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Title: Digital follow-up. Can patients with well-controlled type 2 diabetes have digital annual follow-up without compromising quality of care?

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Digital follow-up. Can well-regulated patients with type 2 diabetes have digital annual follow-ups without compromising quality of care?

1.1.1/ Introduction

Type 2 diabetes (T2D) is a chronic, increasingly prevalent condition, making delivery of personalized, effective care a growing challenge. In Denmark, demographic changes, resource constraints, and workforce shortages are driving major health system reforms. To use future resources efficiently, care must be more precisely targeted so that support is focused on those with the greatest need. For diabetes services, this will mean that people with well-controlled T2D will inevitably be seen less often or supported through different models of care, than they are today.

A review from 2024 showed that for persons with T2D who had not achieved cardiometabolic control, intensifying encounter frequency could enhance medication adherence, shorten the time to achieve the treatment target, and improve the patients' quality of life. However, for the patients who had already achieved the treatment targets, less frequent encounters were equivalent to intensive encounters in maintaining their cardiometabolic control and could save considerable healthcare costs without lowering the quality of care and patient satisfaction (5).

A growing proportion of people with type 2 diabetes in Denmark are well controlled. This supports the exploration of alternative follow-up models for this large patient group from a healthcare perspective.

From the patients' perspective, it is also considered relevant, as recent research indicates that a key factor in the well-being and treatment of persons with diabetes, is avoiding unnecessary interventions in their daily lives (14).

This study focuses on management of care for persons with well-controlled type 2 diabetes in general practice, looking into alternative ways for safe annual follow-ups for this group.

1.1.2/ Background

In Denmark, 345,000 people are living with type 2 diabetes (2). The number is increasing and expected to rise further in the coming years; by 2030, at least 420,000 Danes are projected to have T2D (2).

In Denmark, most people with type 2 diabetes are managed by their general practitioner (1). In 2023 patients with type 2 diabetes generated 4,114,535 GP contacts (3), an average of just under 15 contacts

per person annually; contacts may have been for diabetes care or for other health issues. By contrast, the general population aged over 30 generated average 8.6 GP contacts (4).
Nearly 4 out of ten (38 %) patients with type 2 diabetes in Denmark have normal glycated glucose, HbA1c < 48 mmol/mol, and LDL cholesterol below 2,5 mmol/l and no history of atherosclerotic cardiovascular comorbidity (2).

An audit published in 2025 (1), reviewing 1,398 T2D patients of all ages followed in general practice in the Region of Southern Denmark in 2023, found that in 44% of patients no actions were taken at the annual diabetes follow-up (e.g., change in medication dose, any type of referral, or lifestyle counselling).

Internationally, there is no consensus regarding the optimal consultation frequency for patients with type 2 diabetes, partly due to a lack of evidence in this area. An initial scoping review showed that the scientific literature is limited, and that recommendations for the frequency of diabetes consultations range from every 1 to 12 months and are primarily based on “consensus on good clinical practice” rather than evidence (5).

In the current guideline for the treatment of type 2 diabetes from the Danish College of General Practitioners (DSAM), it is recommended that patients attend diabetes follow-up between 1 and 4 times per year (9). The frequency may depend on the extent to which clinical treatment targets are achieved, the presence of complications, other comorbidities, and the patient’s overall health.

The guideline thus supports a differentiated approach to diabetes care, but it does not provide specific decision models for how this differentiation should be managed, resulting in substantial variation in control frequency between comparable groups of persons with type 2 diabetes.
There is a lack of data-driven decision-support tools to help physicians determine the optimal frequency of consultations for patients with type 2 diabetes. A 2022 systematic review examined 348 studies that attempted to differentiate treatment for patients with type 2 diabetes. The review showed that, in most cases, expert opinion was used to predict glycemic control, complications, and mortality in patients with type 2 diabetes. Data-driven models for stratification were used in only 6.7% of the studies (7).

