BMJ Open

Effect of intensive nutrition training, education and support versus standard therapy in reducing the need for insulin therapy in gestational diabetes (INTENSE-GDM): a protocol for a randomised controlled single-centre trial in Denmark

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To cite: Ewers B, Blond MB, Kelstrup L, *et al*. Effect of intensive nutrition training, education and support versus standard therapy in reducing the need for insulin therapy in gestational diabetes (INTENSE-GDM): a protocol for a randomised controlled single-centre trial in Denmark. *BMJ Open* 2025;**15**:e089231. doi:10.1136/bmjopen-2024-089231

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (https://doi.org/10.1136/bmjopen-2024-089231).

Received 24 May 2024
Accepted 31 January 2025

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ABSTRACT

Introduction Gestational diabetes mellitus (GDM) poses health risks due to hyperglycaemia, which can lead to clinical complications for mother and child. While dietary therapy serves as first-line treatment, approximately one-third of women with GDM require insulin to obtain glycaemic control. However, insulin therapy amplifies hospital care expenses and personal burdens. Intensive nutrition education, training and support may improve dietary intake leading to glycaemic control and reducing the need for insulin therapy. This study investigates the effectiveness of intensified dietary therapy versus standard dietary therapy in reducing the need for insulin and consequently lowering hospital care costs among women with GDM at high risk of requiring insulin therapy. Responses to the dietary interventions will also be examined within ethnic subgroups.

Methods and analysis This study is a randomised controlled parallel-group trial involving women with GDM randomised in a 1:1 ratio to receive either intensive dietary therapy (intensive group) or standard dietary therapy with only one educational consultation (control group). The educational content of the first consultation is according to routine care and similar in both groups. The intensive group receives two additional dietitian consultations and two additional consultations on request to facilitate training and support in addition to education. Assessments are conducted at baseline and 2–3 weeks before planned delivery, with additional data gathered from medical records. The primary outcome is the difference in the proportion of women requiring insulin therapy. Maternal outcomes, neonatal outcomes, patient-reported outcomes, health behaviour and cost-saving aspects of hospital care will also be assessed. Recruitment began in January 2024 and ends in December 2025, with a target enrolment of 214 women.

Ethics and dissemination The study received approval from the Ethics Committee of the Capital Region of Denmark (H-23055674). Results will be disseminated through peer-reviewed journals, and detailed presentations to key stakeholders.

Trial registration number NCT06127823.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The trial uses a randomised controlled study design targeted at women with gestational diabetes mellitus at high risk of requiring insulin therapy, thereby applying a precision medicine approach.
⇒ The trial is designed with a hierarchical hypothesis structure to explore the uptake and effectiveness of the dietary interventions overall and based on ethnic subgroups.
⇒ The trial investigates both clinical effects and hospital care costs, providing data for assessing the intervention's feasibility for routine implementation.
⇒ The methodology and findings are applicable beyond Denmark and may inform future national and international guidelines.
⇒ The trial focuses on immediate outcomes but limiting maternal weekly gestational weight gain and foetal overgrowth may lead to long-term benefits for both the mother and offspring beyond the duration and scope of this trial.

INTRODUCTION

Gestational diabetes mellitus (GDM) presents a significant global health challenge, affecting about 6% of pregnancies in Denmark[1] and 14% worldwide.[2] Notably, the risk of GDM varies based on ethnicity with non-Western women living in Denmark being at heightened risk.[3] GDM is defined as glucose intolerance and is clinically characterised by varying

degrees of hyperglycaemia.[4 5] The hyperglycaemia poses serious complications for both the mother and child, including pre-eclampsia, preterm birth, caesarean section, foetal overgrowth, birth injuries, respiratory distress syndrome, neonatal hypoglycaemia, jaundice and increased risk of admission to neonatal intensive care.[6] Furthermore, it increases the long-term risks of obesity, type 2 diabetes and cardiovascular disease in both the mother and child.[4]

Dietary therapy is first-line treatment following a diagnosis of GDM. Treatment goals include ensuring an adequate intake of calories, micronutrients and macronutrients to support pregnancy needs while improving glycaemic control and promoting appropriate gestational weight gain.[4 7] While routine dietary advise is sufficient for many in achieving glycaemic control, a notable subset of women with GDM may require insulin therapy.[4 8] Register-based studies indicate that around 30% of Danish women with GDM received insulin therapy over the past two decades.[9 10] Insulin therapy in GDM offers benefits such as improved glycaemic control in the mother, reduced foetal overgrowth, lower rates of caesarean sections and decreased risk of neonatal hypoglycaemia.[11 12] However, it also presents several clinical implications, including an increased risk of maternal hypoglycaemia, greater gestational weight gain, elevated blood pressure, heightened likelihood of labour induction and potential alterations in placental and umbilical vessel function.[4 10 12 13] Moreover, its use often leads to intensified obstetric and endocrinologic surveillance, medical expenses for insulin, necessitates additional ultrasound examinations and raises the probability of labour induction as well as more frequent and prolonged admissions to neonatal care, resulting in heightened hospital care and costs.[10 14 15] Finally, the need for intensified blood glucose monitoring and daily insulin injections adds to the emotional burden experienced by women with GDM, overall impacting their daily lives substantially.[16] Therefore, an intensive dietary therapy approach with more frequent dietitian consultations could provide a less costly and less burdensome alternative to insulin therapy.

Positive predictors of need for insulin therapy include pregestational Body Mass Index (BMI), and BMI at diagnosis, earlier diagnosis in pregnancy, haemoglobin A1c (HbA1c) levels at diagnosis, increased plasma glucose levels during an oral glucose tolerance test (OGTT), higher weekly weight gain during pregnancy and previous GDM.[10 17–20] Additionally, research suggests that women with non-white ethnic backgrounds, particularly those from South Asian and South East Asian countries, may be at a higher risk of requiring insulin therapy for GDM compared with Caucasian women in some, but not all studies.[21 22] Overall, these predictors highlight the considerable heterogeneity in the likelihood of initiating insulin therapy indicating that risk levels are not uniform across all women with GDM.

