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study protocol for a randomized controlled trial

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Published in:
Trials

DOI (link to publication from Publisher):
[10.1186/s13063-024-08588-7](https://doi.org/10.1186/s13063-024-08588-7)

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Publication date:
2024

Document Version
Publisher's PDF, also known as Version of record

[Link to publication from Aalborg University](#)

Citation for published version (APA):

Thomsen, C. H. N., Nørlev, J. T. D., Hangaard, S., Jensen, M. H., Hejlesen, O., Cohen, S. R., Kofoed-Enevoldsen, A., Kristensen, S. N. S., Aradóttir, T. B., Kaas, A., Vestergaard, P., & Kronborg, T. (2024). The intelligent diabetes telemonitoring using decision support to treat patients on insulin therapy (DiaTRUST) trial: study protocol for a randomized controlled trial. *Trials*, 25(1), Article 744. <https://doi.org/10.1186/s13063-024-08588-7>

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STUDY PROTOCOL

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The intelligent diabetes telemonitoring using decision support to treat patients on insulin therapy (DiaTRUST) trial: study protocol for a randomized controlled trial

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Abstract

Background Diabetes affects 10.5% of adults globally, with type 2 diabetes accounting for 90–95% of cases. Achieving optimal glycemic control is crucial yet challenging, particularly with insulin therapy, where 30–50% of patients fail to meet treatment targets. Telemedicine can improve diabetes management but generates vast amounts of data, burdening healthcare professionals. Integrating clinical decision support tools into telemonitoring systems may enhance care efficiency and glycemic control.

Methods The trial is a multicenter 3-month, three-arm, open-label, randomized controlled trial. The trial aims to enroll 51 participants with type 2 diabetes on insulin therapy. Participants will be divided with a 3:1:1 ratio into telemonitoring with decision support, telemonitoring without decision support, and usual care groups. The study employs connected insulin pens, continuous glucose monitors (CGMs), and activity trackers to enable telemonitoring. Outcomes measured include CGM time in range, HbA1c, hypo- and hyperglycemia incidents, total daily insulin dose, body weight, treatment satisfaction, and adherence.

Discussion Telemonitoring with decision support has the potential to revolutionize diabetes management by offering personalized treatment suggestions, thereby reducing the burden on healthcare professionals, and improving patient outcomes. This study will provide valuable insights into the effectiveness of such an approach in achieving glycemic control in people with type 2 diabetes on insulin therapy. By evaluating both clinical outcomes and patient and healthcare professionals' satisfaction, the study aims to contribute to the development of efficient, scalable tel-ehealth solutions for diabetes care.

Trial registration ClinicalTrials.gov NCT06185296. Registered on December 14, 2023.

Keywords Diabetes care, Type 2 diabetes, Telemonitoring, Clinical decision support, Insulin therapy

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Introduction

Background and rationale

Diabetes is a growing global health challenge, with 10.5% of the adult population estimated to have diabetes in 2021. The population is projected to rise to 12.2% (783.2 million people) by 2045 due to continued factors like unhealthy diets, obesity, and decreased physical activity [1]. The vast majority (90–95%) of these individuals have type 2 diabetes [2].

Maintaining optimal glycemic control remains a significant challenge despite being crucial for preventing and managing diabetes-related complications [3, 4]. One major hurdle is the difficulty in accurately determining the appropriate medication dosage for each individual, which is a task that is both time-consuming and complex [4–7]. Approximately 30–50% of people with type 2 diabetes on insulin therapy fail to achieve glycemic targets, highlighting a gap between clinical trial outcomes and real-world effects [8, 9]. This underscores the urgent need for innovative approaches in diabetes care.

Telemedicine has emerged as a promising supplement to the standard of care for improving glycemic control. Such approaches may leverage various technologies to support diabetes management remotely, often with healthcare professionals (HCPs) providing guidance from a distance [10–12]. Studies have shown that telemedicine can significantly impact glycemic control, especially when a monitoring component is included [12]. However, telemonitoring often results in a substantial influx of data, which can overwhelm HCPs [13, 14].

