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Integrated health system intervention aimed at reducing type 2 diabetes risk in women after gestational diabetes in South Africa (IINDIAGO): a randomised controlled trial protocol

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ABSTRACT

Introduction South Africa has a high prevalence of gestational diabetes mellitus (GDM; 15%) and many of these women (48%) progress to type 2 diabetes mellitus (T2DM) within 5 years post partum. A significant proportion (47%) of the women are not aware of their diabetes status after the index pregnancy, which may be in part to low postnatal diabetes screening rates. Therefore, we aim to evaluate a intervention that reduces the subsequent risk of developing T2DM among women with recent GDM. Our objectives are fourfold: (1) compare the completion of the nationally recommended 6-week postpartum oral glucose tolerance test (OGTT) between intervention and control groups; (2) compare the diabetes risk reduction between control and intervention groups at 12 months' post partum; (3) assess the process of implementation; and (4) assess the cost-effectiveness of the proposed intervention package.

Methods and analyses Convergent parallel mixed-methods study with the main component being a pragmatic, 2-arm individually randomised controlled trial, which will be carried out at five major referral centres and up to 26 well-baby clinics in the Western Cape and Gauteng provinces of South Africa. Participants (n=370) with GDM (with no prior history of either type 1 or type 2 diabetes) will be recruited into the study at 24–36 weeks' gestational age, at which stage first data collection will take place. Subsequent data collection will take place at 6–8 weeks after delivery and again at 12 months. The primary outcome for the trial is twofold: first, the completion of the recommended 2-hour OGTT at the well-baby clinics 6–8 weeks post partum, and second, a composite diabetes risk reduction indicator at 12 months. Process evaluation will assess fidelity, acceptability, and dose of the intervention.

Ethics and dissemination Ethics approval has been granted from University of Cape Town (829/2016), University of the Witwatersrand, Johannesburg (M170228), University of Stellenbosch (N17/04/032) and the University of Montreal (2019-794). The results of the trial will be disseminated through publication in peer-reviewed journals and presentations to key South African Government stakeholders and health service providers.

Protocol version 1 December 2022 (version #2). Any protocol amendments will be communicated to investigators, Human Ethics Research Committees, trial participants, and trial registries.

Trial registration number PAN African Clinical Trials Registry (https://pactr.samrc.ac.za) on 11 June 2018 (identifier PACTR201805003336174).

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The trial seeks to integrate a continuum of care into routine public health services, while attending to the specificities of gestational diabetes mellitus (GDM) and post-GDM.
⇒ The intervention uses the Capability–Opportunity–Motivation model for behaviour change (COM-B), and active listening to go beyond top-down, didactic and often blame-the-victim behaviour change and 'lifestyle' approaches to support women.
⇒ Through its embeddedness in Global Alliance of Chronic Disease, opportunities for adaptation to and learning from this trial and others will be identified and pursued.
⇒ A limitation of this trial is that the intervention does not attempt to address potential structural drivers of GDM (built and food environment, poverty, gender dynamics). This limitation is partially addressed in that the process evaluation includes exploration of the impacts of structural drivers on women, health workers and the health system, and the exploration of potential implementation at scale includes exploration of structural drivers of both provision and effective access and utilisation of the proposed integrated health system intervention.

BACKGROUND

Women with gestational diabetes mellitus (GDM) are at high risk of developing type 2

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diabetes mellitus (T2DM) and represent a unique target group for intervention. A systematic review reported that GDM is associated with a sevenfold increased risk of developing T2DM.[1] GDM is also reported to increase long-term cardiovascular disease risk,[2] while offspring exposed to GDM are at high risk of later metabolic disease. In South Africa (SA), two studies found that 45%–48% of women with hyperglycaemia first detected in pregnancy (HFDP), which includes GDM, progressed to T2DM within 6 years post partum,[3] with 47%–53% being unaware of their diabetes status, while a third of their offspring were either overweight or obese at preschool age.[4] Recognition of the effects of GDM on both the mother and infant has led to calls from national and international organisations to intervene with women with prior GDM and their offspring. This includes improving the rate of postpartum testing to identify women with or at high risk for T2DM, providing or referring high-risk women to early treatment and prevention interventions, and supporting the mother in promoting the health of her infant to prevent childhood obesity and subsequent risk of metabolic disease.[5 6]

There is compelling evidence that lifestyle interventions for high-risk groups reduce the progression to T2DM.[7 8] These initial diabetes prevention trials showed benefit using intensive behaviour change interventions for people with pre-diabetes or impaired glucose tolerance. Interventions were equally effective among women with and without self-reported prior history of GDM[9]; although there are only limited data for women with prior GDM. Shyam and colleagues found that with Malaysian women post-GDM, lowering the Glycaemic Index of diets significantly improved glucose tolerance and reduction in body weight as compared with conventional low-fat diets with similar energy prescription.[10] Recently, Tandon and colleagues found that a lifestyle intervention was not effective in reducing T2DM risk of South Asian women with recent GDM,[11] but to our knowledge there are no such trials in African women.[7]