In 2023 SCORE2-Diabetes was published by European Society of Cardiology. SCORE2-Diabetes is an algorithm which predicts the 10-year risk of fatal and non-fatal atherosclerotic cardiovascular (ASCVD) disease in T2D patients aged between 40-69 years without previous ASCVD. Thus, SCORE2-Diabetes can help GPs determine cholesterol management intensity and the need for antithrombotic therapy in T2D patients without prior ASCVD and may also guide follow-up frequency for these patients.

The limitation of using SCORE2-Diabetes to guide treatment intensity and follow-up frequency is that it does not capture the risk of developing microvascular complications. Clinicians should therefore also assess microvascular risk when planning therapy and follow-up. The strongest risk factors for microvascular complications are elevated HbA1c and long diabetes duration (13). While albuminuria indicates already established microvascular endothelial damage in the kidney.
By contrast, the strongest risk factors for macrovascular complications, which Score2-Diabetes primarily considers, are age, smoking, and systolic blood pressure, while cholesterol and HbA1c rank lower (14).

Thus, optimal prediction of complications requires balancing indicators of both micro- and macrovascular disease, which is inherently complex.

Every GP in Denmark can access a comprehensive list of their T2D population via the Careplan overview. The list automatically pulls data from the medical record and displays the GP’s complete population of

type 2 diabetes patients. It offers an overview of who is well controlled across key indicators and who is not. The list contains year of birth, HbA1c, LDL, eGFR, UACR, blood pressure, year of diabetes diagnosis, SCORE2-Diabetes, date of last annual review, and flags for ongoing organ protective therapies (e.g., SGLT-2i). Using this data, GPs might be able to tailor follow-up frequency for their patients with type 2 patients, as key risk indicators are shown in the Careplan overview.

Recent research indicates that a key factor for the well-being and treatment of persons with diabetes is avoiding interventions that unnecessarily disrupt their lives, a concept known as Minimal Disruptive Medicine (8). Because younger, well-managed patients face many years with diabetes, minimizing their lifetime disease burden is essential. With Denmark's rising retirement age, an increasing share of people with type 2 diabetes will remain in the workforce longer, underscoring the need for flexible follow-up models that reduce unnecessary visits and alleviate diabetes related stress.

Previous studies e.g., DiabetesFlex (6) have shown that patient-initiated check-ups in people with type 1 diabetes who were followed on an outpatient basis, versus established check-ups, improved diabetes-related well-being and decreased face-to-face visits, while maintaining safe diabetes management.

On behalf of the organization "Danish Patients," the research institute Voxmeter, in 2023 published a survey (11) of 1,004 representative Danes about their preferences and experiences with access to general practice. The results showed that across all age groups, half of Danes wished to have the option of digital consultations with their GP.

In the 2024 Danish Healthcare Reform, digital health is a key focus. The reform establishes a new patient's right: Danes must be offered digital contact (video, phone, or message) with the healthcare system when it is clinically appropriate, and the patient requests it (12).

In summary, with the rising prevalence of people with type 2 diabetes and a growing share being well-regulated, combined with GPs under increasing pressure to manage chronic diseases, and an increasing demand for digital contact from patients and health authorities, there is a clear need to study how general practice can differentiate in follow-ups for persons with type 2 diabetes and assessing whether digital contact can be implemented safely with respect to key diabetes indicators.

1.2/ Aim and hypothesis

The overall purpose of the study is to gain knowledge on how general practice can safely differentiate care for people with type 2 diabetes with the aim of increasing health equity. In addition, the study contributes knowledge on how digital care can support differentiation in general practice.

The study will investigate whether digital annual follow-up can be implemented for patients with well-controlled type 2 diabetes (as defined by predefined indicators) without compromising treatment quality.

