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# A culturally tailored personaliseD nutrition intErvention in South ASIan women at risk of Gestational Diabetes Mellitus (DESI-GDM): a randomised controlled trial protocol

Rosain N Stennett ,[1] Kristi B Adamo,[2] Sonia S Anand ,[1,3,4] Harpreet S Bajaj,[5] Shrikant I Bangdiwala ,[1,4] Dipika Desai,[1,4] Hertzel C Gerstein ,[3,4] Sujane Kandasamy ,[1] Farah Khan,[4] Scott A Lear ,[4,6] Sarah D McDonald,[1,7,8,9] Tayler Pocsai,[4] Paul Ritvo ,[10] Andrea Rogge,[4] Karleen M Schulze ,[3,4] Diana Sherifali ,[1,11] Jennifer C Stearns,[3,7,12] Gita Wahi,[1,13] Natalie C Williams,[3] Michael A Zulyniak ,[14] Russell J de Souza [1,4]

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For numbered affiliations see end of article.

**Correspondence to**
Dr Russell J de Souza; desouzrj@mcmaster.ca

## ABSTRACT

**Introduction** South Asians are more likely to develop gestational diabetes mellitus (GDM) than white Europeans. Diet and lifestyle modifications may prevent GDM and reduce undesirable outcomes in both the mother and offspring. Our study seeks to evaluate the effectiveness and participant acceptability of a culturally tailored, personalised nutrition intervention on the glucose area under the curve (AUC) after a 2-hour 75 g oral glucose tolerance test (OGTT) in pregnant women of South Asian ancestry with GDM risk factors.

**Methods and analysis** A total of 190 South Asian pregnant women with at least 2 of the following GDM risk factors—prepregnancy body mass index>23, age>29, poor-quality diet, family history of type 2 diabetes in a first-degree relative or GDM in a previous pregnancy will be enrolled during gestational weeks 12–18, and randomly assigned in a 1:1 ratio to: (1) usual care, plus weekly text messages to encourage walking and paper handouts or (2) a personalised nutrition plan developed and delivered by a culturally congruent dietitian and health coach; and FitBit to track steps. The intervention lasts 6–16 weeks, depending on week of recruitment. The primary outcome is the glucose AUC from a three-sample 75 g OGTT 24–28 weeks' gestation. The secondary outcome is GDM diagnosis, based on Born-in-Bradford criteria (fasting glucose>5.2 mmol/L or 2 hours post load>7.2 mmol/L).

**Ethics and dissemination** The study has been approved by the Hamilton Integrated Research Ethics Board (HiREB #10942). Findings will be disseminated among academics and policy-makers through scientific publications along with community-orientated strategies.

**Trial registration number** NCT03607799.

## STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The personaliseD nutrition intErvention in South ASIan women at risk of Gestational Diabetes Mellitus (DESI-GDM) study intervention is informed by the findings of a previous qualitative study, which assessed barriers and facilitators of lifestyle changes to prevent GDM, as well a birth cohort study completed in a similar population.

⇒ This study uses an end-user codeveloped approach to intervention study, which seeks to improve participant engagement and buy in.

⇒ The study is powered to detect a moderate treatment effect on the glycaemic response to the oral glucose tolerance test, however, not GDM.

## INTRODUCTION

Gestational diabetes mellitus (GDM) is a condition in which a woman without existing diabetes develops high blood sugar levels during pregnancy.[1] Complications for the baby include neonatal hypoglycaemia and intensive care admission.[2] GDM is a strong risk factor for future type 2 diabetes (T2DM): up to 50% of women with GDM develop T2DM within 5 years of giving birth[3 4] and face up to sevenfold higher lifetime risk of T2DM compared with women who have a non-GDM pregnancy.[3 5] Additionally, GDM is associated with future atherosclerosis and cardiovascular disease (CVD) in the mother and increases the risk of T2DM in offspring up to eightfold.[5–8]

South Asians (SA), whose ancestors are from India, Pakistan, Bangladesh or Sri Lanka, are the largest non-white ethnic group in Canada and are at high risk of T2DM and early CVD. GDM increases the risk of future T2DM and CVD. The development of GDM is influenced by several factors, including prepregnancy

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body mass index (BMI),[9 10] family history,[11] genetics[12 13] and notably ethnicity[11 14 15] and diet.[11 14 16–18] SA are two times more likely to develop GDM relative to white European women,[14 15] and risk factors for future T2DM in the offspring, including higher birth weight, more adipose tissue and reduced insulin sensitivity, are more common in SA infants of mothers with GDM than infants born to mothers without GDM.[14] Furthermore, a low-quality diet (diet higher in meat, meat dishes, processed meats, organ meats, poultry, fish, seafood, rice, fried foods, refined grains (breads and cereals), fast foods and eggs) during pregnancy increases one's odds of developing GDM (OR: 1.62; 95% CI: 1.20 to 2.19).[14] It is assumed that approximately 13% of GDM cases in SA could be prevented by a healthy diet (population attributable risk: 12.8%).[14]

Food-based interventions show the most potential for preventing GDM.[16–18] A network meta-analysis (21 randomised trials during pregnancy; n=1865 women)[19] reported that diets with reduced glycaemic load and/or increased fibre intake, compared with gestational weight gain advice, improved fasting glucose levels. In another meta-analysis of randomised control trials, diet modification alone led to the largest reduction in risk of excessive maternal weight gain and (3 trials; n=409 women) reduced the incidence of GDM (relative risk (RR): 0.68; 95% CI: 0.48 to 0.96); however, the overall evidence rating was low to very low for the latter outcome.[20] There is a need for more robust food-based intervention studies that consider additional factors in the development of GDM in order to provide optimal prevention strategies for women at higher risk of developing the condition.

