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Flash Glucose Monitoring in gestational diabetes mellitus: study protocol for a randomised controlled trial

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Study title:

Long study title: Flash Glucose Monitoring in gestational diabetes mellitus: study protocol for a randomized controlled trial.

Short study title: FLAsh glucose Monitoring IN GestatiOnal diabetes mellitus (FLAMINGO)
Study Acronym: FLAMINGO

Key words: Gestational Diabetes Mellitus, Flash Glucose Monitoring, Hyperglycemia, Self-monitoring of Blood Glucose.

Abstract

Introduction

Gestational diabetes mellitus (GDM) is glucose intolerance occurring in 3-10% of women and being a risk factor for multiple maternal and fetal complications. The risk of perinatal complications is proportional to the level of maternal hyperglycemia. Proper glycemic control is therefore one of the key elements of GDM therapy. Until recently, determination of blood glucose concentration was performed using glucose meters, which involved multiple fingerpricks. Nowadays, due to the flash glucose monitoring (FGM) availability, it is possible to collect measurements at any time without routine puncturing. The aim of the presented study is to assess the impact of FGM on the efficacy of treatment in population of patients diagnosed with GDM.

Methods and analysis

This is a prospective, randomized study, that will recruit 100 women at 24–28 weeks of gestation at the 1st Department of Obstetrics and Gynecology, Medical University of Warsaw, Poland. Women diagnosed with GDM, who will meet the inclusion criteria, will be individually randomized to the FGM or Self Blood Glucose Monitoring (SBGM) groups. Further on, clinical and laboratory results of the mother and their newborns will be collected for analysis during the course of pregnancy. Primary outcome is mean glycemia result in each group after one month analysis. The secondary objectives will be to compare the two groups for maternal and neonatal outcomes in conjunction with long-term glycemic control using blood glycated hemoglobin (HbA1c) and fructosamine serum concentrations.

Ethics and dissemination

The study is exempt from regional ethics review due to its nature of quality improvement in patient care. The study has been approved by the Bioethics Committee at the Medical University of Warsaw and the patient privacy protection boards governing over the

recruitment sites. Results of the study will be presented in peer-reviewed journals and at conferences.

Trial registration number: NCT04422821

Strengths and limitations of this study

- FLAMINGO study (Flash glucose monitoring in gestational diabetes mellitus) is a prospective and randomized trial that will include follow-up visit after the first month of glycemia control to ascertain metabolic status in pregnant women
- FLAMINGO study will provide scientific evidence on the superiority of FGM over SBGM in glycemia control during treatment of GDM and may improve the neonatal and maternal outcomes by declining the amount of GDM complications through more efficacious glycemic control.
- FLAMINGO trial protocol adopts rigorous methodology and is written in accordance with the *Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT)*.
- In the study, we will include small groups of participants; thus, the results must be treated as preliminary.
- The study recruitment process will be performed at single obstetric department which may have an impact on patient's characteristics.

Introduction

Gestational diabetes mellitus (GDM) is glucose intolerance diagnosed for the first time in pregnancy. It affects 3-10% of pregnant women and is a risk factor for multiple maternal and fetal complications (1). During pregnancy GDM significantly increases the risk of fetal macrosomia, shoulder dystocia, birth trauma and Cesarean section (2). Furthermore, the long-term complications of GDM include increased risk of development of diabetes mellitus type 2 in the mother (3), as well as increased risk of obesity, diabetes and metabolic syndrome occurrence in their children (3); (4). It has been well-documented that the risk of above-mentioned complications increases with the level of maternal hyperglycemia (5).

Proper glycemia control is one of the key elements in the effective treatment of GDM. Until recently, glucose monitoring was solely performed using glucose meters, which required multiple fingerpricks (Self-Monitoring of Blood Glucose, SMBG). Nowadays, due to the glycemia monitoring systems development, such as flash glucose monitoring (FGM), glucose levels may be measured less invasively through subcutaneous sensor application. Apart from continuous glucose concentration measurements the system provides additional data by creating a 24-hour glycemic profile. As shown in one of the studies, FGM due to the ease of use, was 3 times more often applied as a method of glycemia control than SMBG. As a result, patients from FGM group had significantly better blood glucose control (6). Moreover, results of the IMPACT study showed that the use of FGM in patients with diabetes mellitus type 1 significantly reduced the incidence of hypoglycemia episodes (7).

The main purpose of our study is to evaluate the impact of new method of glycemia control (FGM) on the efficacy of treatment of GDM. By analyzing results of this study, such as mean glycemia levels, number of women requiring insulin therapy and maternal-fetal

perinatal outcomes we will provide a scientific basis for more common use of FGM in the population of pregnant women affected by GDM.

Methods and analysis

The study protocol was written in accordance with the Standard Protocol Items: Recommendations for Interventional Trials statement (SPIRIT).

Study design

FLAMINGO is a single-center, non-blinded, randomized, parallel-group trial with a nested qualitative evaluation and 1:1 allocation ratio. The study will be conducted at the 1st Department of Obstetrics and Gynecology, Medical University of Warsaw, Poland over a period of 2020-2021.

Study population and eligibility criteria

We aim to recruit 100 pregnant women diagnosed with GDM based on the results of 75g oral glucose tolerance test (OGTT), performed between 24-28 gestational weeks, in accordance with the criteria defined by WHO (8). Patients will be randomly divided into two groups: FGM - study group comprising 50 women who will receive subcutaneous sensor for glucose monitoring, and SBGM - control group comprising 50 women who will monitor glycemia through use of standard glucose meter.

Inclusion criteria

Women aged 18 years or older, in singleton pregnancy, diagnosed with GDM will be invited to participate in the study.

Exclusion criteria

Multiple pregnancy, fetal malformations, pre-gestational diabetes mellitus, chronic or pregnancy-induced hypertension, chronic renal or hepatic disease, in-vitro fertilization, delivery <37 weeks of gestation, pre-mature rupture of membranes, placenta previa, stillbirth, smoking in pregnancy, intake of medications including: methyldopa, tetracyclin, acetylosalicylic acid, acetaminofen, ibuprofen, L-dopa, tolazamide, tolbutamide will constitute study exclusion criteria.

All women eligible for the study will provide written informed consent prior to enrollment.

Aim of the study and objectives

The aim of the FLAMINGO trial is to assess the impact of FGM on the efficacy of treatment of GDM. Our primary outcome is mean glycemia results (fasting and 1-h postprandial glucose concentrations) in each group (FGM/SMBG) during the first month following GDM diagnosis. The secondary objectives will be to compare the two groups for the number of patients requiring insulin therapy, as well as to assess long-term glycemic control using blood glycated hemoglobin (HbA1c) and fructosamine serum concentrations. We also aim to compare both groups with respect to maternal-fetal perinatal outcomes, including pregnancy weight gain, fetal birth-weight and neonatal glycemia.

Participant selection and recruitment

Pregnant women diagnosed with GDM who will meet study inclusion criteria will be invited to participate in the project (see Figure 1). Recruitment will begin in September 2020 and is estimated to end in October 2021.

Recruitment brochures that contain general information of the study will be placed at the website of the Department. During the recruitment process, trial research staff (AM, PS) will inform potential candidates about the study both verbally and with written information. Women who are agreeable to participate will be obliged to provide written informed consent. Those patients who decline to participate will continue to receive their routine antenatal care. Obstetric care provided to each pregnant woman will not be affected nor influenced by the woman's decision to either participate or not participate in the study.

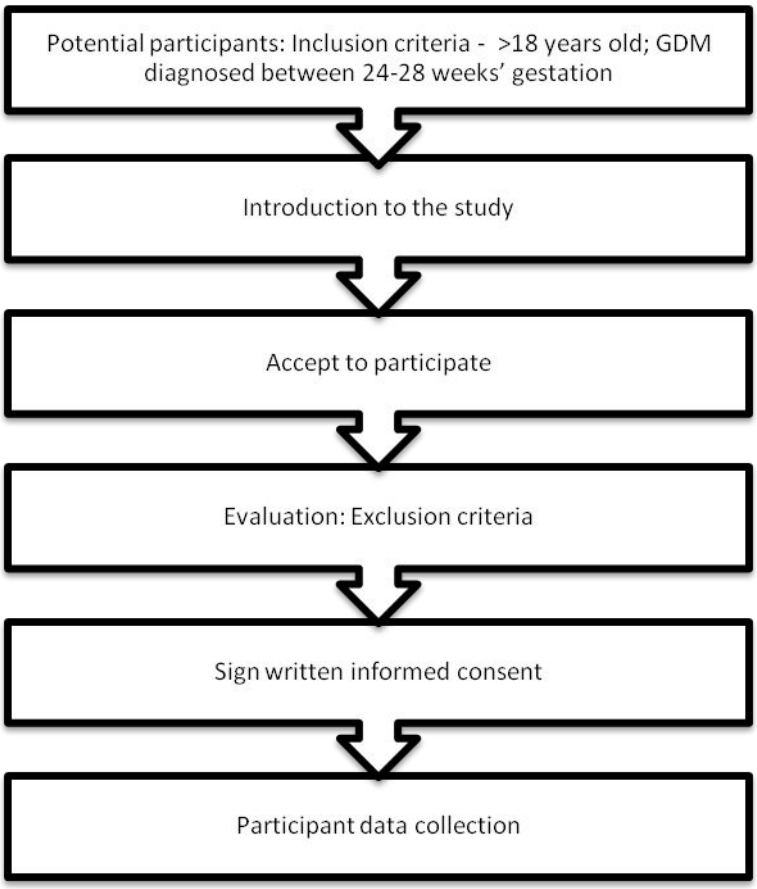

Figure 1 Patient flow scheme

Randomization

Simple randomization with the computer-generated list and sealed envelopes will be used for patient's randomization process. The process of randomization and sealing will be conducted at the 1 st Department of Obstetrics and Gynecology, Medical University of Warsaw by the non-member of the trial research staff.

Blinding

This is a non-blinded trial. As the device used for glycemia monitoring (FGM/SBGM) will be clearly visible to both participants and trial research staff blinding is not feasible for patients and researchers.

Study procedures

Patients included in the study will undergo five visits comprising one recruitment and four follow-up visits (see Figure 2).

Recruitment visit (Visit 1)

At the recruitment visit (24-28 weeks of gestation), after providing the informed consent, patients will be interviewed for sociodemographic data and past medical history to analyze study exclusion criteria. Next, if eligible for the study, participants will be randomly divided into two consecutive groups. Simple randomization with the computer-generated list and sealed envelopes will be used for patient's randomization process. Study group (FGM) will comprise 50 women who will receive subcutaneous sensor for glucose monitoring (FreeStyle Libre™; Abbott Diabetes Care, Alameda, CA), and the control group (SMBG) will comprise 50 women who will monitor glycemia through use of standard glucose meter (iXell®; Genexo sp; Warsaw, Poland). All patients from the study group will obtain instruction for using Freestyle Libre app to measure and collect glycemia results using a mobile phone. Accordingly, control group will be informed about proper use of glucose meters.

In order to assess daily physical activity all participants will obtain a wristband (Xiaomi Mi Band 4; Xiaomi Corporation, Hong Kong) allowing for footsteps measurement. According to Guidelines for Physical Activity During Pregnancy the minimum recommended amount of footsteps is 10.000 per day (9). All patients included in the study will obtain the instruction for using the wristband and its mobile app, together with recommendations about daily physical activity in pregnancy.