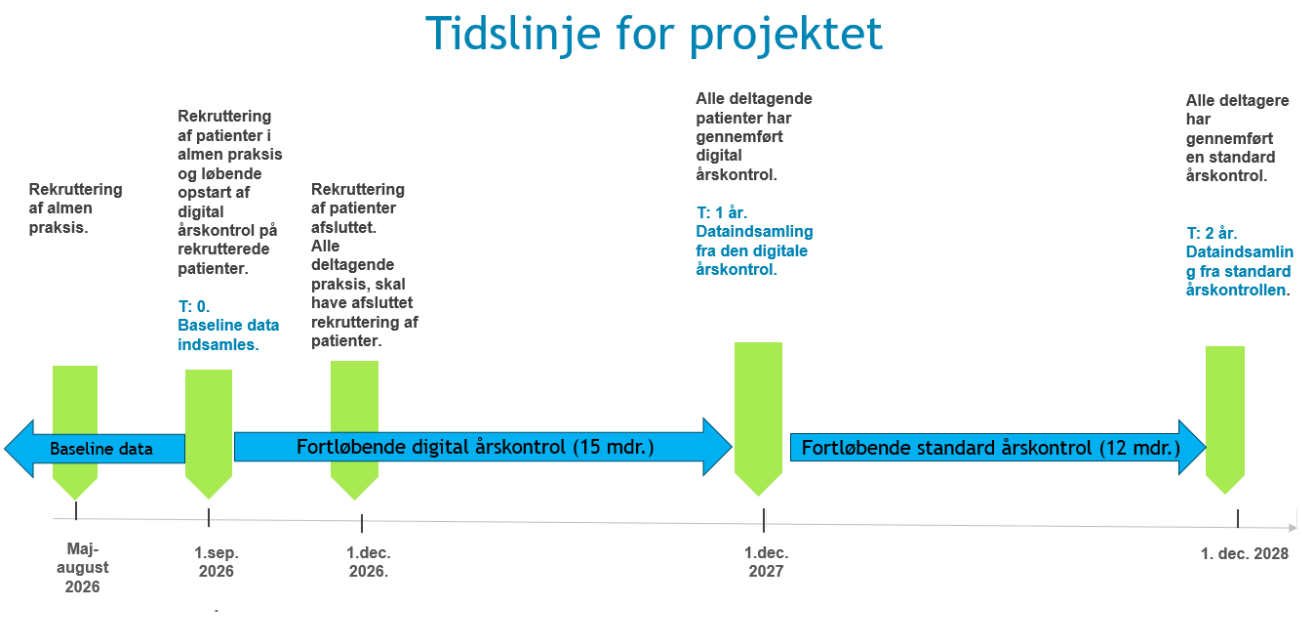
The study also aims to identify factors beyond the obvious paraclinical parameters that GPs consider when evaluating persons with type 2 diabetes, not suitable for digital annual follow-up.

To ensure thorough contextual understanding of the implications this may have on general practice, patients, and their interaction, we qualitatively explore the practices and experiences involved in differentiating diabetes follow-up.

In a prospective follow-up study, we hypothesize the following. For well-regulated persons with type 2 diabetes, replacing annual in-person follow-up with a digital follow-up every second year, can be implemented safely with respect to diabetes management.

In Danish general practice, there is no uniform follow-up schedule for people with well-controlled type 2 diabetes; GPs individually determine their patients' intervals. Visits are usually preceded by blood tests to assess the relevant markers for diabetes (for example HbA1c and renal function).
This study will assess whether it is equally safe for this predefined group of persons with well-regulated type 2 diabetes to undergo a single annual blood test to monitor diabetes status. It will also evaluate whether the annual follow-up—normally a face-to-face consultation in which test results and a yearly diabetes review are provided—can be conducted digitally every other year. Under the digital model, participants will still have blood samples taken, perform measurements (for example blood pressure), complete a lifestyle report on diet, smoking, alcohol, and exercise, and fill in a questionnaire screening for symptoms of complications. The clinician's assessment of test results and communication of results to the participant will be delivered via the clinician's messaging system using the "Min Læge"- app. Thus, the annual check-up communication between doctor and participant will be digital, except for the blood sampling itself, which naturally requires an in-person visit.

