Effects of an integrated mobile health lifestyle intervention among overweight and obese women planning for pregnancy in Singapore: protocol for the single-arm healthy early life moments in Singapore (HELMS) study

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ABSTRACT

Introduction Changes in social and lifestyle factors have led to increasing rates of metabolic and mental health problems. We hypothesise that a transformation of the current maternal and child health system is required to deliver interventions that effectively promote a good start to life in populations at risk of metabolic and mental health problems. We describe a single-arm implementation study ‘Healthy Early Life Moments in Singapore’, which aims to examine whether an integrated lifestyle intervention initiated at preconception and continuing throughout pregnancy and postpartum phases can improve the metabolic and mental health of overweight and obese women, and improve early child growth.

Methods and analysis This single-centre implementation trial is conducted at KK Women’s and Children’s Hospital, Singapore. The trial aims to recruit 500 women, aged 21–40 years with a body mass index of 25–40 kg/m² who plan to get pregnant, with interventions delivered before conception, until 18 months postdelivery. Primary outcomes comprise pregnancy rate, maternal metabolic and mental health status. Secondary outcomes include maternal reproductive health, pregnancy outcomes and offspring growth. The intervention will be delivered using a mobile health application, to provide anticipatory guidance, raise awareness and guide goal-setting on lifestyle behaviours that include diet, physical activity, mental wellness and sleep hygiene from preconception to postpartum. Women who conceive within 1 year of recruitment will be followed through pregnancy and studied with their infants at six-time points during the first 18 months of life. Questionnaires, anthropometric measurements and multiple biosamples will be collected at each visit.

Ethics and dissemination The study has been approved by the Centralised Institutional Review Board of SingHealth (2021/2247). Written informed consent will be obtained from all participants. The findings will be published in peer-reviewed journals and disseminated to national and international policy makers.

Trial registration number NCT05207059.

STRENGTHS AND LIMITATIONS OF THIS STUDY

Healthy Early Life Moments in Singapore (HELMS) aims to examine the impact of integrated interventions, initiated preconceptionally and continued throughout the pregnancy and postpartum phases, on metabolic and mental health of women who are overweight or obese.

Extensive biosampling and detailed phenotyping of mother, father and child will allow longitudinal assessment of changes in health behaviours including diet, physical activity and sleep, maternal metabolic profile and depression risk.

This will provide an important platform for biomarker discovery, validate integrated HELMS interventions and pave the way for new guidelines for lifestyle programmes from preconception to postpartum stages.

The main limitation of this study design includes the inability to distinguish between the effect of an intervention, a placebo effect and the effect of natural history.

HELMS is a single-centre study of the Asian population, involving only English-speaking participants, so external validity may be limited to this population, and caution should be exercised in generalising results across different settings and populations.

INTRODUCTION

Non-communicable diseases (NCDs) represent the predominant cause of morbidity and mortality worldwide.1 Rapid urbanisation, unhealthy diet and sedentary lifestyles have led to an epidemic of metabolic diseases, which are the main drivers of NCDs.1 Coupled with this metabolic epidemic is a rising rate of mental disorders, especially depression, as the leading cause of disability worldwide that commonly affects women.2 Both metabolic and
mental disorders are interrelated, with their co-occurrence frequently observed in individuals living with obesity. The short-term and long-term health risks of maternal obesity and depression in mothers and their children are well documented. Women living with obesity and mental health conditions are at increased risk of infertility, adverse obstetric outcomes and postpartum cardiometabolic complications; and their children are also susceptible to obesity, metabolic disease and psychosocial disturbances in childhood and adolescence. In Singapore, almost one-third of women are overweight or obese (body mass index (BMI) 25–29 kg/m² :17%; BMI ≥30 kg/m² :13%) before pregnancy, while one in ten women experience depression before, during and after pregnancy. To mitigate the impact of maternal obesity and depression, various intervention strategies targeting antenatal and postpartum periods have been studied. These include setting Specific, Measurable, Achievable, Relevant, Time-Bound goals, providing healthy lifestyle counselling or group-based education, perinatal mental health interventions and providing health service support. However, these antenatal and immediate postpartum-phase focused interventions have had modest success, only some showing improvements in eating behaviour, physical activity or weight status, and most failing to prevent adverse mother–offspring outcomes such as gestational diabetes mellitus and macrosomia. This could be attributed to the relatively short duration of the intervention, the lack of continued care from preconception and intervention only beginning in the antenatal and postpartum periods, which may be too late to produce any meaningful impact.

There is increasing focus on interventions during the preconception period, especially for women living with obesity, who are susceptible to both metabolic and mental disorders. Such interventions not only improve the health of the mother, but also provide potential health benefits to the next generation through an improved environment for embryo and fetal development. The preconception period represents a unique opportunity where women are motivated to make a positive change to attain optimal pregnancy outcomes. So far, preconception lifestyle interventions have demonstrated positive maternal behaviour changes, such as increased intake of multivitamins, vegetables and other dietary changes, increased physical activity, as well as smoking cessation and reduced alcohol consumption, resulting in a reduction in BMI and gestational weight gain, higher clinical pregnancy rate and lower preterm delivery. This has led to improved knowledge, self-efficacy and control. Furthermore, women who achieved at least 5% wt loss during such interventions had better cardiometabolic health based on glycaemic and lipid measures 6 years later.

Taken together, this suggests that adopting a life-course perspective in the healthcare model with a continuum of care provided before, during and after pregnancy has the potential to address the trajectory of increased metabolic and mental disorder risk throughout these life stages. Acting upstream before conception to optimise health is crucial to improving reproductive potential while reducing the social and health implications resulting from unplanned pregnancies. Modifying current antenatal care services by empowering women in preparation for pregnancy and childbirth is critical for the well-being of both mother and baby. Optimising postpartum recovery and readiness, and nurturing infants through optimal feeding practices and growth monitoring are important for promoting virtuous life cycles of health in an individual and breaking vicious life cycles of NCDs for the next generation.

**Goals and aims**

We envision an integrated life-course approach with a continuum of care that encompasses preconception preparation, pregnancy optimisation, along with postpartum synchronisation of maternal–child health services in the first 18 months of life. Connecting the preconception, pregnancy and postpartum journeys will achieve synergism in producing greater behavioural change and beneficial outcomes not only for women, but also for the child and family. Therefore, the goal of Healthy Early Life Moments in Singapore (HELMS) is to develop and implement a life-course model of care (MOC) starting from preconception to pregnancy and postpartum phases, to achieve optimal metabolic and mental health.

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**Figure 1** The Healthy Early Life Moments in Singapore (HELMS) framework, comprising preconception, pregnancy and postpartum dyad care. Through maternal behavioural intervention, the overarching aim is to improve metabolic and mental health in women living with obesity, and to improve early child growth. Specifically, HELMS aims to improve women’s fertility, obstetric outcomes, physical and mental recovery from birth, feeding habits and growth of the child.
for both mother and child. This MOC focuses on preventive healthcare, a time where the cost-effectiveness of the intervention is likely to be maximum, and represents the clinical translation of early developmental programming based on the Developmental Origins of Health and Disease paradigm.