Few randomised trials of the effect of diet and/or physical activity on incident GDM have been conducted. One recent randomised trial conducted in Ireland (n=565) found that an exercise and nutrition programme delivered via smartphone did not reduce GDM in overweight and obese women randomised at a mean gestational age of 15.3 weeks (RR: 1.1; 95% CI: 0.71 to 1.66).[21] However, this study aimed to modify only one aspect of diet, which was reducing the glycaemic index. A second trial conducted in Spain (n=1000) found that a Mediterranean dietary pattern supplemented with extra virgin olive oil and pistachios, reduced the incidence of GDM (RR: 0.73; 95% CI: 0.56 to 0.95) compared with standard low-fat dietary advice.[22] A third trial, Project SARAS in Mumbai, India,[23] was an unblinded, individually randomised controlled trial of diet to prevent GDM in women living in slums. The intervention included a daily snack made from leafy green vegetables, fruit and milk for the treatment group, compared with low-micronutrient vegetables (eg, potato and onion) for the control group, on top of the usual diet. Of 6513 women, 35.2% (n=2291) became pregnant; of these, 88.5% (n=2028) reached a gestation of 28 weeks and 50% (n=1008) attended an oral glucose tolerance test (OGTT).[18] In total, 9.9% (n=100) developed GDM using the WHO's 1999 definition.[24] Although there were many challenges of conducting this trial (ie, 50% lost to follow-up), in an intention-to-treat analysis, GDM was reduced in the treatment group (7.3% compared with 12.4% in controls; OR: 0.56; 95% CI: 0.36 to 0.86; p=0.008). The reduction remained significant after adjusting for prepregnancy adiposity and fat or weight gain during pregnancy.

In a qualitative interpretive descriptive study of barriers and facilitators to healthy eating encountered by pregnant and recently pregnant South Asian women and healthcare providers living and working in the Peel Region of Ontario, Canada,[25] women voiced several facilitators to healthy eating such as: (1) knowledge of culturally appropriate healthy foods and (2) access to a healthcare provider able to provide resources and support in a timely fashion. Participants also identified barriers to healthy eating, including difficulty in: (1) changing long-held cultural diet practices, (2) adapting standard dietary advice to personal health beliefs, (3) navigating food choices at family gatherings and (4) accommodating meal needs of others in the household. Women expressed a desire to learn more about healthy eating to prevent diabetes during pregnancy and were keen to use mobile health technology. Healthcare providers identified two major challenges to providing appropriate advice to members of this community: (1) insufficient time for counselling and (2) lack of familiarity with South Asian foods. These findings are consistent with other studies of sociocultural influences on behaviour in pregnancy in South Asian women.[26 27]

These observations have led us to design and evaluate the effectiveness and participant acceptability of a randomised controlled trial of a culturally tailored, personalised nutrition intervention, delivered by a health coach, on the glucose area under the curve (AUC) after a 2-hour 75 g OGTT to pregnant South Asian women at risk of GDM living in Southern Ontario, Canada. The trial protocol follows the guidelines for protocol development and reporting described by the Standard Protocol Items: Recommendations for Interventional Trials 2013 statement (see online supplemental additional file 1).

## METHODS

### Design

The study is a two-arm parallel randomised controlled trial (RCT). The allocation ratio will be 1:1 to the intervention or usual care (control) group. The study schema diagram illustrates the referral and screening procedure (figure 1).

### Setting

The study will be conducted in Southern Ontario with the primary recruitment site being the Regional Municipality of Peel, which consists of three municipalities to the west and northwest of the city of Toronto: the cities of Mississauga and Brampton and the town of Caledon. More than half of the residents of the Region of Peel identify as South Asian.[28] The region has >800 family physicians and >60 obstetricians who see approximately

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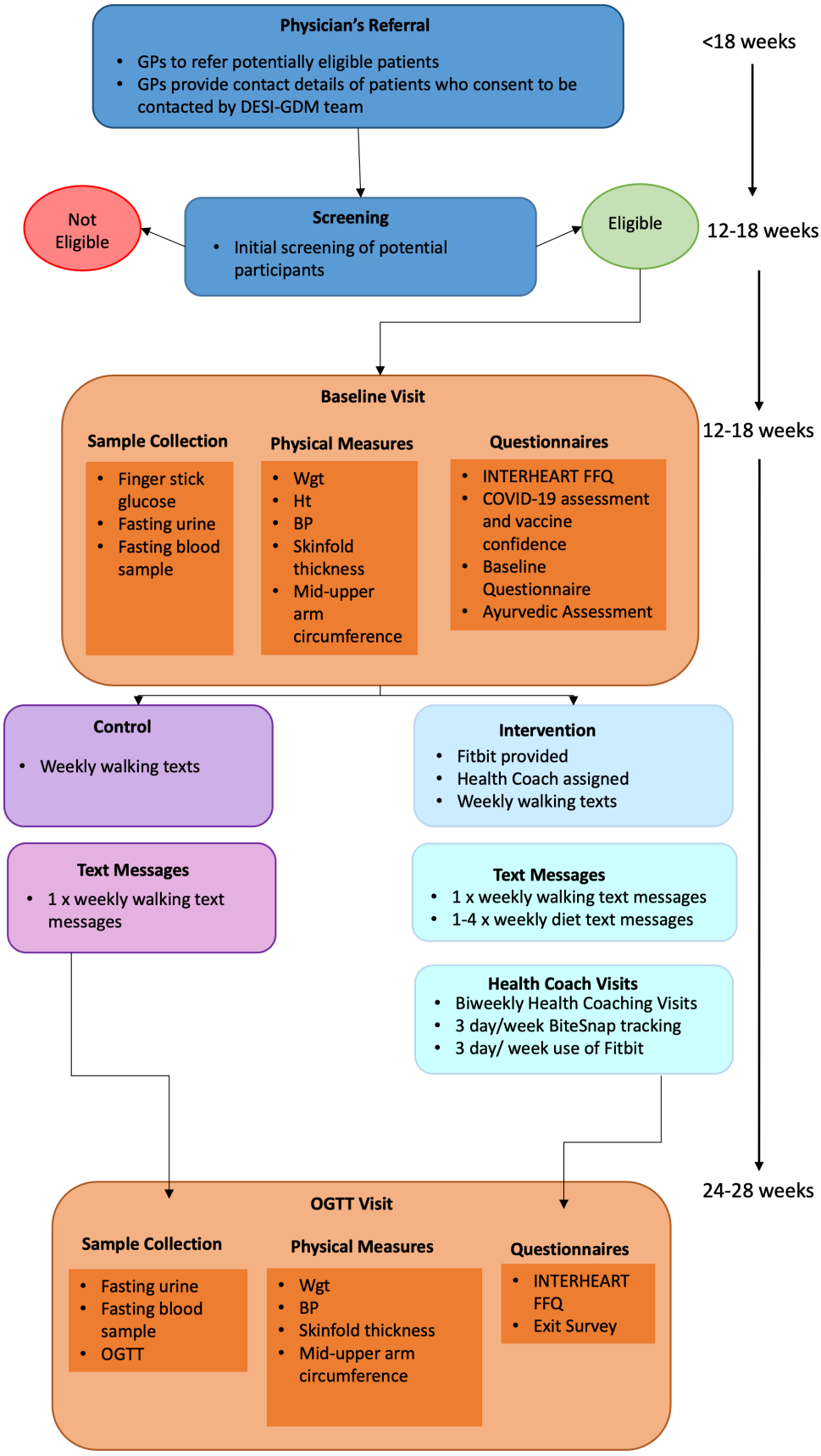


**Figure 1** Study flowchart. BP, blood pressure; FFQ, Food Frequency Questionnaire; GP, general practitioner; Ht, height; OGTT, oral glucose tolerance test; Wgt, weight.