Insights from previous studies and ongoing research, such as the Diabetes teleMonitoring of Patients in Insulin Therapy (DiaMonT) trial (NCT04981808 [15]), also emphasize the necessity for future telemonitoring solutions to incorporate patient-centered treatment suggestions [13, 14, 16–19]. These suggestions can help HCPs manage the large volumes of data generated by telemonitoring. Integrating clinical decision support tools into telemonitoring systems may, therefore, be essential for maintaining resource-effective workflows during telemonitoring. These tools can analyze data, provide treatment-relevant overviews, facilitate clinical decision-making, and reduce the time needed per patient, with the potential for time better spent with patients [20–22]. By incorporating advanced decision support tools, these solutions can thus enhance the efficiency and effectiveness of diabetes care, ultimately leading to better glycemic control and improved patient outcomes [19, 23, 24]. To the best of the authors' knowledge, the integration of advanced decision support tools within telemonitoring systems remains unexplored in the context of insulin-treated people with type 2 diabetes.

Objectives

As part of the Adherence through Cloud-based Personalized Treatment for Type 2 Diabetes (ADAPT-T2D) project, which has the overall objective of improving treatment goals for patients with type 2 diabetes, the present trial aims to explore the feasibility and potential effect in terms of glycemic control of using telemonitoring with integrated decision support for people with type 2 diabetes on or initiating insulin therapy.

Trial design

The trial design is a three-arm, open-label, randomized controlled trial with a 3-month trial period. People with type 2 diabetes will be randomly allocated with a randomization ratio of 3:1:1 to either telemonitoring with integrated decision support (intelligent telemonitoring), telemonitoring without integrated decision support, or usual care (Fig. 1). Due to the nature of the intervention, it is not possible to blind included participants or HCPs to the allocation of participants in the three groups.

The trial will be conducted in accordance with the Helsinki Declaration and the principles of Good Clinical Practice. The Danish Medical Research Ethics Committees (2,313,491) has approved the trial and has been registered at ClinicalTrial.gov (NCT06185296) on December 14, 2023. Any protocol modifications will be approved by the Danish Medical Research Ethics Committees and will be reported to relevant parties.

Methods: participants, interventions, and outcomes

Study setting

The trial will be conducted at two sites: Steno Diabetes Center North Denmark (Aalborg University Hospital, Denmark) and Steno Diabetes Center Zealand (Zealand University Hospital, Nykøbing Falster).

Eligibility criteria

The aim is to include 51 participants. The participants will be people with type 2 diabetes on insulin therapy or about to initiate insulin therapy. Participants will be provided with a connected insulin pen from Novo Nordisk A/S, which is compatible exclusively with Novo Nordisk products. Participants using other insulin brands will transition to Novo Nordisk basal insulin (Tresiba®) at trial initiation, following current guidelines for switching insulin. This transition will be managed by highly trained HCPs to ensure safety. A 24/7 hotline staffed by trained personnel will be available to address any issues or questions related to the transition.

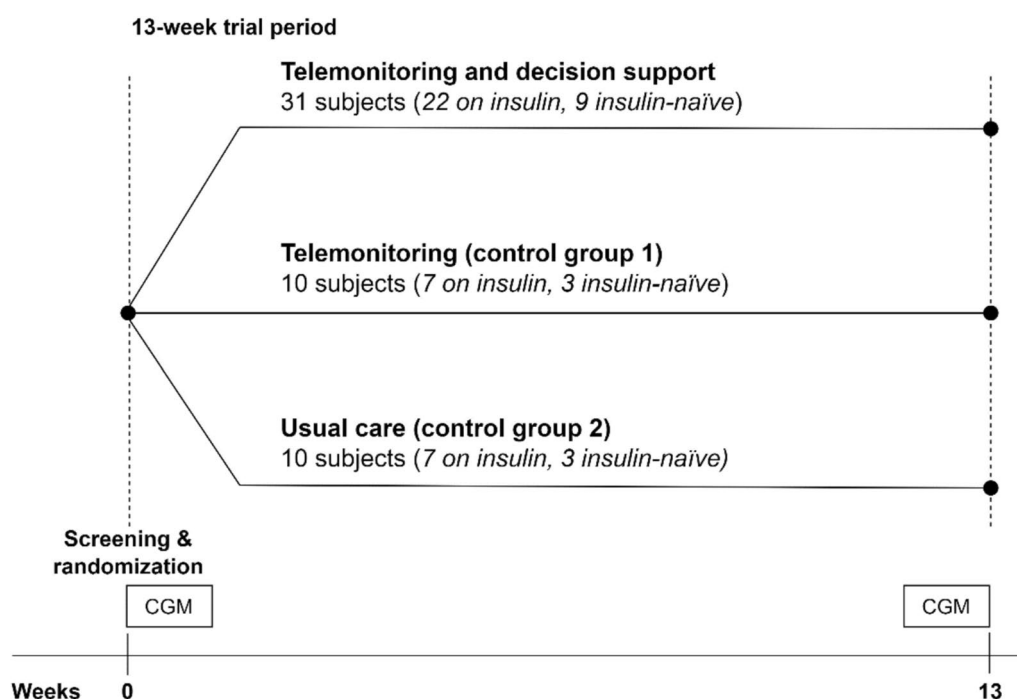


Fig. 1 Trial design. All three groups will visit the trial site two times (indicated by •)