In this study, the overarching aim is to examine whether an integrated intervention beginning preconceptionally and continuing throughout the pregnancy and postpartum phases can improve the metabolic and mental health of women living with obesity, as well as optimise offspring growth and development. At each life-course phase, the study addresses specific hypotheses. We hypothesise that the HELMS MOC lifestyle interventions will promote the metabolic and mental health of overweight and obese women, and thus optimise (1) reproductive outcomes during preconception, (2) obstetric outcomes during pregnancy and (3) postpartum physical and mental well-being, and healthy feeding habits and growth during infancy. We also hypothesise that greater improvements in metabolic and mental health will be observed in obese women with obesity than in those who are overweight. An overview of the study framework is shown in figure 1.

METHODS AND ANALYSIS
Trial design and setting
This study represents a model of implementation to demonstrate the value of adopting a life-course approach and integrated care to maternal–child health. It is conceptualised as a single-arm trial, with a targeted intervention implemented in a group of women living with obesity who are trying to conceive within 1 year after recruitment. The longitudinal intervention will be performed from preconception, throughout pregnancy until 18 months postpartum in the KK Women’s and Children’s Hospital (KKH), Singapore. The protocol is written following the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) guidelines. Written informed consent will be obtained from all participants at the recruitment.

The flow of the trial is shown in figure 2. Participants will be reviewed at multiple time points from preconception through pregnancy, and both participants and their infants will be followed for the first 18 months after delivery, with extensive biosampling and detailed pheno- typing performed longitudinally. Following informed consent at the first preconception clinic visit, participants will complete a set of questionnaires that assess baseline demographics, diet practices, physical activity, sleep, emotion and sexual health. Anthropometric measurements will be taken, together with biosample collection, including blood for a standard 75 g oral glucose tolerance test and stool. Participants will receive a doctor’s consultation, along with prescription of a standard preconception supplement, digitised preconception care and healthy lifestyle guidance. The second preconception clinic visit will take place 6 months later, with questionnaires and

![Figure 2 HELMS study flow diagram. Preconception visits are coloured green, pregnancy visits pink and postpartum visits blue. HELMS, Healthy Early Life Moments in Singapore.](http://bmjopen.bmj.com/ BMJ Open: first published as 10.1136/bmjopen-2022-061556 on 12 December 2022. Downloaded from http://bmjopen.bmj.com/ on December 29, 2022 by guest. Protected by copyright.)
measurements being performed, and compliance with the intervention being reviewed. Phone contact will be made 3 and 9 months after recruitment to help participants maintain focus on their preconception health and lifestyle goals, and to remind them to perform a urine pregnancy test if periods are missed. If they do not become pregnant, an exit visit will be conducted at 12 months with questionnaires, measurements and biosampling, followed by appropriate evaluations and subfertility referrals thereafter. Participants who become pregnant will be seen between 6 and 10 weeks of gestation at the first pregnancy visit. Questionnaires, measurements and biosampling will again be performed. The second HELMS pregnancy visit will be at 24–28 weeks, and the final HELMS visit in pregnancy will be at 32–36 weeks. Continuous antenatal care and healthy lifestyle guidance during pregnancy will be provided throughout the trimesters. At delivery, maternal and infant biosampling, including placenta collection, will be performed. In the postpartum dyad phase, there will be six visits over an 18-month period, according to the infant vaccination schedule, at 1–2 weeks, 6–8 weeks, 4, 6, 12 and 18 months. An ongoing intervention tailored to this postpartum dyad phase will be delivered, together with questionnaires, measurements and biosampling for the mother and child at each visit. Throughout the study, participants will be asked to log their weight and supplement intake weekly in a digital calendar. For the partner, lifestyle and anthropometric measurements will be collected during the preconception, pregnancy and postpartum periods; blood will be collected once during the pregnancy phase. Meanwhile, partners will be passively engaged in the intervention by receiving the same set of digitised intervention materials. A feedback survey on the HELMS programme will be performed at the end of each preconception, pregnancy and postpartum phase.

**Patients and public involvement**

We have conducted in-depth face-to-face interviews with preconception, pregnant and postpartum women who were overweight and obese to understand their needs throughout the preconception-pregnancy-postpartum journey, enablers and barriers to a healthy lifestyle, intervention preferences and delivery methods. This work enabled the development of the intervention package and dissemination plans.

**Participants and recruitment**

Potential participants from the public or KKH (patients/staff) or referred from other healthcare institutes who fulfil the inclusion criteria will be invited to participate in the HELMS study. KKH houses the largest Obstetrics and Gynaecology department in Singapore, managing approximately 12,000 deliveries a year with patients made up of a wide sociodemographic spectrum. Invitation letters, emails, messages, webpages, brochures and posters will be used for advertising. Interested women can contact the study team by email or phone.

Inclusion criteria include (1) a woman who plans to conceive in the next 12 months; (2) BMI 25–40 kg/m²; (3) age 21–40 years; (4) Chinese, Malay, Indian ethnicity or any combination of these three ethnic groups; (5) intending to reside in Singapore for the next 4 years; (5) can access the Internet through any digital platform and (6) can provide written informed consent. Exclusion criteria include (1) currently pregnant; (2) difficulty in understanding the English language; (3) known type 1 or type 2 diabetes; (4) being on anticonvulsant medication, oral steroid, contraception or fertility medication in the past 1 month; (5) on HIV or Hepatitis B or C medication in the past 1 month. If a woman is pregnant within 1 month from the baseline visit, they will be censored from the analyses. If a woman has a pregnancy loss and wishes to rejoin the study, she will be recharacterised at the preconception baseline visit at least 1 month after a negative urine pregnancy test and will receive intervention as before.

Women who suffer from a miscarriage or termination event, experience multiple pregnancies, with fetal congenital anomalies, cannot comply with the study protocol or wish to discontinue their participation will be withdrawn from the study.

**Intervention overview**

All participants will receive an intervention via a mobile health application, designed to address and improve women’s knowledge, attitude and practice in terms of preconception-pregnancy-postpartum care and health behaviours. There will be four modules, namely the HELMS Journey, the HELMS Model, the HELMS Lifestyle and the HELMS Community. The HELMS Journey will provide anticipatory guidance on examinations and measurements performed during clinic visits. The HELMS Model will deliver the 4S (Screening, Size, Supplementation, Special considerations) care plans. The HELMS Lifestyle will provide support in healthy eating, physical activity, mental wellness and sleep hygiene. Finally, the HELMS Community will provide social support and improve participation in the programme. Each of these modules contains phase-specific information developed by obstetricians, neonatologists, paediatricians, dietitians, physiotherapists, psychiatrists and psychologists.

**Intervention details**

**HELMS journey**

Details of each preconception, pregnancy and postpartum visit of HELMS will be available here to provide anticipatory guidance on these visits. This will ensure that participants are aware of the study measurements, as well as the required routine examinations.

**HELMS model**

The HELMS life-course interventions, namely 4S, are developed to provide care throughout the journey from preconception to postnatal. 4S is represented...
by ‘Screening’, ‘Size’, ‘Supplementation’ and ‘Special considerations’.

- Screening involves health and risk assessments through physical and biomarker (eg, Anti-Mullerian hormone, glucose, insulin and lipid profile) measurements, as well as emotion and sleep evaluations for mothers, and developmental assessment for children.
- Body Size management encompasses education on weight status awareness and mother–child health implications, both mother–child weight tracking, healthy eating and physical activity guidance.
- Supplementation includes multimicronutrient, vitamin D, calcium and/or DHA supplements, which are phase specific for mother, and vitamin D supplement drops for the child.
- Special considerations include the management of preconception sexual health and function, the management of pregnancy symptoms and postpartum recovery, and the monitoring of infant growth and feeding management.