Consensus exists on the importance of regulating carbohydrate intake[4 23] to improve glycaemic control. However, evidence supporting a particular diet for managing GDM has not been found.[7] Carbohydrates act as the primary energy source in our diet, significantly influencing postprandial blood glucose responses and overall energy intake, thereby potentially impacting glycaemic control and gestational body weight gain.[4 7] Current international guidelines advocate for a minimum daily consumption of 175 g carbohydrates, equivalent to 35%–40% of total energy (E%) requirements for healthy pregnant women.[4] This minimum intake has been recommended to support normal foetal growth and brain development in pregnant women.[7] Research on moderately carbohydrate-restricted diets (40–45 E%) compared with higher carbohydrate diets (45–60 E%), which are recommended in the general population,[24] among women with GDM is limited.[25–27] One study reported improved glycaemic control, lower rates of insulin therapy initiation, fewer caesarean deliveries and fewer infants large for gestational age (LGA) with the carbohydrate-restricted diet.[26] However, another trial found no decrease in rates of initiating insulin therapy in the carbohydrate-reduced group, while a separate trial demonstrated improved glycaemic control without specifically assessing the prevalence of insulin therapy.[25 27] Dietary interventions, focusing on the efficacy of low glycaemic index (GI) diets in reducing the proportion of women with GDM requiring insulin therapy, are better documented. One study demonstrated that adherence to a low GI diet resulted in a 50% reduction in insulin requirements.[28] A systematic review and meta-analyses based on four randomised controlled trials (RCTs) found that low GI diets decreased the proportion of women requiring insulin (relative risk 0.77) and reduced infant birth weight compared with control diets, while carbohydrate-restricted diets (based on two RCTs) did not affect maternal or infant outcomes.[29]

Understanding potential ethnic disparities in response to dietary interventions for reducing the need for insulin therapy is also important, given the high prevalence of ethnic minorities, constituting 23% of women diagnosed with GDM in Denmark.[3] Migration-related barriers to care, as highlighted in qualitative studies, pose challenges for immigrant women in accessing healthcare, healthy foods and engaging in physical activity, affecting their ability to achieve glycaemic control.[30] Reviews stress the need for culturally sensitive dietary guidance in GDM with tailored dietary interventions based on ethnic origin and food culture.[30 31] The preference for carbohydrate-rich diets with a high GI (eg, white bread and rice),[32] commonly observed in South-Asian, East-Asian, Arab and African diets, further emphasises the importance of addressing this issue. A small pilot study has examined the effects of an ethnicity-specific dietary intervention in GDM, yielding intriguing yet inconclusive results regarding improvements in metabolic control and reduction of gestational weight gain.[33]

At present, there is a lack of evidence-based guidelines, supported by high-quality research, on the optimal dietitian-delivered model of care, including the

frequency of dietitian consultations needed to provide effective dietary therapy and support for women with GDM to improve clinical outcomes. According to empirical data from Danish hospitals, standard routine dietary therapy typically comprises a single consultation with a dietitian following GDM diagnosis, primarily focusing on nutrition education. However, research involving individuals with overweight or type 2 diabetes has shown that more frequent visits to a dietitian including training and support are associated with improved health outcomes, including greater weight loss[34 35] and glycaemic control.[36] Therefore, intensive nutrition training and support may be crucial for minimising postprandial glucose fluctuations and controlling weekly gestational weight gain in women with GDM. This approach could reduce the need for initiating insulin therapy and mitigating pregnancy complications, including foetal overgrowth, thereby diminishing obstetric and endocrinologic implications and associated hospital care costs.

This study aims to investigate the effectiveness of intensified dietary therapy compared with standard dietary therapy in reducing the need for initiating insulin therapy and consequently lowering hospital care costs among women with GDM at high risk of requiring insulin therapy. Furthermore, the study will explore variations in response to the dietary interventions within ethnic subgroups.

METHODS

Trial design

The INTENSE-GDM study is a non-blinded, single-centre, randomised, controlled, parallel-group two-armed trial including women with GDM comparing the delivery of intensive nutrition training, education and support (intensive group) with repeated dietitian consultations with only one educational consultation with a dietitian (control group). See figure 1 for study design and figure 2 for study flow. The trial follows the guidelines of Standard Protocol Items for Randomised Trials (SPIRIT).[37]

Participants

Inclusion criteria

Inclusion criteria are newly diagnosed women with GDM at Department of Obstetrics and Gynaecology, Herlev-Gentofte University Hospital with gestational age (GA) at diagnosis ≤34 weeks. GDM diagnosis in Denmark is currently based on either a 2-hour OGTT plasma glucose value ≥9.0 mmol/L or a 6 points 24-hour profile with at least two plasma glucose measurements above targets (either preprandial>6.0 mmol/L, or 2 hours postprandial>8.0 mmol/L). Participants must provide voluntary written informed consent, available in either Danish or English. For non-Danish and non-English speaking women, consent can be translated by an interpreter. To personalise the treatment and efficiently utilise dietary resources, we only include women with an estimated risk of initiating insulin therapy during pregnancy of ≥20%, as outlined below.

Exclusion criteria

Exclusion criteria are bariatric surgery, concomitant illness (eg, cancer, ulcerative colitis), uncontrolled medical and mental issues as judged by the investigators, concomitant participation in other randomised clinical trials, unable to understand the informed consent and procedures.