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5000 South Asian women/year in the second trimester of pregnancy. Expectant women routinely attend their first visit between 12–18 weeks of pregnancy and then every 4 weeks until 30 weeks' gestation; every 2 weeks from 32 to 36 weeks' gestation; and once a week from 37 weeks' gestation until birth.[29]

### Sample size

With 86 participants per group (total n=172), the study will have 90% power to detect at least a 15% between-group difference in AUC glucose, the primary outcome, assuming 70% adherence to the intervention (ie, goal setting, health coach contacts, food tracking) and SD of AUC glucose=173 mmol/min.[14] A change in glucose of at least this magnitude has been observed in trials of similar design to test fibre supplements,[30] high-protein[31] or high-fat diets.[32] A 10% loss to follow up is assumed, which is low for dietary interventions; however, given the frequent expected contact with healthcare providers during pregnancy, the virtual nature of our intervention and our pilot data,[33] it is believed to be feasible. The sample size has been inflated to 95 per group (total n=190) to account for the expected high lost to follow up. The study will have low power to detect a moderate treatment effect on the secondary outcome of GDM (ie, 20%–30% between-treatment difference) and higher power to detect very large treatment effects in GDM (ie, 80% power to detect a 61% relative risk reduction). The study will look to see if GDM incidence, measured as a dichotomous outcome, is nominally improved.

### Inclusion criteria

Singleton pregnant South Asian women will be enrolled between 12 and 18 weeks' gestation. This timeframe avoids the early pregnancy window, when women are most likely to experience nausea, and is past the highest period of risk for spontaneous abortion. In addition to being South Asian, a high-risk ethnic group for GDM,[11] participants will also need to meet at least 2 GDM risk factors: age>29,[14] low diet quality (assessed with a short diet screener),[14 34] family history of DM/GDM during a previous pregnancy[11 35] or a prepregnancy body mass index (BMI)≥23.[14]

### Exclusion criteria

Expectant mothers with any of the following will be excluded from the study: (a) pre-existing T1DM or T2DM;[11] (b) hypertension (≥140 mm Hg systolic or ≥90 mm Hg diastolic) or on medication for the condition;[36–38] (c) serious difficulty understanding health information in English, based on the screening conversation, that would preclude informed consent and participation (93% of Canadian South Asian women in the National Household Survey could conduct a conversation in one or both official languages (English and French));[39 40] (d) those unwilling or unable to modify their eating habits, based on a screening question; (e) those at high risk of adverse pregnancy outcomes other than GDM (eg, twins or higher-order multiples,[36 41] use of fertility treatments,[42] history of hypertension/pre-eclampsia, history[38] of placenta previa[43] or preterm delivery;[44] or (f) enrolment in another intervention study that would compromise full participation in the personaliseD nutrition intErvention in South ASIan women at risk of Gestational Diabetes Mellitus (DESI-GDM) trial.

### Recruitment

Because of the COVID-19 pandemic, and the university research policies, the study recruitment was delayed but began in November 2021 and is expected to be completed by March 2024. The study team will provide study information to primary care physicians and obstetricians who will identify and refer participants into the study.

Randomisation and blinding: Women will be randomised 1:1 to intervention or control using a centralised integrated web response system (IWRS) at the Population Health Research Institute (PHRI) in Hamilton, Ontario. A statistician will generate a randomisation list using a permuted blocks algorithm with randomly chosen block sizes to ensure balance in numbers and avoid predictability.[45] The nature of the intervention precludes blinding of the participants to the treatment assignment; however, those providing the analysis of blood glucose levels for assessing the primary and secondary outcomes will be blinded to treatment assignment.

At the baseline visit, the research assistant (RA) will confirm eligibility and obtain consent, either in person, verbally via telephone or web conferencing, or electronically via Research Electronic Data Capture (REDCap). These three options are believed to be flexible and responsive to participant preference, and possible regulations regarding COVID-19 public health measures. After confirming eligibility and the informed consent discussion, the RA will collect baseline measures.

After collecting baseline physical measures, the study personnel completing the visit will activate the IWRS to randomly allocate participants to control or intervention in a concealed fashion using a computer-generated random sequence. Those assigned to the intervention will be assigned to a health coach, who will contact the participant for a baseline nutrition assessment and goal-setting session. Planned assessment visits take place at three time points regardless of the study arm: (1) baseline of 12–18 weeks' gestation, (2) follow-up of 24–28 weeks' gestation and (3) post delivery—pregnancy and birth outcomes.

### Intervention

In our intervention study that seeks to address behavioural changes, we used goal setting, behavioural contracting through bi-weekly checkups and tailored health communication (text messaging). These strategies were drawn from the social cognitive theory of behavioural changes[46] and applied stages of change construct of the transtheoretical model.[47] The activities used in the intervention are guided by the findings of (1) the SouTh Asian biRth cohorT (START) study,[14] which identified diet as a key

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modifiable risk factor for GDM and (2) a qualitative study of barriers and facilitators to healthy eating encountered by pregnant and recently pregnant South Asian women and healthcare providers living and working in Ontario.[25]

### Duration

Treatment/intervention duration will be between 6 and 16 weeks, depending on the gestational age at enrolment. Effects of dietary intervention on glycaemic endpoints are detectable in <6 weeks[48 49] and reach maximal effectiveness after 8–10 weeks (~2 months) of intervention.[50] In-person or Zoom study visit, contact will occur two times: once for the baseline visit and once for the OGTT. Between these visits, all participants receive weekly text messages, and intervention participants will also have bi-weekly telephone or video conferencing (Zoom/WhatsApp).