HELMS lifestyle

Metabolic health support (diet and physical activity modules).

The diet module is developed based on the 6P tool, which is designed as a platform to address metabolic health based on the principles of energy input and expenditure, as well as motivation as the basis for dietary change. It is a simple, self-administered instrument based on the concept of a mental model, which can lead to self-awareness, self-evaluation and self-education, over time resulting in a positive change in eating habits and health. The 6P comprises six components as presented in Table 1. Multiple modalities are incorporated that include feedback on 6P behaviour, 6P self-monitoring, 6P goal setting and 6P nudges along with the use of the 6P tool. By including these six main discrete dietary and activity components under a single ‘package’, it will provide an overview of the mental model of nutrition based on the principle of energy input and expenditure, promoting self-awareness of unhealthy lifestyle behaviours and nudging individuals into actual implementation via concrete, personalised feedback and increasing intrinsic motivation. This is based on the theoretical framework of the theory of planned behaviour, which has been widely used to predict behavioural intention and health-related behaviours.

The physical activity module seeks to engage women with the importance, type and intensity of exercise during each phase. It consists of a series of appropriate, tailored exercise videos developed by physiotherapists and obstetricians with the support of scientific evidence. Wearable activity trackers will be used to provide real-time feedback on physical performance and help participants monitor their energy expenditure. Sustainability will be supported with the use of nudges (both text messages and images) delivered weekly to influence behaviour and decision-making.

Mental health support (Mental health and Sleep modules)

The mental health module serves as the main way to support, screen and guide women’s mental health longitudinally. Upstream screening of depressive symptoms at the preconception stage allows women at high risk to be triaged earlier for receiving targeted mental health support from KKH’s mental health team comprising a clinical coordinator, case manager and psychiatrist. Women at medium risk will be engaged more intensively, while those at low risk will continue to participate, enabling and preparing for different stages through a package of clinical care and lifestyle support, especially in the late stages of pregnancy and early stages of postpartum. The sleep module aims to support mental wellness by promoting healthy sleep practices throughout the life-course. A wearable sleep tracker will be used to provide real-time feedback on sleep performance and help participants to monitor their sleep patterns.

HELMS community

An online community platform is being established as part of supporting mental health among HELMS participants. This allows women to share their experiences, identify common problems among peers and generate solutions that work for them in the online chat group.

Our intervention approach will be based on the SIGN strategy (Support, Inform, Guide and Nudge) to deliver the 4S and healthy lifestyle support. Close monitoring of women’s health allows timely support provided by the healthcare staff. Setting up mobile health education helps to inform women about the importance and warning points in different stages. Educational materials in various formats, including diagrams and videos, provide guidance on phase-specific care and healthy lifestyles that focus on nutrition, physical activity, mental health and sleep hygiene. Health nudges in the form of key messages related to preconception, pregnancy and postpartum dyad care, as well as healthy lifestyles, facilitate care support and behavioural changes. The use of nudges represents a preferred architecture strategy that is widely used in public policy making, to alter people’s behaviour and influence decision making.

Table 1 Components of the 6P tool

<table>
<thead>
<tr>
<th>6P</th>
<th>Healthy mental model of nutrition</th>
<th>Description</th>
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<tbody>
<tr>
<td>P1</td>
<td>Portion</td>
<td>Amount of food intake</td>
</tr>
<tr>
<td>P2</td>
<td>Proportion</td>
<td>Caloric density of food intake</td>
</tr>
<tr>
<td>P3</td>
<td>Pleasure</td>
<td>Frequency of snacks and sugary beverages and irregular intake</td>
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<tr>
<td>P4</td>
<td>Period</td>
<td>Time of day of food intake</td>
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<tr>
<td>P5</td>
<td>Physicality</td>
<td>Physical activity and sedentary behaviour</td>
</tr>
<tr>
<td>P6</td>
<td>Psychology</td>
<td>Readiness for change</td>
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In summary, we will apply an interactive and personalised approach to conducting the intervention, supported by real-time feedback. This involves goal setting, individual education, self-awareness, self-monitoring, motivation and outcome review process. These techniques are commonly used in behavioural interventions and can improve health outcomes.\textsuperscript{33,34}

**Intervention adherence**

Adherence to the intervention will be established throughout the study with regular logbook charts of supplement intake, sexual activity and weight, which will be reviewed at each study visit or by telephone reminders. The use of a digital tracker for activity and sleep allows off-site monitoring of wearing adherence, and research staff will take action to check for reasons for non-adherence.

**Outcomes and assessments**

The primary outcome is the pregnancy rate in overweight and obese women trying to conceive within 1 year of baseline assessment. It is defined as a positive urine pregnancy test, followed by ultrasound confirmation of an intrauterine gestational sac after 6 weeks of amenorrhoea. If an ultrasound scan is not available or inconclusive, the diagnosis of pregnancy will be made clinically. A successful conception is one of the most important clinical outcomes, and it represents the culmination of improved metabolic and mental health, leading to optimised gametogenesis.

Coprimary outcomes include maternal metabolic health and mental health status in each phase, with 18 months postdelivery serving as the principal endpoint. Maternal metabolic health is assessed by metabolic syndrome criteria. Mental health is evaluated using the Edinburgh Postnatal Depression Scale (EPDS).\textsuperscript{35}

Other key outcomes include:

**Women/mothers**

- Reproductive health as assessed by fecundability, pregnancy loss and live birth rates, and sexual function based on Female Sexual Function Index.\textsuperscript{19,36}
- Pregnancy outcomes include pain, obstetric and delivery complications.
- Health behaviours assessed by dietary practice (6P tool,\textsuperscript{30} 4-day food diary, Food Frequency Questionnaire,\textsuperscript{37} Three Factor Eating Questionnaire,\textsuperscript{38} alcohol and supplement intake), smoking exposure, physical activity and sedentary behaviours (International Physical Activity Questionnaire,\textsuperscript{39,40} Sedentary Behaviour Questionnaire,\textsuperscript{41} accelerometer), and sleep (Pittsburgh Sleep Quality Index,\textsuperscript{42} digital tracker).
- Metabolic profile, including weight status, body fat distribution, blood pressure, lipid and glycaemic measures.
- Gut microbiome profile assessed by stool sample.
- Nutrient status based on diet, blood and breast milk composition (breast milk will be collected at five time points through the first year postdelivery).
- Ocular health as assessed by retinal vessel calibre characteristics.

**Offspring**

- Anthropometry and growth assessed by antenatal serial ultrasound scans, infant weight, length and head circumference.
- Neonatal complications such as hypoglycaemia and admission to neonatal care facilities; infant health and well-being, and skin biopsy for a subset of infants with eczema.
- Infant feeding assessed by breastfeeding behaviours, time of weaning, nutrition milestone, dietary intake and eating behaviours.

**Partners**

- Physical and metabolic health assessed by weight, BMI and body fat distribution.
- Health behaviours assessed by smoking exposure, alcohol intake, meal pattern, stress level, physical activity and sedentary behaviours.

Programme effectiveness will be evaluated based on women’s quality of life, healthcare utilisation and participant feedback surveys. Blood, cord blood, stool, urine, saliva, placenta and breast milk samples will be stored for analyses on biochemical, micronutrient, metabolomic, genomic, epigenetic, immunological and molecular profiles.

