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Real-time continuous glucose monitoring versus self-monitoring of blood glucose in adults with insulin-treated type 2 diabetes: a protocol for a randomised controlled single-centre trial

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ABSTRACT

Introduction Medical treatment options for type 2 diabetes (T2D) have increased over the last decade and enhance the possibility of individualised treatment strategies where insulin is still one of them. In spite of the advancements in treatment options, less than one-third of the population with T2D obtain their optimal glycaemic goal. In persons with type 1 diabetes, continuous glucose monitoring (CGM) has shown to be the most important driver for improvement in glycaemic control, even more than insulin-pump therapy. The use of technology in T2D has only been investigated in few studies.

The overall objective of the research study is to examine the effectiveness of the use of CGM versus self-monitoring of blood glucose (SMBG) in persons with insulin-treated T2D on glycaemic variables and patient-reported outcomes on treatment satisfaction, health behaviour and well-being. The independent effect of peer support will also be studied.

Methods and analysis The study is a single centre, prospective, randomised, open-labelled, three-armed study with the randomisation 2:1:2 in group A with CGM, group B with CGM and peer support, and group C as a control group with SMBG. The participants receive a training course unique for the allocation group. The study runs for 12 months and includes 100 adult participants with insulin-treated T2D, treated at the outpatient clinic at Steno Diabetes Center Copenhagen. Primary outcome is difference in change in time in range. Recruitment begins in August 2020 and ends in July 2021. Final 12-month follow-up is anticipated to be in August 2022.

Ethics and dissemination The study will be carried out in accordance with the Helsinki Declaration and is approved by the Scientific Ethics Committee of the Capital Region (H-20000843). Data collection and handling will be performed in accordance with the General Data Protection Regulation and is approved by the Danish Data Protection Agency (J-2020-100). Dissemination will be in international peer-reviewed journals, conferences and a plain-language summary for participants.

Strengths and limitations of this study

► The study will provide new evidence of the effectiveness of the use of continuous glucose monitoring in treatment of type 2 diabetes especially on time in range, potentially shaping clinical guidelines for self-monitoring of blood glucose frequency and timing.
► Robustly designed three-armed randomised controlled trial with a long study period of 12 months.
► Including a wide collection of patient-reported outcomes as health behaviour and their association with time in range.
► The study's generalisability could be limited by the exclusion criteria, especially according to conditions that impact the stability of a haemoglobin A1c (HbA1c) measurement, comorbidity which does not allow lowering of HbA1c to 53 mmol/mol and the single-centre set-up of the trial.
► The unblinded nature of the trial and unbalanced dropout rates could bias the results.

INTRODUCTION

Long-term microvascular and macrovascular complications are still a serious burden of type 2 diabetes (T2D). To delay these, well-treated blood pressure and lipids, smoking cessation and physical activity, as well as good glycaemic control, are crucial.[1] In spite of the advancements in treatment options, less than one-third of the population with T2D obtain their optimal glycaemic goal. The optimal glycaemic goal in most individuals with diabetes is haemoglobin A1c (HbA1c) 53 mmol/mol (7.0%); and for those with a

short diabetes duration and no significant comorbidity, an even lower HbA1c is desirable.[2] However, HbA1c does not give any information about the glycaemic variation, the proportion of time in good glycaemic range (TIR) (3.9–10 mmol/L), in the time above or below the optimal range. This information can be obtained with the use of continuous glucose monitoring (CGM), but only few persons with T2D use CGM daily. Evidence suggests that glycaemic variability is an independent risk marker for late diabetes complications and mortality,[3] and merely a 5% increase in TIR is associated with clinically significant benefits for persons with type 1 diabetes (T1D) or T2D.[4–6]

In T1D, several studies have demonstrated that the use of technology such as insulin pumps and CGM used either separately or in combination with insulin pumps is effective in obtaining the glycaemic goals.[7 8] Studies indicate that CGM is the most important driver for improvement in glycaemic control,[9] even more than insulin delivery method (pen or pump).[10] Even though T2D counts for 90% of all diabetes cases, data are sparser on the use of technology in T2D, and the use of real-time CGM (RT-CGM) in persons with insulin-treated T2D has only been investigated in few studies with results showing reduced HbA1c and increased TIR.[11–13]

The use of CGM as a behavioural tool has the potential to improve diabetes outcomes, but the reason behind is not fully elucidated and the majority of studies on CGM in T2D have not described the included education programme on CGM use which complicates interpretation of study results.