After meeting study inclusion criteria patient will obtain diet recommendations for GDM prepared by clinical dietician. To evaluate participants' dietary habits, we will use Eating Assessment Test prepared by the Polish National Institute of Public Health – National Institute of Hygiene. This is a short questionnaire (20 items for diet) intended to evaluate dietary habits in patients diagnosed with GDM. Based on the summary points obtained from the test patients will be assigned to one of the four diet groups (good/ satisfactory/ demanding diet modification/ not satisfactory).

According to Polish Society of Obstetricians and Gynecologists (PSOG) recommendations all participants will be obliged to measure fasting and 1-h postprandial glucose concentrations in a daily manner, together with once per week midnight measurement (10). Postprandial glucose measurements will be performed after three main meals (breakfast, dinner, supper) as well as after three additional meals. At the end of the visit, all participants will undergo blood tests (HbA1c, fructosamine) and selected biometric maternal-fetal parameters will be measured (patient weight, ultrasound estimated fetal weight).

Visit 2 (14 days after the recruitment)

At the second follow-up visit glycemia levels, diet control and physical activity will be analyzed. Based on glycemia results participants will obtain modified diet recommendations and will be qualified to insulin therapy if required. According to PSOG standards for management of GDM fasting glucose level <90mg/dl and 1-h postprandial glucose level <140mg/dl are indicative of proper glycemic control (10). The study group will obtain new FGM sensor. At the end of the visit, research staff will collect biometric measurements from all patients included in the study (the same as during Visit 1).

Visit 3 (28 days after the recruitment)

At the third visit glycemia levels, diet control and physical activity will be analyzed. Based on glycemia results participants will obtain modified diet recommendations and will be qualified to insulin therapy if required. In patients already treated with insulin, dosage will be modified according to glycemia results. The study group will obtain glucose meter. All patients will end physical activity control with a wristband. Eating Assessment Test will be performed to test whether dietary recommendations and glycemia control in the study have an impact on eating habits of the participants. At the end of the visit, all participants will undergo blood tests (HbA1c, fructosamine) and selected biometric parameters will be measured.

Visit 4 (34-36 gestational weeks)

At the fourth visit glycemia levels, diet control and insulin therapy will be analyzed. Based on glycemia results participants will obtain modified diet recommendations and will be qualified to insulin therapy if required. In patients already treated with insulin, dosage will be modified according to glycemia results. Eating Assessment Test will be performed to test whether dietary recommendations and glycemia control in the study have an impact on eating habits of the participants. Additionally, research staff will collect selected biometric measurements from all patients included in the study. At the end of the visit, all participants will undergo blood tests (HbA1c, fructosamine).

Visit 5 (after delivery)

24-72 hours after the delivery, research staff will retrieve maternal and neonatal outcomes from patients medical history.

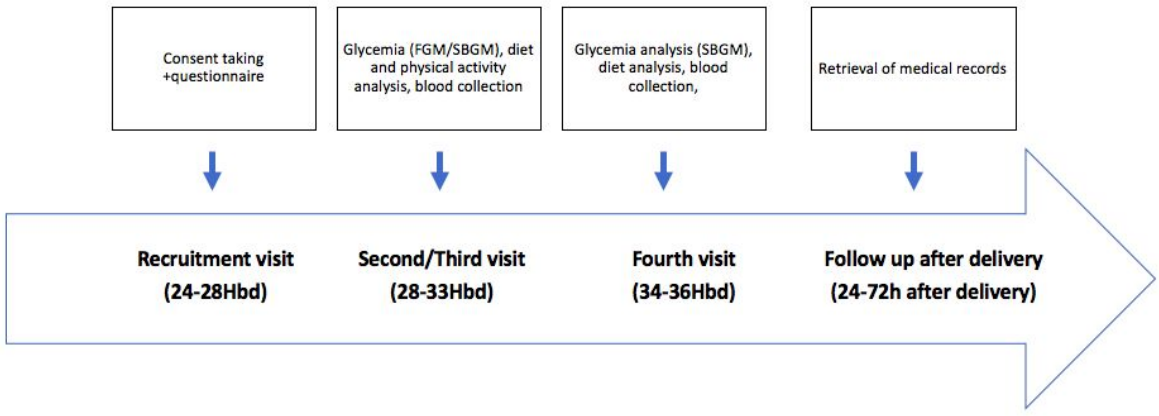

Figure 2. The flow diagram of the study

Study outcome

The primary outcome will be mean glycemia results (fasting and 1-h postprandial glucose concentrations) in each group (FGM/SBGM) during the first month following the diagnosis of GDM.

The secondary objectives will be to compare both groups for:

- Number of patients requiring insulin therapy (2, 4 and 8 weeks after the recruitment visit)

- Long-term glycemic control using blood HbA1c concentrations (2, 4 and 8 weeks after the recruitment visit)
- Long-term glycemic control using fructosamine serum concentrations (2, 4 and 8 weeks after the recruitment visit)
- Number of hypoglycemia episodes (glucose concentration <70 mg/dl) during one month analysis (episodes per day in 0-4 weeks after the recruitment visit)
- Physical activity during one month analysis based on a footsteps daily count (0-4 weeks after the recruitment visit)
- Compliance with diet recommendations according to Eating Assessment Test (2, 4 and 8 weeks after the recruitment visit)
- Gestational weight gain (2, 4 and 8 weeks after the recruitment visit)
- Mode of delivery (rate of vaginal delivery/ Cesarean section)
- Fetal birth-weight
- Neonatal glycemia

Sample size calculation and statistical analysis

The performed power analysis (power of 80%, a significance level of 5%, two-sided) estimated a required sample size of 76 patients (38 patients in each group). The analysis was based on the results of the IMPACT Study, and assuming an expected 38% decrease in the time spent in hypoglycemia in patients using FGM compared to patients using SMBG (6). Considering potential exclusions and losses during follow-up, we decided to recruit a total of number of 100 patients in the study.

Continuous data will be compared using the Mann-Whitney U test, and for categorical variables the chi square test will be applied. The results will be presented as medians and inter-quartile ranges (IQR), or as a frequency (%). For within-group comparisons, the Wilcoxon test for paired differences will be used. The relationship between glucose, HbA1c and fructosamine concentrations, and selected maternal-fetal parameters will be examined with the use of Pearson's correlation coefficient. Multivariable logistic regression analysis will be performed to evaluate the potential impact of selected predictors on primary outcomes. All tests will be carried out at a significance level of 0.05.

Patient and public involvement

Patients and the public will not be involved in the process of the design, conduct, reporting or dissemination plans of the study. All participants will be informed about the trial results at the end of the study.

Ethics and dissemination

The study is exempt from regional ethics review due to its nature of quality improvement in patient care. The study has been approved by the Bioethics Committee at the Medical University of Warsaw and the patient privacy protection boards governing over the recruitment sites. All data sets will be password protected and only available to project investigators. Results of the study will be presented in peer-reviewed journals and at conferences.

Discussion

According to epidemiological data GDM affects about 5.4 % of pregnant women in Europe and the prevalence is continuously increasing (11). As a result, there is an urgent need to search for the new methods of effective glucose monitoring facilitating glycemia control, and thus, allowing for a decrease in the rate of maternal and fetal complications.

Flash glucose monitoring is a new method, that is already commonly used in pediatric patients diagnosed with diabetes mellitus type 1 (7). As one multicentre study demonstrated, due to easiness of FGM use, patients measured glycemia 3 times more often per day in comparison with those using standard glucose meters. Consequently, patients significantly improved their diurnal glucose profile (6). In addition, the results of IMPACT study proved that use of FGM among type 1 diabetic patients is effective in reduction of hypoglycemia episodes (7). Finally, in the study by Dunn C T et al. a positive correlation between the number of scans per day and HbA1c levels was found, showing a significant decrease in HbA1c concentration among patients who monitored glycemia more frequently (12).

To conclude, although limited in number, available studies suggest that use of FGM may help to improve monitoring and treatment results in patients affected by glucose tolerance disorders during pregnancy. Based on that, we would like to investigate the impact of FGM on maternal and neonatal outcomes in population of patients diagnosed with gestational diabetes mellitus.

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Footnotes

Contributors AM is the principal investigator and has coordinated trial design and drafting of the protocol. PS and DBO revised and supervised the trial design and protocol. All the authors have read and approved the final version of the manuscript.
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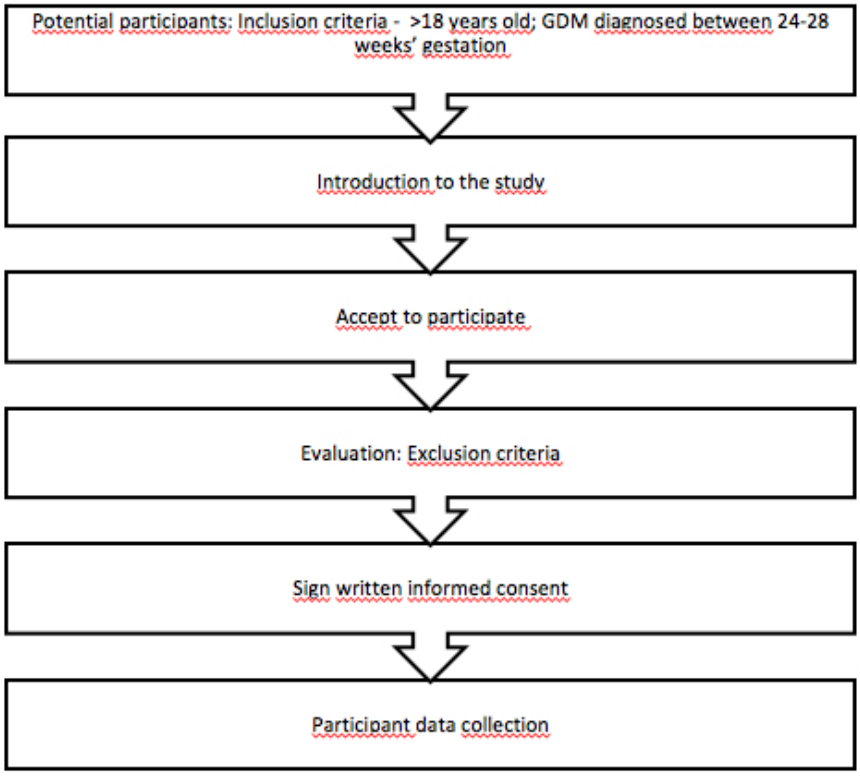
Competing interests None declared.
Ethics approval – The Bioethics Committee at the Medical University of Warsaw; Approval Number: KB/50/2020
Provenance and peer review Not commissioned; externally peer reviewed.