**Planned analyses**

Continuous variables will be presented as means and SD, or medians and 25th–75th centiles, as appropriate. Categorical variables will be presented as numbers and percentages. The pregnancy rate will be determined by the number of women who became pregnant (defined as stated previously) divided by the total number of women who completed the 1-year follow-up during the preconception phase. The time to pregnancy (TTP) will be estimated by the number of menstrual cycles required to achieve pregnancy over 1 year of follow-up. We will use the discrete-time proportional hazards model, which analyses TTP as a discrete scale based on the number of menstrual cycles, to estimate the fecundability ratio (FR) and the 95% CI.\textsuperscript{33,34} accounting for left truncation and right censoring. For the other two coprimary outcomes, a linear mixed effects model will be used to examine changes in means between the baseline and follow-up metabolic markers and EPDS scores, with adjustment for baseline potential confounders (including partner’s characteristics) and duration of the intervention received. In addition to the pre–post comparison of outcomes stated above, differences in pregnancy and birth outcomes will also be compared with a similar observational cohort in Singapore called Singapore PREconception Study of long-Term maternal and child Outcomes (S-PRESTO).\textsuperscript{45} using multiple linear or logistic regression models, adjusting for potential confounders. These confounders, such as age, ethnicity and education, will be determined from...
literature review, directed acyclic graph and/or observed statistically significant associations with exposures and outcomes.

We will impute missing data using multiple imputation analyses by chained equations. The number of imputations will be determined based on a percentage of missing values, and the results of total imputations will be pooled using Rubin’s rule. To determine whether the imputation of the missing data may have affected the results, we will perform sensitivity analyses on participants with a complete set of data.

**Sample size calculation**

Based on the S-PRESTO study, which is an observational cohort recruited from preconception and followed up through postpartum periods, preconception overweight or obese women (BMI ≥25 kg/m²) had a 38% pregnancy rate, while those with normal weight (BMI 18.5–24.9) had 47% pregnancy rate. Among overweight and obese women, those with healthy metabolic profiles characterised by absence of the metabolic syndrome or insulin resistance had a 52% pregnancy rate. We anticipated that HELMS intervention will improve overweight or obese women’s pregnancy rate from 38% to 50% within 12 months of trying. Using a two-sided α level of 5% and a power of at least 90%, 400 participants are needed in the preconception phase, leading to 200 pregnancies. Considering a 20% drop-out rate, 500 participants are required for recruitment. We estimated that 15% of women will experience pregnancy loss and another 10% drop-out, leaving 150 dyad pairs to be followed.

**Quality control**

Procedures and actions will be implemented throughout the study to ensure that information provided to all participants is standardised, data collected is as complete as possible and of high quality. Research staff responsible for recruiting and follow-up participants will receive training from study leads on recruitment, consent taking, questionnaire and data management, intervention delivery and compliance monitoring. An operation database will be developed to monitor participant progression throughout the study, schedule study visits and monitor visit/measure completeness. A quarterly meeting will be held among study leads and research staff to review recruitment process, intervention delivery, data collection and participants’ feedback. An annual audit on the study will be performed by an independent party.

**Data monitoring**

All data will be pseudonymised. Participants’ identifiers will be kept separately in a password-protected file and only be assessed by specific research staff. Electronic data will be managed using a secure, encrypted online data-capturing system approved by the institution. A data monitoring team will perform data checking on completeness, errors and outliers. To facilitate data monitoring procedure, algorithms are programmed to autodetect implausible value while entering data and to prompt messages for incomplete entry. Ad hoc discussions will be organised with study leads to clarify actions required to resolve data issues.

**ETHICS AND DISSEMINATION**

The study has been approved by the Centralised Institutional Review Board of SingHealth (2021/2247). Written informed consent will be obtained from all participants (online supplemental file 1). The findings will be published in peer-reviewed journals and disseminated to national and international policy makers.

**DISCUSSION**

The existing MOC in maternal–child health in Singapore and in many developed countries emphasises disease treatment with less emphasis on health promotion. Most women are not prepared for pregnancy, and many have poor metabolic and mental health. This lack of preparedness carries over in the postpartum phase after the child is born. A woman’s own needs are often neglected in the immediate postpartum phase when the attention is primarily focused on caring for the newborn. Coupled with unexpected physical and emotional challenges in this new phase of life, it culminates in a cycle of poor metabolic and mental health. Women living with overweight and obesity represent a particularly high-risk group for poor metabolic and mental health. The current obesity management strategy has three fundamental gaps. First, the timing of intervention is too far downstream in adulthood. Second, there is weak foundational knowledge of nutrition and physical activity, with poor awareness and insight into metabolic health. Third, there is no structured and coordinated care plan for these women while planning to conceive, which would be an ideal window for intervention during the crucial period of gametogenesis. To address these challenges, there is a need to invert the pyramid of care and focus our effects upstream, starting from preconception.

HELMS aims to address the twin challenges of metabolic and mental health disorders through a series of interventions, to provide the best and most equal start to life for children. Through its life-course approach, HELMS recognises the additive effects of influences on a person’s life that will impact the future health trajectory. It aims to impart new mental models of nutrition, physicality and mental wellness, by guiding, supporting and empowering women through an integrated journey from preconception to postpartum, to address metabolic and mental health challenges. We hope this unique holistic approach with a continuum of care across the early life-course, starting from preconception and pregnancy until the postpartum period will build a strong foundation for healthy women and secure a healthy start for future generations.
The environment of the woman plays an important role in health behaviours including diet, physical activity and sleep, maternal metabolic profile and depression risk. The biosamples will provide an important platform for biomarker discovery, validate integrated HELMS interventions and pave the way for new guidelines for lifestyle programmes from the preconception to postpartum stages.

Despite the strong evidence base for adverse maternal and child outcomes in overweight and obese women, as well as the benefit of lifestyle interventions in the preconception and pregnancy phases, integrated HELMS interventions are novel and have not established unequivocal evidence of benefit. Thus, HELMS is conceptualised as a single-arm intervention trial in women living with overweight or obesity to obtain preliminary evidence of the efficacy of intervention. A subsequent larger pragmatic trial is envisaged to validate the efficacy of the intervention. The main limitations of this study design include the inability to distinguish between the effect of intervention, a placebo effect and the effect of natural history, including regression to the mean. Given the similarity in study design to the prospective observational cohort S-PRESTO, with similar time points of follow-up and biosampling, there is the potential for comparison with this historical cohort. HELMS is a single-centre study of the Asian population, involving only English-speaking participants, thus, the external validity may be limited to this population, and caution will need to be exercised in generalising results across different settings and populations. Finally, the interventions are tailored to the woman/mother, with only passive intervention for her partner. The environment of the woman plays an important role in her compliance to lifestyle interventions, which may undermine the impact of our programme. On the other hand, if the success of the HELMS interventions extends to that of her immediate family, we would also have limited insights with minimal measurements on the partner, to reduce the burden of involvement in the study.

The major strength of this study is the extensive biosampling and detailed phenotyping of mother, father and child, which will allow longitudinal assessment of changes in health behaviours including diet, physical activity and sleep, maternal metabolic profile and depression risk. This provides an important platform for biomarker discovery, validation of integrated HELMS interventions and paves the way for new guidelines for lifestyle programmes throughout the life-course. We acknowledge the main limitation of this single-arm trial, where we are unable to distinguish between the effect of intervention, a placebo effect or the effect of natural history. In addition, HELMS is conducted in a developed country with only English-speaking Asian participants, since English is the language used in our assessment tools and advisories, which may limit its external validity and caution should be exercised before generalising our findings to other settings and population.