Identifying women with GDM at high risk of initiating insulin therapy

The risk model used for inclusion of participants was designed with the aim of providing personalised care focusing on optimising cost-benefit by reducing the number of low-risk individuals included in the trial, while still retaining a large proportion of all women who would need insulin therapy. The cut-point for the estimated probability of initiating insulin therapy during pregnancy is ≥20% based on three variables, which result in approximately 50% of a local cohort having an increased risk of initiating insulin therapy. The primary risk model used for inclusion (shown in figure 3) is based on the following three variables: GA at diagnosis, pregestational

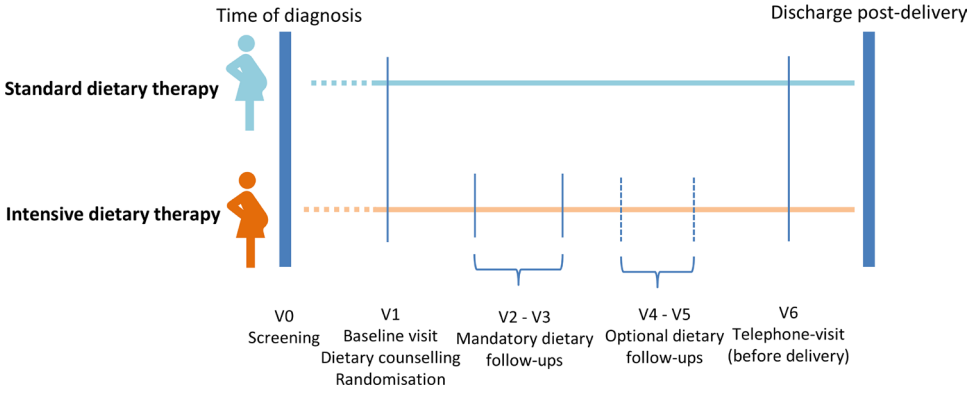

Figure 1 Study design. A minimum of three consultations and two additional optional consultations with a dietitian will be provided in the intensive dietary therapy group compared with only one consultation with a dietitian in the standard dietary therapy group. Visit 0 (screening) and 1 (baseline with first dietary consultation) can be combined if convenient.

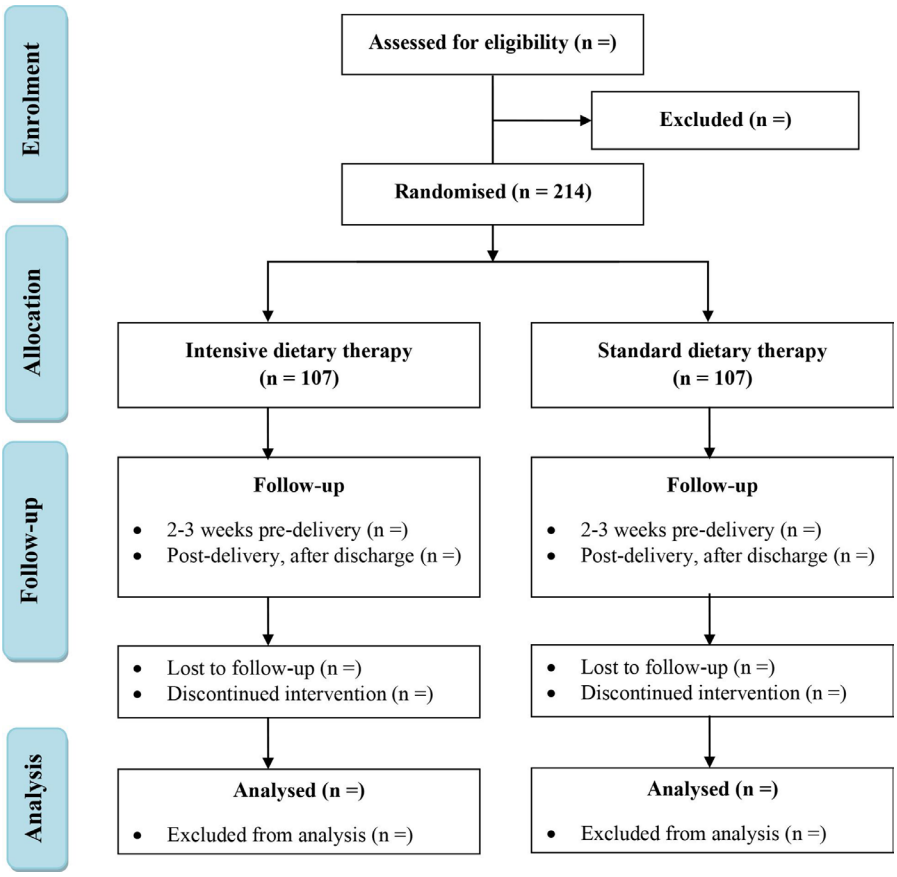

Figure 2 Study flow diagram. The planned flow of participants through the stages of the trial.

BMI and HbA1c at diagnosis. In cases where HbA1c has not been measured at the screening visit, 2-hour OGTT at diagnosis will be used together with GA at diagnosis and pregestational BMI (model shown in figure 4) to estimate the probability of initiating insulin therapy. Further details on the creation of the risk models are provided in online supplemental appendix A.

Definition of ethnicity

Women are categorised into two groups (white and non-white ethnic backgrounds) based on their country of origin (immigrant or second-generation immigrants) to explore the differences in response to the dietary interventions within ethnic subgroups. Immigrant women represent 23% of women diagnosed with GDM in Denmark.[3] However, at our hospital, we have observed that up to 45% belonged to a non-white ethnic group (unpublished). Women with a white ethnic background are defined as individuals with European ancestral origins who are identified as white (also called European, or in terms of racial classifications, the group known as 'Caucasian'). Women with a non-white ethnic background are the remaining, often belonging to minority populations. These include Asian (Indian, Pakistani, Bangladeshi, Chinese and any other Asian background), Caribbean, Black, African, Middle East, Hispanic/Latino and any mixed or multiple ethnic background.[38]