1.3/ Timeline and Methods



Methods

The study comprises two methodological components:

1. Prospective follow-up study

A prospective cohort study with an intervention and two-year follow-up, comparing intervention participants to a matched control group of non-intervention participants identified via registries in the Central Region of Denmark BI database. Prespecified outcomes include diabetes-related clinical indicators, morbidity, primary and secondary healthcare utilization, and medication use. Register-based outcomes are available for all participants.

2. Qualitative study

A qualitative study exploring the experiences and practices of patients and healthcare professionals in the intervention group, with a particular focus on their experiences and practices concerning digital annual follow-up and the differentiation of follow-up intensity. This includes examining how the transition to digital follow-up influences patients' everyday life, including their sense of security, self-management of diabetes, and engagement with their own health. Data will be collected through participant observations in consultations in general practice and semi-structured qualitative interviews, aiming to provide in-depth insight into how digital follow-up is experienced and implemented in clinical practice. The project will be solely qualitative and will not make use of surveys.

Approximately fifteen participants who, in accordance with the identification and recruitment process described in section 1.3.3.-1.3.4, have consented to participate in the study will be interviewed by a trained anthropologist within 1-2 months after enrollment, and again in relation to their digital annual follow-up. The participants will be selected purposefully in cooperation between the qualitative researcher and the GPs to obtain variation in relation to age, gender, and years with type 2 diabetes. The participant's GP or GP nurse will, in the absence of the interviewer, ask the participant, either verbally or in writing, whether they wish to be interviewed.
For participants who accept to be interviewed, the interviews will take place in the participant´s home or at the GP clinic. Furthermore, if accepted by the participants, the anthropologist will participate in diabetes-related interactions with general practice to observe and gain knowledge of practices of diabetes care.
Interviews will be transcribed and coded in qualitative research software (Nvivo) along with observational fieldnotes. The semi-structured interviews will be based on an interview guide that will address themes of 1) everyday life with diabetes, 2) disease and treatment burden, 3) interactions with and use of general practice, 4) confidence in diabetes care, and 4) changes in the patient's role and responsibility in diabetes care. Through participant observation in general practice the study will also explore how health professionals in general practice consider and negotiate differentiation in diabetes care and identify factors that play beyond the paraclinical parameters when GPs consider patients eligible to digital annual follow-up. The qualitative researcher will follow GP's and nurses' work in the clinics. Before observing consultations, patients will be informed of the purpose of the qualitative study by the GP or nurse and will be able to decline the presence of the researcher.

1.3.1./ Setting and study population

The study will be conducted in selected general practices located in the Central Region of Denmark. All general practices within this region are invited to participate.

1.3.2/ Inclusion criteria for the intervention group

When selecting criteria to be included in the study population, we thoroughly evaluated key micro- and macrovascular risk factors and pragmatically aligned them with indicators available in the Careplan overview, while also ensuring the selection process remains meaningful and simple for GPs.
As listed in the "Background" section, the strongest risk factors for microvascular complications are elevated HbA1c and long diabetes duration (13). While albuminuria indicates already established microvascular endothelial damage in the kidney.
The strongest risk factors for macrovascular complications are prior ASCVD, age, smoking, and systolic blood pressure, while cholesterol and HbA1c rank lower (14).

According to the European Society of Cardiology presence of severe target organ damage (TOD) gives persons with T2D a very high risk for macrovascular complications. Severe target organ damage is present if any of the following applies: 1. eGFR < 45 ml/min. 2. Proteinuria (UACR > 300 mg/g). 3. microalbuminuria (UACR: 30-300 mg/g) with eGFR < 60 ml/min. or 4. Presence of microvascular disease at least three different sites (e.g., microalbuminuria, plus retinopathy plus neuropathy (24). Based on the above and pragmatically aligned with indicators available in the Careplan overview, we selected the following inclusion criteria.