Trial status
HELMS recruitment commenced in April 2022 and is expected to be completed in June 2024. The current protocol is version 1, dated 16 December 2021.

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Contributors Conceptualisation, JC, FY, CWK and SLL; methodology, JC, FY, KG, CWK and SLL; writing—original draft preparation, CWK, SLL and YF; writing—review and editing, all authors; funding acquisition, MCC, FY and JC. All authors have read and agreed to the published version of the manuscript.

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Competing interests KG and YF received reimbursement for speaking at conferences sponsored by companies that sell nutritional products. KG is part of an academic consortium that received research funding from Abbott Nutrition, Nestle and Danone. All other authors declare no competing interests.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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Chee Wai Ku http://orcid.org/0000-0003-3719-3005

REFERENCES
40. IPAQ research committee. Guidelines for data processing and analysis of the international physical activity questionnaire-short and long forms; 2004.


PARTICIPANT INFORMATION SHEET AND CONSENT FORM

You are being invited to participate in a research study. Your participation in this study is entirely voluntary. Before you take part in this research study, the study must be explained to you and you must be given the chance to ask questions. Your questions will be answered clearly and to your satisfaction. Please read carefully the information provided here. If you agree to participate, please sign the consent form. You will be given a copy of this document.

If you are a parent or legal guardian giving consent for a child to participate in the study, please note that the word “you” refers to your child.

STUDY INFORMATION

Protocol Title:
Healthy Early Life Moments in Singapore (HELMS)

Principal Investigator:
Prof. Jerry Chan Kok Yen
Senior Consultant
Department of Reproductive Medicine
KK Women's and Children's Hospital
100 Bukit Timah Road
Singapore 229899

PURPOSE OF THE RESEARCH STUDY

The purpose of this study is to implement a behavioural intervention to address the challenges of poor outcomes relating to fertility, perinatal and eventual chronic diseases through an integrated continuum of care from the preconception phase, across maternity until the early postnatal phase. We hope to learn the optimal life course model of care in breaking vicious life cycles and promote virtuous life cycles for our women, children and family.

You were selected as a possible participant in this study because you are planning for a child in the near future and falling within the body mass index (BMI) of 25 to 40 kg/m².

This study targets to recruit 300 participants from the general population in Singapore where the study visits will take place at KK Women's and Children's Hospital.

STUDY PROCEDURES & YOUR RESPONSIBILITIES IN THIS STUDY

If you agree to take part in this study, you will be asked to begin participating before you are pregnant, to attend the study visits during pregnancy and for a further 18 months after the birth of your child.
The table below indicates the study visits and the procedures which will be done at each visit:

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Preconception</th>
<th>Pregnancy</th>
<th>Delivery</th>
<th>Postnatal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Base-line</td>
<td></td>
<td>Birth</td>
<td>1-2w</td>
</tr>
<tr>
<td>Questionnaires</td>
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<td>Phone calls</td>
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<td>✓</td>
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<td></td>
<td>3m</td>
<td></td>
<td>6-10w</td>
<td>6-8w</td>
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<td>6m</td>
<td></td>
<td>24-28w</td>
<td>4m</td>
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<td></td>
<td>9m</td>
<td></td>
<td>32-36w</td>
<td>6m</td>
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<tr>
<td></td>
<td>Exit</td>
<td></td>
<td>Birth</td>
<td>12m</td>
</tr>
<tr>
<td></td>
<td>Exit</td>
<td></td>
<td>1-2w</td>
<td>18m</td>
</tr>
<tr>
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<td></td>
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<td>6-10w</td>
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<td>24-28w</td>
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<td>32-36w</td>
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<td>Birth</td>
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<td>(30ml)</td>
<td>✓</td>
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<tr>
<td></td>
<td>Placenta collection</td>
<td></td>
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<td>✓</td>
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<tr>
<td>Stool collection</td>
<td>✓</td>
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<tr>
<td>Activity tracker</td>
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<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Sleep tracker</td>
<td></td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

*C: child, M: mother

You will be provided with lifestyle intervention initiatives since preconception (before pregnancy), throughout pregnancy and until 18 months postnatal (after delivery of baby). Throughout the study, you will be
- asked to administer a nutrition intervention tool known as ‘6P’ to assess and monitor your dietary behaviour;
- prescribed with multi-micronutrients supplements by the study team doctors;
- provided with phase specific education materials related to preconception care, pregnancy care and dyad care;
- provided with exercise guidance;
- provided with Vitamin D drops for your child.

You will need to visit the study clinics for
- 3 times during the preconception phase (2 times if successfully getting pregnant over 1 year after enrollment into the study);
- 3 times during the pregnancy phase; and
- 6 times during the postnatal phase.

Each visit will take approximately 2 hours to complete. Additional visits may be required depending on the clinical care investigations and reviews as per necessary. A feedback survey will be performed at the end of each preconception, pregnancy and postnatal phases and upon study exit for women who are withdrawn at specific phase of the study.

Details of study measures at respective time-point are described below:

**Preconception:**
At the first visit, your will be asked to come after a minimum of 8 hours overnight fasting. You will be
- screened for eligibility;
- assessed for lifestyles, sexual health and anthropometry (weight, height, waist-hip circumference);
- undergoing an eye assessment including retinal photography to take a photo at the back of your eye.
- undergoing blood collection, at most 35ml of blood (less than 3 tablespoons):
  - Blood lipids (cholesterol and triglycerides)
o Hormonal profile
o Infection screen
o Full blood count (FBC)
  o Oral glucose tolerance test (OGTT)*
  o Insulin (hormone which regulates blood glucose levels)
  o C-peptide (a marker of insulin production)
  o HbA1c (blood test that gives an indication of your average blood glucose levels over the past three months)
○ Additional blood for research analyses (12ml / less than 1 tablespoon)
• self-administering a nutrition intervention tool, known as the 6P tool to assess and monitor your dietary behaviour
• receiving education related to preconception health from the clinical staff/ doctors
• receiving exercise guidance and an activity tracker (Actigraph device, Figure 1) to track for your 24-hour activity. The tracker is to be worn on the wrist and captures activity levels, sleep and light exposure. Arrangement will be made to collect the tracker back from you after 10 days.

![Figure 1: Actigraph device](image)

* A 75g (approximately 5 tablespoons) oral glucose tolerance test (OGTT) to determine how quickly sugar is cleared from your blood. This involves a total of 2 blood-taking time points; at fasting and 2 hours after drinking the glucose drink. At the 2-hour time point, we will also collect blood for triglycerides, insulin and C-peptide (approximately 5ml / 1 teaspoon). Your blood will be taken from your arm at each time-point.

We will also make arrangement to collect stool sample from your home. The stool sample will be used for research analyses.

You will receive preconception care provided by the doctors and follow-up visits will be arranged based on the clinical reviews/investigations as per necessary. Blood test results will be reviewed by the doctors.

6 months after the first visit, you will be followed up in the clinic for 6P, personality, lifestyles, physical activity and eye assessments, health and weight review as per necessary. 10ml (2 teaspoons) of blood will be collected for fasting glucose, lipid profile and insulin tests. Stool sample will also be collected at this time point.

At 3, 9 and 12 months, you will be followed-up through phone calls to track for pregnancy status and asked to self-administer the 6P tool for dietary behaviour monitoring and to continue with the exercises. Arrangement will also be made to collect the stool samples from your home. Throughout the preconception phase, preconception health and dietary related messages will be delivered to you by the study team.