Recruitment and informed consent

Recruitment will take place at the outpatient clinic at Steno Diabetes Center Copenhagen (SDCC), Denmark and target women with newly diagnosed GDM at the Department of Obstetrics and Gynaecology at Herlev-Gentofte University Hospital. Prior to study entry, written informed consent will be obtained from all participants (online supplemental appendix B). A participant information sheet, available in both Danish and English, will be electronically delivered to all women with GDM treated at Herlev-Gentofte University Hospital via E-Boks alongside the invitation to the initial consultation with the dietitian postdiagnosis, according to standard procedure. During the initial consultation with one of the research dietitians, who routinely conducts consultations for all women with GDM, time will be allocated for thorough oral presentation of study details. The research dietitian will ascertain whether the participant has read the provided information and remains interested in learning more about the clinical trial. If affirmative, the research dietitian will provide oral information in Danish, English or with interpreter assistance as necessary. If immediate acceptance of participation is chosen, the woman and the research dietitian will sign an electronic consent form, available in Danish or English. Subsequently, a screening will be conducted by the research dietitian to assess eligibility for study inclusion. Eligible women will then undergo

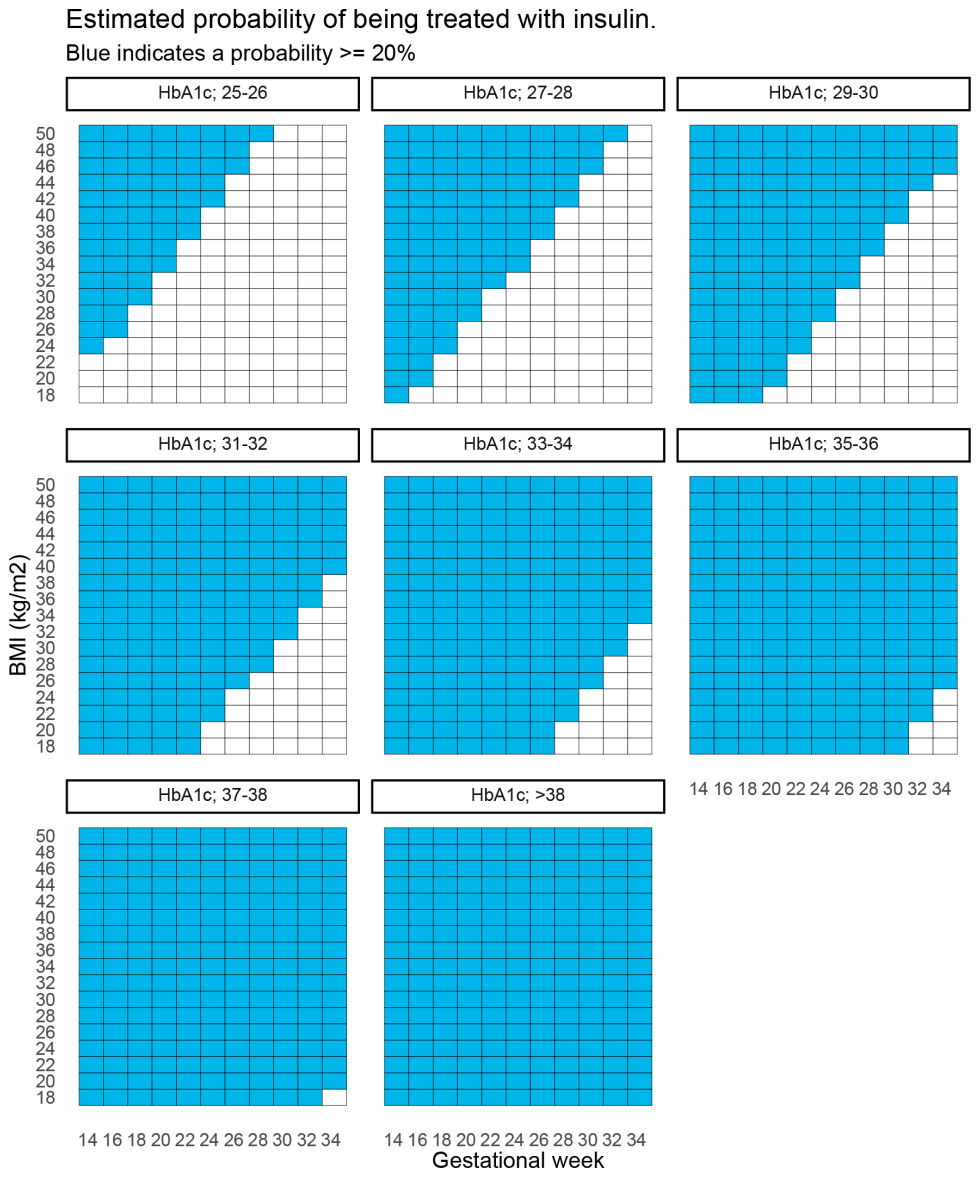

Figure 3 Risk assessment form for identifying women with GDM at high risk (probability≥20%) for initiating insulin therapy (shown in blue) and lower risk (shown in white) based on their HbA1c (mmol/mol) values displayed on top, while pregestational BMI values (kg/m^2) are represented on the Y-axis, and gestational age at diagnosis (in weeks) on the X-axis. BMI, Body Mass Index; HbA1c, haemoglobin A1c.

baseline measurements, receive the first dietary consultation and then be randomised to one of the two groups in the specified order by the research dietitian. Women requiring additional time for consideration or those who have not yet read the provided information will be scheduled for a follow-up meeting within 2 days. Recruitment for the study commenced in January 2024 and is anticipated to conclude by December 2025.

Randomisation

Participants will be randomised in a 1:1 ratio to receive either intensive dietary therapy (intervention group) or standard dietary therapy (control group). The randomisation will be conducted using simple randomisation through a computer-generated randomisation module in research electronic data capture (REDCap), a secure web-based application designed to facilitate research data management.[39] A research dietitian will execute the randomisation process. The randomisation list has been generated by a research assistant not involved in the trial, who will be the sole individual with access to it throughout the trial. If this individual is unable to fulfil this assigned role, a new impartial person will be designated to maintain and manage the sequence.