Patient flow scheme

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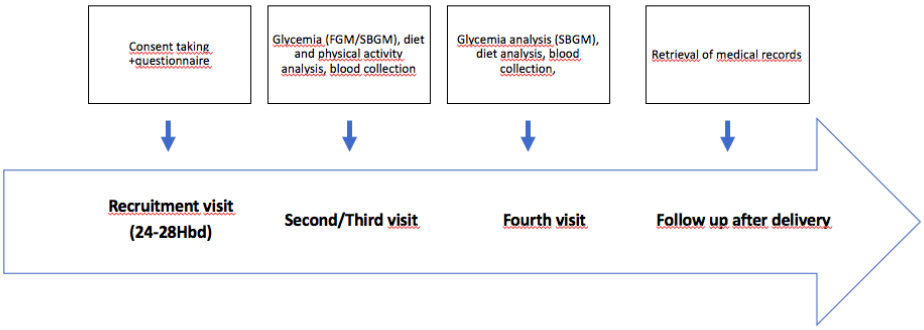

The flow diagram of the study

349x159mm (72 x 72 DPI)

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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In your methods section, say that you used the SPIRITreporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, Hróbjartsson A, Mann H, Dickersin K, Berlin J, Doré C, Parulekar W, Summerskill W, Groves T, Schulz K, Sox H, Rockhold FW, Rennie D, Moher D. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. Ann Intern Med. 2013;158(3):200-207

		Reporting Item	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	2
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	2
Protocol version	#3	Date and version identifier	1
Funding	#4	Sources and types of financial, material, and other support	9
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1, 9

Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	n/a
Roles and responsibilities: sponsor and funder	#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
Roles and responsibilities: committees	#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)	n/a
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	2
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	2
Objectives	#7	Specific objectives or hypotheses	3
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, non-inferiority, exploratory)	2
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	3

		obtained	
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)	3
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	4-6
Interventions: modifications	#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)	5-6
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	n/a
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	n/a
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	6-7
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)	6
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
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	3-4

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	4
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	4
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	4
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	n/a
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	n/a
Methods: Data collection, management, and analysis			
Data collection plan	#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	6

		protocol	
Data collection plan: retention	#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	n/a
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	7
Statistics: outcomes	#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	7
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	7
Statistics: analysis population and missing data	#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)	n/a
Methods: Monitoring			
Data monitoring: formal committee	#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	n/a
Data monitoring: interim analysis	#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	n/a
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	n/a
Auditing	#23	Frequency and procedures for auditing trial conduct, if	n/a

		any, and whether the process will be independent from investigators and the sponsor	
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	9
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)	n/a
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	n/a
Consent or assent: ancillary studies	#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	7
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	9
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	n/a
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: trial results	#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	7
Dissemination policy:	#31b	Authorship eligibility guidelines and any intended use of	7

authorship		professional writers	
Dissemination policy: reproducible research	#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

BMJ Open

Flash Glucose Monitoring in gestational diabetes mellitus: study protocol for a randomised controlled trial

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Abstract

Introduction

Gestational diabetes mellitus (GDM) is a glucose intolerance occurring in 3-10% of pregnant women and being a risk factor for multiple maternal and fetal complications. The risk of perinatal complications is proportional to the level of maternal hyperglycemia. Proper glycemic control is therefore one of the key elements of GDM therapy. Until recently, determination of blood glucose concentration was performed using glucose meters, which involved multiple fingerpricks. Nowadays, due to the flash glucose monitoring (FGM) availability, it is possible to collect measurements at any time without routine puncturing. The aim of the presented study is to assess the impact of FGM on the efficacy of treatment in population of patients diagnosed with GDM.

Methods and analysis

This is a prospective, randomized study, that will recruit 100 women at 24–28 weeks of gestation at the 1st Department of Obstetrics and Gynecology, Medical University of Warsaw, Poland. Women diagnosed with GDM, who will meet the inclusion criteria, will be individually randomized to the FGM or self-monitoring of blood glucose (SMBG) groups. Further on, clinical and laboratory results of the mother and their newborns will be collected for analysis during the course of pregnancy. Primary outcome is mean glycemia result in each group after one month analysis and percentage of results in the target glycemic range. The secondary objectives will be to compare the two groups for maternal and neonatal outcomes in conjunction with long-term glycemic control using blood glycated hemoglobin (HbA1c) and fructosamine serum concentrations.

Ethics and dissemination

The study is exempt from regional ethics review due to its nature of quality improvement in patient care. The study has been approved by the Bioethics Committee at the Medical

University of Warsaw and the patient privacy protection boards governing over the recruitment sites. Results of the study will be presented in peer-reviewed journals and at conferences.

Trial registration number: NCT04422821

Strengths and limitations of this study

- FLAMINGO study (Flash glucose monitoring in gestational diabetes mellitus) is a prospective, open-label and randomized trial
- FLAMINGO study will provide scientific evidence on the superiority of FGM over SMBG in glycemia control in GDM-complicated pregnancies.
- FLAMINGO trial protocol adopts rigorous methodology and is written in accordance with the *Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT)*.
- In the study, we will include small groups of participants at a single obstetric department, and thus the results must be treated as preliminary.
- To reduce costs FGM device will be applied only for the one third of the trial which might have an impact on the results of the study.

Introduction

Gestational diabetes mellitus (GDM) is a glucose intolerance diagnosed for the first time in pregnancy. It affects 3-10% of pregnant women and is a risk factor for multiple maternal and fetal complications (1). During pregnancy GDM significantly increases the risk of fetal macrosomia, shoulder dystocia, birth trauma and Cesarean section (2). Furthermore, the long-term complications of GDM include increased risk of development of diabetes mellitus type 2 in the mother (3), as well as increased risk of obesity, diabetes and metabolic syndrome occurrence in their children (3); (4). It has been well-documented that the risk of above-mentioned complications increases with the level of maternal hyperglycemia (5).

Proper glycemia control is one of the key elements in the effective treatment of GDM. Until recently, glucose monitoring was solely performed using glucose meters, which required multiple fingerpricks (Self-Monitoring of Blood Glucose, SMBG). Nowadays, due to the glycemia monitoring systems development, such as flash glucose monitoring (FGM), glucose levels may be measured less invasively through subcutaneous sensor application. FGM is a factory-calibrated sensor measuring glucose concentrations in the interstitial fluid. Although it represents different measurement technique than SMBG, previous studies have shown, that glycemia levels obtained by both methods are comparable (6); (7). Apart from continuous glucose concentration measurements the system provides additional data by creating a 24-hour glycemic profile. In comparison, SMBG provides only single, intermittent measurements, that limits detection of glycemic variability or nocturnal hypoglycaemic events (6). As shown in one of the studies, FGM due to the ease of use, was 3 times more often applied as a method of glycemia control than SMBG. As a result, patients from FGM group had significantly better blood glucose control (7). In the study by Bühling et al. continuous glucose monitoring had overall better sensitivity in detecting abnormal glucose levels (8). Furthermore, results of the IMPACT study demonstrated that the use of FGM in

patients with diabetes mellitus type 1 significantly reduced the incidence of hypoglycemia episodes(7) . Although hyperglycemia is the most common alteration occurring in GDM patients, there is also an increased risk of masked hypoglycemia. It was showed that almost one third of GDM patients experienced hypoglycemic events during the course pregnancy that could have been easily detected using methods for continuous glycemia control (9). Diagnosis of these hypoglycemic episodes may be of particular importance in GDM patients before qualifying to insulin therapy.

The main purpose of our study is to evaluate the impact of a new method of glycemia control (FGM) on the efficacy of treatment of GDM. Assuming, that the first month after diagnosis of GDM is essential for the proper implementation of dietary and physical activity recommendations by the patients, the favorable cost-effective strategy will be to apply FGM device only during that period of pregnancy. By analyzing results of this study, such as fasting and postprandial glycemia levels, number of nocturnal hypoglycemic episodes, number of women requiring insulin therapy, daily dosage of insulin and maternal-fetal perinatal outcomes, we will provide a scientific basis for more common use of FGM in the population of pregnant women affected by GDM.

Methods and analysis

The study protocol was written in accordance with the Standard Protocol Items: Recommendations for Interventional Trials statement (SPIRIT).

Study design

FLAMINGO is a single-center, non-blinded, randomized, crossover study with a nested qualitative evaluation and 1:1 allocation ratio. The study will be conducted at the 1st Department of Obstetrics and Gynecology, Medical University of Warsaw, Poland over a period of 2020-2021.

Study population and eligibility criteria

We aim to recruit 100 pregnant women diagnosed with GDM based on the results of 75g oral glucose tolerance test (OGTT), performed between 24-28 gestational weeks, in accordance with the universal criteria defined by World Health Organization (10). Patients will be randomly divided into two groups: FGM - study group comprising 50 women who will receive subcutaneous sensor for glucose monitoring, and SMBG - control group comprising 50 women who will monitor glycemia through use of standard glucose meter.

Inclusion criteria

Women aged 18 years or older, in singleton pregnancy, diagnosed with GDM will be invited to participate in the study.

Exclusion criteria

Multiple pregnancy, fetal malformations, pre-gestational diabetes mellitus (overt diabetes in pregnancy), chronic or pregnancy-induced hypertension, chronic renal or hepatic disease diagnosed prior to study entry, in-vitro fertilization, pre-mature rupture of membranes, placenta previa, smoking in pregnancy, intake of medications including: methyldopa, tetracyclin, acetylosalicylic acid, acetaminofen, ibuprofen, L-dopa, tolazamide, tolbutamide will constitute study exclusion criteria.

All women eligible for the study will provide written informed consent prior to enrollment.

Aim of the study and objectives

The aim of the FLAMINGO trial is to assess the impact of FGM on the efficacy of treatment of GDM. Our primary outcome is mean glycemia results (fasting and 1-h postprandial glucose concentrations) in each group (FGM/SMBG) during the first month following GDM diagnosis in conjuction with the percentage of results in the target glycemic range. The secondary objectives will be to compare the two groups for the number of patients requiring insulin therapy, dosage of insulin, number of hypoglycemic episodes, as well as to compare blood glycated hemoglobin (HbA1c) and fructosamine serum concentrations as potential markers of long-term glycemic control and predictors of perinatal complications, based on previous studies (11); (12). Simultaneously, we aim to compare patient's physical activity level based on a daily steps number counted by a wristband and to assess compliance with diet recommendations using Eating Assessment Test. Finally, we aim to compare both groups with respect to maternal-fetal perinatal outcomes, including pregnancy weight gain, fetal birth-weight and neonatal glycemia.

Participant selection and recruitment

Pregnant women diagnosed with GDM by the trial research staff (AM, PS) who will meet study inclusion criteria will be invited to participate in the project (see Figure 1). Recruitment will begin in September 2020 and is estimated to end in October 2021.

Recruitment brochures that contain general information of the study will be placed at the website of the Department. During the recruitment process, trial research staff (AM, PS) will inform potential candidates about the study both verbally and with written information. Women who are agreeable to participate will be obliged to provide written informed consent. Those patients who decline to participate will continue to receive their routine antenatal care. Obstetric care provided to each pregnant woman will not be affected nor influenced by the woman's decision to either participate or not participate in the study.

Randomization

Simple randomization with the computer-generated list and sealed envelopes will be used for patient's randomization process. The process of randomization and sealing will be conducted at the 1 st Department of Obstetrics and Gynecology, Medical University of Warsaw by the non-member of the trial research staff.

Blinding

This is a non-blinded trial. As the device used for glycemia monitoring (FGM/SMBG) will be clearly visible to both participants and trial research staff blinding is not feasible for patients and researchers.

Study procedures

Patients included in the study will undergo five visits comprising one recruitment and four follow-up visits (see Figure 2). The trial research staff (AM, PS) will be responsible for analyzing participants glycemia results, diet control and physical activity as well as for the modifications of health interventions during the follow-up visits.

Recruitment visit (Visit 1)

At the recruitment visit (24-28 weeks of gestation), after providing the informed consent, patients will be interviewed for sociodemographic data and past medical history to analyze study exclusion criteria. Next, if eligible for the study, participants will be randomly divided into two consecutive groups. Simple randomization with the computer-generated list and sealed envelopes will be used for patient's randomization process. Study group (FGM) will comprise 50 women who will receive subcutaneous sensor for glucose monitoring (FreeStyle Libre™; Abbott Diabetes Care, Alameda, CA), and the control group (SMBG) will comprise 50 women who will monitor glycemia through use of standard glucose meter (iXell®; Genexo sp; Warsaw, Poland; ISO 15197:2015). All patients from the study group will obtain instruction for using Freestyle Libre app to measure and collect glycemia results using a mobile phone. Patients without mobile phone will obtain Freestyle Libre Reader and instructions for using the device. Accordingly, control group will be informed about proper use of glucose meters. The results from FGM and SMBG will be collected during the follow up visits.