During the preconception follow-up, if you have a positive urinary pregnancy test, an ultrasound scan will be arranged for you to confirm clinical pregnancy. If you do not conceive within one year from the first visit, you will be contacted to arrange for a final anthropometry, lifestyles, eye assessments and blood tests (FBC, fasting glucose, insulin, C-peptide, HbA1c,
lipid profile and some additional blood for research analyses) before withdrawal from the study. Another stool sample will be collected as well.

**Pregnancy:**
There will be 3 visits (6-10, 24-28 and 32-36 weeks) during your pregnancy that coincide with your routine antenatal visits, where lifestyle and anthropometry assessments will be performed. The 6P tool will also be administered at each visit and blood test reviews will be provided by the doctor.

By tagging along with routine antenatal clinical blood draw, we will collect additional blood at the same time:

- **6-10 weeks:** Lipid profile, FBC, fasting glucose, insulin, C-peptide, HbA1c and additional blood for research analyses.
- **24-28 weeks:** Lipid profile, FBC, OGTT, insulin, C-peptide and additional blood for research analyses.

As per standard clinical practice, the OGTT during pregnancy consists of 3 time points: fasting, 1 and 2 hour(s) after drinking the glucose drink. We will also collect blood for triglycerides, insulin and C-peptide (approximately 5ml / 1 teaspoon) at the 1 and 2-hour time-points.

In total, at most 30ml of blood (2 tablespoons) will be collected at each visit, inclusive of 12ml (less than 1 tablespoon) for research analyses mentioned above.

At 24-28 weeks, you will receive an activity tracker to track for your 24-hour activity. Arrangement will be made to collect the tracker back from you after 10 days.

At 6-10 and 32-36 weeks, eye assessment will be done.

Stool samples will be collected from you for the 3 visits, arrangement will be made to collect the stool samples from your home. The stool samples will be used for research analyses.

You will also receive trimester-specific education on antenatal care, healthy lifestyles and exercise guidance throughout the pregnancy phase.

**Delivery:**
After you have delivered, placenta and 20 ml (less than 2 tablespoons) of cord blood will be collected if you have given consent. It is likely that there will not be enough cord blood left for banking after it has been collected for study purposes. However, if you wish to bank your child’s cord blood at any point during the study, your decision will be respected by the study team. 10ml (2 teaspoons) of your blood will be collected and stool sample from your child will also be collected for research analyses.

**Postnatal:**
After delivery, there will be 6 visits (1-2 weeks, 6-8 weeks, 4, 6, 12 and 18 months) during the postnatal phase coinciding with the child vaccination time points. During these visits, there will be

- lifestyle and anthropometry assessments;
- dyad care by the clinical staff/ doctors for both mother and child, including reviews on dietary measures and weight outcomes/ child growth monitoring;
- continuous intervention emphasising on dietary behaviours, physical activity and lifestyle changes

HELMs PiS+CF: Version 5 dated 08 Apr 2022
At 6-8 weeks and 18 months, OGTT, insulin, C-peptide, HbA1c and lipid profile assessment will be performed. In total, at most 30ml of blood (2 tablespoons), inclusive of 12ml (less than 1 tablespoon) for research analyses, will be collected at the respective visits.

At 6-8 weeks and 12 months, you will also receive an activity tracker to track for your 24-hour activity. Arrangement will be made to collect the tracker back from you after 10 days.

We would also like to collect 10ml (2 teaspoons) of breast milk up to the 12-month visit or until the cessation of lactation, whichever is earlier. Stool samples will be collected from your child for the 6 visits and from you at 6-8 weeks, arrangement will be made to collect the stool samples from your home. The breast milk and stool samples will be used for research analyses.

The human biological material may be tested in Singapore or Norway, and only coded human biological materials and/or data will be transferred out of Singapore. To protect your confidentiality, all the human biological materials will be coded. All identifiable information (e.g., names, IC numbers) will be kept separate from the human biological materials. The link between your identifiable information and the code number will be kept confidential by the Principal Investigator or a trusted third-party. The human biological materials and data collected will not be used in research involving human-animal combinations, which is restricted by laws imposed by the Ministry of Health, Singapore.

**Sleep tracking**

You will receive a device (Oura Ring, Figure 2) to track your sleeping patterns throughout the study period. The device can be worn on any finger (except the thumb) and records movement, heart rate and temperature. The device is water-proof up to 100m and can be worn while showering or swimming. Wearing the device while scuba diving or keeping it submerged underwater for over 12 hours should be avoided. Arrangement will be made to collect the device back from you upon study completion.

If you agree to participate in this study, you should follow the study visit schedules, measures, advice and directions given to you by the study team.

**WHAT IS NOT STANDARD CARE OR IS EXPERIMENTAL IN THIS STUDY**

The study is being conducted because the lifestyle intervention designed to start from the preconception, through pregnancy until the postnatal phase are not yet proven to be a standard care in women with high BMI. We hope that your participation will help us to determine whether the intervention is equal or superior to existing clinical care.

Although anthropometric measurement and retinal photography, as well as blood glucose, FBC and lipid profile tests may be part of standard medical care, in this study these procedures are being performed for the purposes of the research, and are not part of your routine care.
POSSIBLE RISKS, DISCOMFORTS OR INCONVENIENCES

Personal privacy and confidentiality:
This study uses health information that may affect your privacy. To protect your confidentiality, only a unique code number will be used to identify data and/or biological material that we collected from you.

As there will be a link between the code and your identifiable information, there is still a possibility of data breach. A data breach is when someone sees or uses data without permission. If there is a data breach, someone could see or use the data we have about you. Even without your name, there is a chance someone could figure out who you are. They could misuse your data. We believe the chance of this is very small, but it is not zero.

Questionnaires/ surveys/ interviews:
Some of the questions might make you feel uncomfortable or upset. You may refuse to answer any of the questions and/or take a break at any time during the study.

Collection of blood:
Taking blood may cause momentary discomfort, pain, bleeding, bruising or swelling at the site of the needle stick. Rarely, taking blood may cause fainting or infection. If possible, the research blood sample(s) will be collected at the same time you have blood drawn for clinical care or through an existing catheter already inserted into a vein.

Collection of placenta:
Collection of placenta is safe, non-invasive and there will be no adverse effects.

Collection of stool and breast milk samples:
Collection of stool and breast milk may cause inconveniences and momentary discomfort.

Retinal photography:
Retinal photography may cause mild and temporary discomfort. You may experience the flashlight as very intense and see spots for a short time following the examination.

Oura Ring:
Wearing the device may cause mild and temporary discomfort. If you experience redness or skin irritation on your finger, remove the ring immediately.

POTENTIAL BENEFITS

If you participate in this study, you may reasonably expect to benefit from the study by receiving lifestyle intervention and relevant education starting from preconception, through pregnancy until the postnatal phase.

ALTERNATIVE PROCEDURES/ TREATMENTS IF YOU DO NOT PARTICIPATE IN THE STUDY

If you choose not to take part in this study, the alternative is to have what is considered standard care for your condition. In our institution, this would be routine clinical care for women.
at who are trying for pregnancy, during and after pregnancy, and you do not need to undergo the research activities mentioned above.

COSTS & PAYMENTS IF PARTICIPATING IN THIS STUDY

There is no cost to you for participating in this research study.