### Treatment group

A personalised nutrition plan will be developed for each woman by a culturally congruent dietitian. Our dietary intervention will focus on: (1) providing personalised food recommendations that consider a woman's current dietary habits by identifying food choices and substitutions that will optimise the diet, (2) providing dietary advice that is sensitive to religious belief/practice if desired by the participant (eg, vegetarian foods maybe preferred by Hindu, Buddhists, Jainists, etc; while inclusion of meat may be more appropriate for Sikhs and Christians) and regional (eg, Northern vs Southern India, Sri Lanka, Bangladesh, Pakistan) culinary practices and (3) involving the household meal preparer, if this is not the participant herself, in the coaching contacts; and use mobile health technology to reduce the amount of in-office time a healthcare practitioner spends on dietary counselling. Additionally, participants assigned to the intervention group will be given a Fitbit to track their steps along with encouragement to increase walking.

The health coach will codesign a plan with each participant that considers baseline dietary intake, energy balance for recommended gestational weight gain, personal values and preferences, and set 2–4 'SMART' (specific, measurable, achievable, realistic and timely) goals. Nutrition and behaviour change experts have developed text messages that support 11 categories of nutrition goals (table 1), targeted to address eating behaviours identified by participants in our qualitative study, designed to optimise energy balance for weight gain and improve dietary quality.

### Both groups

Participants in both groups receive weekly text messages, aimed at increasing walking, as this was identified as a way to increase physical activity during pregnancy that was acceptable to South Asian women to undertake during pregnancy,[25] and is critical for glucose homeostasis during pregnancy.[51 52] Both groups will be given resources that provide advice on healthy eating, physical activity and other lifestyle factors during pregnancy (paper handouts) plus additional materials adapted specifically for the South Asian community. Healthcare providers in Peel Region use these tools routinely (Diabetes Canada: https://bit.ly/2m8r2tT or Heart & Stroke: https://bit.ly/2lDubl7).

### Study measurements and schedule

#### Baseline assessment (for both intervention and control participants)

At the baseline visit, participants' physical measurement (height, weight, blood pressure, skinfold thickness and mid-upper arm circumference), fasting urine and blood sample will be collected. Additionally, an ayurvedic assessment and three questionnaires (baseline instrument, INTERHEART Food Frequency Questionnaire (FFQ) and COVID-19 assessment and vaccine confidence questionnaire) will be administered.

The baseline instrument is a researcher developed and has four sections: (1) sociodemographics, (2) medical history, (3) obstetric history and (4) lifestyle history.

The Ayurvedic 'prakriti' assessment is a way of characterising a population into set subgroups, based on traditional Indian medicine called Ayurveda. This is a method of taking a person-centred approach to health care,[53] based on phenotypic characteristics such as appearance, mannerisms, etc, and is used for personalising medicine and ways of healthy living for individual. We will use the validated Topiwala National Medical College (TNMC) *Prakriti* questionnaire from 2004.[54] The decision to use this tool was taken during the development of the protocol, through conversations with members of the team and potential participants who practice Ayurveda. We may explore differences in the primary outcome according to prakriti; however, these are post hoc, exploratory analyses only.

**Table 1** Categories of nutrition goals

| | |
|---|---|
| 1. Eating out healthy | 2. Reduce indulgence in sweets/desserts |
| 3. Controlling over-eating | 4. Reduce intake of sugary beverages |
| 5. Reducing high-fat, fried foods | 6. Cooking meals at home more |
| 7. Reducing highly refined carbohydrates | 8. Improving meal planning |
| 9. Encouraging mindful eating | 10. Eating more fruits and vegetables |
| 11. Increasing quality protein intake | |



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The INTERHEART FFQ (modified for use in pregnancy) is a semiquantitative FFQ that assesses intake of fruits and vegetables and fast foods consumption. The FFQ was adapted from the 19-item INTERHEART FFQ,[55] which has been used in studies that included SA.[56 57]

The COVID-19 assessment and vaccine confidence questionnaire is a short two-part, self-administered questionnaire. We have decided to administer this because the COVID-19 pandemic has impacted all aspects of day-to-day life, and its impact on our participants will help contextualise our findings. The first part is the Vaccination Attitudes Examination Scale,[58] a validated and reliable tool that assesses general vaccination attitudes across four domains: (1) mistrust of vaccine benefit, (2) worries about unforeseen future events, (3) concerns about commercial profiteering and (4) Preference for natural immunity. The second section comprises additional questions about preferred types of COVID-19 vaccines, preferred location of receiving the vaccine and general attitudes/concerns about vaccines.

Participants will be given an option to provide their health card number, which will enable future linkage with administrative data sources from Ontario such as the Institute for Clinical Evaluative Sciences for potential health economic evaluation and for long-term follow-up of the mother and her child.

### Weekly and health coach visit

Participants in both control and intervention groups receive one text message every week up to the date of the OGTT with one of the six walking tips, sent by an automated outbound messaging system developed by MemoTXT (Toronto, Ontario, Canada). The intervention group only will also be sent weekly text messages to reinforce individual nutrition goals at times of day requested by the participant. Participants assigned to the intervention group will be given a Fitbit to track their steps and will be requested to track food consumption in Bitesnap, a photo food journal app, for two weekdays and one weekend day bi-weekly (up to eight assessments). Health coaches will be able to view both Fitbit and Bitesnap data via the Health Coaching Platform.

Coaching contacts to the intervention group will be made bi-weekly up to the date of their OGTT. These coaching calls will be recorded using an audio recording device. At each scheduled contact, intervention participants review agreed-upon diet goals, and assess, on a Likert scale, how often they were able to achieve the goals (ranging from 'never' to 'all of the time'); the coach will work with the participant to overcome barriers using our Brief Action Planning Guide. After each coaching call, participants and health coaches will complete a Visit Reflection Questionnaire.

The central coordinator will review data regularly for completion, and ad hoc calls may be made to clarify items for either arm, but no counselling is provided to control group participants (see table 2 for details).

### Follow-up assessment/second visit

At the second clinic visit (24–28 weeks' gestation), INTERHEART FFQ, fasting urine sample collection and fasting blood sample collection are repeated (this may be done virtually or in-person) and a 75 g OGTT is performed. Additional blood samples will be collected at three time points (0, 1 and 2 hours) during the OGTT (based on referral and participant willingness) and stored for future analysis.

In Peel, pregnant women usually undergo a 50 g glucose challenge at 24–28 weeks, with a 1-hour value≥7.8 mmol/L being an indication for a 75 g OGTT.[59] Rather than this two-step process, we have chosen to administer the 75 g OGTT to all women because: (1) it was used to establish South Asian-specific diagnostic criteria for GDM, and thus the study's outcomes will be directly comparable;[15] (2) it avoids the high false-negative rate of the 50 g Glucose Challenge Test among SA;[60 61] (3) one-step screening has potential for long-term cost-saving;[62–64] and (4) Diabetes Canada recognises that the one-step strategy can identify a subset of women who would not otherwise be identified as having GDM and who may benefit with regard to certain perinatal outcomes.[11] The study team will coordinate with the healthcare provider to ensure participants receive the 75 g OGTT between 24 and 28 weeks, avoiding the two-step screen.