Participants will be included according to the following criteria:

- Adults ≥ 18 years
- Diagnosed with type 2 diabetes ≥ 12 months prior to screening
- Willing to travel to one of the two trial sites to attend in-person visits
- Have an internet connection at home
- Have the personal digital ID, MitID, a Danish national online digital authenticator
- Willing to use a smartphone and the connected devices used in the trial
- Able to understand and read Danish

Participants will be excluded according to the following criteria:

- Pregnancy or breastfeeding
- Major surgery planned during the trial
- Cancer diagnosis within the last 5 years
- Participation in other interventional trials
- Limited literacy affecting the use of trial devices
- Having worn a continuous glucose monitor (CGM) ≤ 6 months prior to the screening
- Treated with mixed insulin
- Conditions deemed by the sub-investigator or investigator to make the participant unfit for the trial,

including insufficient understanding or physical/cognitive ability to participate.

Recruitment

Participants will be recruited through a multifaceted approach. Initially, participants will be recruited at the endocrinology clinics at Aalborg University Hospital or Zealand University Hospital, Nykøbing Falster when attending visits. A poster with trial information will also be displayed at the endocrinology clinics, and hospital staff will hand out a leaflet to interested patients. During a visit to the endocrinology clinics, patients can consent to be contacted by a trial representative to receive further information. Additionally, a group of patients has volunteered to be contacted for new trials at the endocrinology clinic at Aalborg University Hospital, and they will receive initial phone calls followed by mailed information if interested. Furthermore, recruitment efforts will extend to newspaper ads, advertisements in the Danish diabetes magazine, social media, patient organizations, and relevant regional websites.

Informed consent

Patients expressing interest will be invited to an information interview, where they can bring a companion if desired. Detailed in the participant information letter provided beforehand, this interview outlines the trial's

purpose and design. The interview will be conducted at Aalborg University Hospital or Zealand University Hospital, Nykøbing Falster, in a private setting led by the investigator, a sub-investigator, or a delegated project team member possessing requisite expertise related to the trial. Participants are informed of their right to take time for reflection before consenting, and withdrawal of consent is permitted without explanation at any stage. The trial commences only upon the signing of informed consent by both participant and investigator or sub-investigator.

The randomization process

In case of informed consent, the participant will be randomized to either intelligent telemonitoring, telemonitoring alone, or usual care during the initial visit to the endocrinology clinic at Aalborg University Hospital or Zealand University Hospital, Nykøbing Falster. Randomization will be conducted in REDCap (2020 Vanderbilt University) using a computer-generated block-randomized list (3:1:1 ratio) stratified on the proportion of insulin-naïve, resulting in 30% insulin-naïve in each group. The allocations will remain concealed until interventions are assigned. Participants will be enrolled and informed about the trial by HCPs. Participant consent and assignment of interventions will also be handled by HCPs. At the first visit, several basic information about the participants will be obtained together with responses to eight questionnaires (Table 1). Furthermore, a venous blood sample will be drawn to address secondary endpoints and establish baseline data with a lab technician or nurse overseeing the sampling procedure.

The intervention

The intelligent telemonitoring group

At the first visit, participants in the intelligent telemonitoring group will be provided with a CGM (Dexcom G7), Novo Nordisk insulin pen(s) (NovoPen6), an activity tracker (Fitbit Charge 4), and a smartphone. Participants treated or initiated with long-acting insulin only will be provided with one insulin pen, while participants treated with long- and short-acting insulin (or will initiate short-acting insulin during the trial) will be provided with two insulin pens. Participants will be asked to use the Novo Nordisk insulin pen(s) to administer insulin for the entire trial period. Participants will also be asked to wear the CGM and an activity tracker for the entire trial period. Participants will use the provided wearable devices continuously at home to collect, log, and transfer tissue glucose levels, insulin administration, activity, and sleep for the entire trial duration. During the trial, participants will be asked to use three smartphone apps: one for activity tracker data (Fitbit:

Health and Fitness), one for CGM data (Dexcom G7 app), and one for transferring insulin data recorded by the insulin pen(s) (ADAPT app). Participants will use the provided smartphone to access the apps. Furthermore, participants will be asked to use a web portal (ADAPT portal for patients), which can be accessed via the Internet on a computer. In the web portal, participants will be able to see a combined view of CGM, insulin, and activity data. Participants will therefore need a computer with internet access during the trial to access the combined overview of the data collected from the wearable devices. If participants do not have a computer, they will be provided with one for the trial period. HCPs will train participants in using the technologies at the first visit and provide assistance during the trial.