Self-care is one of the cornerstones in the treatment of diabetes but is very complex, and reviews on adherence have shown low adherence on medication as well as health behaviour such as following guidelines on diabetes management, dietary intake and physical activity.[14 15] To our knowledge, only limited evidence exists on the effect of CGM on both health behaviour and medication adherence,[16–19] furthermore studies on patient-related outcomes (PROs) such as treatment satisfaction and diabetes distress are sparse.[20] Whether CGM can be a help in designing the appropriate treatment regimen at the individual level for T2D has not yet been examined just as there is no consensus regarding optimal frequency and timing for the measurements of self-monitoring of blood glucose (SMBG) in relation to both TIR and the different treatment options in T2D.[2]

The use of peer support in diabetes self-management intervention programmes has shown improvements in diabetes outcomes.[21] To our knowledge, no studies combining CGM and peer support for persons with diabetes exist. In a systematic review by Fisher *et al*, examining the effect of a peer-support programme in disease management with special reference to diabetes peer support was associated with a significant improvement in glycaemic control in 20 out of 24 studies with an average decrease in HbA1c of 0.76%. In another review by Dale *et al*,[22] peer support was associated with a significant improvement in blood pressure, cholesterol, body mass index (BMI) and weight, physical activity, self-efficacy, depression and perceived social support.

In the present study, the overall aim is to investigate the effect of RT-CGM in persons with insulin-treated T2D on glycaemic variables, change in behavioural adherence on medicine use, diet and exercise, and PROs such as well-being, diabetes distress and treatment satisfaction. Furthermore, the independent effect of peer support on these variables will be examined.

METHODS

Trial design

The Steno2tech CGM study is a single-centre, prospective, randomised, open-labelled, three-armed study in adults with T2D treated with insulin comparing the use of RT-CGM (without peer support (group A), RT-CGM with peer support (group B)) with standard SMBG measurements (group C). Each participant will be in the study for 12 months.

Participants

Recruitment will take place at the outpatient clinic at Steno Diabetes Center Copenhagen (SDCC), Denmark. Inclusion criteria are: age ≥18 years, clinical diagnosed T2D with duration ≥1 year, treated with insulin injections at least once daily, ≥1 year on top of diet and exercise recommendations (can be additionally treated with one or more different oral antidiabetic drugs (except sulfonylurea (SU)) and/or glucagon-like peptide 1 analogues), HbA1c ≥58 mmol/mol and attending the outpatient clinic at SDCC ≥1 year.

Exclusion criteria are: inability to understand the patient information, missing informed consent, treatment with SU during the last 3 months before study starts, new antidiabetic treatment the last 3 months, use of systematic corticosteroids, severe visual impairment, severe skin allergy for adhesive tape to the patch of CGM or other skin condition that inhibits the use of a CGM device, comorbidity which does not allow lowering of HbA1c to 53 mmol/mol (7.0%), hypoglycaemic unawareness, impaired renal disease with estimated glomerular filtration rate (eGFR) <45 mL/min/1.73 m^2, conditions that impact the stability of an HbA1c measurement (chronic liver disease, haemoglobinopathy, anaemia and so on), known or suspected alcohol or drug abuse, enrolled in another clinical study or pregnancy, intention to become pregnant, breast feeding or not using adequate contraceptive methods. Furthermore, persons with prior experience with Flash Glucose Monitoring (Libre) or CGM, will be excluded, as prior use could potentially bias the results.