At the completion of their OGTT, each woman will be asked to complete the DESI-GDM exit survey. This is a 9-item questionnaire based on previous tools created and used by the study team. Responses to each question are provided using a 5-item Likert scale (from strongly disagree through strongly agree).

### Postnatal assessment

Study participants will be contacted after delivering their baby to self-report the birth weight and length of their baby. Participants will also be asked to provide details of any complications during delivery.

## Study outcomes

The primary clinical outcome of this trial is the area under the curve (AUC) of glucose following the 2-hour, three-sample 75 g OGTT. A measure of glycaemic response, glucose AUC is a continuous measure of the response to a 75 g OGTT that accounts for variations in fasting plasma glucose levels between individuals. It is calculated by the trapezoidal method using the fasting, 1-hour and 2-hour glucose[65] (figure 2). The AUC is superior to a single measure, that is, fasting or 2-hour glucose only, which may not provide complete information regarding plasma glucose processing after a load.[66]

The secondary outcome is GDM, classified using the cut-offs derived in the Born-in-Bradford (BiB) cohort, which were found to be associated with 75% higher risk of LGA or infant adiposity (infant birth weight >90th percentile for gestational age or adiposity (sum of skinfold measurements>90th percentile for gestational age) in a study of 5408 SA women). These values are fasting

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Table 2 Schedule of study activities

| Activity | Baseline visit | Weekly | Health coach visits (bi-weekly) | OGTT visit | Postbirth Follow-up |
|---|---|---|---|---|---|
| Screening | x | | | | |
| Informed consent | x | | | | |
| Randomisation | x | | | | |
| Physical measures (height, weight, blood pressure, skinfold thickness, mid-upper arm circumference) | x | | | | |
| INTERHEART Food Frequency Questionnaire | x | | | x | |
| Finger stick for glucose | x | | | | |
| COVID-19 Assessment and Vaccine Confidence Questionnaire | x | | | | |
| 75 g OGTT | | | | x | |
| Urine sample collection | x | | | x | |
| Blood sample collection (optional) | x | | | x | |
| Baseline questionnaire | x | | | | |
| Ayurvedic assessment | x | | | | |
| Device identification* | x | | | | |
| FitBit distribution* | x | | | | |
| Bitesnap downloaded* | x | | | | |
| Resource handouts | x | | | | |
| Walking tips via MemoTXT | | x | | | |
| Diet reinforcement via MemoTXT* | | x | | | |
| Calls with health coach (set and review SMART goals, Brief Action Planning Guide) * | | | x | | |
| Visit reflection* | | | x | | |
| Bitesnap food journal* | | x | | | |
| FitBit return* | | | | x | |
| Exit questionnaire | | | | x | |
| Mother-reported infant physical measures | | | | | x |

*Intervention group only.
OGTT, oral glucose tolerance test; SMART, specific, measurable, achievable, realistic and timely.

glucose>5.2 mmol/L or 2 hours post load>7.2 mmol/L.[15] Current clinical cut-offs for the 75 g OGTT used to diagnose GDM in the general population as defined by the Diabetes Canada's clinical practice guidelines are: fasting glucose>5.3 mmol/L, 1-hour>10.6 mmol/L or 2-hour>9.0 mmol/L.[11] The study team will assess the sensitivity and specificity of the BiB definition against the International Association of the Diabetes and Pregnancy Study Groups or WHO criteria (see table 3 for diagnostic criteria).

## Planned data analysis

The study will assess the main effect of the diet intervention (β1) based on two outcomes as well as conduct process and acceptability assessments:

### Primary clinical outcome

The study will assess the main effect of the diet intervention (β1) on the primary outcome of glucose AUC with a linear regression model with *intervention* as the main effect (a dummy variable, where 1=treatment; 0=control).

### Secondary clinical outcome

The study will assess the main effect of the diet intervention (β1) on the secondary outcome of GDM by fitting a logistic regression model with *intervention* as the main effect (a dummy variable, where 1=treatment; 0=control).

Table 4 provides a summary of the planned analysis objectives, outcome, hypothesis and methods of analysis, and figure 3 is our proposed Consolidated Standards of Reporting Trials flow diagram.

### Process and acceptability assessments

These data will be presented descriptively and include monthly process feedback (eg, recruitment, retention, adherence), which the team will discuss on an ongoing basis (eg, adherence, unmet goals/targets). The study team will review qualitative and quantitative data to refine implementation processes. Acceptability will be explored using semistructured exit interviews after the OGTT visit, which allow each participant to reflect on



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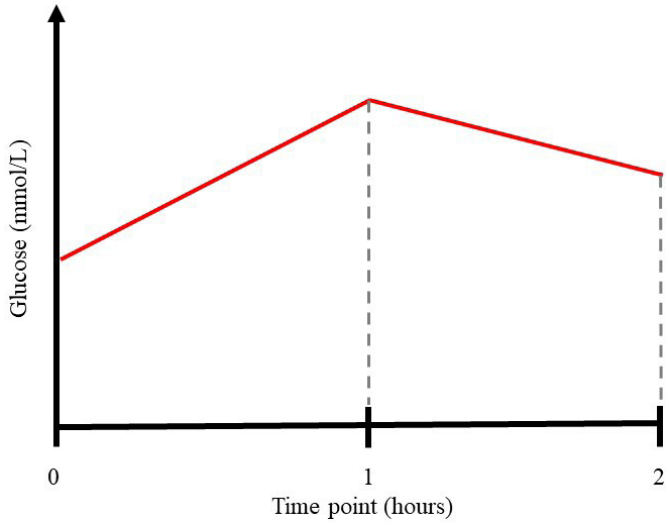


**Figure 2** Area under the curve (AUC) of glucose calculation. The area under the curve of the 75 g OGTT (mmol/L × min) is calculated by the trapezoidal method using the fasting, 1-hour and 2-hour glucose. The AUC of the time–blood glucose curve of the OGTT approximately equals the areas of two trapezoids as follows: 1/2 (0 hour blood glucose + 1 hour blood glucose) × 60 min/hr + 1/2 (1 hour blood glucose + 2 hours blood glucose) × 60 min/hr.

their experiences with the programme and convey what they liked and disliked about the study, and if they would recommend the programme to a friend, as we have in previous studies of similar design.[67 68]

### Handling of missing outcome data

Missing outcome data (OGTT) will be handled via multiple imputation as a sensitivity analysis if we have >30% missing outcome data.