INTERVENTION

All participants

All participants will receive a one-hour individual in-person consultation with a dietitian, covering

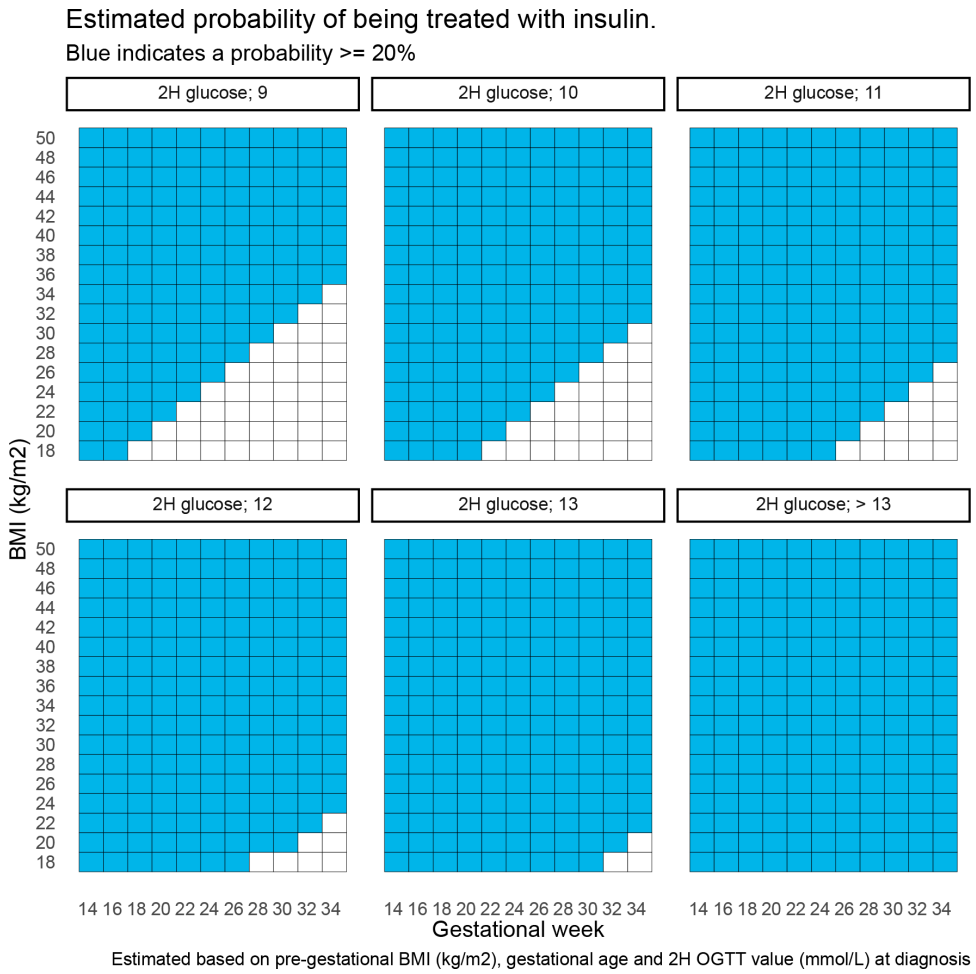

Figure 4 Risk assessment form for identifying women with GDM at high risk (probability≥20%) for initiating insulin therapy (shown in blue) and lower risk (shown in white) based on 2-hour OGTT (mmol/L) values displayed on top, while pregestational BMI values (kg/m^2) are represented on the Y-axis, and gestational age at diagnosis (in weeks) on the X-axis. BMI, Body Mass Index; 2 H glucose, 2-hour oral glucose tolerance test.

dietary recommendations for women diagnosed with GDM, personalised goal setting for behavioural changes addressing individual dietary challenges, food culture and preferences (examples provided in online supplemental appendix C). Recommendations for weekly gestational weight gain will also be provided. During the consultation, participants will receive education on basic carbohydrate counselling, including methods for carbohydrate identification and counting. This can be achieved through various approaches, including calculating carbohydrate content from food labels, using carbohydrate food tables or smartphone apps such as the well-established 'Kulhydrattælleren' app developed by the Danish Diabetes Association, available on both Google Play and the App Store (only available in Danish).

Each participant will receive a personalised carbohydrate plan outlining the recommended daily carbohydrate intake, aiming for approximately 175 g carbohydrates per day, with approximately 150 g sourced from the major carbohydrate food groups such as bread, rice, pasta, potatoes, dairy and fruits. The plan will also include recommendations for timing carbohydrate intake at different meals and snacks to ensure optimal distribution throughout the day. A carbohydrate distribution of 10%–15% at breakfast, 30% at lunch and dinner and the remaining 25%–30% divided into 2–4 snacks is recommended to aim for a postprandial glycaemic response within the target area for women with GDM.[40–42] In practice, women are often advised to consume approximately 20 g for breakfast, 40–50 g for lunch, 40–50 g for dinner and 10–20 g for snacks up to three times daily. Participants will also receive guidance on selecting carbohydrates with a low GI and are encouraged to adhere to their carbohydrate plan until delivery.

During the consultation, the 'Carbs & Cals: Diet & Diabetes' app from the UK, available on both Google Play and the App Store, featuring photo-based portion sizes of various high-carbohydrate foods, along with culturally sensitive images of high-carbohydrate foods, will be utilised to assist the dietitian in estimating each woman's current carbohydrate intake and for providing visual guidance and recommendations for intake.

Intensive dietary group only

Women assigned to the intensive dietary therapy group will have two mandatory 30-min follow-up consultations with the dietitian in addition to the initial consultation. The follow-up consultations will involve repeated training and support, feedback on postprandial plasma glucose measurements in relation to meals consumed and monitoring of gestational weight gain. Adjustments to the dietary plan will be made as necessary until delivery. These consultations will be carried out either by phone, video or in-person based on personal preference. The first follow-up will take place 3–4 days after the initial consultation, and the second follow-up will take place approximately 1 week after the first follow-up (figure 1). Furthermore, participants will have the option to request two additional follow-up consultations (15–30 min each) by phone or video with the dietitian. The timing of these optional follow-ups is flexible and may occur at any point up to delivery.