In order to assess daily physical activity all participants will obtain a wristband (Xiaomi Mi Band 4; Xiaomi Corporation, Hong Kong) allowing for footsteps measurement. According to Polish Society of Obstetricians and Gynecologists (PSOG) the recommended number of footsteps in pregnancy is 10.000 per day(13). As previously demonstrated mild physical activity, such as walking has protective effect on excessive gestational weight gain and decreases the risk of preterm birth and fetal macrosomia (14-17).
All patients included in the study will obtain the instruction for using the wristband and its mobile app, together with recommendations about daily physical activity in pregnancy.

After meeting study inclusion criteria patient will obtain diet recommendations for GDM prepared by clinical dietician. To evaluate participants' dietary habits, we will use Eating Assessment Test prepared by the Polish National Institute of Public Health – National Institute of Hygiene. This is a short questionnaire (20 items for diet) intended to evaluate dietary habits in patients diagnosed with GDM. The summary points base on a number of meals per day, length of breaks between meals, daily portions of fruits and vegetables, frequency of fried food and sweets consumption per week (questionnaire and list of points for each element provided in Supplementary files). The maximum test result is 42 points, the minimum 4 points. Based on the points obtained patients will be assigned to one of the four diet groups (good: 39-42, satisfactory: 30-38, demanding diet modification 12-29, and not satisfactory < 12 points).

According to PSOG recommendations all participants will be obliged to measure fasting and 1-h postprandial glucose concentrations in a daily manner, together with once per week midnight measurement (18). Postprandial glucose measurements will be performed after three main meals (breakfast, dinner, supper). To avoid excessive data collection, we do not aim to analyze all the results obtained with the FGM. At the end of the visit, all participants will undergo blood tests (HbA1c, fructosamine) and selected biometric maternal-fetal parameters will be measured (patient weight, ultrasound estimated fetal weight).

Visit 2 (14 days after the recruitment)

At the second follow-up visit glycemia levels, diet control and physical activity will be analyzed. Based on glycemia results participants will obtain modified diet recommendations and will be qualified to insulin therapy, if required (fasting blood glucose concentrations above 90 mg/dL or postprandial glycemia results above 140 mg/dl). Initial predetermined

insulin dose planned for the study is four units for long-acting insulin and three units per meal for short-acting insulin. The final insulin dosage will be individualized based on the glycemic results during the follow-up visits (19). According to PSOG standards for management of GDM fasting glucose level <90mg/dl and 1-h postprandial glucose level <140mg/dl are indicative of proper glycemic control (18). The study group will obtain new FGM sensor. At the end of the visit, research staff will collect biometric measurements from all patients included in the study (the same as during Visit 1).

According to the criteria proposed by Tudor-Locke we will divide patients into four groups of physical activity based on a number of daily steps collected by the wristband: sedentary (< 5000 daily steps), low active (5000~7500 daily steps), somewhat active (7500~10000 daily steps) and active (≥ 10000 daily steps)(20).

Visit 3 (28 days after the recruitment)

At the third visit glycemia levels, diet control and physical activity will be analyzed. Based on glycemia results participants will obtain modified diet recommendations and will be qualified to insulin therapy if required. In patients already treated with insulin, dosage will be modified according to glycemia results. The study group will obtain glucose meter. All patients will end physical activity control with a wristband. Eating Assessment Test will be performed to test whether dietary recommendations and glycemia control in the study have an impact on eating habits of the participants. At the end of the visit, all participants will undergo blood tests (HbA1c, fructosamine) and selected biometric parameters will be measured.

Visit 4 (34-36 gestational weeks)

At the fourth visit glycemia levels, diet control and insulin therapy will be analyzed. Based on glycemia results participants will obtain modified diet recommendations and will be qualified to insulin therapy, if required. In patients already treated with insulin, dosage will be modified according to glycemia results. Eating Assessment Test will be performed to test whether dietary recommendations and glycemia control in the study have an impact on eating habits of the participants. Additionally, research staff will collect selected biometric measurements from all patients included in the study. At the end of the visit, all participants will undergo blood tests (HbA1c, fructosamine).

Visit 5 (after delivery)

24-72 hours after the delivery, research staff will retrieve maternal and neonatal outcomes from patient's medical history.

Study outcome

The primary outcome will be mean glycemia results (fasting and 1-h postprandial glucose concentrations) in each group (FGM/SMBG) during the first month following the diagnosis of GDM and the percentage of results in the target glycemic range.
The secondary objectives will be to compare both groups for:

- Number of patients requiring insulin therapy (2, 4 and 8 weeks after the recruitment visit)
- Dosage of insulin (2, 4 and 8 weeks after the recruitment visit)

- Long-term glycemic control using blood HbA1c concentrations (2, 4 and 8 weeks after the recruitment visit)
- Long-term glycemic control using fructosamine serum concentrations (2, 4 and 8 weeks after the recruitment visit)
- Number of hypoglycemic episodes (glucose concentration <70 mg/dl) during one month analysis (episodes per day in 0-4 weeks after the recruitment visit)
- Physical activity during one month analysis based on a footsteps daily count (0-4 weeks after the recruitment visit)
- Compliance with diet recommendations according to Eating Assessment Test (2, 4 and 8 weeks after the recruitment visit)
- Gestational weight gain (2, 4 and 8 weeks after the recruitment visit)
- Mode of delivery (rate of vaginal delivery/ Cesarean section)
- Fetal birth-weight
- Neonatal glycemia

Sample size calculation and statistical analysis

The performed power analysis (power of 80%, significance level of 5%, two-sided) estimated a required sample size of a total of 80 patients (40 patients in each group). The analysis was based on the results of a previous report comparing FGM with SMBG and estimation to detect a difference in the percentage of results in the target glycemic range between study and control groups (21). Sample size is further increased to 100 patients to account for a potential exclusions and drop out of approximately 10%. l

Continuous data will be compared using the Mann-Whitney U test, and for categorical variables the chi square test will be applied. The results will be presented as medians and inter-quartile ranges (IQR), or as a frequency (%). For within-group comparisons, Bland Altman, Passing-Bablok and Deming regression analysis will be performed. The relationship between glucose, HbA1c and fructosamine concentrations, and selected maternal-fetal parameters will be examined with the use of Pearson's correlation coefficient. Multivariable logistic regression analysis will be performed to evaluate the potential impact of selected predictors on primary outcomes. All tests will be carried out at a significance level of 0.05. Statistical analyses will be performed using SAS software, version 9.2 or later (SAS Institute, Cary, NC).

Patient and public involvement

Patients and the manufacturers (Abbott Diabetes Care, Genexo sp, Xiaomi Corporation) will not be involved in the process of the design, conduct, reporting or dissemination plans of the study. All participants will be informed about the trial results at the end of the study.

Trial monitoring and management

Patient retention strategy:

Patients recruited to the study will obtain an email with the schedule of the follow up visits. They will also obtain regular phone contact before each visit.

Strategies for the management of missing data:

For missing glycemic data, in particular in the SMBG group mean glycemia levels from the past 5 days will be calculated, in accordance with the time of measurement (fasting, postprandial).

Ethics and dissemination

The study is exempt from regional ethics review due to its nature of quality improvement in patient care. The study has been approved by the Bioethics Committee at the Medical University of Warsaw and the patient privacy protection boards governing over the recruitment sites. All data sets will be password protected and only available to project investigators. Results of the study will be presented in peer-reviewed journals and at conferences.

Discussion

According to epidemiological data GDM affects about 5.4 % of pregnant women in Europe and the prevalence is continuously increasing (22). As a result, there is an urgent need to search for the new methods of effective glucose monitoring facilitating glycemia control, and thus allowing for a decrease in the rate of maternal and fetal complications.

Flash glucose monitoring is a new method, that is already commonly used in pediatric patients diagnosed with diabetes mellitus type 1 (23). As one multicentre study demonstrated, due to easiness of FGM use, patients measured glycemia 3 times more often per day in comparison with those using standard glucose meters. Consequently, patients significantly improved their diurnal glucose profile (7). In addition, the results of IMPACT study proved that use of FGM among type 1 diabetic patients is effective in reduction of hypoglycemia episodes (23). Finally, in the study by Dunn C T et al. a positive correlation between the number of scans per day and HbA1c levels was found, showing a significant decrease in HbA1c concentration among patients who monitored glycemia more frequently (24).

Apart from the relatively small group of participants, the presented single-centre study is limited by the fact that FGM will be applied only for one month following the GDM diagnosis. Nonetheless, we believe that these first four weeks after the recruitment are of crucial importance for proper implementation of dietary and physical activity recommendations by the patients (25). Moreover, if primary objectives are accomplished proposed strategy may significantly reduce costs of FGM application.

To conclude, although limited in number, available studies suggest that use of FGM may help to improve monitoring and treatment results in patients affected by glucose tolerance disorders during pregnancy. Based on that, we would like to investigate the impact of FGM on maternal and neonatal outcomes in population of patients diagnosed with gestational diabetes mellitus.

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Footnotes

Contributors AM is the principal investigator and coordinated trial design, drafting and critically revising of the protocol. PS and DBO were involved in drafting the manuscript for publication. AM and PS developed the statistical design and sample size estimation. PS, DBO and MW critically revised and supervised the trial design and protocol. DBO and MW contributed to the ethical and regulatory aspects of the research. All the authors have read and approved the final version of the manuscript.
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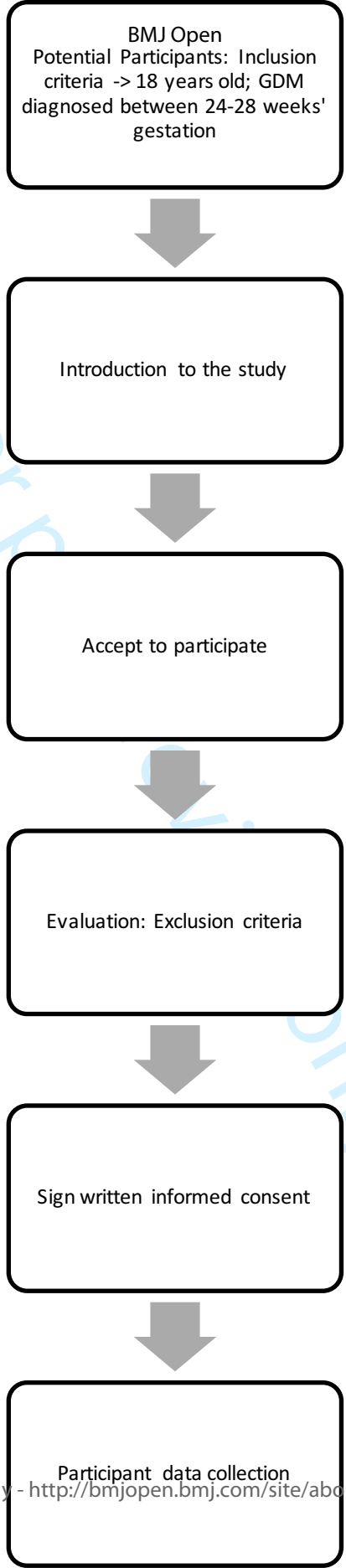
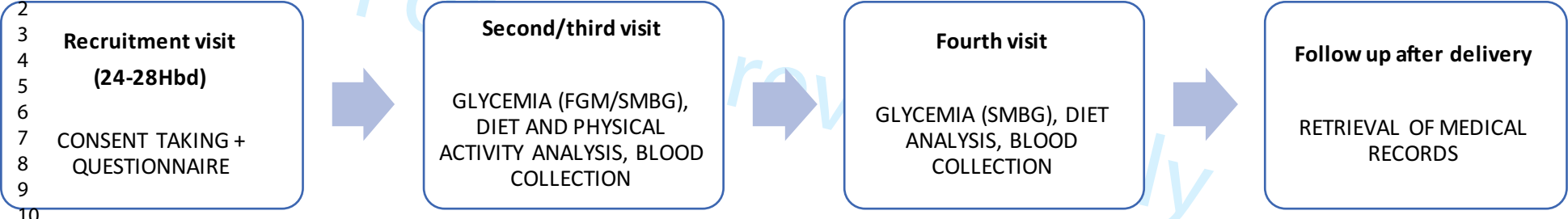
Provenance and peer review Not commissioned; externally peer reviewed.
Data availability statement Data are available on reasonable request.

