SPAROW STUDY PROTOCOL

Objectives:

1. To conduct a randomized control trial to examine the efficacy of an INTERACTIVE SMARTPHONE APP, customized for Singaporean women with recent GDM, in optimizing post-delivery weight and metabolic profiles compared with standard care.

   - Primary outcome: Restoration of booking weight if previous booking BMI = 23; Weight loss of 5% with respect to booking weight if BMI > 23
   - Secondary outcomes: Improved cardiometabolic and inflammatory markers: fasting and 2h post-glucose load plasma glucose in an oral glucose tolerance test, HbA1C, advanced glycation end-products, C-peptide, HOMA-IR, lipid profile, liver function, hsCRP, IL-6.2.

2. Evaluate the relative cost-effectiveness of this INTERACTIVE SMARTPHONE APP compared to standard care within the Singapore healthcare system in terms of improvements in quality of life, feasibility, acceptability, scalability and sustainability.

Design:

During the antenatal period, subjects will be informed about the study during regular NUH GDM consultations. After delivery, women will be offered the opportunity to join the study. Informed consent will be obtained at the 36-41 week follow-up visit or if the patient is admitted to hospital between 36-41 weeks of gestation. An appointment will be given for the first study visit at 6-12 weeks post-delivery. After delivery before discharge, subject's height and weight will be taken. Women will undergo a 75gm OGTT. Fasting blood would be stored for metabolic assessments. Validated questionnaires on health status, diet, physical activity, and quality of life as listed below in secondary outcomes will be obtained.

RANDOMIZATION:

Participants would be randomized after informed consent has been obtained to either STANDARD care or INTERACTIVE SMARTPHONE APP arms of the study. The team aims to randomize 200 subjects (n=100 in each arm) and estimate that a minimum of 64 subjects will complete the study in each arm. The team has factored in a total of 15% attrition from postnatal diagnosis of type 2 diabetes, voluntary attrition and lost to follow-up.

INTERVENTIONS:

A) STANDARD CARE ARM: Subjects in the standard care arm will be informed of their increased risk of developing type 2 diabetes in the future, and given general lifestyle advice to maintain a healthy weight, eat a well-balanced diet and do regular exercise during their 6-week postnatal visit. Women found to have impaired fasting glucose (6.1-6.9 mmol/L) or impaired glucose tolerance (2H post glucose of 7.8-11.0 mmol/L) will be issued a letter reinforcing lifestyle changes namely weight loss (if raised BMI), diet, exercise, and encouragement to consult a family physician to discuss the appropriateness of starting medications that can prevent the progression to type 2 diabetes, or restore the blood glucose to normal levels. Those with a normal OGTT result will just be informed that it is normal.

B) INTERACTIVE SMARTPHONE APP ARM: Participants will download the INTERACTIVE SMARTPHONE APP and will be briefed on its use by our team of nutritionists/ dieticians, exercise physiologists and lifestyle coaches. Patients will also be given a digital weighing

machine to chart their weight weekly if they do not already own one. About 4 months after delivery, participants will return to the outpatient clinic for OGTT, HbA1C, advanced glycation end-products, C-peptide, HOMA-IR, lipid profile, liver function, hsCRP, and IL-6 testing, as well as the same validated questionnaires that they had completed during their previous visit. This will be their last visit pertaining to the study and will be discharged from the study.

Methods:

For the main analysis, the primary outcomes are the proportion of women attaining a satisfactory weight at 4 months post-delivery. The team will aim for a minimally important effect of a doubling in the proportion of women who attain their target weight, corresponding to 40% of women in the intervention group attaining their target weight (or less) and 20% in the control group. For a standard power of 80% and alpha of 0.05, the sample size required in each group to detect this effect is 64 individuals. To account for a potential 15% attrition rate, the team aims to recruit 75 individuals in each group.

Subject's visits:

VISIT 1 (6-12 weeks postnatal): Blood taking: at 0hr and 2hr for oral glucose tolerance test. HbA1C, advanced glycation end-products, C-peptide, HOMA-IR, lipid profile, liver function, hsCRP, and IL-6. Questionnaires: Patients will be asked to fill up a series of questionnaires that will cover their health status, diet, physical activity, and quality of life. An optional 10ml of additional blood will be collected for storage for use in future studies regarding the management of recent gestational diabetes.

VISIT 2 (about 4 months postnatal): Blood taking: at 0hr and 2hr for oral glucose tolerance test. HbA1C, advanced glycation endproducts, C-peptide, HOMA-IR, lipid profile, liver function, hsCRP, and IL-6. Patients will be asked to fill up a series of questionnaires that will cover their health status, diet, physical activity, and quality of life. An optional 10ml of additional blood will be collected for storage for use in future studies regarding the management of recent gestational diabetes.

Details of investigations performed:
- Blood taking for: OGTT, blood metabolic markers (C-peptide, insulin, HbA1C, lipid profile, liver function, hsCRP), blood for future research
- Measurements: Height, weight
- Questionnaires:
    1) 3-Day food diary,
    2) Self-Efficacy to regulate eating habits questionnaire,
    3) Self-Efficacy to regulate exercise questionnaire,
    4) Health Education Impact (heiQ),
    5) RAND-12 health questionnaire,
    6) Health Expenditure questionnaire.

Inclusion criteria:

Female aged 21 years and above; Plans to deliver in NUH; Diagnosed with GDM antenatally (between 12-34 weeks gestation) defined using the 2013 World Health Organization criteria;

Has a smartphone and able to independently use a smartphone app; Willing to provide a blood sample; Able to give written informed consent; Able to speak and read English.

Exclusion criteria:

Subjects with type 1 and type 2 diabetes (including suspected cases diagnosed by an abnormal oral glucose tolerance test in the 1st and early 2nd trimesters of pregnancy); Drugs that affect glucose or lipid metabolism; Terminal or life threatening condition; Physical or mental condition that would prevent completion of a majority of study instruments.