We estimate that the SA prevalence of GDM is greater than 15% based on a systematic review we conducted of GDM prevalence in Africa and projections using other published data,[12–14] alongside findings from Soweto[15] and Johannesburg.[16] Currently, in poor urban settings of Cape Town and Soweto, where the diabetes burden is high, women with GDM receive their antenatal care including delivery at their nearest tertiary facility and, in contrast to their intensive antenatal care, they receive little attention post partum. Several barriers impede good follow-up: (1) poor understanding of postpartum GDM risks for the development of diabetes by the mother; (2) the mother attends community postnatal care clinics, which do not provide care for women with GDM through screening for diabetes and on-going lifestyle counselling; and (3) when women with GDM are referred back into primary care for on-going follow-up, they must navigate two separate health service systems, one for herself and one for her baby. This gap between antenatal and postnatal care is being investigated in high-income settings where, despite many women reporting an intention to change their lifestyles post GDM pregnancy to prevent diabetes, they find the effort challenging and where the postpartum oral glucose tolerance test (OGTT) has a high rate of attrition.[17]

A systematic review suggested leveraging scheduled 'well-baby' visits at health services, including the child's vaccination programme and follow-up, to conduct necessary tests and provide follow-up advice to mothers post-GDM.[17] This requires not only a deeper understanding of women's individual experiences and motivations, but also an intervention-oriented understanding of health systems opportunities and barriers to such an integrated approach to continuum of care. The South African Strategic Plan for the prevention and control of NCDs commits the government to macro-level, legislative and policy interventions in line with WHO recommendations. These are essential for creating a more enabling environment for individuals to adopt and sustain healthier lifestyles, particularly in SA's highly unequal social and healthcare context. SA has adopted a comprehensive tobacco control policy, mandated the replacement of trans-fats and reduction of salt in manufactured foods and is formulating legislation for the regulation of marketing unhealthy food to children. An additional component is to strengthen the primary healthcare system's capacity for prevention; including proactively identifying individuals and communities at risk and behaviour change counselling to assist individuals to modify their behaviour.

The overall aim of this trial is to evaluate a novel health system intervention to reduce the subsequent risk of developing T2DM among women with recent GDM. Our objectives are fourfold: (1) compare the completion of the nationally recommended 6-week postpartum OGTT between intervention and control groups; (2)compare the diabetes risk reduction between control and intervention groups at 12 months post partum; (3) assess the process of implementation; and (4) assess the cost-effectiveness of the proposed intervention package.

METHODS

Participant and public involvement

In 2015, we started with key informant interviews and consultation with various stakeholders around the development of the trial protocol and potential intervention. In 2016, we constituted Patient Groups with local women as part of the formative work and explored qualitatively the lived experience of GDM. Later we involved these women in reviewing the intervention and preparatory phase to support greater acceptance and feasibility of the trial. In 2017, several stakeholder meetings and key informant interviews were held with the SA Department of Health at district and provincial levels with regard to policy and potential integration of the intervention in the community public health clinics. In 2018, we hosted an open GDM symposium summarising the evidence

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base, our formative results and presented the initial study protocol for discussion.

Study design

The trial was designed following the Standard Protocol Items (Recommendations for Interventional Trials; SPIRIT 2013 statement)—see online supplemental file 2. A convergent parallel mixed-methods study comprising of an exploratory, individually randomised control trial to evaluate the uptake and outcomes of postpartum screening and prevention of T2DM among women with recent GDM, with concurrent qualitative and quantitative process evaluation of implementation and economic evaluation of the intervention. Participants and intervention staff will not be blinded. However, the data collection team, laboratory staff and research team will be blinded.

Setting and participants

The trial will take place in urban, public sector health services settings in Cape Town and Soweto (Johannesburg) to capture the diversity of GDM management currently in SA, where the population is of lower socioeconomic status, and diabetes prevalence is high. Study participants (n=370) will be women diagnosed with GDM receiving antenatal care at Groote Schuur Hospital (GSH), Mowbray Maternity Hospital (MMH), New Somerset Hospital and Tygerberg Hospital in Cape Town and Chris Hani Baragwaneth Academic Hospital (CHBH) in Soweto. At all of these sites the International Association of Diabetes and Pregnancy Study Group criteria diagnoses GDM if one or more values equal or exceed thresholds of fasting plasma glucose (FPG) of 5.1 mmol/L and/or a 2-hour plasma glucose level of 8.5 mmol/L following a 75 g OGTT. Participants from these recruitment sites with GDM will be identified through clinic records and the fieldwork team will approach them to be enrolled into IINDIAGO. The postpartum study clinics will be well-baby clinics in Cape Town and Soweto that are served by the above-mentioned hospitals. If we detect comorbidities in any of the participants during the process of the trial and data collection they will be referred for clinical management as per standard of care guidelines.