Figure Legend:

Figure 1 Patient flow scheme.
Figure 2. The flow diagram of the study.





Kwestionariusz oceny jakościowej jadłospisów pacjentek z cukrzycą ciążową

Lp.	Wyróżnik	Punkty
1.	**Liczba posiłków**	
	I Śniadanie	1
	II Śniadanie	1
	Obiad	1
	Podwieczorek	1
	Kolacja	1
	II Kolacja	1
2.	**Przerwa między posiłkami w ciągu dnia**	
	do 3 godz.	2
	do 4 godz.	1
	powyżej 4 godz.	0
3.	**Przerwa nocna**	
	do 10 godz.	1
	powyżej 10 godz.	0
4.	**Uwzględnienie wody do picia w ilości co najmniej 2-2,5 l/dzień**	
	Tak	1
	Nie	0
5.	**Ilość warzyw spożywana w ciagu dnia**	
	5 porcji	5
	4 porcje	4
	3 porcje	3
	2 porcje	2
	1 porcja	1
	w żadnym posiłku	0
6.	**Ilość owoców spożywana w ciągu dnia**	
	2 porcje	2
	1 porcja	1
	w żadnym posiłku	0
7.	**Uwzględnienie porcji surowych warzyw i/lub owoców**	
	przynajmniej w 2 posiłkach	2
	przynajmniej w 1 posiłku	1
	w żadnym posiłku	0
8.	**Różnorodność warzyw i/lub owoców w jadłospisach**	
	Tak	1
	Nie	0
9.	**Produkty zbożowe z pełnego przemiału**	
	przynajmniej w 3 posiłkach	3
	w 2 posiłkach	2
	w 1 posiłku	1

	w żadnym posiłku	0
10.	**Różnorodność produktów węglowodanowych w jadłospisach**	
	Tak	1
	Nie	0
11.	**Mleko i przetwory mleczne w tym napoje fermentowane**	
	≥ 3w posiłkach	3
	w 2 posiłkach	2
	w 1 posiłku	1
12.	**Białko pełnowartościowe (zwierzęce lub strączkowe) w głównych posiłkach**	
	w 3 posiłkach	3
	w 2 posiłkach	2
	w 1 posiłku	1
	w żadnym posiłku	0
13.	**Nasiona roslin strączkowych**	
	6x na 2 tygodnie	2
	4x na 2 tygodnie	1
	< 2 x na 2 tygodnie	0
14.	**Ryby i/lub przetwory rybne**	
	6x na 2 tygodnie	2
	4x na 2 tygodnie	1
	< 2 x na 2 tygodnie	0
15.	**Różnorodność gatunkowa mięs i przetworów mięsnych w jadłospisach**	
	Tak	1
	Nie	0
16.	**Przekąski między posiłkami**	
	warzywa/orzechy	2
	owoce	1
	słone przekąski	0
	słodycze	0
17.	**Zróżnicowanie technik przygotowywania potraw (uwzględnienie niskiego IG)**	
	Tak	1
	Nie	0
18.	**Zróżnicowanie konsystencji i strawności poszczególnych składników posiłku**	
	Tak	1
	Nie	0
19.	**Potrawy smażone w jadłospisach**	
	4x na 2 tygodnie	2
	6x na 2 tygodnie	1
	> 6 x na 2 tygodnie	0

20.	**Dodatek przypraw do potraw**	
	używanie ziół zamiast soli	1
	dosalanie potraw przy stole	0
	dodatek cukru do potraw	0

Lp.	**Ocena końcowa jadłospisów pacjentek z cukrzycą ciążową**	**Przedział punktowy**
1.	prawidłowy	39-42
2.	zadowalający	30-38
3.	wymagający poprawy	12-29
4.	niezadowalający	≤ 12

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRITreporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, Hróbjartsson A, Mann H, Dickersin K, Berlin J, Doré C, Parulekar W, Summerskill W, Groves T, Schulz K, Sox H, Rockhold FW, Rennie D, Moher D. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. Ann Intern Med. 2013;158(3):200-207

		Reporting Item	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	2
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	2
Protocol version	#3	Date and version identifier	1
Funding	#4	Sources and types of financial, material, and other support	9
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1, 9

Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	n/a
Roles and responsibilities: sponsor and funder	#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
Roles and responsibilities: committees	#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)	n/a
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	2
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	2
Objectives	#7	Specific objectives or hypotheses	3
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, non-inferiority, exploratory)	2
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	3

		obtained	
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)	3
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	4-6
Interventions: modifications	#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)	5-6
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	n/a
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	n/a
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	6-7
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)	6
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
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	3-4

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	4
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	4
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	4
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	n/a
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	n/a
Methods: Data collection, management, and analysis			
Data collection plan	#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	6

		protocol	
Data collection plan: retention	#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	n/a
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	7
Statistics: outcomes	#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	7
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	7
Statistics: analysis population and missing data	#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)	n/a
Methods: Monitoring			
Data monitoring: formal committee	#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	n/a
Data monitoring: interim analysis	#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	n/a
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	n/a
Auditing	#23	Frequency and procedures for auditing trial conduct, if	n/a

		any, and whether the process will be independent from investigators and the sponsor	
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	9
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)	n/a
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	n/a
Consent or assent: ancillary studies	#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	7
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	9
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	n/a
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: trial results	#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	7
Dissemination policy:	#31b	Authorship eligibility guidelines and any intended use of	7

authorship		professional writers	
Dissemination policy: reproducible research	#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

ŚWIADOMA ZGODA NA UDZIAŁ W BADANIU KLINICZNYM

Tytuł badania: *Ocena wpływu zastosowania ciągłego monitorowania glikemii na wyniki leczenia cukrzycy ciążowej.*

Ja niżej podpisany(a).....
oświadczam, że przeczytałem/am i zrozumiałem/am powyższe informacje dotyczące opisanego badania klinicznego oraz otrzymałem/am wyczerpujące, satysfakcjonujące mnie odpowiedzi na zadane pytania. Wyrażam dobrowolnie zgodę na udział w tym badaniu klinicznym i jestem świadomy/świadoma faktu, iż w każdej chwili mogę wycofać zgodę na udział w dalszej części badania klinicznego bez podania przyczyny. Przez podpisanie zgody na udział w badaniu nie zrzekam się żadnych należnych mi praw. Otrzymam kopię niniejszego formularza opatrzoną podpisem i datą.

Wyrażam zgodę, by dla kontroli poprawności wykonania badania klinicznego przedstawiciele krajowych, zagranicznych lub międzynarodowych instytucji nadzorujących badanie, mieli wgląd w moje dane osobowe oraz dokumentację medyczną (dane dotyczące mego stanu zdrowia) pod warunkiem, że są oni związani z badaniem.

Przez podpisanie tego dokumentu potwierdzam również, że zostałem/zostałam poinformowany/poinformowana o sposobie przetwarzania danych z badania i że dane te będą weryfikowane przez ich porównanie z moją dokumentacją medyczną oraz że dane te są zbierane jedynie w celu naukowej analizy badania.

Wyrażam zgodę na przetwarzanie danych w tym badaniu zgodnie z obowiązującym w Polsce prawem (Rozporządzenie Parlamentu Europejskiego i Rady (UE) 2016/679 z dnia 27 kwietnia 2016 r. w sprawie ochrony osób fizycznych w związku z przetwarzaniem danych osobowych i w sprawie swobodnego przepływu takich danych oraz uchylenia dyrektywy 95/46/WE). Zgadzam się na przekazanie moich anonimowych danych do innych krajów, zarówno w obrębie Europy jak i poza nią.

Dane analizowane przez odnośnie władze, reprezentantów Ministerstwa Zdrowia, agencje rządowe oraz Komisje Bioetyczne dostępne będą jedynie w postaci anonimowej. Zostałem/zostałam poinformowany/poinformowana, iż w przypadku wycofania zgody na udział w badaniu zgromadzone do tej pory dane mogą zostać wykorzystane i przetwarzane jako część bazy danych badania.

Zgodnie z art. 13 ogólnego rozporządzenia o ochronie danych osobowych z dnia 27 kwietnia 2016 r. informuję, iż:

1. Administratorem Pani/Pana danych osobowych jest Uniwersyteckie Centrum Zdrowia Kobiety i Noworodka WUM z siedzibą w Warszawie, pl.Starynkiewicza 1/3, 02-015,
2. Inspektorem Ochrony Danych w UCZKiN jest adres email iod@uczkin.pl,
3. Pani/Pana dane osobowe przetwarzane będą w celu realizacji badania klinicznego *Ocena wpływu zastosowania ciągłego monitorowania glikemii na wyniki leczenia cukrzycy ciążowej* w I Katedrze i Klinice Położnictwa i

Ginekologii WUM na podstawie art. 9 ust. 2 lit. a ogólnego rozporządzenia o ochronie danych osobowych z dnia 27 kwietnia 2016 r.,

4. Pani/Pana dane osobowe mogą być ujawniane wyłącznie:

1) osobom upoważnionym u administratora do przetwarzania danych osobowych,

2) podmiotom przetwarzającym na mocy umowy powierzenia,

3) przedstawicielom krajowych, zagranicznych lub międzynarodowych instytucji nadzorujących badanie kliniczne po spełnieniu warunków określonych w Rozdziale V ogólnego rozporządzenia o ochronie danych osobowych z dnia 27 kwietnia 2016 r.,

4) innym podmiotom upoważnionym na podstawie przepisów prawa,

1. Pani/Pana dane osobowe przechowywane będą wyłącznie przez okres wymagany przez obowiązuję przepisy prawa,
2. posiada Pani/Pan prawo dostępu do treści swoich danych, prawo do ich sprostowania, usunięcia, ograniczenia przetwarzania, prawo do przenoszenia danych, prawo do wniesienia sprzeciwu i prawo do cofnięcia zgody w dowolnym momencie,
3. posiada Pani/Pan prawo wniesienia skargi do Urzędu Ochrony Danych Osobowych, gdy uzasadnione jest, że Pani/Pana dane osobowe przetwarzane są przez administratora niezgodnie z ogólnym rozporządzeniem o ochronie danych osobowych z dnia 27 kwietnia 2016 r.,
4. podanie danych osobowych jest dobrowolne,
5. decyzje nie będą podejmowane w sposób zautomatyzowany, nie będzie Pan/Pani podlegał profilowaniu.

Pacjent:

.....
.....

Imię i nazwisko (drukowanymi literami) Podpis data złożenia podpisu

(ręką pacjenta)

Oświadczam, że omówiłem/omówiłam przedstawione badanie z pacjentem/pacjentką używając zrozumiałych, możliwie prostych sformułowań oraz udzieliłem/udzieliłam informacji dotyczących natury i znaczenia badania.

Osoba uzyskująca zgodę na badanie

.....
.....