If you take part in this study, the following will be performed at no charge to you:

- All assessments and examinations done at the HELMS study clinic
- Preconception hormonal blood tests, infection screen, OGTT, fasting glucose, insulin, C-peptide, HbA1c, lipid profile and FBC at the HELMS study visits
- Multi-micronutrients supplements
- Vitamin D drops for your child
- Doctor consultations during the preconception phase and 6-10w visit during pregnancy phase at the HELMS study clinic

These costs will be borne by KK Women’s and Children’s Hospital.

The cost of your usual medical care (procedures, medications and doctor visits) will continue to be billed to you.

You will be reimbursed for your time, inconvenience and transportation costs. Reimbursement for each study specific visit will be as follows:

- Preconception phase:
  a. S$70 for baseline visit
  b. S$60 for 6m visit
  c. S$100 for 12m/Exit visit
- Pregnancy phase:
  a. S$100 for 6-10w visit
  b. S$100 for 24-28w visit
  c. S$80 for 32-36w visit
- Delivery: S$20 for placenta, maternal and cord blood collection
- Postnatal phase:
  a. S$100 for 1-2w visit
  b. S$100 for 6-8w visit
  c. S$80 for 4m, 6m and 12m visit
  d. S$120 for 18m visit
- Reimbursement upon submission:
  a. S$30 for participation in Actigraph data collection where the device is worn for 10 consecutive days
  b. S$50 for participation in Oura Ring data collection where the device is worn for at least 3 consecutive months in each phase
  c. S$5 for each stool collection.
  d. S$10 for each breast milk collection.
INCIDENTAL FINDINGS

There will not be any incidental findings arising in this research. “Incidental findings” are findings that have potential health or reproductive importance to research participants like you and are discovered in the course of conducting the study, but are unrelated to the purposes, objectives or variables of the study.

WHAT HAPPENS TO THE SAMPLES COLLECTED FOR THE RESEARCH

The biological materials collected for this research study will be deemed to be donated to KK Women’s and Children’s Hospital as a gift. By agreeing to this, you give up your rights to the biological materials. If the use of your biological materials and/or your data results in intellectual property rights and commercial benefits, you will not receive any financial benefits or proprietary interest.

The biological materials will be used only for the purpose of this research and will be discarded or destroyed upon completion of the research study.

PARTICIPANT’S RIGHTS

Your participation in this study is entirely voluntary. You have a right to ask questions, which the study team will do their best to answer clearly and to your satisfaction.

In the event of any new information becoming available that may be relevant to your willingness to continue in this study, you (or your legal representative, if relevant) will be informed in a timely manner by the Principal Investigator or his/her representative and will be contacted for further consent if required.

WITHDRAWAL FROM STUDY

You are free to withdraw your consent and discontinue your participation in the study at any time, without your medical care being affected. If you decide to stop taking part in this study, you should tell the Principal Investigator.

However, any of your data and your child’s data that have been collected until the time of your withdrawal will be kept and analysed. Your or your child’s medical information will be retrieved from the hospital medical records even after your withdrawal. The reason is to enable a complete and comprehensive evaluation of the study.

The biological materials that have been collected for the study will not be returned to you. However, you retain your right to ask the Principal Investigator to discard or destroy any remaining samples if they have not been anonymised and/or have not been used.

Your study doctor, the Principal Investigator of this study may stop your participation in the study at any time for one or more of the following reasons:

- Failure to follow the instructions of the Principal Investigator and/or study staff.
- The Principal Investigator decides that continuing your participation could be harmful to your health or safety.
- You require treatment not allowed in the study.
- The study is cancelled.
RESEARCH RELATED INJURY AND COMPENSATION

If you follow the directions of the Principal Investigator of this research study and you are injured due to the research procedure(s) given under the plan for the research study, our institution will provide you with the appropriate medical treatment.

Payment for management of the normally expected consequences of your treatment (i.e. consequences of your treatment which are not caused by your participation in the research study) will not be provided.

You still have all your legal rights. Nothing said here about treatment or compensation in any way alters your right to recover damages where you can prove negligence.

CONFIDENTIALITY OF STUDY AND MEDICAL RECORDS

Your participation in this study will involve the collection of Personal Data. “Personal Data” means data about you which makes you identifiable (i) from such data or (ii) from that data and other information which an organisation has or likely to have access. Examples of personal data include name, national registration identity card (NRIC), nationality, passport information, date of birth, and telephone number.

Personal Data collected for this study will be kept confidential. Your study records and medical records, to the extent required by the applicable laws and regulations, will not be made publicly available. Only the study team will have access to the personal data being collected from you. In the event of any publication regarding this study, your identity will remain confidential.

However, the monitor(s), the auditor(s), the Institutional Review Board, and the regulatory authority(ies) will be granted direct access to your original medical records and study records to verify study procedures and data, without making any of your information public. The HELMS study may gain access to your/ your child’s information records held by healthcare providers and government agencies (e.g. Singapore’s National Disease Registries, National Immunisation Registry, Ministry of Health, Ministry of Education) in Singapore for the purpose of studying health outcomes.

By signing the Consent Form, you consent to (i) the collection, access to, use and storage of your Personal Data by KK Women’s and Children’s Hospital, and (ii) the disclosure of such Personal Data to our authorised service providers and relevant third parties as mentioned above.

Any information containing your Personal Data that is collected for the purposes of this research will be stored in Singapore. To protect your identity, your Personal Data will be labelled with a unique code number. The code will be used in place of your name and other information that directly and easily identifies you. The study team will keep a separate file that links your code number to your Personal Data. This will be kept in a safe place with restricted access. In the event of any international collaboration in data analysis, your coded data will be transferred out of Singapore.

All data collected in this study are the property of KK Women’s and Children’s Hospital. The data will be used for the purpose of this research study only, unless you give permission for
your data to be made available for future use in other research studies. For this purpose, consent for future research will be sought from you.

By participating in this research study, you are confirming that you have read, understood and consent to the SingHealth Data Protection Policy, the full version of which is available at www.singhealth.com.sg/pdpa.

**WHO HAS REVIEWED THE STUDY**

This study has been reviewed by the SingHealth Centralised Institutional Review Board for ethics approval.

If you have questions about your rights as a participant, you can call the SingHealth Centralised Institutional Review Board at 6323 7515 during office hours (8:30 am to 5:30pm).

**WHO TO CONTACT IF YOU HAVE QUESTIONS REGARDING THE STUDY**

If you have questions about this research study or in the case of any injuries during the course of this study, you may contact:

**Principal Investigator**
Prof. Jerry Chan Kok Yen  
Department of Reproductive Medicine  
KK Women's and Children's Hospital  
100 Bukit Timah Road  
Singapore 229899  
Tel: 6394 1060 / 8125 3639 (after office hours)

If you have any feedback about this research study, you may contact the Principal Investigator or the SingHealth Centralised Institutional Review Board.
Protocol Title:
Healthy Early Life Moments in Singapore (HELMS)

Principal Investigator:
Prof. Jerry Chan Kok Yen
Department of Reproductive Medicine
KK Women’s and Children’s Hospital
100 Bukit Timah Road
Singapore 229899

I agree to participate in the research study as described and on the terms set out in the Participant Information Sheet.

The nature, risks and benefits of the study have been explained clearly to me and I fully understand them.

I understand the purpose and procedures of this study. I have been given the Participant Information Sheet and the opportunity to discuss and ask questions about this study and am satisfied with the information provided to me.