We aim to recruit a total of 100 participants. Recruitment for the study will begin August 2020 and will end in July 2021. Final 12-month follow-up is anticipated to be in August 2022.

Table 1 Participant study timeline

	Prestudy procedures and enrolment			12-month intervention							
Visit	0	1	2	3	4	5	6	7	8	9	10
Time point in weeks	−1	0	2½	8	10	20	30½	32	44	58½	60
Recruitment	x										
Eligibility screening and informed consent		x									
Allocation (randomisation)			x								
Interventions											
Group A CGM				←——————————————————→							
Group B CGM+peer support				←——————————————————→							
Group C SMBG				←——————————————————→							
Training course unique for each of the allocated groups				x							
Peer support (group B)					x	x		x			
Assessments											
Blood and urine samples		x			x	x		x	x		x
Questionnaires		x						x			x
10 days of blinded CGM		x					x			x	
Data collection and CGM, SMBG upload			x		x	x		x	x		x
Treatment intensification					x	x		x	x		
Registration of adverse events			x	x	x	x	x	x	x	x	x
End of study											x

CGM, continuous glucose monitoring; SMBG, self-monitoring of blood glucose.

INTERVENTION
Devices
Self-monitoring of blood glucose
Participants assigned to the SMBG group are required to perform SMBG according to the clinical guidelines used in the outpatient clinic in accordance with the Danish Endocrinology Society, European Association for the Study of Diabetes and American Diabetes Association. The daily number of recommended SMBG measurements therefore varies from 1 to 7 measurements per day depending on the individual's medical treatment and actual glycaemic control, which is stated in a standard operating procedure (SOP). All participants will be using their own SMBG device and will be reinstructed in the test procedure.

CGM (DexCom G6 CGM)
For CGM (both blinded and real-time use), we will use CE-marked DexCom G6 (DexCom, San Diego, California, USA) CGMs. The DexCom G6 is Food and Drug Administration-approved and commercially available by prescription and indicated for persons with both T1D and T2D.[23]

Communication platform
Glucose data will be downloaded via Diasend (Glooko) to a computer for review and analysis.

Participant timeline
Recruitment
Potentially eligible participants will be identified by information about diagnosis, insulin treatment, HbA1c, diabetes duration, comorbidities, age and allergies by the healthcare professionals (HCPs) in the outpatient clinic. If potentially eligible, the persons will be asked whether they are interested in participation. A written patient information will be given along with the brochure: 'Forsøgspersoners rettigheder i et sundhedsvidenskabeligt forskningsprojekt' ('Rights of study subjects in a health science research project'). Investigator will ensure that the potentially eligible participants are adequately informed about the study rationale and design, in written and spoken words. Before signing the consent form (in online supplemental materials), the person is given a minimum of 24 hours to reconsider. Potentially eligible participants are informed that they may, at any time, withdraw their informed consent without these having consequences for their future treatment.

Included participants will attend the clinic for two prestudy visits and eight visits during the 12 months' study period (table 1).

Assignment of interventions
Participants will be randomised to three different study groups (2:1:2), A CGM group, B CGM group using

peer support and C the control group, using REDCap (REsearch Data CAPture software), a secure web-based application designed to support research data capture.[24] The allocation sequence will be centrally prepared by a person without relation to the specific study and generated using www.sealedenvelope.com.

Training course for the participants

After randomisation, the participants in the three study groups will attend a 3-hour training course with different contents depending on the group allocation. The aim of this training course is to ensure that the participants have the knowledge, support and confidence to work collaboratively with their HCPs to increase TIR and HbA1c. The training courses will be of similar length to avoid the influence of more time with the investigator/HCPs on outcome for the CGM group A versus the control group C. All participants will receive education on health behaviour, the influence of different food items and exercise on glucose levels and how to measure SMBG correctly. Furthermore, participants in group A and B (intervention) will receive a CGM education and training session led by the study investigator, including interactive and hands-on, using case studies. The training session will include spoken and written instructions on how to insert and wear the CGM device and how to interpret the CGM information to better understand the relation between participants' blood glucose and their diabetes self-management.