Inclusion criteria

Women who fulfil the following criteria at recruitment will be eligible for inclusion:

- Diagnosed with GDM by the antenatal clinic.
- Currently living in the community served by the clinics and planning to remain in the area for the next year.
- Participant willing and able to give informed consent for participation in the study.
- Able to communicate in one of the predominant official languages spoken in the Western Cape (Cape Town) and Gauteng (Johannesburg) provinces (eg, English, Afrikaans, isiXhosa, isiZulu and Sesotho).

Exclusion criteria

Women will not be included in the study if they fulfil the following criteria:

- Women who have had type 1 or T2DM prior to the index pregnancy. For all recruitment hospitals, T2DM is defined as FPG ≥7.0 mmol/L, 2-hour OGTT plasma glucose ≥11.1 mmol/L, glycated haemoglobin (HbA1c) ≥6.5% (48 mmol/mol), or self-reported use of diabetes drugs.
- Women who carried/delivered twins.
- Postdelivery women who have stillbirths or infants who die before 6 weeks of age.
- If any women based on the OGTT at 6–8 weeks are diagnosed with diabetes, they will be excluded from any analyses pertaining to 12 months secondary outcomes.

Randomisation

Trial participants will be individually randomised (1:1 ratio) to the intervention arm or to the standard of care (control) arm during pregnancy. The sequence (computer-generated random numbers) will be generated by an independent statistician for each stratum. These strata will comprise the two cities (Cape Town and Soweto).

Allocation concealment

Sequentially numbered, opaque, sealed envelopes will be used to conceal the sequence until interventions are assigned. The recruiting staff will enrol participants and obtain informed consent. Thereafter, the recruiter will contact an independent study member or independent statistician not involved in the recruitment who will receive the study number, write the study number, date and time on the physical envelope and then open the envelope and inform the recruiter about the study number for the participant. Envelope numbers as well as randomisation codes are entered in REDCap, then intervention team can see if this is their participant or not. The hard copies of envelopes with codes are filed by the study coordinator with each participant study ID so sequential opening of envelopes can be confirmed.

Blinding

The measurement team, research team, statisticians and the trial management teams will be blinded throughout the trial. However, participants and intervention staff will not be blinded to the intervention arm. Post partum, the participants in the intervention arm will be assigned to specific well-baby clinic facilities where the intervention will be delivered in comparison to the control arm where participants will receive standard of care. In Cape Town it is typically a referral letter to their local day hospital (clinic) or a private doctor of their choice, and in Soweto this is done at a tertiary hospital endocrine clinic.

Control arm (standard of care)

Typically, GDM women receive some health education and advice on lifestyle from healthcare providers during

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routine antenatal care and they are monitored more closely following diagnosis. Post partum, GDM women are encouraged to return to the clinic 6 weeks following delivery for an OGTT to determine diabetes risk. Usual healthcare providers at both the tertiary and the primary level in the public sector are not trained in behaviour change counselling skills and do not usually have access to good quality health education/motivational resources on diet, physical activity, smoking or alcohol use. Currently, there is no organised lifestyle modification intervention for women with GDM in the postpartum period.The control group will be asked to attend the usual antenatal and postpartum health services in place for each trial site. The study will remain in contact with the control arm participants to update contact information.

Intervention arm

The IINDIAGO intervention deviates from standard of care in the following way: (1) the intervention delivery staff are trained in effective behaviour change skills; (2) two additional antenatal counselling sessions are offered; (3) health literacy material will be provided; (4) a convenient point of care OGTT will be offered at the 6-week visit at the well-baby clinic; (5) four counselling sessions will be offered when the mom presents herself at the well-baby clinic routine vaccinations for their baby; and (6) three home or community or telephonic counselling sessions in-between the well-baby clinic sessions. In total the intervention participants will receive upto nine contact points of counselling support.

Theory

The intervention was developed utilising the Capability–Opportunity–Motivation model for behaviour change (COM-B model) outlined in the Behaviour Change Wheel.[18] The COM-B model allows contextual developing of behaviour change interventions, and a systematic way to analyse the target behaviour and effects of interventions. Behaviour is viewed as a consequence of the interaction between the three main components of the model, which are capability, opportunity and motivation. The COM-B model is used to analyse barriers to and enablers that affect contextual behaviour change, and therefore enables intervention developers to set achievable behaviour change goals.[19 20] The intervention components were informed by the logic model developed from both published data and formative research (figure 1). The intervention will take place in the hospital, clinic and community setting delivered by nurses and lay counsellors (who will be of the same profile as either the existing health promoters or the HIV lay counsellors employed in the public-sector health services)—see table 1 for a summary of the implementation of the intervention.