General instructions

All participants will receive guidance to engage in moderate-intensity aerobic activities throughout their pregnancy, such as brisk walking in addition to recommendations to prioritise optimal sleep duration and quality. Furthermore, participants will follow the usual obstetric care at the Department of Obstetrics and Gynaecology.

Assessment of need for insulin therapy

Based on the recommendations outlined in the Danish National guidelines for GDM management, the target for preprandial and postprandial plasma glucose levels is <6.0 mmol/L and <8.0 mmol/L, respectively.[43] However, national recommendations for insulin therapy thresholds have been changed, effective from 1 January 2025 to <5.5 mmol/L for preprandial and <7.0 mmol/L for postprandial plasma glucose levels, measured 1.5 hours from the start of a main meal.[44] When dietary strategies fail to achieve the desired glucose goals for the woman with GDM, insulin therapy is initiated. According to the Danish National guidelines, this is the case if two or more preprandial and postprandial plasma glucose values are above targets within a week without an obvious explanation. In such cases, initiation of insulin therapy and referral to diabetes care by an endocrinologist is recommended.[43 44] When insulin therapy is initiated, the endocrinologist's consultations take place at 1- to 2-weeks interval until delivery. While obstetricians and endocrinologists are not blinded to participant allocation in the study, they do not actively participate in the study recruitment or management.

Data collection at baseline and predelivery

Prior to study inclusion, gestational age at onset of GDM, HbA1c measured at the time of diagnosis and self-reported pregestational BMI data are collected from the electronic medical record to identify women at high risk of insulin therapy. At the baseline visit, body weight and height are measured, and self-reported data on country of origin and ethnicity, family status, educational status and dietary habits are collected. Following the visit, participants will receive a series of electronic questionnaires integrated using the REDCap software system. Two to three weeks before delivery, a telephone interview will be conducted to reassess dietary intake, followed by the distribution of the same set of electronic questionnaires. Figure 5 illustrates the study flow from recruitment to the final study visit.

Outcomes

The primary outcome is the difference in percentage of women with GDM initiating treatment with insulin therapy prior to delivery in the two groups.

Secondary outcomes include maternal outcomes (weekly gestational weight gain (gram) from time of diagnosis to delivery; changes in HbA1c (mmol/mol) from time of diagnosis to delivery; time to prescription of insulin (in days) from study inclusion until delivery; mean initial and maximal insulin dose (units/kg body weight)); and neonatal outcomes (percentage of new-borns small for gestational age (SGA); LGA; with macrosomia (birth weight >4500 g): neonatal hypoglycaemia (defined as plasma glucose <2.5 mmol/L after the first two postnatal hours); new-borns admitted to the neonatal intensive care unit (NICU), duration of NICU stay).

Descriptive/exploratory outcomes include changes in the following from inclusion until delivery:

Maternal outcomes

Pre-eclampsia (defined as new-onset gestational hypertension with a blood pressure ≥140/90 mm Hg after GA of 20 weeks combined with proteinuria (≥0.3 g protein in 24-hour urine or ≥0.1 g protein in a midstream urine spot), pulmonary oedema and/or specific symptoms of end-organ dysfunctions (eg, headache, nausea and vomiting), preterm births (defined as GA <37 completed weeks), acute and planned caesarean sections and shoulder dystocia.

Neonatal outcomes

Neonatal jaundice defined as elevated total serum bilirubin >68–137 µmol/L and clinically manifests as yellowish discolouration of the skin).

Person-reported outcomes: the following validated questionnaires will be used: Diabetes Diet-related Quality of Life (DDRQOL),[45] WHO-Five Well-being Index (WHO-5),[46] Healthcare Climate Questionnaire (HCCQ),[47] Perceived Competence in Diabetes Scale (PCDS),[47] and Pregnancy Physical Activity Questionnaire (PPAQ).[48] These questionnaires are available in both Danish and English and are administered electronically through REDCap. Assessments will occur after the baseline visit and the after the telephone interview 2–3 weeks prior to expected delivery, with an estimated completion time of 20 min.