### Sensitivity analyses (for primary and secondary outcomes only)

The study team anticipate possible variation in treatment effect according to time in study and by clinic site (if multiple clinics refer participants). Women will be enrolled in the study between weeks 12 and 18 of pregnancy. The outcome will be assessed at weeks 24–28 of pregnancy. Therefore, the length of time that each woman will receive the intervention may vary. The first sensitivity analysis will adjust the primary outcome for time in study (OGTT date minus enrolment date). In the second sensitivity analysis, if there are multiple sites of enrolment, the study team will consider a random effect of study site.

**Table 3** Diagnostic criteria for secondary outcome, gestational diabetes mellitus

| Threshold | Fasting | 1 hour | 2 hours |
|---|---|---|---|
| BiB | ≥5.2 | – | ≥7.2 |
| IADPSG | ≥5.1 | ≥10.0 | ≥8.5 |
| WHO | ≥7.0 | – | ≥7.8 |
| Diabetes Canada | ≥5.3 | ≥10.6 | ≥9.0 |

BiB, Born-in-Bradford; IADPSG, International Association of the Diabetes and Pregnancy Study Groups; WHO, World Health Organization.

### Interim data analysis

No interim data analysis is planned.

## Ethical considerations

The study has been approved by the Hamilton Integrated Research Ethics Board (HiREB #10942), and the trial is registered with clinical trials.gov (NCT03607799). Participants will provide written, verbal or electronic informed consent. If providing verbal consent, participants will be sent the full consent via email or paper mail, to read and refer to while being consented. If providing electronic consent via REDCap, participants will be sent a link that contains the full consent and will review the consent over telephone or web conferencing with study staff. The participant will select whether they agree to participate at the bottom of the consent page. Participant data will be deidentified to protect confidentiality and will only be reported and published in aggregate. Any modifications made to the study protocol will be shared with HiREB as stipulated and we will follow their advice regarding implementation and dissemination.

## Data monitoring and management

### Study coordination and management

The principal investigator will take responsibility for the oversight of the study. The coordinating centre for the trial will be PHRI in Hamilton, Ontario, Canada. The coordinating centre, under the direction of the study statistician, will receive all data and take process steps to reduce missing data. A junior project manager, along with a graduate student, will oversee the of recruitment of participants and handle central trial coordination. At weekly meetings, the study will review recruitment, minor adverse events, study inventories and review any expressed concerns by participants or the team. The steering committee will direct operational/process, nutrition, coaching and statistical aspects of the trial.

### Data and safety monitoring

For a previous pilot study, the study team had convened a Data and Safety Monitoring Committee (DSMC), consisting of two internal medicine specialists (one being an experienced endocrinologist) and a biostatistician. This committee advised that a DSMC was not required for the pilot, voting for a safety officer and disbanded. The committee advised the same for this trial. Therefore, at prespecified meeting times, the safety officer, trained in internal medicine, will review data, noting any of the eight minor (mother—induced labour, anaemia, urinary tract infection, fall/injury/accident related to study, low mood or high blood pressure; child—premature labour (<36 weeks) or shoulder dystocia) or six major maternal events (hyperemesis gravidarum, caesarean section, pre-eclampsia, primary postpartum haemorrhage>500 mL, miscarriage or maternal mortality,) or two major infant

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Table 4 Analysis plan: objectives, outcome, hypothesis and methods of analysis

| Objective | Outcomes | Measurement | Criteria for success | Method of analysis |
|---|---|---|---|---|
| Primary clinical | Glycaemic response to the 75 g oral glucose tolerance test | Area under the curve of glucose | Mean statistically significant reduction of 15% in the intervention arm | Linear regression* |
| Secondary clinical | Gestational diabetes diagnosed by 75 g oral glucose tolerance test | Fasting glucose>5.2 mmol/L, or 2 hours post 75 g load>7.2 mmol/L | OR<0.9=signal of benefit OR>1.1=signal of harm | Logistic regression* |
| Acceptability | Acceptability | Answer to the question 'Would you recommend this programme to a friend?' | ≥80% of participants reply 'agree or strongly agree' | Descriptive statistic (proportion) |

*Mixed models will be considered to adjust for centre effects using random intercepts.

events (mortality—(fetal and neonatal) or stillbirth). The safety officer will determine whether they are related to study participation. To evaluate safety outcomes, maternal blood pressure at baseline and the OGTT follow-up visit will be measured, and notes of any pregnancy complications at coaching contacts.

The safety officer will review an interim data analysis, comparing (a) mean AUC glucose and (b) GDM incidence between treatment and control (blinded) after the first 25 participants have completed their OGTT visit. Thereafter, the safety officer will review the data following each additional 50 participants. There is no early stopping rule for this study. The study will only collect data at baseline and the OGTT visit.

## Patient and public involvement

The study included recently pregnant SA women living in Peel (Ontario), public health practitioners and primary care providers who work with pregnant SA women in the development of our intervention through focus groups and semistructured interviews. The coinvestigators who work with the SA community and serve on guidelines committees have been closely involved with developing this research proposal. The study's physician collaborators will be involved in the recruitment progress to help troubleshoot challenges and refine intervention implementation strategies during the grant cycle.