The telemonitoring system incorporating decision support will support the monitoring HCPs in telemonitoring the participants. An overview of the system and the exchange of data across the parts of the system is seen in Fig. 2. The monitoring HCPs will receive training in using the system prior to trial initiation to equip them to use the system to telemonitor participants.

HCPs affiliated with the clinical trial sites will perform the telemonitoring using the HCP-facing part, ADAPT Portal, of the telemonitoring system which will comprise visualizations of data collected by the wearable devices (CGM, insulin pen(s), and activity tracker) and provide decision support using two algorithms built into the system, a treatment insights algorithm, and a basal insulin dosage suggestion algorithm:

- 1) The treatment insights algorithm will provide insights into trends in data that may elucidate treatment-relevant issues for a participant's current treatment (e.g., misalignment between insulin doses taken and the ones prescribed, missed insulin doses, etc.).
- 2) The basal insulin dosage algorithm will provide the HCPs with a suggestion for basal insulin dose based on the CGM and insulin pen data collected from the participants.

Decision support will also be directed at participants through the ADAPT app, as they can choose to acquire their risk of nocturnal hypoglycemia before going to bed by actively requesting this risk by pushing a button in the ADAPT app. An algorithm will generate the risk. This algorithm is part of the intelligent telemonitoring system.

HCPs, in collaboration with an endocrinologist, make all treatment decisions during the trial. Thus, the intelligent telemonitoring system will only provide information that the monitoring HCPs may choose to act according to if they agree with the treatment suggestion.

Table 1 Overview of assessments, blood samples, and questionnaires collected at trial visits to the endocrinology clinic. *Only participants in the intelligent telemonitoring and telemonitoring group will be asked to answer the DHSS questionnaire

	Screening	13-week trial period
Visit (V)	Visit 1	Visit 2
Time of visit (weeks)	0	13
Visit windows (days)		84–105
Person related assessments		
Date of birth	X	
Gender	X	
Highest education level achieved	X	
Income level	X	
Marital status	X	
Duration of diabetes	X	
Diabetes complications	X	
Concomitant medications	X	
Concomitant illness	X	
Smoking	X	
Alcohol habits	X	
Exercise and diet	X	X
Number of severe cases of hypoglycemia within the last 12 months (severe hypoglycemia will be defined based on the latest recommendations from the American Diabetes Association)	X	
Information on insulin use prior to trial		
• Time for insulin initiation	X	
• Insulin regimen		
• Dosing schedule (number of units prescribed and recommended dosing times)		
• Administration device		
Number of diabetes-related visits or contacts (by phone, e-consultations, etc.) with HCPs at a healthcare facility (e.g., endocrinology department, general practitioner, etc.) within the last 12 months	X	
Number of hospitalizations within the last 12 months	X	
Clinical assessments		
Height	X	
Body weight	X	X
Blood pressure	X	
Laboratory assessments		
HbA _{1c}	X	X
C-peptide in serum	X	
Lipids in plasma	X	
Glucose in plasma	X	
Insulin in serum	X	
Other assessments		
Health literacy (The European Health Literacy Survey Questionnaire Short Form (HLS-EU-Q short form))	X	
Hypoglycemia unawareness status (Clarke hypoglycemia awareness survey)	X	
Fear of hypoglycemia (HFS-II short form)	X	X
Health-related quality of life (EQ-5D)	X	X
Diabetes-related quality of life (DIDP questionnaire)	X	X
Patient adherence (MMAS-8)	X	X
Treatment satisfaction (DTQS questionnaire)	X	X
Perceived competences in diabetes (PCD questionnaire)	X	X
Participants and HCPs' satisfaction with telemonitoring solution (DHSS questionnaire, 10-items for participants* and 11-items for monitoring HCPs)		X