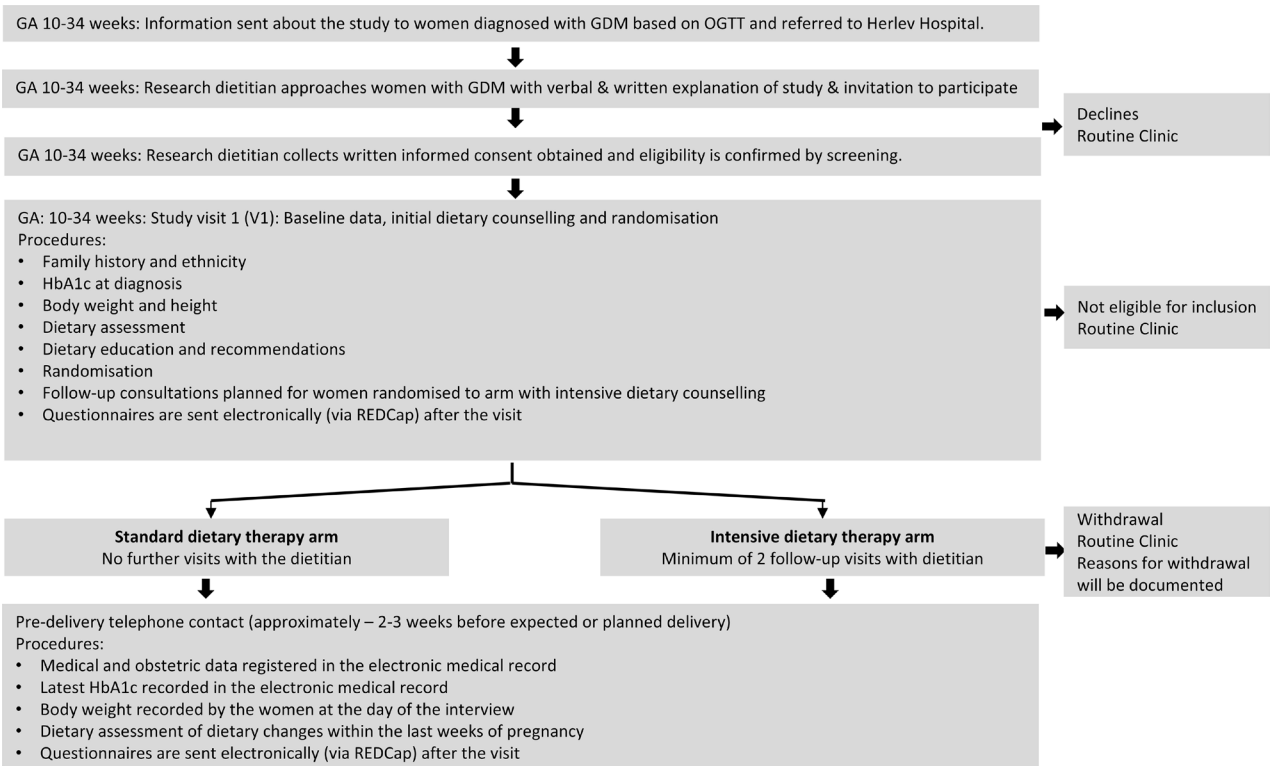

Figure 5 INTENSE-GDM protocol summary. GA, gestational age; GDM, gestational diabetes; HbA1c, haemoglobin A1c; OGTT, oral glucose tolerance test; REDCap, research electronic data capture.

Outcomes related to adherence and interventions

Outcomes related to adherence and interventions including changes in carbohydrate intake (total daily intake and per meal) from baseline until 2–3 weeks prior to delivery, weekly gestational weight gain from inclusion until 2–3 weeks prior to delivery, frequency and types of dietitian contacts (face-to-face, video and telephone) from inclusion until delivery (compliance goal: attendance of two mandatory follow-up consultations in the intervention group) and adverse events.

Hospital costs

Hospital costs will be derived from registry data provided by the Danish Health Data Authority (National Patient Register). These data will be utilised to analyse differences between the two study groups, encompassing hospital DRG-costs (Diagnosis Related Groups) incurred from GDM referral to discharge postdelivery. These net costs will also be categorised into outpatient hospital contacts, inpatient costs before delivery due to GDM, delivery costs, postdelivery inpatient costs for both mother and offspring separately, including NICU costs.

Data collection

Table 1 presents the collected data, methods, timing, and participants data are collected from.

Statistical methods

Hypothesis for the primary outcome

We hypothesise that intensive dietary therapy is superior to standard dietary therapy (control group) in reducing the incidence of insulin use from inclusion to delivery. The following hypothesis hierarchy will be used for the primary outcome. The type 1 error will be controlled in the strong sense using the following hierarchical (fixed sequence A–C) testing procedure. This is based on priority ordering of the hypotheses and testing them in this order until an insignificant result appears:

1. We hypothesise that intensive dietary therapy is superior to standard dietary therapy in reducing the need for insulin therapy in all women with GDM regardless of ethnicity.
2. We hypothesise that intensive dietary therapy is superior to standard dietary therapy in reducing the need for insulin therapy in women with a white ethnic background.
3. We hypothesise that intensive dietary therapy is superior to standard dietary therapy in reducing the need for insulin therapy in women with a non-white ethnic background.

Sample size calculation

Based on register data from Herlev Hospital from the period of 2019–2022, the incidence of insulin therapy among women with GDM receiving standard care was 30% (unpublished data). By including women with GDM with a high risk of insulin therapy, the expected incidence of insulin therapy use was 50%. A 50% difference in the incidence of insulin therapy between the two study groups during the study period was defined as the minimally important difference for the primary outcome. Thus, the

Table 1 Data collection in the INTENSE-GDM trial

Variable	Measurement/method	Participant	Screening	Baseline	Predelivery	Postdelivery
			V0	V1	V6	No visit
Ethnicity and socio-economy	Self-constructed questions	W		•		
Medical history	EMR	W	•	•		
Diet history	Personal interview	W		•	•	
Alcohol, sleep, smoking	Self-constructed questions	W		•	•	
Obstetric history	EMR	W	•	•	•	•
Medication	EMR	W		•	•	
Glycose control	HbA1c	W		•	•	
	7-point SMGB	W			•	
	Neonatal hypoglycaemia	N				•
	Admission to NICU	W, N				•
Anthropometry	Height, BW, BMI	W		•	•	
	Delivery weight (EMR)	N				•
	LGA (EMR)	N				•
	SGA (EMR)	N				•
	Macrosomia (EMR)	N				•
Delivery complications	Preterm birth (EMR)	W				•
	Pre-eclampsia (EMR)	W				•
	Caesarean section (EMR)	W				•
	Jaundice (EMR)	N				•
Well-being	The WHO-Five Well-being Index (WHO-5)[46]	W		•	•	
Diet-related quality of life	Diabetes Diet-Related Quality of Life (DDRQOL)[45]	W		•	•	
Autonomy support	Healthcare Climate Questionnaire (HCCQ)[47]	W		•	•	
Perceived competences	Perceived Competence in Diabetes Scale (PCDS)[47]	W		•	•	
Treatment satisfaction	Self-constructed questions	W			•	
Physical activity	Pregnancy Physical Activity Questionnaire (PPAQ)[48]	W		•	•	
Adherence	EMR data	W				•
Hospital costs	EMR and registry data	W, N				•
Safety	Adverse events	W			•	•

BMI, Body Mass Index; BW, body weight; EMR, electronic medical record; HbA1, haemoglobin A1c; LGA, large for gestational age; N, neonate delivered by women with GDM in the study; NICU, neonatal intensive care unit; SGA, small for gestational age; SMGB, self-monitoring of blood glucose; W, woman with GDM.

sample size estimation was based on a logistic regression model (outcome=group) and the following assumptions: an allocation ratio of 1:1; alpha=0.05; 0.8 power, an incidence of insulin therapy of 50% in the standard therapy group and 25% in the intervention group.