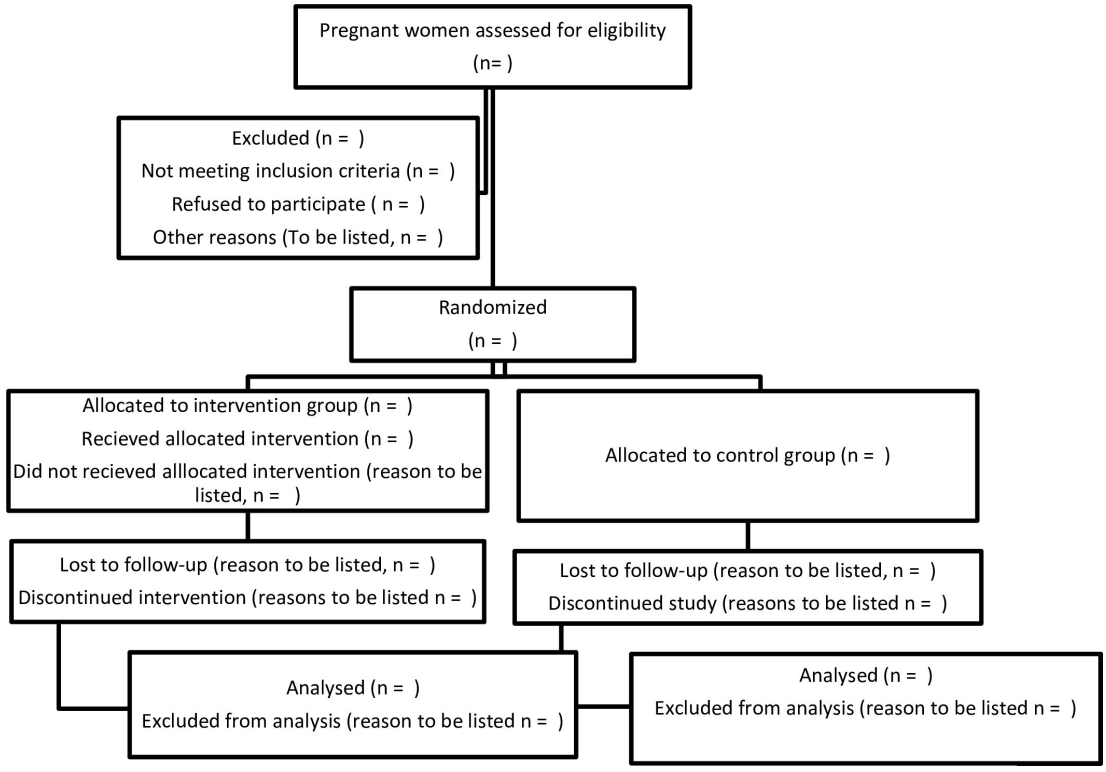


Figure 3 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram exemplar.

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### Dissemination plans

The findings of the study will be important in guiding future evidence-based recommendations and public health policies to manage gestational glycaemia in pregnant women at risk of GDM. Throughout the study, a strategy for integrated knowledge translation will be used to develop a series of digital projects (short digital story-based videos) that capture: (1) participant experiences that include key messages about successful approaches to healthy eating that women would like to share with their communities and (2) key study findings regarding effective dietary changes to reduce risk of GDM and public health messages tailored for researchers, practitioners and policy-makers. A community event will be organised to share participant results with the group.

The study team involved community organisations that they have worked with over the past 10 years to engage the SA community and healthcare professionals. The study will disseminate its findings among academics and policymakers using traditional methods including scientific publications, and if indicated, guideline development. The study will collaborate with family physicians, Region of Peel Public Health and Diabetes Canada through talks and briefing reports to disseminate to community partners and Health Canada, Diabetes Canada, Heart and Stroke, Canadian Medical Association, as well as targeted communication. Peel Public Health supports 'scale-up' of individual interventions using population health methods that complement clinician efforts, including mass media, social media and text messaging campaigns. If the study demonstrates that providing tailored, culturally specific dietary advice during pregnancy to SA women is feasible and effective, the study foresee adapting the approach to other at-risk populations, including white European, African Canadian or First Nations communities.

## DISCUSSION AND IMPLICATIONS

This study protocol describes the first RCT that examines the effect of a culturally tailored, personalised nutrition intervention on gestational glycaemia in South Asian women living in Canada. In addition to proximal complications for the newborn, including life-threatening low blood sugar (hypoglycaemia) and intensive care admission, GDM is a risk factor for future atherosclerosis and CVD in the mother and childhood adiposity, type 2 diabetes,and CVD in her offspring.[33] Over the past two decades, studies have shown that starting interventions as early as infancy and perhaps before—may be an especially effective approach to maintaining lifelong heart health.[69] This intervention in pregnancy, aimed at reducing glycaemia and its effect on the newborn infant, has great potential to 'break the cycle' of maternal hyperglycaemia and excess infant adiposity and insulin resistance and eventually CVD in both mother and baby.

Previous intervention studies that have sought to reduce the risk of GDM have reported mixed results, perhaps due to population heterogeneity of the maternal metabolic profile, inconsistent application of GDM diagnostic criteria, along with varied implementation.[16–18 70]

The DESI-GDM study is unique because it is culturally tailored for South Asian pregnant women living in Canada, and it builds on a qualitative study of the barriers and facilitators of lifestyle changes to prevent GDM,[25] as well a birth cohort study completed in a similar population.[71] Such culturally tailored and participant/end-user codeveloped approaches to intervention studies improve engagement, by adding relevance to the intervention for participants.[9 72] By involving the members of the community likely to benefit from the intervention in the design of the study through previous and ongoing work, the DESI-GDM intervention is tailored to the needs and challenges of participants and is feasible. The study team's connections with family physicians help encourage high rates of recruitment and engagement as well as transferability and scale-up, as appropriate, of study results.

A limitation of the study is that participants in our study will be exposed to the intervention only after becoming pregnant. Some researchers have posited that GDM prevention measures are the most effective prior to pregnancy so that modifiable risk factors can be 'optimised' prior to pregnancy.[10] However, an umbrella review by Giannakou, *et al*[73] found that among 61 risk factors for GDM, prepregnancy BMI was associated with increased risk of GDM, and the authors assessed the level of evidence to be 'highly suggestive'. Furthermore, a prevalence meta-analysis of 70 studies involving 671 945 women found that every 1-unit increase in prepregnancy BMI increased the prevalence of GDM by 0.92% (95% CI: 0.73 to 1.10).[74] A final limitation is that the genetic risk carried by South Asian women may overwhelm the effects of our dietary intervention.[12]

The study is unique in that it is designed to deliver and test the uptake of a dietary intervention to reduce gestational dysglycaemia in a high-risk population in Canada. This intervention in pregnancy, aimed at reducing dysglycaemia, has great potential to 'break the cycle' of maternal gestational dysglycaemia and excess infant adiposity and insulin resistance, and eventual CVD and T2DM, both of which are complications of GDM in both mother and baby.

