

Study subjects will be identified on all study-related CRFs and databases only by the study ID number, which will not include any personal identifying information. Collected data will be reviewed intermittently by PI and Co-PI to assure the accuracy of the data.

7.2. Data Entry and Storage

Data will be stored electronically after each subject encounter and will be stored in KKH.

8. SAMPLE SIZE AND STATISTICAL METHODS

8.1. Determination of Sample Size

This is an exploratory pilot study. There has been no prior study with data that can be used for a sample size and power calculation.

8.2. Statistical and Analytical Plans

1. The STATA software will be used for descriptive analysis of the sleep and physical activity data collected in terms of mean, median, standard deviation, frequency and percentages.

2. The independent t-test and chi-squared test will be used to explore associations between maternal characterises (e.g., age, pre-pregnancy weight) with outcomes of sleep markers (sleep onset latency, wake after sleep onset, time in bed and heart rate variability) as well as higher or lower physical activity markers (energy expenditure, and step count).

9. DIRECT ACCESS TO SOURCE DATA/DOCUMENTS

The investigator(s)/institution(s) will permit study-related monitoring, audits and/or IRB review and regulatory inspection(s), providing direct access to source data/document.

10. QUALITY CONTROL AND QUALITY ASSURANCE

Data will be evaluated for adherence with the protocol and for accuracy in relation to source documents every 6 months. PI and Co-PI will be responsible for the evaluation of data quality.

11. ETHICAL CONSIDERATIONS

This study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with the Good Clinical Practice and the applicable regulatory requirements.

This final Study Protocol, including the final version of the Participant Information and Consent Form, must be approved in writing by the Centralised Institutional Review Board (CIRB), prior to enrolment of any patient into the study.

The principle investigator is responsible for informing the CIRB of any amendments to the protocol or other study-related documents, as per local requirement.

11.1. Informed Consent

All patients included in this study will need to sign on the consent forms. All the Clinical Research Coordinators will be sufficiently trained to administer the consent form of this study.

11.2. Confidentiality of Data and Patient Records

To minimize the risk of loss of confidentiality all information related to study subjects will be confidential and kept in secure cabinets or password-protected computer files. Study subjects will be identified on all study-related CRFs and databases only by the study ID number, which will not include any personal identifying information. Research records, samples, and consent forms will be maintained by Division of O&G at KKH to allow for retrospective analysis.

12. PUBLICATIONS

Publication policy for study findings will follow the international guideline published elsewhere.

13. RETENTION OF STUDY DOCUMENTS

Records for all participants, including CRFs, all source documentation (containing evidence to study eligibility, history and physical findings, laboratory data, results of consultations, etc.) as well as IRB records and other regulatory documentation will be retained by the PI in a secure storage facility. The records will be accessible for inspection and copying by authorized authorities within 7 years after trial completion.

14. FUNDING and INSURANCE

National Medical Research Council

List of Attachments

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