Training and approach

The IINDIAGO lay counsellors will be trained in a patient-centred counselling method blended from three evidence-based methods: (1) Motivational Interviewing, (2) the 5As (Assess, Advise, Agree, Assist, Arrange) and (3) 'Healthy Conversations'.[21] During the training they will learn how to: approach behaviour change; ask open,

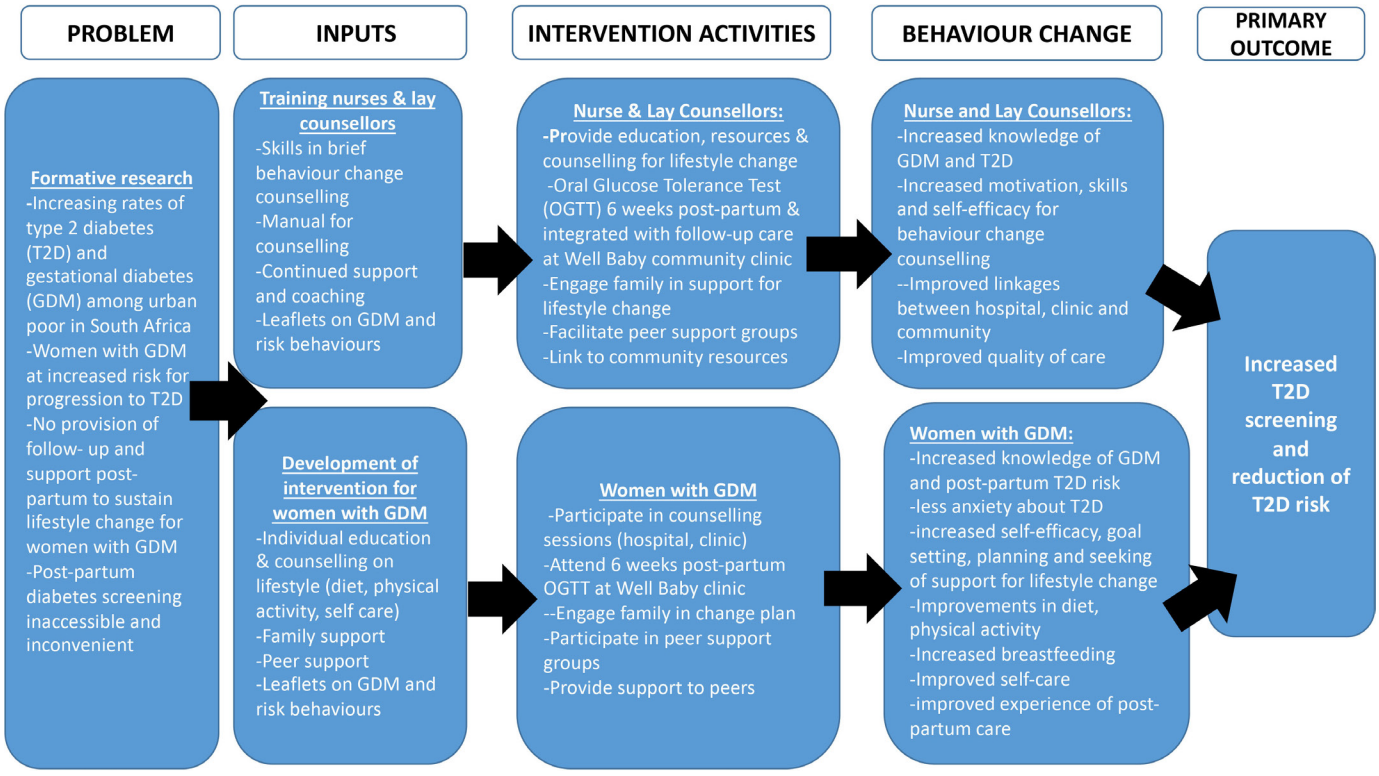


Figure 1 Logic model outlining the pathway of impact of the IINDIAGO intervention. GDM, gestational diabetes mellitus.

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Table 1 Implementation of the *IINDIAGO* intervention-arm components

Step 1	Step 2	Step 3	Step 4	Step 5	Step 6	Step 7
Pregnancy	Pregnancy	Before delivery	Post delivery	6 weeks post partum	10, 14, 36 weeks post partum	In community
Introduce intervention, make appointment for session 1 to coincide with next routine GDM clinic visit	BBCC session 1, make appointment for BBCC session 2 to coincide with next routine GDM clinic visit before delivery date	BBCC session 2, prime for 6 weeks postpartum OGTT at well-baby clinic, advise BBCC will continue post partum to support continued behaviour change	Make appointment for 6 weeks postpartum OGTT and BBCC session 3 at well-baby clinic	Point of care OGTT with result in real-time, refer women with type 2 diabetes to hospital, deliver BBCC session 3	BBCC sessions at well-baby clinic	Peer group sessions, home visits

BBCC, brief behaviour change counselling; GDM, gestational diabetes mellitus; OGTT, oral glucose tolerance test.

discovery questions to better understand a woman's context and perspective; and support women to identify opportunities for change and set goals that are realistic and feasible in their circumstances. The training will also include content knowledge on the nature of GDM and T2DM and the relevant behavioural risk factors. The blended method is congruent with empowerment models for self-management of chronic disease and the 'guiding style' of Motivational Interviewing, which aims to actively engage patients in a conversation about behaviour change, evoke their own motivations to change, promote autonomy in decision making and enhance self-efficacy. The training will consist of three intensive training sessions, plus individual follow-up coaching by the trainer and intervention team support sessions every month. Knowledge of and competency in the method will be evaluated before and after the training. The intervention team will be required to reach a level of acceptable competency before they are tasked with implementing the intervention. The trainer will provide at least one session of follow-up observation and coaching in the real life, clinic setting before the intervention starts. The intervention team will be provided with a comprehensive resource package containing guidelines on the counselling method and information on GDM, T2DM and their behavioural risk factors.