**Author affiliations**
[1]Department of Health Research Methods, Evidence, and Impact, Faculty of Health Sciences, McMaster University, Hamilton, Ontario, Canada
[2]School of Human Kinetics, Faculty of Health Sciences, University of Ottawa, Ottawa, Ontario, Canada
[3]Department of Medicine, McMaster University, Hamilton, Ontario, Canada
[4]Population Health Research Institute, Hamilton, Ontario, Canada
[5]LMC Healthcare, Toronto, Ontario, Canada
[6]Faculty of Health Sciences, Simon Fraser University, Burnaby, British Columbia, Canada
[7]Department of Obstetrics & Gynecology, Faculty of Health Sciences, McMaster University, Hamilton, Ontario, Canada
[8]Division of Maternal-Fetal Medicine, Faculty of Medicine, McMaster University, Hamilton, Ontario, Canada
[9]Department of Radiology, Faculty of Health Sciences, McMaster University, Hamilton, Ontario, Canada

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[10]Kinesiology and Health Science, York University, Toronto, Ontario, Canada
[11]School of Nursing, Faculty of Health Sciences, McMaster University, Hamilton, Ontario, Canada
[12]Farncombe Family Digestive Health Research Institute, McMaster University, Hamilton, Ontario, Canada
[13]Department of Pediatrics, McMaster University, Hamilton, Ontario, Canada
[14]Food Science and Nutrition, University of Leeds, Leeds, UK

**Twitter** Michael A Zulyniak @Mike_Zuly and Russell J de Souza @DrRussRD

**Contributors** RNS drafted the manuscript. RJdS, KBA, SSA, HSB, SIB, HCG, SK, SAL, SDM, PR, DS, MAZ and GW conceived and designed the study. RJdS, HSB, SIB, DD, FK, TP, AR, KMS, DS, JCS, NCW and MAZ participated in the development of the protocol and data acquisition methods. RJdS, KMS and SIB developed the statistical analysis plan. RJdS, DD, FK, TP, AR, KMS and DS participated in the design of the visits. All authors read and approved the final manuscript.

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**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.

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**ORCID iDs**
Rosain N Stennett http://orcid.org/0000-0003-3386-2558
Sonia S Anand http://orcid.org/0000-0003-3692-7441
Shrikant I Bangdiwala http://orcid.org/0000-0002-3111-0689
Hertzel C Gerstein http://orcid.org/0000-0001-8072-2836
Sujane Kandasamy http://orcid.org/0000-0003-4326-2783
Scott A Lear http://orcid.org/0000-0001-7614-755X
Paul Ritvo http://orcid.org/0000-0003-1141-0083
Karleen M Schulze http://orcid.org/0000-0002-7481-5697
Diana Sherifali http://orcid.org/0000-0002-4423-3848
Michael A Zulyniak http://orcid.org/0000-0003-4944-5521
Russell J de Souza http://orcid.org/0000-0001-8945-513X

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SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

| Section/item | Item No | Description | Addressed on page number |
|---|---|---|---|
| **Administrative information** | | | |
| Title | 1 | Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym | 1 |
| Trial registration | 2a | Trial identifier and registry name. If not yet registered, name of intended registry | 3 |
| | 2b | All items from the World Health Organization Trial Registration Data Set | N/A |
| Protocol version | 3 | Date and version identifier | N/A |
| Funding | 4 | Sources and types of financial, material, and other support | 23 |
| Roles and responsibilities | 5a | Names, affiliations, and roles of protocol contributors | 1&3 |
| | 5b | Name and contact information for the trial sponsor | N/A |
| | 5c | Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities | N/A |
| | 5d | Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee) | 20-21 |

**Introduction**

| | | | |
|---|---|---|---|
| Background and rationale | 6a | Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention | 4-6 |
| | 6b | Explanation for choice of comparators | N/A |
| Objectives | 7 | Specific objectives or hypotheses | 6 |
| Trial design | 8 | Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory) | 7 |

**Methods: Participants, interventions, and outcomes**

| | | | |
|---|---|---|---|
| Study setting | 9 | Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained | 7 |
| Eligibility criteria | 10 | Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists) | 8 |
| Interventions | 11a | Interventions for each group with sufficient detail to allow replication, including how and when they will be administered | 10 |
| | 11b | Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease) | N/A |
| | 11c | Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests) | 12-16 |
| | 11d | Relevant concomitant care and interventions that are permitted or prohibited during the trial | 8 |
| Outcomes | 12 | Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended | 16-17 |
| Participant timeline | 13 | Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure) | 7&fig 1 |

| | | | |
|---|---|---|---|
| Sample size | 14 | Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations | ____7-8_____ |
| Recruitment | 15 | Strategies for achieving adequate participant enrolment to reach target sample size | _____9_____ |
| **Methods: Assignment of interventions (for controlled trials)** | | | |
| Allocation: | | | |
| Sequence generation | 16a | Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions | _____9_____ |
| Allocation concealment mechanism | 16b | Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned | _____9_____ |
| Implementation | 16c | Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions | ____9-10____ |
| Blinding (masking) | 17a | Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how | _____9_____ |
| | 17b | If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial | _____9-10____ |
| **Methods: Data collection, management, and analysis** | | | |
| Data collection methods | 18a | Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol | _____9_____ |
| | 18b | Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols | ___13-16____ |

| | | | |
|---|---|---|---|
| Data management | 19 | Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol | ___19-20____ |
| Statistical methods | 20a | Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol | ___17-18____ |
| | 20b | Methods for any additional analyses (eg, subgroup and adjusted analyses) | ___18-19____ |
| | 20c | Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation) | ___18-19____ |
| **Methods: Monitoring** | | | |
| Data monitoring | 21a | Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed | _____20_____ |
| | 21b | Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial | ___19-20____ |
| Harms | 22 | Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct | ____19-20___ |
| Auditing | 23 | Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor | ____N/A_____ |
| **Ethics and dissemination** | | | |
| Research ethics approval | 24 | Plans for seeking research ethics committee/institutional review board (REC/IRB) approval | ____2&19____ |
| Protocol amendments | 25 | Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators) | _____19_____ |

| | | | |
|---|---|---|---|
| Consent or assent | 26a | Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32) | _____9_____ |
| | 26b | Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable | _____N/A____ |
| Confidentiality | 27 | How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial | _____19_____ |
| Declaration of interests | 28 | Financial and other competing interests for principal investigators for the overall trial and each study site | ___24-25____ |
| Access to data | 29 | Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators | _____25_____ |
| Ancillary and post-trial care | 30 | Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation | _____N/A____ |
| Dissemination policy | 31a | Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions | ____21-22___ |
| | 31b | Authorship eligibility guidelines and any intended use of professional writers | _____N/A_____ |
| | 31c | Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code | _____N/A_____ |
| **Appendices** | | | |
| Informed consent materials | 32 | Model consent form and other related documentation given to participants and authorised surrogates | _____N/A_____ |
| Biological specimens | 33 | Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable | _____N/A_____ |

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.