Eligibility criteria

- Adults of legal age, 18 years or older, with type 2 diabetes (ICD-10: E11) and follow-up in general practice.
- eGFR >59 mL/min/1.73 m^2
- HbA1c:
  - <48 mmol/mol, or
  - 48–53 mmol/mol if the individual HbA1c treatment target is <53 mmol/mol
- Urine albumin-to-creatinine ratio (UACR):
  - <30 mg/g, or
  - 30–300 mg/g with ongoing treatment with organ-protective medication: SGLT-2i or GLP1 agonist *and* RAS-blockade with ACE-I or ARB (ATC-code: C09, A10BK, A10BD, A10BJ)
- LDL <2.6 mmol/L
- Ability to use the Danish national healthcare website (www.sundhed.dk)
- Ability to read and understand Danish.

Criteria for exclusion:

- Pregnancy (ICD-10 O00-O99)
- Withdrawal of informed consent.
  The following diagnosis, ICD-10 code:
- F00–F03: Dementia – all forms
- F70-F79: Intellectual disability.
- I50: Heart failure
- Z51.5: Palliative care.
- Any diagnoses or circumstances, that by the GPs judgement, makes digital annual follow-up inadvisable or unsafe.

1.3.3.1/ Identification of intervention participants

Identification of participants will be conducted by general practices.
Data required for the identification and recruitment of study participants will be passed on to the researcher prior to obtaining consent.

The average GP in Denmark has approximately 1,500 registered patients. With a national type 2 diabetes prevalence of 7.1%, this corresponds to roughly 100 patients with type 2 diabetes per GP. To identify potential study participants, each GP will therefore need to review the entire clinic's population of T2D patients — approximately 100 individuals.

For these patients, the following data from the period September 2025 to December 2026 are required to identify which individuals meet the inclusion criteria relating to eGFR, HbA1c, UACR, LDL, and organ-protective treatment — hereafter referred to collectively as the paraclinical criteria:

- Diagnosis of type 2 diabetes (ICD-10: E11)
- Name and CPR number
- eGFR
- HbA1c
- UACR
- LDL
- Ongoing medical organ-protective treatment with ATC code: C09, A10BK, A10BD and A10BJ

This data are available through the Careplan overview, and therefore a full medical record review is not required to identify which potential participants meet the paraclinical inclusion criteria.
As we expect participation from 25 general practices with an average of 2.4 GPs per practice (see section 1.3.8/ Analysis), the above process will need to be carried out for approximately 6,000 potential participants.

We estimate that approximately 30 out of these 100 T2D individuals per GP will meet the paraclinical inclusion criteria.
For each of these approximate 30 potential participants per GP, and for the project in total 1800 potential participants, the GP must review each individual medical to assess chronic conditions and determine whether any comorbidities preclude digital annual follow-up.

The medical record review will focus on the following chronic comorbidities which exclude participation:
Diagnoses listed with ICD-10 code and name:

- F00–F03: Dementia – all forms
- F70-F79: Intellectual disability.
- I50: Heart failure
- Z51.5: Palliative care – all forms.

Chronic diagnoses are assessed without temporal limitation, as they are by definition considered persistent and clinically relevant.
Data on chronic diagnoses for each potential participant are necessary to assess whether digital annual follow-up is clinically advisable for the individual potential participant.
Additional diagnoses or circumstances not listed above that cannot be anticipated may, in the GP's professional judgement, render digital annual follow-up clinically unadvisable. These could be conditions which affect the potential participant's ability to understand the study concept, to read, interpret, and respond appropriately to messages from the GP. It may also be other comorbidities where the combination with type 2 diabetes may pose a clinical risk, making digital annual follow-up clinically unadvisable, and thereby placing the potential participant outside the target group for this study.
We estimate that approximately half of the potential participants meeting the paraclinical inclusion criteria will be excluded following medical record review based on exclusion criteria, reducing the number of potential participants to approximately 900, who will proceed to the recruitment process.