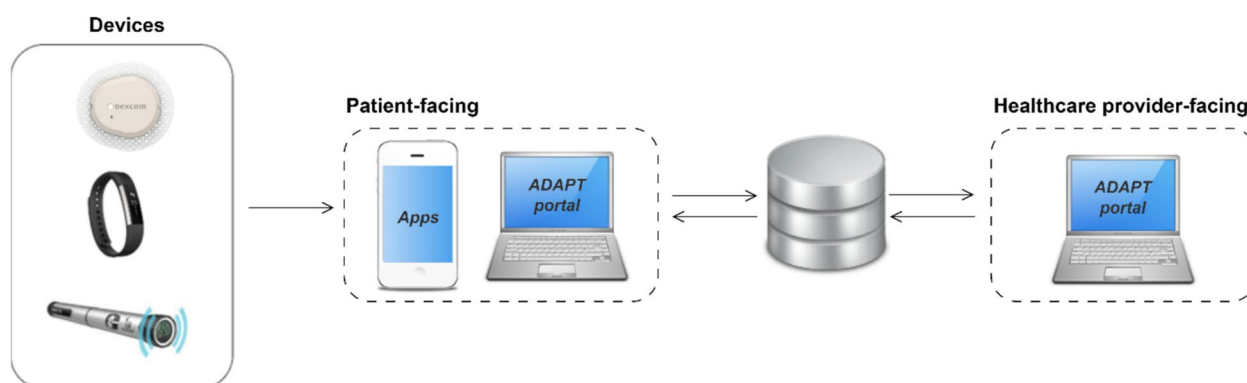


Fig. 2 Overview of the different parts of the developed decision support system and the exchange of data across these parts from the wearable devices (CGM, activity tracker, and insulin pen) to the patient-facing app on a smartphone to a cloud server from where the healthcare professionals can assess the participants data and update insulin treatment

The HCPs will initiate telephone contact with participants on at least two occasions—1 week and 1 month after inclusion in the trial. However, the monitoring frequency will be customized to suit each participant's requirements, and participants may receive ongoing contact if deemed relevant by the monitoring HCPs. All calls to participants are recorded in trial notes, and any treatment-related information from the calls will be recorded in their respective electronic patient journals.

The telemonitoring group

Participants in the telemonitoring group will be monitored in the same manner as those in the intelligent telemonitoring group. They will also be asked to use a CGM (Dexcom G7), Novo Nordisk insulin pen(s) (NovoPen6), an activity tracker (Fitbit Charge 4), and a smartphone. The only difference between the two groups is that no decision support will be provided to either the participants or the HCPs monitoring participants in the telemonitoring group.

The usual care group

Participants in the usual care group will receive usual care but will be provided with a blinded CGM (Dexcom G7) with a receiver, insulin pen(s) (NovoPen6), and a smartphone with the ADAPT app. Usual care of people with type 2 diabetes typically covers an annual or biannual consultation. Other contacts with HCPs are on the patient's initiative and, therefore, the frequency of contacts with HCPs varies greatly from person to person. People with type 2 diabetes treated with or initiating insulin are encouraged to measure blood glucose using a glucometer at least once daily if treated only with basal insulin and at least thrice daily if treated with basal insulin in combination with bolus insulin daily (39). Participants will be asked to wear the blinded CGM during two

periods: in continuation of the first visit and before end of trial visit. Each period will have a duration of 20 ± 3 days. These participants will get a receiver to collect the data, as they will not have the Dexcom G7 app. Furthermore, they will be asked to use the insulin pen(s) for the entire trial period and to transfer insulin data to the ADAPT app. Participants will not be able to view their CGM data or insulin data during the trial. No changes in insulin dosage will be performed based on the blinded devices, as neither participants nor monitoring HCPs have access to data. CGM data will be used to analyze primary and secondary outcomes. Recorded insulin data will be used for later analysis and comparison of adherence between the three groups.

Criteria for discontinuing

In case of any serious adverse events related to the trial are identified, as determined by the primary investigator, the trial will be stopped. If a participant reacts unexpectedly to the trial according to the primary investigator's assessment, or if a participant is otherwise not suited for further participation (e.g., not using the devices as assigned or not attending visits at the endocrinology outpatient clinic), participation can be terminated at any time.

Strategies to improve adherence to intervention

Intervention adherence will be assessed using data obtained from the connected devices and from interactions between participants and HCPs.

End of trial

At the end of the trial visit to the endocrinology clinic, participants from all three groups will be asked to answer several questionnaires, and a HCP will perform assessments and take a venous blood sample (see Table 1).

Furthermore, participants who transitioned to Tresiba® from other insulins will be carefully monitored to ensure a smooth transition back to their pre-trial insulin brand if necessary.

Outcome measures

All CGM-based endpoints are defined using the International Consensus Report from 2019 [25].

Primary endpoint

Change from baseline in CGM time in range (3.9–10.0 mmol/L) three months after randomization.