Peer support

After the training course, participants in group B will get an email on the peer-support set-up, concept and content. The participants will be asked to share their wishes for topics to be discussed during the following peer-support sessions. The peer support will be facilitator-led by the primary investigator with peer exchange in group sessions (three sessions over the study period, 3 hours per session) with four to six participants in every group. The approach will be participatory and adaptable to allow flexibility in the content of the peer-support sessions and involve customised use of participatory methods, that is, dialogue tools and exercises from 'In Balance with Chronic Illness: Tools for Patient Education' from SDCC.[25] The first session will include the involvement of participants in planning the content of the three peer-support sessions and a discussion on confidentiality among the participants.

CGM training course for HCPs

All participating HCPs will attend a CGM education and training session, similar to the participants. The aim of the CGM training course is to ensure that the HCPs have the knowledge and support and confidence to work collaboratively with study participants to increase TIR and decrease HbA1c.

Outcomes

Included outcome measures are shown in the following box 1.

DATA COLLECTION, MANAGEMENT AND ANALYSIS
Data collection

At the screening visit, informed consent will be retrieved, and inclusion and exclusion criteria will be reviewed. The following baseline data will be recorded: sex, age, highest education level, civil status, occupation, race/ethnicity, diabetes duration, total daily insulin dose (average of previous 7 days) and number of insulin injections per day, frequency and mean of SMBG/day, number of severe hypoglycaemia events in previous 12 months, hypoglycaemia awareness, allergies, medical history, medications prescribed (use of non-insulin glucose-lowering medication), height, weight, BMI, blood pressure and heart rate. During the screening visit, hypoglycaemia awareness will be evaluated using Pedersen-Bjergaard *et al* classification of hypoglycaemia awareness.[26 27] According to the exclusion criteria, a potential participant will be excluded in case of unawareness.

Participants will be advised to document any severe hypoglycaemic episodes throughout the study in a glucose diary provided. Episodes of severe hypoglycaemia will be defined as 'a hypoglycaemic event serious enough to require the help of another person' (self-reported).

Blood and urine samples

Blood samples during the study will be collected for analysis of HbA1c, blood glucose, creatinine, eGFR, alanine aminotransferase, thyroid stimulating hormone, cholesterol, triglycerides, low-density lipoprotein and high-density lipoprotein. Urine samples will be analysed for albumin, creatinine and Urine-Human Chorionic Gonadotrophin to test for pregnancy (U-HCG) where relevant.

Questionnaires

The following standardised validated PRO questionnaires will be provided at visits 1, 7 and 10: The WHO Five Well-Being Index,[28] the Diabetes Distress Scale,[29] the revised short-form Hypoglycaemia Fear Survey,[30] the Glucose Monitoring Satisfaction Scale,[31] the Diabetes Treatment Satisfaction Questionnaire[32]; status questionnaire for baseline characteristics and a change questionnaire for intervention end point measurements,[33 34] the Swedish National Board of Health and Welfare questionnaire for assessing Physical Activity,[35] a Danish questionnaire inspired by the Perceived Dietary Adherence Questionnaire[36] and a Danish questionnaire on Medical Adherence.[37]

Blinded CGM

Participants in all three groups will wear a blinded CGM (DexCom G6) for a 10-day period before randomisation, after 30.5 weeks and after 58.5 weeks. The participants will receive both spoken and written information about the blinded CGM, instructions on how to insert and wear the CGM, skin preparation and observation of skin reactions.

Participants in the two CGM groups will wear the open CGM according to treatment, and participants in all of

the three groups will wear the blinded CGM to measure the effect of the treatment.

Clinical visits: data collection, upload and treatment intensification

There are five clinical follow-up visits (visits 4, 5, 7, 8, 10) planned during the 60 weeks' study period (see table 1). During these visits, SMBG or CGM data will be uploaded via Diasend and data will be collected.