The sample size is estimated to be 107 women for detecting a between-group difference. However, to ensure sufficient power for the ethnic subgroup analysis, a sample size of 214 is required (table 2).

Statistical analysis

Intention-to-treat analyses will be conducted, using all available data, to compare treatment effects between the two study groups for the primary outcome, as well as all

Table 2 Sample size estimations

N total	Power all	Power ethnic subgroups
107	0.80	0.51
150	0.92	0.65
175	0.95	0.72
200	0.97	0.78
214	0.98	0.80

secondary and exploratory outcomes. Logistic regression models will be applied to analyse dichotomous outcomes, including the primary outcome. Baseline-adjusted linear mixed-effects models will be used to analyse continuous outcomes for secondary and exploratory outcomes, with participants in the control group placed at baseline for baseline correction. Generalised linear models will be applied for other outcomes, including count data. Ethnic subgroup will be included as covariate in the regression models. Non-parametric statistical tests will be used for outcomes that do not meet model assumptions even after logarithmic transformation. Results will be presented as estimated mean differences in change (95% CI) between and within groups. Minimal to no missing data is expected due to written consent from all participants to collect clinical data through their electronic medical records, where all information is automatically recorded during routine medical pregnancy visits. If participants drop out before delivery or before the final study visit (conducted by telephone), we request permission to retrieve their clinical data from their electronic medical records. In the case of missing data, multiple imputation of missing outcome data will be performed under the assumption that data are missing at random. The multiple imputation model will include the following auxiliary variables: HbA1c or 2-hour OGTT at diagnosis, gestational age at diagnosis, prepregnancy BMI, ethnicity and intervention group. If more than 10% outcome data are missing, a sensitivity analysis will be performed. For this analysis, we will impute data using a similar model as described above, except that the outcomes for participants with missing data will be assumed similar to the outcomes of participants in the control group. All participants with missing outcome data will therefore be placed in the control group during the imputation. Statistically significant findings will be determined with a significance level of $p<0.05$ (two-tailed). A more detailed Statistical Analysis Plan will be prepared and uploaded to ClinicalTrials.gov prior to the conclusion of the intervention, and the primary outcome will be evaluated by an investigator blinded to the treatment allocation.

Patient and public involvement

Prior to finalising the trial design and intervention, we conducted a comprehensive needs assessment in the Autumn 2022. The needs assessment included interviews with 20 women with GDM, comprising individuals with white and non-white ethnic backgrounds, and receiving treatment solely through diet or additionally with insulin. Furthermore, we engaged in workshops and interviews with 12 healthcare professionals, including endocrinologists, obstetricians, nurses and dietitians from the Department of Obstetrics and Gynaecology at Herlev-Gentofte University Hospital, Department of Diabetes Care at SDCC and Centre for Pregnant Women with Diabetes at Rigshospitalet. The findings based on this needs assessment underscored the requirement for ongoing training and support for women with GDM to sustain an optimal diet and engage in physical activities. Drawing on these insights and informed by existing literature, we developed various educational components tailored women with GDM including group sessions and individual consultations with a dietitian and physiotherapist, as well as physical exercise classes. These educational components underwent pilot testing in 2023, during which women with GDM were given the autonomy to select the components they preferred. This approach led to the final study design only including the educational components that women deemed important to participate in. The pilot test revealed that women predominantly prioritised individual consultations with a dietitian. Consequently, all other educational components were excluded from the final study design. Thus, the perspectives, preferences and choices of women with GDM played a pivotal role in shaping the development of the intervention and the final study design.

ETHICS, RISK OF HARM AND DISSEMINATION

The trial has received approval from the Ethics Committee of the Capital Region of Denmark (#H-23055674), adhering to the principles outlined in the Declaration of Helsinki. Protocol changes will be reported to the Ethics Committee and a new study protocol will be uploaded at Clinicaltrials.gov. Furthermore, the trial conforms to the Danish Data Protection Agency and the General Data Protection Regulation for the handling and storage of data. Only appointed researchers affiliated with SDCC will have access to the data, with the principal investigator facilitating access to source data and documents for regulatory inspections. To maintain confidentiality, all personal data will be adequately blinded during processing and publication.

No clinical measurements specific to the study will be conducted and adverse effects due to this trial are not anticipated. However, any possible harm or side-effects from this non-medical trial will be recorded. Participants are covered by the Patient Compensation Association as per the Danish Act on the Right to Complain and Receive Compensation within the Health Service.

Investigators are responsible for disseminating both positive and negative findings as well as inconclusive results. Findings will be presented at conferences and published in international peer-reviewed journals. The first draft of the manuscript based on the main study results will be authored by BE. All coauthors are expected to adhere to the Vancouver rules for publication standards.

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Contributors BE, MBB and ERM conceptualised the study. All authors (BE, ERM, HS, MBB, MJH, LK, PH, SF and TB) contributed to the study's design and content. BE, MBB and MJH collected the data and conducted all analyses. BE drafted and registered the study protocol with the Ethics Committee of the Capital Region of Denmark and at ClinicalTrials.gov, as well as wrote the first draft of the manuscript. All authors critically reviewed the manuscript for significant intellectual content and approved the final version for publication. Furthermore, all authors agree to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. BE is the guarantor for this.

Funding This work was financed by an internal grant provided by Steno Diabetes Center Copenhagen (SDCC). The investigators have no economic interest in the study results.

Competing interests Steno Diabetes Center Copenhagen (SDCC) is a hospital providing health services within the public healthcare system. The research project and SDCC are partially funded by the Novo Nordisk Foundation through unrestricted grants. The Novo Nordisk Foundation has no financial interest in the study and has no influence on the (1) study design; (2) collection, analysis and interpretation of data; (3) writing of the study report and publication and (4) decision to submit the paper for publication. The investigators have no financial, personal or professional associations that could be perceived as influencing the study. They will not benefit economically from conducting this study and have no competing interest to declare.

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

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

Provenance and peer review Not commissioned; externally peer reviewed.

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