Secondary endpoints

- 1) Change from baseline in HbA1c three months after randomization.
- 2) Change from baseline in CGM time in level 1 hypoglycemia (3.0–3.8 mmol/L) three months after randomization.
- 3) Change from baseline in CGM time in level 2 hypoglycemia (<3.0 mmol/L) three months after randomization.
- 4) Change from baseline in CGM time in level 1 hyperglycemia (10.1–13.9 mmol/L) three months after randomization.
- 5) Change from baseline in CGM time in level 2 hyperglycemia (>13.9 mmol/L) three months after randomization.
- 6) Change from baseline in total daily dose three months after randomization.
- 7) Change from baseline in CGM endpoints three months after randomization: episodes (hypoglycemia and hyperglycemia) 15 min and area under the curve.
- 8) Change from baseline in body weight three months after randomization.
- 9) Use of telemonitoring equipment: The frequency of use during the trial is assessed directly from the delivered devices.
- 10) Time-to-target with respect to individualized treatment targets.
- 11) Time efficiency: Between-group differences in time spent on contact with participants and treatment evaluation/telemonitoring of participants by HCPs during the 3-month trial.
- 12) Fear of hypoglycemia: Between-group differences measured by the hypoglycemia Fear Survey-II short form (HFS-II short form) questionnaire at baseline and the 3-month assessment.
- 13) Diabetes-related quality of life: Between-group differences measured by the DAWN Impact of Dia-

betes Profile questionnaire (DIDP) at baseline and the 3-month assessment.

- 14) Quality of Life: Between-group differences measured by the EQ-5D questionnaire at baseline and the 3-month assessment.
- 15) Patient adherence: Between-group differences measured by the Morisky Medication Adherence Scale 8-item (MMAS-8) at baseline and 3-month assessment.
- 16) Participants' and HCPs' satisfaction with telemonitoring. Measured by Digital Health Solution Satisfaction questionnaire (DHSS) at the 3-month assessment.
- 17) Treatment satisfaction: Between-group differences measured by the Diabetes Treatment Satisfaction Questionnaire (DTSQ) at baseline and the 3-month assessment.
- 18) Perceived competence in Diabetes: Between-group differences measured by the Perceived Competence in Diabetes questionnaire (PCD) at baseline and the 3-month assessment.

Exploratory endpoints

The exploratory endpoints are based on questionnaires and monitoring data and include the following:

- 19) Self-reported adherence information. During contact between HCPs and participants in the two telemonitoring groups, participants will be asked about their insulin adherence during the previous week.
- 20) Insulin doses and times. Any differences in the use of insulin between the three groups are examined based on data from the insulin pens.
- 21) Change from baseline in CGM endpoints three months after randomization: number of days worn, percentage of time active, mean glucose, glycaemic variability, and glucose management indicator.
- 22) Changes from baseline in diet and exercise habits.
- 23) Self-reported information on diet and exercise habits was collected during contact between HCPs and participants in the two telemonitoring groups.

In addition, qualitative interviews and usability testing will be conducted with selected participants and HCPs from the trial sites to gain deeper insights into the participants' and HCPs' experience of the design and use of the intelligent telemonitoring solution and telemonitoring alone.

Data management

Data management involves both manual archiving and storage on a computer system within REDCap. The storage duration is in accordance with regulations notified to the Danish Data Protection Agency. Signed informed consent forms are securely stored and kept under lock and key. Questionnaire responses and other patient data are housed within REDCap. Access to all data is restricted, known only to the investigator, sub-investigator, and select project members.

Any review or manipulation of third-party data will occur only with agreement between the sub-investigator and the primary investigator. Data will be retained for the duration specified by the Danish Data Protection Agency. If renewal is requested, the trial will be reevaluated for permission. Data cleaning procedures are carried out throughout the trial, including cross-validation of dates, duplicate searches, and source data verification. Corrections to source data adhere to ICH guidelines for good clinical practice.

Confidentiality

During the trial, participant information will be collected, encompassing health status, medication, and comorbidities. This data serves three purposes: ensuring subject suitability for study inclusion, facilitating later analysis in anonymized forms, and aiding HCPs in providing appropriate patient care. Information retrieval occurs only after informed consent is obtained, granting primary investigators, sub-investigators, and designated project members direct access to patient journals, including electronic records. Retrieved data includes health conditions vital for trial completion and for monitoring and quality control purposes. Access to patient information is restricted to HCPs and relevant project team members at Steno Diabetes Centers, with no access granted to personally identifiable data for other ADAPT-T2D consortium members. Regulatory authorities may access patient journals to fulfill monitoring and quality control obligations essential for study completion.