Hospital-based antenatal intervention

Women recruited into the intervention arm at 24–36 week's gestation will be eligible to receive two face-to-face, individual counselling sessions from an IINDIAGO lay counsellor at the hospital where they are receiving their routine antenatal GDM care for approximately 30 min. These sessions will focus on the nature of GDM, the risks to both the mother and baby and the importance of a healthy lifestyle, not just for the pregnancy, but for the long term. It will be emphasised that the GDM diagnosis provides an opportunity and cue for the woman, as well as her family, to review their current lifestyle and take measures to prevent T2DM and other non-communicable disease. The benefits of breast feeding and how to cope with stress and anxiety will also be raised as topics for discussion. The first session will take place as soon as possible after recruitment and the second, any time before delivery.

Postpartum clinic-based intervention

As part of our formative research we examined the possibility of performing clinic-based point of care OGTT across several instruments versus laboratory glucose assessments. We found that not all glucometers are suitable for GDM screening but three were accurate enough compared with the laboratory-derived glucose measurement (particularly at fasting of the OGTT). Importantly, in our SA study population, 80% of GDM cases was diagnosed on the fasting sample.[22] Given the significant practical advantages of a point of care OGTT assessment in the community clinic, we opted to use the Freestyle Optium Neo device as that provided the more accurate assessments compared with laboratory methods. All women in the intervention group will receive a point of care OGTT at the well-baby clinic during the routine 6-week postpartum visit, scheduled for the mother to bring the infant to the clinic for immunisation. The participants will have a fasting finger prick blood sample drawn. They will then be asked to drink 75 g glucose in 250 mL water and a second finger prick sample will be drawn 120 min later. This test will be performed by the lay counsellor employed by the IINDIAGO. Participants will be contacted in the week prior to the appointment and another reminder SMS will be sent the day before the appointment to reinforce the need for fasting. The IINDIAGO lay counsellor will liaise with the clinic staff to facilitate completion of the routine 6-week baby visit.

Behaviour change counselling

Women in the intervention arm will be offered a total of four brief (approximately 10 min), individual, face-to-face or telephonic counselling sessions at the well-baby clinic with the IINDIAGO lay counsellor at each of the routine visits for immunisation, that is, 6, 10, 14 and 36 weeks post partum. These sessions will focus on supporting the woman to achieve and maintain healthy lifestyle changes in the postpartum period. From the outset, the counsellor will negotiate, with the woman, which target behaviours will be prioritised in the four sessions. These may include

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diet, physical activity, weight loss, smoking, alcohol use, breast feeding and stress or anxiety, depending on a brief risk assessment and the woman's expressed needs and readiness to change. The counsellor will actively engage the woman in setting behaviour change goals and developing a personalised risk reduction plan appropriate to her circumstances, resources and preferences. Follow-up counselling will be offered by the same counsellor and focus on enhancing self-efficacy, positively reinforcing progress, problem solving and dealing constructively with relapse. The counsellor will keep contact with study participants via mobile phone messaging and follow-up any women who do not attend for their scheduled clinic visits. This will communicate continued social support and caring, in addition to reducing potential drop out from the study.

Community-based intervention

In between the counselling sessions at the clinic, women may receive a discretionary home visit by the same lay counsellor, with whom she has built up a relationship during the well-baby clinic counselling sessions. These visits could take place at around 8, 12 and 16 weeks post partum and will focus on assisting the family (and/or another member of the household) engage with healthy lifestyle change. The lay counsellor will also organise a minimum of three peer support group sessions, once there are sufficient numbers of women in the intervention arm living in the same general residential area. These will take place at an agreed local venue or at one of the women's homes if preferred and at a time agreed on by participants. Women will be encouraged to bring along their support person or buddy. The group sessions will be tailored to the expressed needs of each group, and will focus on sharing experiences, problem solving common barriers to lifestyle modification and exploring how to access available community resources and opportunities. They will also involve practical activities such as demonstrations on how to prepare healthy meals and how to shop for healthier products, as well as physical activity classes. It is envisaged that these sessions would last several hours at a time. The lay counsellor will encourage the formation of WhatsApp groups among women for additional social support and will discuss how the peer support groups could possibly be sustained beyond the study.

Health literacy resources

During the counselling sessions, participants will be offered education/self-help materials that will provide further information on lifestyle change and teach behaviour change skills. These tools have already been researched and developed on physical activity, diet, alcohol use and smoking (see www.ichangeforhealth.co.za). These will be made available for this intervention. These materials include real-life testimonials from the same target community who model successful lifestyle change, despite facing many of the barriers to achieving change experienced by people of low socioeconomic status. Further complementary resources will include leaflets on GDM and T2DM; postnatal depression and breast feeding.