Imię i nazwisko (drukowanymi literami) Podpis data złożenia podpisu

Formularz Świadomej Zgody na badanie wersja nr 1 z dnia 06.02.2020

BMJ Open

Flash Glucose Monitoring in gestational diabetes mellitus: study protocol for a randomised controlled trial

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-041486.R2
Article Type:	Protocol
Date Submitted by the Author:	20-Jan-2021
Complete List of Authors:	Majewska, Agata; Medical University of Warsaw, 1st Department of Obstetrics and Gynecology Stanirowski, Paweł; Medical University of Warsaw, 1st Department of Obstetrics and Gynecology Wielgoś, Mirosław; Medical University of Warsaw, 1st Department of Obstetrics and Gynecology Bomba-Opon, Dorota; Medical University of Warsaw, 1st Department of Obstetrics and Gynecology
Primary Subject Heading:	Obstetrics and gynaecology
Secondary Subject Heading:	Diabetes and endocrinology
Keywords:	OBSTETRICS, Maternal medicine < OBSTETRICS, DIABETES & ENDOCRINOLOGY

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Study title:

Long study title: Flash Glucose Monitoring in gestational diabetes mellitus: study protocol for a randomised controlled trial.

Short study title: FLAsh glucose Monitoring IN GestatiOnal diabetes mellitus (FLAMINGO)
Study Acronym: FLAMINGO

Key words: gestational diabetes mellitus, flash glucose monitoring, hyperglycemia, self-monitoring of blood glucose.

Abstract

Introduction

Gestational diabetes mellitus (GDM) is a glucose intolerance occurring in 3-10% of pregnant women and being a risk factor for multiple maternal and fetal complications. The risk of perinatal complications is proportional to the level of maternal hyperglycemia. Proper glycemic control is therefore one of the key elements of GDM therapy. Until recently, determination of blood glucose concentration was performed using glucose meters, which involved multiple fingerpricks. Nowadays, due to the flash glucose monitoring (FGM) availability, it is possible to collect measurements at any time without routine puncturing. The aim of the presented study is to assess the impact of FGM on the efficacy of treatment in population of patients diagnosed with GDM.

Methods and analysis

This is a prospective, randomised study, that will recruit 100 women at 24–28 weeks of gestation at the 1st Department of Obstetrics and Gynecology, Medical University of Warsaw, Poland. Women diagnosed with GDM, who will meet the inclusion criteria, will be individually randomised to the FGM or self-monitoring of blood glucose (SMBG) groups. Further on, clinical and laboratory results of the mother and their newborns will be collected for analysis during the course of pregnancy. Primary outcome is mean glycemia result in each group after one month analysis and percentage of results in the target glycemic range. The secondary objectives will be to compare the two groups for maternal and neonatal outcomes in conjunction with long-term glycemic control using blood glycated hemoglobin (HbA1c) and fructosamine serum concentrations.

Ethics and dissemination

The study is exempt from regional ethics review due to its nature of quality improvement in patient care. The study has been approved by the Bioethics Committee at the Medical

University of Warsaw and the patient privacy protection boards governing over the recruitment sites. Results of the study will be presented in peer-reviewed journals and at conferences.

Trial registration number: NCT04422821

Strengths and limitations of this study

- FLAMINGO study (Flash glucose monitoring in gestational diabetes mellitus) is a prospective, cross-over, open-label and randomised trial
- FLAMINGO study will compare flash glucose monitoring with self-monitoring of blood glucose in glycemia control in GDM-complicated pregnancies.
- FLAMINGO trial protocol adopts rigorous methodology and is written in accordance with the *Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT)*.
- FGM device will be applied only for the one third of the trial due to budgetary restrictions.
- The trial will include small groups of participants at a single obstetric department, that is a limitation of the study.

Introduction

Gestational diabetes mellitus (GDM) is a glucose intolerance diagnosed for the first time in pregnancy. It affects 3-10% of pregnant women and is a risk factor for multiple maternal and fetal complications (1). During pregnancy GDM significantly increases the risk of fetal macrosomia, shoulder dystocia, birth trauma and Cesarean section (2). Furthermore, the long-term complications of GDM include increased risk of development of diabetes mellitus type 2 in the mother (3), as well as increased risk of obesity, diabetes and metabolic syndrome occurrence in their children (3); (4). It has been well-documented that the risk of above-mentioned complications increases with the level of maternal hyperglycemia (5).

Proper glycemia control is one of the key elements in the effective treatment of GDM. Until recently, glucose monitoring was solely performed using glucose meters, which required multiple fingerpricks (Self-Monitoring of Blood Glucose, SMBG). Nowadays, due to the glycemia monitoring systems development, such as flash glucose monitoring (FGM), glucose levels may be measured less invasively through subcutaneous sensor application. FGM is a factory-calibrated sensor measuring glucose concentrations in the interstitial fluid. Although it represents different measurement technique than SMBG, previous studies have shown, that glycemia levels obtained by both methods are comparable (6); (7). Apart from continuous glucose concentration measurements the system provides additional data by creating a 24-hour glycemic profile. In comparison, SMBG provides only single, intermittent measurements, that limits detection of glycemic variability or nocturnal hypoglycaemic events (6). As shown in one of the studies, FGM due to the ease of use, was 3 times more often applied as a method of glycemia control than SMBG. As a result, patients from FGM group had significantly better blood glucose control (7). In the study by Bühling et al. continuous glucose monitoring had overall better sensitivity in detecting abnormal glucose levels (8). Furthermore, results of the IMPACT study demonstrated that the use of FGM in

patients with diabetes mellitus type 1 significantly reduced the incidence of hypoglycemia episodes(7) . Although hyperglycemia is the most common alteration occurring in GDM patients, there is also an increased risk of masked hypoglycemia. It was showed that almost one third of GDM patients experienced hypoglycemic events during the course pregnancy that could have been easily detected using methods for continuous glycemia control (9). Diagnosis of these hypoglycemic episodes may be of particular importance in GDM patients before qualifying to insulin therapy.

The main purpose of our study is to evaluate the impact of a new method of glycemia control (FGM) on the efficacy of treatment of GDM. Assuming, that the first month after diagnosis of GDM is essential for the proper implementation of dietary and physical activity recommendations by the patients, the favorable cost-effective strategy will be to apply FGM device only during that period of pregnancy. By analyzing results of this study, such as fasting and postprandial glycemia levels, number of nocturnal hypoglycemic episodes, number of women requiring insulin therapy, daily dosage of insulin and maternal-fetal perinatal outcomes, we will provide a scientific basis for more common use of FGM in the population of pregnant women affected by GDM.

Methods and analysis

The study protocol was written in accordance with the Standard Protocol Items: Recommendations for Interventional Trials statement (SPIRIT).

Study design

FLAMINGO is a single-center, non-blinded, randomised, crossover study with a nested qualitative evaluation and 1:1 allocation ratio. The study will be conducted at the 1st Department of Obstetrics and Gynecology, Medical University of Warsaw, Poland over a period of 2020-2021.

Study population and eligibility criteria

We aim to recruit 100 pregnant women diagnosed with GDM based on the results of 75g oral glucose tolerance test (OGTT), performed between 24-28 gestational weeks, in accordance with the universal criteria defined by World Health Organization (10). Patients will be randomly divided into two groups: FGM - study group comprising 50 women who will receive subcutaneous sensor for glucose monitoring, and SMBG - control group comprising 50 women who will monitor glycemia through use of standard glucose meter.

Inclusion criteria

Women aged 18 years or older, in singleton pregnancy, diagnosed with GDM will be invited to participate in the study.

Exclusion criteria

Multiple pregnancy, fetal malformations, pre-gestational diabetes mellitus (overt diabetes in pregnancy), chronic or pregnancy-induced hypertension, chronic renal or hepatic disease diagnosed prior to study entry, in-vitro fertilization, pre-mature rupture of membranes, placenta previa, smoking in pregnancy, intake of medications including: methyldopa, tetracyclin, acetylosalicylic acid, acetaminofen, ibuprofen, L-dopa, tolazamide, tolbutamide will constitute study exclusion criteria.

All women eligible for the study will provide written informed consent prior to enrollment.

Aim of the study and objectives

The aim of the FLAMINGO trial is to assess the impact of FGM on the efficacy of treatment of GDM. Our primary outcome is mean glycemia results (fasting and 1-h postprandial glucose concentrations) in each group (FGM/SMBG) during the first month following GDM diagnosis in conjuction with the percentage of results in the target glycemic range. The secondary objectives will be to compare the two groups for the number of patients requiring insulin therapy, dosage of insulin, number of hypoglycemic episodes, as well as to compare blood glycated hemoglobin (HbA1c) and fructosamine serum concentrations as potential markers of long-term glycemic control and predictors of perinatal complications, based on previous studies (11); (12). Simultaneously, we aim to compare patient's physical activity level based on a daily steps number counted by a wristband and to assess compliance with diet recommendations using Eating Assessment Test. Finally, we aim to compare both groups with respect to maternal-fetal perinatal outcomes, including pregnancy weight gain, fetal birth-weight and neonatal glycemia.

Participant selection and recruitment

Pregnant women diagnosed with GDM by the trial research staff (AM, PS) who will meet study inclusion criteria will be invited to participate in the project (see Figure 1). Recruitment will begin in September 2020 and is estimated to end in October 2021.

Recruitment brochures that contain general information of the study will be placed at the website of the Department. During the recruitment process, trial research staff (AM, PS) will inform potential candidates about the study both verbally and with written information. Women who are agreeable to participate will be obliged to provide written informed consent. Those patients who decline to participate will continue to receive their routine antenatal care. Obstetric care provided to each pregnant woman will not be affected nor influenced by the woman's decision to either participate or not participate in the study.

Randomization

Simple randomization with the computer-generated list and sealed envelopes will be used for patient's randomization process. The process of randomization and sealing will be conducted at the 1 st Department of Obstetrics and Gynecology, Medical University of Warsaw by the non-member of the trial research staff.

Blinding

This is a non-blinded trial. As the device used for glycemia monitoring (FGM/SMBG) will be clearly visible to both participants and trial research staff blinding is not feasible for patients and researchers.

Study procedures

Patients included in the study will undergo five visits comprising one recruitment and four follow-up visits (see Figure 2). The trial research staff (AM, PS) will be responsible for analyzing participants glycemia results, diet control and physical activity as well as for the modifications of health interventions during the follow-up visits.

Recruitment visit (Visit 1)

At the recruitment visit (24-28 weeks of gestation), after providing the informed consent, patients will be interviewed for sociodemographic data and past medical history to analyze study exclusion criteria. Next, if eligible for the study, participants will be randomly divided into two consecutive groups. Simple randomization with the computer-generated list and sealed envelopes will be used for patient's randomization process. Study group (FGM) will comprise 50 women who will receive subcutaneous sensor for glucose monitoring (FreeStyle Libre™; Abbott Diabetes Care, Alameda, CA), and the control group (SMBG) will comprise 50 women who will monitor glycemia through use of standard glucose meter (iXell®; Genexo sp; Warsaw, Poland; ISO 15197:2015). All patients from the study group will obtain instruction for using Freestyle Libre app to measure and collect glycemia results using a mobile phone. Patients without mobile phone will obtain Freestyle Libre Reader and instructions for using the device. Accordingly, control group will be informed about proper use of glucose meters. The results from FGM and SMBG will be collected during the follow up visits.