Plans for collection, laboratory evaluation, and storage of biological specimens

Blood samples will be drawn from all participants at the initial and the final visit. These samples are analyzed for HbA1c, lipids, c-peptide, glucose, and insulin levels. Approximately 30 mL of blood will be collected per participant. After extraction, the samples are analyzed at Aalborg University Hospital or Zealand University Hospital, Nykøbing Falster and subsequently disposed of. HCPs at Steno Diabetes Center North Denmark and Steno Diabetes Center Zealand will manage the blood

collection and processing. All biological material will be discarded once all relevant analyses for the research project are completed at its conclusion.

Sample size calculation

The sample size calculation follows this formula:

$$n = \frac{2\sigma_d^2}{\tau^2} \left(z_{\frac{\alpha}{2}} + z_{\beta} \right)^2$$

τ represents the minimum detectable difference in mean, while σ_d represents the standard deviation of the difference. Assuming a difference in CGM time of 15.9 ($\tau=15.9$) and a standard deviation of the difference of 15.5% ($\sigma_d = 15.5$) [34], with a significance level of 0.05 and a power of 0.8, the required number of participants is 39. The assumed difference in CGM time in range and the standard deviation of the difference is based on preliminary data from the DiaMonT trial (NCT04981808). Accounting for an estimated dropout rate of 30%, 51 participants need to be included. The high anticipated dropout rate is primarily expected in the usual care group. To mitigate loss to follow-up, HCPs will provide participants in the usual care group with 2 months telemonitoring after trial completion.

Statistical analysis

The trial's objective will be explored using a range of statistical methods. No formal analysis is planned during the data collection phase.

All analyses will adhere to both intention-to-treat and per-protocol principles. The intention-to-treat analysis will encompass all participants randomized across the trial's three groups, while the per-protocol analysis will exclude those lost to follow-up.

The primary endpoint will be investigated using data from all participants via a primary analysis utilizing a statistical model incorporating multiple imputation using multivariate imputation by chained equations (MICE). This technique fills in missing CGM data using information from participants in the usual care group (treatment policy). An ANCOVA analysis with CGM time in range at baseline as a covariate will estimate the effect of intelligent telemonitoring on CGM time in range compared to the telemonitoring alone and usual care.

Secondary endpoints, CGM metrics, and HbA1c will undergo similar ANCOVA analyses, also with baseline values serving as covariates. The treatment policy will be employed to impute missing data points.

Sensitivity analyses with similar configurations will be applied to subgroups. Subgroup analyses will differentiate between participants already receiving insulin treatment

pre-trial and those who are insulin naïve. Furthermore, the total daily insulin dose will be investigated in a sensitivity analysis among subgroups, and the total daily dose of basal and bolus insulin will be investigated.

Researchers from the project group will conduct the data analysis without blinding to group assignments due to practical and financial considerations.

Monitoring

Composition of the coordinating center and trial steering committee

The ADAPT-T2D consortium's steering committee will supervise the trial and fulfill the role of the data monitoring committee. Additionally, an independent research member from Steno Diabetes Center North Denmark, uninvolved directly in the trial, will conduct audits on data quality throughout the trial duration.

The core team responsible for managing the trial will include lab technicians and research project managers. They will convene regular meetings as needed throughout the trial period, with monthly status meetings scheduled. The primary investigator, the data auditing research member, and other relevant project members will be invited to these meetings and participate as required.

Adverse event reporting

The risks and potential side effects of participating in the trial are deemed minimal. Any adverse events linked to the trial will be documented in both the electronic patient journal and the trial master file in REDCap if attributed to the trial by the primary investigator or his/her authorized representative. All trial-associated adverse events will be included in the primary trial publication.

Discussion

The DiaTRUST trial is designed to investigate the feasibility and potential effect of telemonitoring with integrated decision support on glycemic control for people with type 2 diabetes who are either already on insulin therapy or initiating it. By including both insulin-treated and insulin-naïve people with type 2 diabetes, the trial seeks to broaden its potential impact. Effective diabetes management can reduce the risk of complications, leading to improved quality of life and potentially lower healthcare costs. By addressing a growing global health challenge, the study seeks to contribute to better public health outcomes.

Various interventional elements will be employed in the DiaTRUST trial, including multiple connected devices, three decision support algorithms, and monitoring by HCPs. This complexity makes it challenging to isolate the specific source(s) of potential effect(s) from the intelligent telemonitoring setup. Nevertheless, the primary aim

of this trial is to evaluate the feasibility of telemonitoring with integrated decision support as a whole, with future studies potentially exploring the contribution of individual components in more detail.