Primary outcomes

A team of trained research assistants will collect all the survey, measurement and clinical data as outlined in table 2 using harmonised and standardised operating procedures between the two sites. Either validated surveys and/or survey instruments used for SA populations will be utilised. The first primary outcome will be completion of the 6 weeks OGTT (yes/no variable), and the second primary outcome will be change in diabetes risk between 6 weeks and 12 months post partum.The second primary outcome will be defined as a composite measure at the participant level and is made up of the sum of three risk indicators: (1) weight (this will be an indicator variable scored as '1' if the percentage weight loss from postpartum weight is more than 5% at 12 months and '0' if otherwise); (2) waist circumference (this will be an indicator variable scored as '1' if the percentage reduction in waist circumference from postpartum waist circumference is more than 3% at 12 months and '0' if otherwise) and (3) dysglycaemia (this will be an indicator variable scored as '1' if the blood glucose concentrations measured from the OGTT were within normal ranges according to the WHO guidelines of 1998 at 12 months and '0' if otherwise).

Sample size

For the primary outcome (postnatal 6-week OGTT), for a 15% difference (increase) in follow-up visits in the intervention arm the study would need 242 participants at 80% power. For the other primary outcome, positive diabetes risk reduction at 1 year defined as a positive outcome in any of the three diabetes risk indicators (percentage weight loss >5%; percentage waist circumference reduction of >3%; normoglycaemia status at 1 year). The prevalence of >5% wt change from Penn *et al* (2013) was 38% in the intervention arm and 14% in the control arm. These values and difference formed the basis of the sample size calculations. In the intervention arm, participants will be handled by a limited of number of well-baby clinics with linked intervention counsellors. The total anticipated attrition for the study is 30%: the a priori expected exclusion of recruited participants due to diabetes status at delivery or at the 6 weeks visit determined by OGTT using WHO criteria is 15%. We estimate that a further 15% will be lost to follow-up between birth and 12 months. Therefore, the study sample size required, accounting for attrition, is 370 participants; 185 in each of the intervention and control arms. While the number of control and intervention participants will be matched in Cape Town and Soweto, the total sample in each city does not need to be split equally. This sample size will have 90% power to detect a minimum difference of 20% (35% vs 15% used) in the prevalence of the secondary outcome at 1 year between the intervention and control

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Table 2 Longitudinal data collection in IINDIAGO (M: mother, I: infant)

Domain	Measure	Pregnancy	6–8 Weeks post partum	12 Months post partum
Demography	Demographic and socioeconomic data, household composition, occupation, education, living environment	M		M
Anthropometry	Height/length		M/I	M/I
	Weight	M	M/I	M/I
	Body mass index		M	M
	Circumferences (waist, hip, mid-upper arm)		M	M
	Child (arm and head circumferences, triceps, subscapular skinfolds)		I	I
Clinical	Pregnancy complications	M		
	HIV status	M		
	Blood pressure		M	M
	Oral glucose tolerance test		M	M
	Plasma and serum sample collection		M	M
Lifestyle and health behaviour	Dietary intake (SA food frequency questionnaire)	M	M	M
	Physical activity (Global Physical Activity Questionnaire)[27]	M	M	M
	Tobacco, alcohol and drug use: Exposure Questionnaire (WHO-STEPS, AUDIT-Questionnaire)[28]	M	M	M
	Past behaviour change attempts	M	M	M
	Body Shape Questionnaire	M	M	
	Breast feeding		M	M
Mental and physical health	Depression (Patient Health Questionnaire (PHQ-9))[29]	M	M	M
	Stress (Chronic Burden Scale), social support and general life satisfaction	M	M	M
	Perceived behaviour control and perceived barriers to healthy eating and physical activity questionnaires	M	M	M
	Medical history, family history, medication and supplement history	M	M	M
	Self-Determination Theory Questionnaire	M	M	M
	Health service utilisation and events (hospitalisation events)	M	M/I	M/I

arms under the assumptions given above. This sample size will have 80% power to detect a 16% difference in prevalence of the secondary outcomes at 1 year, under the same assumptions.

Secondary outcomes

Secondary maternal outcomes at 12 months post partum will include: weight and waist circumference, T2DM and dysglycaemia measured using fasting and 2-hour OGTT blood glucose, insulin resistance (HOMA-IR) and 2-hour OGTT insulin, HbA1c, blood pressure, diet, physical activity, perception of body shape and image, indicators of psychosocial health and breastfeeding history. Secondary infant outcomes at 12 months will include weight and length (see table 2).