In general, during the study, the goal is to achieve HbA1c 53 mmol/mol or below and most possible glucose values measured with CGM or SMBG in the range 3.9–10 mmol/L with all possible means. The treatment intensification will be depending on: patterns from downloaded SMBG/CGM, history of medication since last visit, issues regarding exercise and food intake, and episodes of hypoglycaemia and symptoms of hyperglycaemia. For each group, a group-specific SOP for the treatment intensification will be used, based on the existing guidelines and procedures in the outpatient clinic. The treatment intensification will be done by a specialist in diabetology specifically experienced in treating T2D. The patterns they observe on the downloads and the specific actions they are recommending in response to the patterns will be recorded.

Data management

The data management is performed in accordance with the General Data Protection Regulation and approved by the Danish data protection agency (J-2020-100). All information on study participants is protected according to law on processing of personal data and the law of health. The electronic study database in REDCap is password protected and located on the hospital network server which is continuously backed up. All information on paper that is personally identifiable will be kept in a locked filing cabinet in a double-locked office. Only the study sponsor and investigators will have access to the study database.

Statistical methods

A sample size of 74 (37 in each group (A+C)) was calculated to have 90% power to detect a difference in mean time in target glycaemic range, TIR (3.9–10.0 mmol/L) between group A and C of 75 min/day equivalent to a 5% increase in TIR, which is associated with clinically significant benefits,[4] SD of 100 min[11] and a 2-sided α-level of 0.05. Sample size is increased to 80 (40 in group A+C) to account for a potential dropout of approximately 10%. In this study, the effect of peer support will be considered hypothesis-generating for later studies, and 20 participants in group B will be included for that purpose.

Blinding of the study will not be possible as the treatment advice is dependent on the different treatments in the groups. Participant characteristics at baseline will be summarised for each group. Comparable statistics with continuous outcome will be calculated by t-test for parametric and Wilcoxon rank sum for non-parametric

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Box 1   Outcome measures

Primary outcome measure

Time frame: from baseline to 12 months with the interim measurement at 6 months

► Difference between change in time in range (TIR) (3.9–10 mmol/L) in per cent, assessed via blinded continuous glucose monitoring (CGM) device, between CGM group (A) and self-monitoring of blood glucose (SMBG) group (C) in percentages.

Secondary outcome measures

Time frame: from baseline to 12 months with the interim measurement at 6 months

► Difference between change in haemoglobin A1c (HbA1c) in mmol/mol between the CGM group (A) and the SMBG group (C).

► Difference between change in mean sensor glucose concentration in mmol/L measured by 2 weeks blinded CGM between the CGM group (A) and the SMBG group (C).

► Difference between change in time below range (TBR) (<3.9 mmol/L, <3.0 mmol/L), in percentages, measured by 2 weeks blinded CGM between the CGM group (A) and the SMBG group (C).

► Difference between change in time above range (TAR) (>10 mmol/L, >13.9 mmol/L), in percentages, measured by 2 weeks blinded CGM, between the CGM group (A) and the SMBG group (C).

► Difference between change in glycaemic variability (SD, coefficient of variance and others), in percentages, measured by 2 weeks blinded CGM between the CGM group (A) and the SMBG group (C).

► Difference between change in number of severe hypoglycaemic episodes with the need of assistance between the CGM group (A) and the SMBG group (C).

► Difference between change in insulin dose in IU/day/kg between the CGM group (A) and the SMBG group (C).

► Difference between change in body mass index (in kg/m^2) between the CGM group (A) and the SMBG group (C).

► Difference between change in antidiabetic medicine (new medication, change in doses, discontinuation of medicine) between the CGM group (A) and the SMBG group (C).

► Difference between change in patient-related outcome measures on general well-being, between the CGM group (A) and the SMBG group (C) measured by the questionnaire WHO Five Well-Being Index (WHO-5).

► Difference between change in patient-related outcome measures on diabetes-related distress, between the CGM group (A) and the SMBG group (C) measured by the Diabetes Distress Scale.