I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reasons and without my medical care being affected.

By participating in this research study, I confirm that I have read, understood and consent to the SingHealth Data Protection Policy.

Should withdrawal from the study occur, please indicate your choice using the relevant checkbox.

- [ ] I do not agree to be contacted for other related research studies after withdrawal.
- [ ] I agree to be contacted for other related research studies after withdrawal.

<table>
<thead>
<tr>
<th>Name of participant</th>
<th>Signature/Thumbprint (Right / Left)</th>
<th>Date of signing</th>
</tr>
</thead>
</table>

HELMS PIS+CF: Version 5 dated 08 Apr 2022
To be completed by parent / legal guardian / legal representative, where applicable

I hereby give consent for _________________________ (Name of Participant) to participate in the research study. The nature, risks and benefits of the study have been explained clearly to me and I fully understand them.

I confirm that I have read, understood and consent to the SingHealth Data Protection Policy.

| Name of participant’s parent/ legal guardian/ legal representative | Signature/Thumbprint (Right / Left) | Date of signing |

To be completed by translator, if required

The study has been explained to the participant/ legal representative in ____________________________ by ____________________________.

Language

| Name of translator |

To be completed by witness, where applicable

I, the undersigned, certify that:

- I am 21 years of age or older.
- To the best of my knowledge, the participant or the participant’s legal representative signing this informed consent form had the study fully explained to him/her in a language understood by him/ her and clearly understands the nature, risks and benefits of the participant's participation in the study.
- I have taken reasonable steps to ascertain the identity of the participant or the participant's legal representative giving the consent.
- I have taken reasonable steps to ascertain that the consent has been given voluntarily without any coercion or intimidation.

Witnessed by: ________________________________ __________________ ________________

| Name of witness | Date of signing |

Signature of witness

1. An impartial witness (who is 21 years of age or older, has mental capacity, who is independent of the research study, and cannot be unfairly influenced by people involved with the research study) should be present during the entire informed consent discussion if a participant or the participant’s legal representative is unable to read, and/or sign and date on the consent form (i.e. using the participant’s or legal representative’s thumbprint). After the written consent form and any written information to be provided to participant is read and explained to the participant or the participant’s legal representative, and after the participant or the participant’s legal representative has orally consented to the participant's participation in the study and, if capable of doing so, has signed and personally dated the consent form, the witness should sign and personally date the consent form. This is applicable for Clinical Trials regulated by HSA and Human Biomedical Research under the HBRA.

2. For HBRA studies, the witness may be a member of the team carrying out the research only if a participant or the participant’s legal representative is able to read, sign and date on the consent form.
Investigator’s Statement

I, the undersigned, certify to the best of my knowledge that the participant/ participant’s legal representative signing this consent form had the study fully explained to him/her and clearly understands the nature, risks and benefits of the participant's participation in the study.

________________________       _______________________ ________________
Name of Investigator/Person obtaining consent    Signature    Date
INFORMATION & CONSENT FORM FOR FUTURE RESEARCH

This is an optional component that is separate from the research study. You may still participate in the research study if you say "No" to this. Please ask questions if you do not understand why we are asking for your permission.

In this Consent Form for Future Research, we seek your permission to keep your data for future research. The data will be kept in KK Women’s and Children’s Hospital. Except if you withdraw your consent or there are limits imposed by law, there is no limit on the length of time we will store your data. Researchers will use your data for research long into the future.

This is what will be done with your stored data:

- We may use the data to answer additional research questions in other research studies. This is outside the scope of the research study but still related to maternal-child health and disease development.
- We may share the data with other researchers at Agency for Science, Technology and Research (A*STAR), National University of Singapore, Duke-NUS Medical School, Singapore Management University etc. and with researchers outside of Singapore, such as collaborators from University of Southampton, UK etc.
- The stored data will be labelled with a code instead of information that directly identifies you (e.g. your name, NRIC, date of birth, etc.). We will keep a separate file (key) that links your code to your identifiable information.
- When we share your data with other researchers, it will be in a coded manner. They will not be able to identify you from the coded data.
- If you decide at a later time that you do not want your data to be used for future research, you can contact the Principal Investigator or study team at any time. All your stored data that has not been used or shared with other researchers will be removed and discontinued from further use, unless this information is already included in analyses or used in publications.
CONSENT FORM FOR FUTURE RESEARCH

This component is optional. You do not have to agree to it in order to participate in the research study.

Please indicate your choice using the relevant checkbox.

☐ I do not agree to have my data stored for future use in other research studies.

☐ I agree to have my data stored for future use in other research studies.

____________________      ___________________________          _____________
Name of participant                   Signature/Thumbprint (Right / Left)       Date of signing

To be completed by parent / legal guardian / legal representative, where applicable

I hereby give consent for _________________________ (Name of Participant)’s data obtained from the research study to be stored for future use in other research studies in the interest of medical progress as described in and on terms set out in the Information & Consent Form for Future Research.

I understand that his/her participation is voluntary and I can withdraw his/her participation at any time, without giving reasons.

The nature of this optional component has been explained clearly to me and I fully understand them.

I have been given the Information & Consent Form for Future Research and the opportunity to discuss and ask questions about this optional component and am satisfied with the information provided to me.

I confirm that I have read, understood and consent to the SingHealth Data Protection Policy.

____________________      ____________________________        ______________
Name of participant’s parent/ legal guardian/ legal representative      Signature/Thumbprint (Right / Left)      Date of signing

To be completed by translator, if required

The optional component (storage of data for future use in other research studies) has been explained to the participant/ participant’s legal representative in

Language                                               by                                               Name of translator

HELMS PIS+CF: Version 5 dated 08 Apr 2022
To be completed by witness, where applicable

I, the undersigned, certify that:

- I am 21 years of age or older.
- To the best of my knowledge, the participant or the participant’s legal representative signing this Information & Consent Form for Future Research had the optional component fully explained to him/her in a language understood by him/her and clearly understands the purpose and the nature of the participant’s participation in the study.
- I have taken reasonable steps to ascertain the identity of the participant or the participant’s legal representative giving the consent.
- I have taken reasonable steps to ascertain that the consent has been given voluntarily without any coercion or intimidation.

Witnessed by: ________________________________ ___________________

Name of witness      Date of signing

________________________________
Signature of witness

1. An impartial witness (who is 21 years of age or older, has mental capacity, who is independent of the research study, and cannot be unfairly influenced by people involved with the research study) should be present during the entire informed consent discussion if a participant or the participant’s legal representative is unable to read, and/or sign and date on the consent form (i.e. using the participant’s or legal representative’s thumbprint). After the written consent form and any written information to be provided to participant, is read and explained to the participant or the participant’s legal representative, and after the participant or the participant’s legal representative has orally consented to the participant’s participation in the study and, if capable of doing so, has signed and personally dated the consent form, the witness should sign and personally date the consent form. This is applicable for Clinical Trials regulated by HSA and Human Biomedical Research under the HBR A.

2. For HBRA studies, the witness may be a member of the team carrying out the research only if a participant or the participant’s legal representative is able to read, sign and date on the consent form.

Investigator’s Statement

I, the undersigned, certify to the best of my knowledge that the participant/ participant’s legal representative signing this Information & Consent Form for Future Research had the optional component (storage of data for future use in other research studies) fully explained to him/her and clearly understands the purpose and the nature of the participant’s participation in the study.

Name of Investigator/ Person obtaining consent

Signature                      Date