Statistical analysis

For the analysis at 12 months the participants who test positive for T2DM at 6–8 weeks will be excluded from the complete randomised population resulting in a modified intention to treat study population and analysis. Descriptive statistics will be calculated by arm at the participant level. For the primary outcomes a participant level binomial regression model will be used with arm and stratification as the main effect. The intervention effect (difference in proportions) will be reported with 95% CIs. Multiple imputation for missing 1 year measurements will be done. For the secondary outcome analysis such as absolute weight change this will also be analysed using linear regression model. For categorical secondary outcomes the binomial regression models will be used. The primary outcomes will also be analysed in a regression model using baseline variables as covariates in the model.

Process evaluation

We will determine the degree to which the intervention was implemented as planned, the extent to which it reached the target population, adaptations which may have been made to the intervention[23] and how the implementation of the intervention is perceived by the participants and may affect the routine functioning of the health services and systems in which it is meant to be integrated. The process evaluation thus has two components: evaluation of the process of implementing the behavioural prevention intervention by counsellors to women; and documentation and analysis of actual,

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Table 3 Data collection for process evaluation

Well-baby clinics	Focus group discussions two in each clinic (one with nursing and other clinic staff, and one with Community Health Worker) during months 1, 6 (optional) and 11 of the trial.
	Individual interviews with facility managers, 1–2 nurses, 1–2 counsellors or Community Health Workers in three clinics at each site at months 1 or 2, and 11.
	Non-participant observation of clinic practice: 2 half-days in each clinic in each site in months 1 and 11.
Managers	Key informant interviews with city and provincial managers in month 12.
Hospital	Implementation team interviews and key informant interviews with one doctor, one obstetric nurse/midwife and a nutritionist/dietician at three hospitals (Chris Hani Baragwanath in Soweto and Groote Schuur and Mowbray in Cape Town) midway through the intervention.
Women (beneficiaries)	In-depth interviews with women within 2 weeks of the 6-week visit (n=50) to explore their experiences to date, and after completion of the intervention (n=30) to explore overall experiences, as well as, reasons for retention and attrition. Special attention will be paid to reach women who have dropped out of the study and explore their experiences in a non-judgmental manner.
	Brief exit interviews (5 min) with women after their clinic intervention in months 2 and 12 (n=5 women from 6–7 clinics twice).
Intervention teams	Individual interviews and focus group discussions with intervention team members in both sites in months 2 and 12 to document their perceptions of the intervention and explore their perspectives on integration into routine health services.

likely and possible interactions with and effects on health service and health system functioning (see table 3 for process evaluation data collection). The analysis of the findings will integrate both of these components, and these process evaluation findings will support the interpretation of the trial data. Fidelity to the guiding style and the use of behaviour change skills in practice will be measured through observation by the process evaluation team, and the use of a proforma evaluation form developed for this purpose. Other process measurement tools will include the case records compiled and kept by the nurse and lay counsellor on all counselling sessions and a log of follow-up phone calls and/or SMSs. Process evaluation of the behavioural prevention intervention will be informed by the COM-B (Capabilities, Opportunities and Motivation for Behaviour Change) dimensions of the Behaviour Change Wheel. Process evaluation of the overall implementation and potential integration within public health systems will be informed by UK-MRC guidance for process evaluation of complex interventions.[24] Our intent is to understand why participants did not fully engage with the intervention or withdrew from the trial, and we aim to follow-up with these participants and interview them.

We will conduct interviews with healthcare workers including facility managers and the implementation team involved in IINDIAGO intervention to document whether the intervention is delivered as it was designed, we will monitor any changes made from the original design and steps taken to adapt it to the facility context, and we will explore facility staff and managers' perspectives on both adherence and adaptation in relation to future implementation and scale-up during routine practice. While fidelity and adaptation are sometimes considered opposing ideas in implementation research,[25] we believe that both are necessary for complex interventions like IINDIAGO to be integrated into (and influence changes in) existing services. The dose of the intervention itself will be assessed through time–motion assessment and documentation of the intervention implementation. This will be evaluated in relation to routine workdays and workloads, evaluated through non-obtrusive observation and during the health worker interviews and through summary assessments of facility registers, to explore the extent to which integration of the intervention as delivered during the study is likely to increase workload. The level of health worker, manager and policymaker (the participants on the health system side of the intervention) engagement will be evaluated through interviews directly soliciting their perspectives (positive, negative, neutral) as well as through ethnographic non-participant observation to explore how health system staff react to the IINDIAGO trial (eg, apparent indifference, proactive expressions of interest, support or reservations). We will analyse the data through thematic content analysis and descriptive statistics to determine critical features that distinguish the IINDIAGO intervention from routine practice, as well as those which seem likely to be very close to/indistinguishable from routine practice.[26]

The process evaluation of the IINDIAGO intervention will thus consider not only the intervention design but also the possible unplanned positive and negative outcomes, as well as, the process through which these were identified and managed by the intervention team and how this is perceived by health system personnel. This will allow us to evaluate the feasibility of integration of IINDIAGO into routine practice, and at which level of integration, as the main health system implementation outcome and to explore perceptions regarding how to optimise the intervention sustainability .