In order to assess daily physical activity all participants will obtain a wristband (Xiaomi Mi Band 4; Xiaomi Corporation, Hong Kong) allowing for footsteps measurement. According to Polish Society of Obstetricians and Gynecologists (PSOG) the recommended number of footsteps in pregnancy is 10.000 per day(13). As previously demonstrated mild physical activity, such as walking has protective effect on excessive gestational weight gain and decreases the risk of preterm birth and fetal macrosomia (14-17).
All patients included in the study will obtain the instruction for using the wristband and its mobile app, together with recommendations about daily physical activity in pregnancy.

After meeting study inclusion criteria patient will obtain diet recommendations for GDM prepared by clinical dietician. To evaluate participants' dietary habits, we will use Eating Assessment Test prepared by the Polish National Institute of Public Health – National Institute of Hygiene. This is a short questionnaire (20 items for diet) intended to evaluate dietary habits in patients diagnosed with GDM. The summary points base on a number of meals per day, length of breaks between meals, daily portions of fruits and vegetables, frequency of fried food and sweets consumption per week (questionnaire and list of points for each element provided in Supplementary files). The maximum test result is 42 points, the minimum 4 points. Based on the points obtained patients will be assigned to one of the four diet groups (good: 39-42, satisfactory: 30-38, demanding diet modification 12-29, and not satisfactory < 12 points).

According to PSOG recommendations all participants will be obliged to measure fasting and 1-h postprandial glucose concentrations in a daily manner, together with once per week midnight measurement (18). Postprandial glucose measurements will be performed after three main meals (breakfast, dinner, supper). To avoid excessive data collection, we do not aim to analyze all the results obtained with the FGM. At the end of the visit, all participants will undergo blood tests (HbA1c, fructosamine) and selected biometric maternal-fetal parameters will be measured (patient weight, ultrasound estimated fetal weight).

Visit 2 (14 days after the recruitment)

At the second follow-up visit glycemia levels, diet control and physical activity will be analyzed. Based on glycemia results participants will obtain modified diet recommendations and will be qualified to insulin therapy, if required (fasting blood glucose concentrations above 90 mg/dL or postprandial glycemia results above 140 mg/dl). Initial predetermined

insulin dose planned for the study is four units for long-acting insulin and three units per meal for short-acting insulin. The final insulin dosage will be individualized based on the glycemic results during the follow-up visits (19). According to PSOG standards for management of GDM fasting glucose level <90mg/dl and 1-h postprandial glucose level <140mg/dl are indicative of proper glycemic control (18). The study group will obtain new FGM sensor. At the end of the visit, research staff will collect biometric measurements from all patients included in the study (the same as during Visit 1).

According to the criteria proposed by Tudor-Locke we will divide patients into four groups of physical activity based on a number of daily steps collected by the wristband: sedentary (< 5000 daily steps), low active (5000~7500 daily steps), somewhat active (7500~10000 daily steps) and active (≥ 10000 daily steps)(20).

Visit 3 (28 days after the recruitment)

At the third visit glycemia levels, diet control and physical activity will be analyzed. Based on glycemia results participants will obtain modified diet recommendations and will be qualified to insulin therapy if required. In patients already treated with insulin, dosage will be modified according to glycemia results. The study group will obtain glucose meter. All patients will end physical activity control with a wristband. Eating Assessment Test will be performed to test whether dietary recommendations and glycemia control in the study have an impact on eating habits of the participants. At the end of the visit, all participants will undergo blood tests (HbA1c, fructosamine) and selected biometric parameters will be measured.

Visit 4 (34-36 gestational weeks)

At the fourth visit glycemia levels, diet control and insulin therapy will be analyzed. Based on glycemia results participants will obtain modified diet recommendations and will be qualified to insulin therapy, if required. In patients already treated with insulin, dosage will be modified according to glycemia results. Eating Assessment Test will be performed to test whether dietary recommendations and glycemia control in the study have an impact on eating habits of the participants. Additionally, research staff will collect selected biometric measurements from all patients included in the study. At the end of the visit, all participants will undergo blood tests (HbA1c, fructosamine).

Visit 5 (after delivery)

24-72 hours after the delivery, research staff will retrieve maternal and neonatal outcomes from patient's medical history.

Study outcome

The primary outcome will be mean glycemia results (fasting and 1-h postprandial glucose concentrations) in each group (FGM/SMBG) during the first month following the diagnosis of GDM and the percentage of results in the target glycemic range.
The secondary objectives will be to compare both groups for:

- Number of patients requiring insulin therapy (2, 4 and 8 weeks after the recruitment visit)
- Dosage of insulin (2, 4 and 8 weeks after the recruitment visit)

- Long-term glycemic control using blood HbA1c concentrations (2, 4 and 8 weeks after the recruitment visit)
- Long-term glycemic control using fructosamine serum concentrations (2, 4 and 8 weeks after the recruitment visit)
- Number of hypoglycemic episodes (glucose concentration <70 mg/dl) during one month analysis (episodes per day in 0-4 weeks after the recruitment visit)
- Physical activity during one month analysis based on a footsteps daily count (0-4 weeks after the recruitment visit)
- Compliance with diet recommendations according to Eating Assessment Test (2, 4 and 8 weeks after the recruitment visit)
- Gestational weight gain (2, 4 and 8 weeks after the recruitment visit)
- Mode of delivery (rate of vaginal delivery/ Cesarean section)
- Fetal birth-weight
- Neonatal glycemia

Sample size calculation and statistical analysis

The performed power analysis (power of 80%, significance level of 5%, two-sided) estimated a required sample size of a total of 80 patients (40 patients in each group). The analysis was based on the results of a previous report comparing FGM with SMBG and estimation to detect a difference in the percentage of results in the target glycemic range between study and control groups (21). Sample size is further increased to 100 patients to account for a potential exclusions and drop out of approximately 10%. l

Continuous data will be compared using the Mann-Whitney U test, and for categorical variables the chi square test will be applied. The results will be presented as medians and inter-quartile ranges (IQR), or as a frequency (%). For comparison between groups, Bland Altman and Passing-Bablok method will be performed. The relationship between glucose, HbA1c and fructosamine concentrations, and selected maternal-fetal parameters will be examined with the use of Pearson's correlation coefficient. Multivariable logistic regression analysis will be performed to evaluate the potential impact of selected predictors on primary outcomes. All tests will be carried out at a significance level of 0.05.

Statistical analyses will be performed using SAS software, version 9.2 or later (SAS Institute, Cary, NC).

Patient and public involvement

Patients and the manufacturers (Abbott Diabetes Care, Genexo sp, Xiaomi Corporation) will not be involved in the process of the design, conduct, reporting or dissemination plans of the study. All participants will be informed about the trial results at the end of the study.

Trial monitoring and management

Patient retention strategy:

Patients recruited to the study will obtain an email with the schedule of the follow up visits. They will also obtain regular phone contact before each visit.

Strategies for the management of missing data:

For missing glycemic data, in particular in the SMBG group mean glycemia levels from the past 5 days will be calculated, in accordance with the time of measurement (fasting, postprandial).

Ethics and dissemination

The study is exempt from regional ethics review due to its nature of quality improvement in patient care. The study has been approved by the Bioethics Committee at the Medical University of Warsaw and the patient privacy protection boards governing over the recruitment sites. All data sets will be password protected and only available to project investigators. Results of the study will be presented in peer-reviewed journals and at conferences.

Discussion

According to epidemiological data GDM affects about 5.4 % of pregnant women in Europe and the prevalence is continuously increasing (22). As a result, there is an urgent need to search for the new methods of effective glucose monitoring facilitating glycemia control, and thus allowing for a decrease in the rate of maternal and fetal complications.

Flash glucose monitoring is a new method, that is already commonly used in pediatric patients diagnosed with diabetes mellitus type 1 (23). As one multicentre study demonstrated, due to easiness of FGM use, patients measured glycemia 3 times more often per day in comparison with those using standard glucose meters. Consequently, patients significantly improved their diurnal glucose profile (7). In addition, the results of IMPACT study proved that use of FGM among type 1 diabetic patients is effective in reduction of hypoglycemia episodes (23). Finally, in the study by Dunn C T et al. a positive correlation between the number of scans per day and HbA1c levels was found, showing a significant decrease in HbA1c concentration among patients who monitored glycemia more frequently (24).

Apart from the relatively small group of participants, the presented single-centre study is limited by the fact that FGM will be applied only for one month following the GDM diagnosis. Nonetheless, we believe that these first four weeks after the recruitment are of crucial importance for proper implementation of dietary and physical activity recommendations by the patients (25). Moreover, if primary objectives are accomplished proposed strategy may significantly reduce costs of FGM application.

To conclude, although limited in number, available studies suggest that use of FGM may help to improve monitoring and treatment results in patients affected by glucose tolerance disorders during pregnancy. Based on that, we would like to investigate the impact of FGM on maternal and neonatal outcomes in population of patients diagnosed with gestational diabetes mellitus.

Footnotes

Contributors AM is the principal investigator and coordinated trial design, drafting and critically revising of the protocol. PS and DBO were involved in drafting the manuscript for publication. AM and PS developed the statistical design and sample size estimation. PS, DBO and MW critically revised and supervised the trial design and protocol. DBO and MW contributed to the ethical and regulatory aspects of the research. All the authors have read and approved the final version of the manuscript.

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process of the design, funding, conducting, reporting, dissemination plans of the study, data management and publication.

Competing interests None declared.
Ethics approval – The Bioethics Committee at the Medical University of Warsaw; Approval Number: KB/50/2020
Provenance and peer review Not commissioned; externally peer reviewed.
Data availability statement Data are available on reasonable request.

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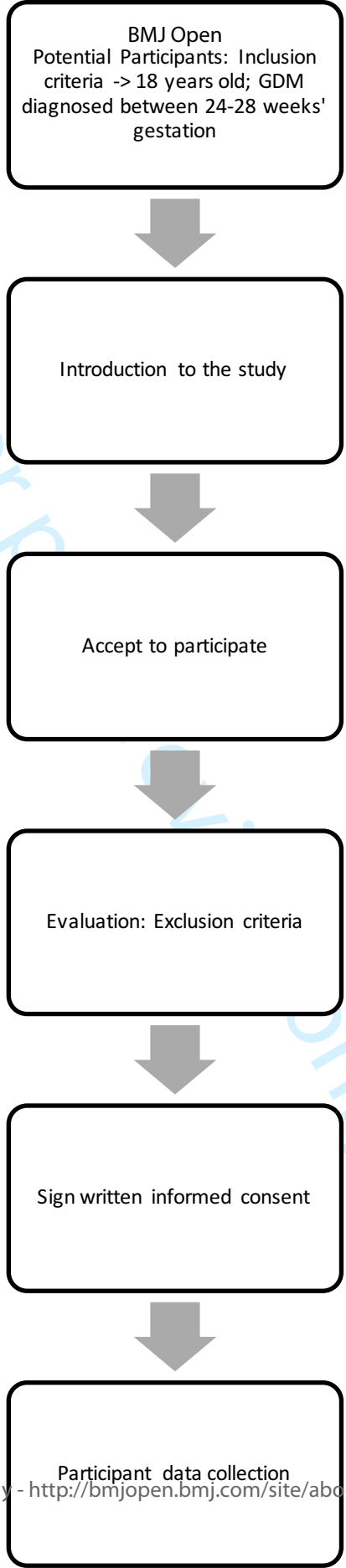
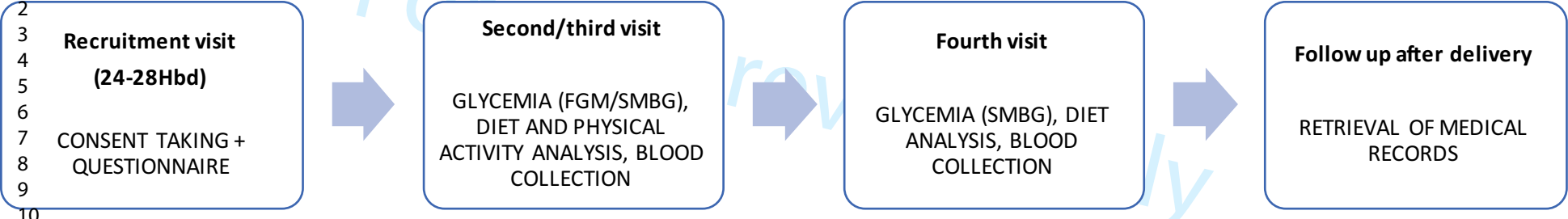
Figure Legend:

Figure 1 Patient flow scheme.