► Difference between change in patient-related outcome measures on hypoglycaemia fear between the CGM group (A) and the SMBG group (C) measured by the short-form Hypoglycaemia Fear Survey.

► Difference between change in patient-related outcome measures on diabetes treatment satisfaction between the CGM group (A) and the SMBG group (C) measured by the Diabetes Treatment Satisfaction Questionnaire.

► Difference between change in patient-related outcome measures on satisfaction with glucose monitor between the CGM group (A) and the SMBG group (C) measured by the Glucose Monitoring Satisfaction Scale.

► Difference between change in health behaviour regarding exercise between the CGM group (A) and the SMBG group (C) measured by the Swedish National Board of Health and Welfare questionnaire for Physical Activity.

Continued

Box 1 Continued

- ► Difference between change in health behaviour regarding diet between the CGM group (A) and the SMBG group (C) measured by the Danish Perceived Dietary Adherence Questionnaire.
- ► Difference between change in health behaviour regarding antidiabetic medication adherence between the CGM group (A) and the SMBG group (C) measured by a Danish Medical Adherence Scale.

Other prespecified exploratory outcome measures
- ► Difference between change in TIR, assessed by 2 weeks blinded CGM device, and HbA1c between the CGM groups (without peer support group A and with peer support group B) in percentages.
- ► Difference between change in general well-being between the CGM groups (without peer support group A and with peer support group B) measured by the questionnaire WHO-5.
- ► Difference between change in diabetes-related distress between the CGM groups (without peer support group A and with peer support group B) measured by the Diabetes Distress Scale.
- ► Difference between change in hypoglycaemia fear between the CGM groups (without peer support group A and with peer support group B) measured by the short-form Hypoglycaemia Fear Survey.
- ► Difference between change in glucose monitoring satisfaction between the CGM groups (without peer support group A and with peer support group B) measured by the Glucose Monitoring Satisfaction Scale.
- ► Difference between change in diabetes treatment satisfaction between the CGM groups (without peer support group A and with peer support group B) measured by the Diabetes Treatment Satisfaction Questionnaire.
- ► Difference between change in health behaviour regarding exercise between the CGM groups (without peer support group A and with peer support group B) measured by the Swedish National Board of Health and Welfare questionnaire for Physical Activity.
- ► Difference between change in health behaviour regarding diet between the CGM groups (without peer support group A and with peer support group B) measured by the Danish Perceived Dietary Adherence Questionnaire.
- ► Difference between change in health behaviour regarding antidiabetic medication adherence between the CGM groups (without peer support group A and with peer support group B) measured by a Danish Medical Adherence Scale.
- ► Difference in mean number of days of CGM use between individuals achieving TIR >70% vs TIR <70% within the CGM groups (group A+B).
- ► Difference in HbA1c (mmol/mol) baseline between individuals achieving TIR >70% vs TIR <70% within the CGM groups (group A+B).
- ► Difference in age in years between individuals achieving TIR >70% vs TIR <70% within the CGM groups (group A+B).
- ► Difference in diabetes duration in years between individuals achieving TIR >70% vs TIR <70% within the CGM groups (group A+B).
- ► Difference in C-peptide (pmol/L) between individuals achieving TIR >70% vs TIR <70% within the CGM groups (group A+B).
- ► Difference in education level between individuals achieving TIR >70% vs TIR <70% within the CGM groups (group A+B).
- ► Difference in social status between individuals achieving TIR >70% vs TIR <70% within the CGM groups (group A+B) measured by civil status and occupation.