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Cost-effectiveness

Analysis will compare the integrated intervention to the control and assess whether the intervention improves the diabetes risk profile and quality of life of mothers with previous GDM at an acceptable cost. The analysis will draw on costs incurred during the trial and changes in health outcomes during that 1 year time horizon. Costs will be estimated from the provider (public health system), patient and societal perspectives. Provider costs will be a product of the unit costs of the service and its utilisation, considering both direct and indirect costs. We will use data from the department of health audits/resources to collect facility and provider unit costs, and we will capture time spent by counsellors delivering the intervention through records of counselling sessions. Healthcare utilisation data of participants will be derived from counselling report forms and through the baseline and final questionnaires. Patient costs will be the sum of direct non-medical costs and opportunity costs (eg, time away from work) incurred during the intervention period. These will be assessed using baseline and final questionnaires and patient exit surveys. Additional programme costs (eg, counsellor training, development of educational materials) will be assessed by reviewing study budgets.

Trial status, impact of the COVID-19 pandemic and limitations

Trial formative research started in 2015, and trial recruitment began in April 2018 for the pilot phase where we examined the data collection procedures and intervention processes. Minor changes were made to the procedures and processes so that these were feasible and acceptable. We shifted into the second main trail phase in the beginning of 2019. The heterogeneity of the health systems across the two provinces and hospitals around GDM diagnosis criteria and non-universal screening proved to be a challenge for recruitment, but it is an important finding that has spurred specific process evaluation research and will form part of our planned stakeholder engagement. Twelve months into the trial the COVID-19 pandemic hit South Africa through a series of waves and lockdown levels. A hard lockdown (level 5) was implemented in South Africa from 26 March to 30 April 2020. Thereafter a level 4 lockdown was implemented until 31 May 2020. Level 3 then lasted until 17 August 2020, when the country moved to level 2 and finally level 1 (September 2021). The recruitment has been severely interrupted particularly in 2020. On resuming community recruitment, additional COVID-19 specific safety protocols were implemented, and intervention face-to-face interactions were replaced with telephonic sessions. Given COVID-19 related delays, re-recruitment efforts and preparation for analytical datasets, IINDIAGO is expected to be completed by end of 2023. We acknowledge that our a priori logic model that informed the intervention may not have fully recognised intermediate outcomes, but this investigation will form part of the process evaluation. We plan to adjust for site population differences but we recognise that this might not account for all the potential differences. We recognise that several of our planned survey instruments are not validated specifically within South Africa and we will examine these for internal validity within the study population.

Data management

All data collection staff will undergo extensive harmonised training. Data will be collected onto a REDCap database with validation and quality checking programming, and regular monitoring by the data coordinator. Only authorised users with appropriate permissions will have database access. Data on numbers recruited and lost to follow-up, as well as reasons for the latter will be maintained for the participating sites. All biomarkers will be analysed by a central laboratory with strict quality assurance (indicators of variance) and these indicators will be presented in all publications.

Data sharing and availability statement

We support the BMJ's Tier two data policy and ICMJE guidelines for trial data to be made available on reasonable request. IINDIAGO will be completed by end 2023 and the main trial analyses will be completed within 12 months thereafter. From January 2025, deidentified trial participant and process evaluation (qualitative transcripts) data are available on reasonable request. Please contact Naomi Levitt (ORCID identifier: 0000-0001-6480-80; Naomi.Levitt@uct.ac.za) for data access, which will be granted for all valid scientific enquiries. Data with clinical research forms, codebook and study methods will be supplied. Data sharing policies are consistent with South African government legislation.

ETHICS AND DISSEMINATION

Ethics approval has been granted from all partnering institutions (University of Cape Town (829/2016), University of Stellenbosch, (N17/04/032), University of the Witwatersrand, Johannesburg (M170228) and the University of Montreal (2019-794)) and permissions have been secured from all relevant authorities before recruitment of participants. The recruiting team ask participants for written informed consent before randomisation—see online supplemental file 3. All participant research data will be deidentified at collection and signed informed consent documents will be stored separately and securely by the study coordinators. The results of the trial will be disseminated through publication in peer-reviewed journals and presentations to key stakeholders.

GOVERNANCE

Trial management team

The TMC will oversee the day-to-day conduct of the trial. This team will consist of site and task-specific co-ordinators, investigators and the principal investigators. Additional members will be co-opted as needed. The

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management team will meet monthly and be accountable to the principal investigators (NL and CZ).

Trial Steering Committee (TSC)

A TSC will be convened to provide overall supervision of the trial. The principal investigators will report to the TSC, which will consist of three experienced public health researchers and will meet remotely 6–12 monthly.

Advisory group

This group will ensure that various stakeholders provide ongoing input into the development and implementation of the intervention. This group will include representatives from the Department of Health, civil society groups, patient advocacy groups and clinicians.

Data monitoring committee

A data monitoring committee is not required as the trial is a low risk trial. Severe adverse events are not expected and, in the event, that they occur, they will be reported to the TSC and the respective ethics committees.

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Patient consent for publication Consent obtained directly from patient(s).

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