Figure 2. The flow diagram of the study.





Kwestionariusz oceny jakościowej jadłospisów pacjentek z cukrzycą ciążową

Lp.	Wyróżnik	Punkty
1.	**Liczba posiłków**	
	I Śniadanie	1
	II Śniadanie	1
	Obiad	1
	Podwieczorek	1
	Kolacja	1
	II Kolacja	1
2.	**Przerwa między posiłkami w ciągu dnia**	
	do 3 godz.	2
	do 4 godz.	1
	powyżej 4 godz.	0
3.	**Przerwa nocna**	
	do 10 godz.	1
	powyżej 10 godz.	0
4.	**Uwzględnienie wody do picia w ilości co najmniej 2-2,5 l/dzień**	
	Tak	1
	Nie	0
5.	**Ilość warzyw spożywana w ciagu dnia**	
	5 porcji	5
	4 porcje	4
	3 porcje	3
	2 porcje	2
	1 porcja	1
	w żadnym posiłku	0
6.	**Ilość owoców spożywana w ciągu dnia**	
	2 porcje	2
	1 porcja	1
	w żadnym posiłku	0
7.	**Uwzględnienie porcji surowych warzyw i/lub owoców**	
	przynajmniej w 2 posiłkach	2
	przynajmniej w 1 posiłku	1
	w żadnym posiłku	0
8.	**Różnorodność warzyw i/lub owoców w jadłospisach**	
	Tak	1
	Nie	0
9.	**Produkty zbożowe z pełnego przemiału**	
	przynajmniej w 3 posiłkach	3
	w 2 posiłkach	2
	w 1 posiłku	1

	w żadnym posiłku	0
10.	**Różnorodność produktów węglowodanowych w jadłospisach**	
	Tak	1
	Nie	0
11.	**Mleko i przetwory mleczne w tym napoje fermentowane**	
	≥ 3w posiłkach	3
	w 2 posiłkach	2
	w 1 posiłku	1
12.	**Białko pełnowartościowe (zwierzęce lub strączkowe) w głównych posiłkach**	
	w 3 posiłkach	3
	w 2 posiłkach	2
	w 1 posiłku	1
	w żadnym posiłku	0
13.	**Nasiona roslin strączkowych**	
	6x na 2 tygodnie	2
	4x na 2 tygodnie	1
	< 2 x na 2 tygodnie	0
14.	**Ryby i/lub przetwory rybne**	
	6x na 2 tygodnie	2
	4x na 2 tygodnie	1
	< 2 x na 2 tygodnie	0
15.	**Różnorodność gatunkowa mięs i przetworów mięsnych w jadłospisach**	
	Tak	1
	Nie	0
16.	**Przekąski między posiłkami**	
	warzywa/orzechy	2
	owoce	1
	słone przekąski	0
	słodycze	0
17.	**Zróżnicowanie technik przygotowywania potraw (uwzględnienie niskiego IG)**	
	Tak	1
	Nie	0
18.	**Zróżnicowanie konsystencji i strawności poszczególnych składników posiłku**	
	Tak	1
	Nie	0
19.	**Potrawy smażone w jadłospisach**	
	4x na 2 tygodnie	2
	6x na 2 tygodnie	1
	> 6 x na 2 tygodnie	0

20.	**Dodatek przypraw do potraw**	
	używanie ziół zamiast soli	1
	dosalanie potraw przy stole	0
	dodatek cukru do potraw	0

Lp.	**Ocena końcowa jadłospisów pacjentek z cukrzycą ciążową**	**Przedział punktowy**
1.	prawidłowy	39-42
2.	zadowalający	30-38
3.	wymagający poprawy	12-29
4.	niezadowalający	≤ 12

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRITreporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, Hróbjartsson A, Mann H, Dickersin K, Berlin J, Doré C, Parulekar W, Summerskill W, Groves T, Schulz K, Sox H, Rockhold FW, Rennie D, Moher D. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. Ann Intern Med. 2013;158(3):200-207

		Reporting Item	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	2
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	2
Protocol version	#3	Date and version identifier	1
Funding	#4	Sources and types of financial, material, and other support	9
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1, 9

Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	n/a
Roles and responsibilities: sponsor and funder	#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
Roles and responsibilities: committees	#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)	n/a
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	2
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	2
Objectives	#7	Specific objectives or hypotheses	3
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, non-inferiority, exploratory)	2
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	3

		obtained	
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)	3
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	4-6
Interventions: modifications	#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)	5-6
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	n/a
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	n/a
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	6-7
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)	6
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
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	3-4

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	4
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	4
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	4
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	n/a
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	n/a
Methods: Data collection, management, and analysis			
Data collection plan	#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	6

		protocol	
Data collection plan: retention	#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	n/a
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	7
Statistics: outcomes	#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	7
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	7
Statistics: analysis population and missing data	#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)	n/a
Methods: Monitoring			
Data monitoring: formal committee	#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	n/a
Data monitoring: interim analysis	#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	n/a
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	n/a
Auditing	#23	Frequency and procedures for auditing trial conduct, if	n/a

		any, and whether the process will be independent from investigators and the sponsor	
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	9
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)	n/a
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	n/a
Consent or assent: ancillary studies	#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	7
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	9
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	n/a
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: trial results	#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	7
Dissemination policy:	#31b	Authorship eligibility guidelines and any intended use of	7

authorship		professional writers	
Dissemination policy: reproducible research	#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

ŚWIADOMA ZGODA NA UDZIAŁ W BADANIU KLINICZNYM

Tytuł badania: *Ocena wpływu zastosowania ciągłego monitorowania glikemii na wyniki leczenia cukrzycy ciążowej.*

Ja niżej podpisany(a).....
oświadczam, że przeczytałem/am i zrozumiałem/am powyższe informacje dotyczące opisanego badania klinicznego oraz otrzymałem/am wyczerpujące, satysfakcjonujące mnie odpowiedzi na zadane pytania. Wyrażam dobrowolnie zgodę na udział w tym badaniu klinicznym i jestem świadomy/świadoma faktu, iż w każdej chwili mogę wycofać zgodę na udział w dalszej części badania klinicznego bez podania przyczyny. Przez podpisanie zgody na udział w badaniu nie zrzekam się żadnych należnych mi praw. Otrzymam kopię niniejszego formularza opatrzoną podpisem i datą.

Wyrażam zgodę, by dla kontroli poprawności wykonania badania klinicznego przedstawiciele krajowych, zagranicznych lub międzynarodowych instytucji nadzorujących badanie, mieli wgląd w moje dane osobowe oraz dokumentację medyczną (dane dotyczące mego stanu zdrowia) pod warunkiem, że są oni związani z badaniem.

Przez podpisanie tego dokumentu potwierdzam również, że zostałem/zostałam poinformowany/poinformowana o sposobie przetwarzania danych z badania i że dane te będą weryfikowane przez ich porównanie z moją dokumentacją medyczną oraz że dane te są zbierane jedynie w celu naukowej analizy badania.

Wyrażam zgodę na przetwarzanie danych w tym badaniu zgodnie z obowiązującym w Polsce prawem (Rozporządzenie Parlamentu Europejskiego i Rady (UE) 2016/679 z dnia 27 kwietnia 2016 r. w sprawie ochrony osób fizycznych w związku z przetwarzaniem danych osobowych i w sprawie swobodnego przepływu takich danych oraz uchylenia dyrektywy 95/46/WE). Zgadzam się na przekazanie moich anonimowych danych do innych krajów, zarówno w obrębie Europy jak i poza nią.

Dane analizowane przez odnośnie władze, reprezentantów Ministerstwa Zdrowia, agencje rządowe oraz Komisje Bioetyczne dostępne będą jedynie w postaci anonimowej. Zostałem/zostałam poinformowany/poinformowana, iż w przypadku wycofania zgody na udział w badaniu zgromadzone do tej pory dane mogą zostać wykorzystane i przetwarzane jako część bazy danych badania.

Zgodnie z art. 13 ogólnego rozporządzenia o ochronie danych osobowych z dnia 27 kwietnia 2016 r. informuję, iż:

1. Administratorem Pani/Pana danych osobowych jest Uniwersyteckie Centrum Zdrowia Kobiety i Noworodka WUM z siedzibą w Warszawie, pl.Starynkiewicza 1/3, 02-015,
2. Inspektorem Ochrony Danych w UCZKiN jest adres email iod@uczkin.pl,
3. Pani/Pana dane osobowe przetwarzane będą w celu realizacji badania klinicznego *Ocena wpływu zastosowania ciągłego monitorowania glikemii na wyniki leczenia cukrzycy ciążowej* w I Katedrze i Klinice Położnictwa i

Ginekologii WUM na podstawie art. 9 ust. 2 lit. a ogólnego rozporządzenia o ochronie danych osobowych z dnia 27 kwietnia 2016 r.,

4. Pani/Pana dane osobowe mogą być ujawniane wyłącznie:

1) osobom upoważnionym u administratora do przetwarzania danych osobowych,

2) podmiotom przetwarzającym na mocy umowy powierzenia,

3) przedstawicielom krajowych, zagranicznych lub międzynarodowych instytucji nadzorujących badanie kliniczne po spełnieniu warunków określonych w Rozdziale V ogólnego rozporządzenia o ochronie danych osobowych z dnia 27 kwietnia 2016 r.,

4) innym podmiotom upoważnionym na podstawie przepisów prawa,

1. Pani/Pana dane osobowe przechowywane będą wyłącznie przez okres wymagany przez obowiązuję przepisy prawa,
2. posiada Pani/Pan prawo dostępu do treści swoich danych, prawo do ich sprostowania, usunięcia, ograniczenia przetwarzania, prawo do przenoszenia danych, prawo do wniesienia sprzeciwu i prawo do cofnięcia zgody w dowolnym momencie,
3. posiada Pani/Pan prawo wniesienia skargi do Urzędu Ochrony Danych Osobowych, gdy uzasadnione jest, że Pani/Pana dane osobowe przetwarzane są przez administratora niezgodnie z ogólnym rozporządzeniem o ochronie danych osobowych z dnia 27 kwietnia 2016 r.,
4. podanie danych osobowych jest dobrowolne,
5. decyzje nie będą podejmowane w sposób zautomatyzowany, nie będzie Pan/Pani podlegał profilowaniu.

Pacjent:

.....
.....

Imię i nazwisko (drukowanymi literami) Podpis data złożenia podpisu

(ręką pacjenta)

Oświadczam, że omówiłem/omówiłam przedstawione badanie z pacjentem/pacjentką używając zrozumiałych, możliwie prostych sformułowań oraz udzieliłem/udzieliłam informacji dotyczących natury i znaczenia badania.

Osoba uzyskująca zgodę na badanie

.....
.....

Imię i nazwisko (drukowanymi literami) Podpis data złożenia podpisu

Formularz Świadomej Zgody na badanie wersja nr 1 z dnia 06.02.2020