Continued

Box 1 Continued

- ► Difference in ethnicity between individuals achieving TIR >70% vs TIR <70% within the CGM groups (group A+B) measured by white/non-white.
- ► Difference in medicine used between individuals achieving TIR >70% vs TIR <70% within the CGM groups (group A+B).
- ► Difference in change in health behaviour regarding diet between individuals achieving TIR >70% vs TIR <70% within the CGM groups (group A+B) measured by the Danish Perceived Dietary Adherence Questionnaire.
- ► Difference in change in health behaviour regarding exercise between individuals achieving TIR >70% vs TIR <70% within the CGM groups (group A+B) measured by the Swedish National Board of Health and Welfare questionnaire for Physical Activity.
- ► Difference in change in health behaviour regarding medication adherence between individuals achieving TIR >70% vs TIR <70% within the CGM groups (group A+B) measured by a Danish Medical Adherence Scale.
- ► Correlation between mean number of SMBG/day and time points for SMBG in the study period and improvement in HbA1c, in TIR, in TBR, in TAR within the control group C.
- ► Difference between number of participants using CGM versus not using CGM increasing 5% or more in TIR.
- ► Evaluating which blood glucose values (fasting, preprandial or postprandial) measured by SMBG best reflect TIR.

continuous variables, and Fisher's exact test for categorical variables. Changes in primary and secondary outcomes over the intervention period and effects of the treatments will be modelled by linear mixed-effects models with a patient-specific random intercept to account for the correlation of repeated measurements within patients. These will include the interim measurements at 6 months. The p values for secondary outcomes will be corrected by the Benjamini-Hochberg method for multiple comparisons.

Analysis will be performed on an intention-to-treat basis. Furthermore, per-protocol analysis will be performed, including participants in group A and B having used the CGM device as instructed for at least 80% of the entire study period and participants in group B having participated in at least two out of three peer-support sessions.

Missing data will be handled with multiple imputations. Furthermore, dropout rates and characteristics on non-participants including reasons will be examined if informed consent is obtained. Statistical significance will be inferred at a 2-tailed p value of 0.05 with a CI on 95%.

Patient and public involvement
To examine the education concept of the training course prior to the start of the study, we invited a group of patients at SDCC to give us their considerations on our training courses. We adjusted the course concepts considering their input. Likewise, the peer-support concept and contents and all written information were examined by a group of patients at SDCC to secure correct understanding and user influence here on.

At the end of the study, the participants will be asked to evaluate the study, study procedures, education and so on, including interviews and/or questionnaires, on preferred future treatment.

ETHICS AND DISSEMINATION

The study will be carried out in accordance with the Helsinki Declaration after approval by the Scientific Ethics Committee of the Capital Region (H-20000843).

This study focuses on an important clinical problem with significant health and cost implications for persons with T2D, two-thirds of whom have glycaemic levels above recommended target. Our study will provide evidence of the effectiveness of the use of RT-CGM in the treatment for T2D, potentially shaping clinical guidelines for SMBG frequency and timing as well as use of technology in T2D with an impact on both healthcare and healthcare costs. Not being able to recruit enough participants to reach power estimates may be a potential limitation. Unbalanced dropout rates may be a bias risk, by a higher demand on participants allocated to one of the two CGM groups because CGM is not reimbursed in Denmark, and thereby some participants may sign up for the study with the hope of being randomised to CGM.

The risk of side effects when participating in this study is expected to be low. There is a minimal risk of infection and/or allergic skin reaction at the CGM insertion site. In general, insulin therapy is associated with a risk of hypoglycaemia. The risk of hypoglycaemia during the study is no higher than in the everyday life of persons with insulin-treated T2D. There is a minimal risk of an increase in diabetes distress through an increase in diabetes awareness by using CGM, especially with the use of too many alerts/alarms, but studies have shown that a decrease in diabetes distress is more to be expected.[20] The use of alerts/alarms will be individually set and can be set to a minimum, if needed. The occurrence of any side effect will be assessed at every visit throughout the study period. All participants are covered by the mandatory individual insurance at SDCC, Denmark. The investigators are confident that the possible risks and side effects for the participants are outweighed by the expected benefits from the conduct of this study. If the study is prematurely terminated, the investigators will promptly inform the Scientific Ethics Committee of the Capital Region and the participants to assure appropriate therapy and follow-up.

Study results, positive, negative and inconclusive findings, will be presented at national and international scientific meetings and published in scientific papers in international scientific peer-reviewed journals. In addition, plain-language summary results will be communicated to study participants by letter.

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