Although the sample size of 51 participants may limit the statistical generalizability of the results, the purpose of the DiaTRUST trial is to assess feasibility rather than efficacy. The insights gained will inform the planning of larger-scale trials that can more robustly explore the effectiveness of telemonitoring with decision support in this population.

The open-label design of the DiaTRUST trial, a necessary feature given the nature of the intervention, presents potential bias, as both participants and HCPs are aware of the intervention being tested. This may introduce bias into the results, and this will be considered in the interpretation of the trial outcomes. Additionally, the use of blinded CGM in the usual care group could lead to a Hawthorne effect, where participants alter their behavior due to the awareness of being monitored. This will be considered as a potential limitation when interpreting the study results.

While the 3-month duration of the trial is appropriate for assessing the feasibility and short-term effects of the intervention, it may not capture long-term outcomes, such as sustained glycemic control or changes in insulin dose requirements. Future studies with extended follow-up periods will be necessary to evaluate the long-term effects and durability of telemonitoring interventions for people with type 2 diabetes.

Moreover, the single-country nature of the trial, conducted in Denmark, may limit the generalizability of the findings to other healthcare settings or populations. Future multi-national trials will be required to validate these findings across more diverse healthcare settings and populations.

To the best of the authors' knowledge, this trial presents the first attempt to integrate decision support into telemonitoring for people with type 2 diabetes. It holds the potential to offer valuable insights into the future of telemonitoring solutions incorporating decision support to ease the clinical interpretation of the large amount of telemonitoring data by providing actionable insights. The study's findings could potentially inform the development and implementation of more effective telemonitoring solutions within healthcare systems. If successful, the intervention could lead to cost savings by optimizing resource use and improving patient management.

Trial status

The present trial protocol (version number 2, 18.10.2024) is expected to commence participant recruitment in January 2025 and is expected to conclude in May 2026.

Abbreviations

ADAPT-T2D project	Adherence through Cloud-based Personalized Treatment for Type 2 Diabetes project
CGM	Continuous glucose monitor
DiaMonT trial	Diabetes teleMonitoring of Patients in Insulin Therapy trial
DiaTRUST trial	Intelligent Diabetes Telemonitoring Using decision Support to treat patients on insulin Therapy trial
HCP	Healthcare professional

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s13063-024-08588-7>.

Supplementary Material 1.

Acknowledgements

N/A.

Dissemination plans

The study results will be published in international scientific journals in anonymized form only. The results will be published irrespective of their acceptance by international journals and regardless of whether the results are positive, negative, or inconclusive. Authorship in future trial publications will follow the Vancouver Convention.

Authors' contributions

All authors were involved in both the trial's design and the writing of the manuscript. Furthermore, each author has critically reviewed and given approval for the manuscript's final version.

Funding

The ADAPT-T2D project has a total budget of 33 million DKK. The project received 10 million DKK in funding from the Innovation Fund Denmark, with the remaining amount primarily self-financed by Novo Nordisk A/S. This financial support covers staff remuneration, blood sampling and analysis, transportation costs, telemedicine equipment, system development, publication of results, and various trial materials.

Data availability

Access to patient journal information is restricted solely to project team members and HCPs affiliated with Steno Diabetes Center North Denmark. Other members of the ADAPT-T2D consortium will not have access to any personally identifiable data. Review and manipulation of third-party data will occur only with the agreement of the primary investigator. Data will be retained for the duration specified by the Danish Data Protection Agency. All biological material will be disposed of at the project's conclusion once all analyses relevant to the specific research project have been finalized.

Declarations

Ethics approval and consent to participate

The trial protocol has been approved by the Danish Medical Research Ethics Committees (2313491). Any necessary modifications to the original trial protocol will require submission of a supplemental protocol to the Danish Medical Research Ethics Committees for approval. If the Danish Medical Research Ethics Committees determine that any modifications to the original protocol necessitate informing participants, they will be contacted by telephone.

Consent for publication

No personally identifiable information about individual participants will be disclosed. The authors do not anticipate the need for additional consent from participants for future studies using trial data. However, if such consent is unexpectedly required, participants will be contacted via mail.

Competing interests

The principal investigator has no conflicts of interest. Several authors are present employees at Novo Nordisk A/S and/or hold company shares at Novo Nordisk A/S.

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Received: 3 July 2024 Accepted: 28 October 2024

Published online: 08 November 2024

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