During the recruitment process, we estimate that 2 out of 3 potential participants will accept participation, resulting in a total of 600 enrolled participants (see section 1.3.8/ Analysis).

1.3.3.2 Identification of non- intervention participants

Non-intervention participants, (the matching control group), will be identified in the registry database BI Data Warehouse. Matching will be done on diagnosis of type 2 diabetes (ICD-10: E11) age, sex, and baseline HbA1.. The control group will match the intervention group in size, comprising approximately 600 individuals, with data covering the period from September 2025 to December 2028. This matched control group will be used to evaluate whether a transition to digital annual follow-up affects outcomes in the intervention group relative to controls across paraclinical measurements (e.g., HbA1c), healthcare utilization, and medication use.

Through the BI portal's biochemistry repository, data from Labka II system from clinical biochemistry departments at hospitals in Central Denmark Region, we obtain data on total cholesterol, LDL, HbA1c, eGFR, and UACR.
Through the BI portal's Shared Medication Record (FMK), we obtain data on medication prescriptions.
Through the BI portal's data from MidtEPJ on in- and outpatient activity and referrals, we obtain data on secondary healthcare utilization.
Through the database "DPA_praksissektor, we obtain data on contacts with general practice.

Access to the BI Data Warehouse is governed by data protection requirements.

1.3.4/ Recruitment

Recruitment of participant will be conducted in general practice.

Initial contact with potential participants
Potential participants who meet the inclusion criteria and who do not meet by any exclusion criteria will be sent a brief information message (Appendix 3) via the practice's messaging module. The message will include the following information:

1. A brief introduction to the study.
2. Link to written information about the study (appendix 5)
3. A notice stating that potential participants who wish to receive information should contact the clinic to arrange a telephone appointment to receive verbal information about the study. The message asks participants to choose a time when they have sufficient privacy and time to receive verbal information without interruptions and, if desired, with a support person
4. A notice that if the person does not want further information about, or participation in, the project, they can decline by replying to the message with "no thanks".

At the agreed time, the potential participant will receive a phone call from their usual diabetes clinician at their GP clinic. During the call, the clinician will provide oral information about the study, answer questions, and confirm that the participant has understood the information and the implications of consent.
The procedure for recruitment and oral information is thoroughly described in Danish in Appendix 2.

This approach to recruitment was chosen to ensure that recruitment mirrors how general practitioners typically contact patients. In an interview study with general practice clinicians conducted during the planning of the study, most clinicians expressed a preference for calling and informing the potential participants themselves. Furthermore, the contact method of giving oral information by phone aligns with one of the study's intentions; to avoid unnecessary disruptions from the healthcare system.
Informed consent

After the oral information, the potential participant will receive a message (Appendix 4) with a generic link to written participant information (Appendix 5) and the informed consent form (Appendix 6).

The reflection period between the provision of participant information and consent is ensured as follows:

- Both the verbal information and the written patient information materials will inform potential participants of their right to a reflection period of at least 24 hours between receiving the information and giving consent.
- The written information material is attached to both message 1 and message 2. There will be an interval of at least 24 hours between the sending of message 1 and the verbal information session, as this must be scheduled between the general practice and the potential participant.
- The link to the consent form is sent after the verbal information has been provided and will remain active for two weeks.

Consent forms will be submitted directly to a secure digital repository managed by the study team at Steno Diabetes Center Aarhus. The study team will notify the GP via the clinic's E-Boks when a participant has given consent; no information will be disclosed to the study team before a participant has provided written consent.

Declining participation in the intervention

A potential participant may decline further information or refuse participation at any time, verbally or in writing. This decision must be recorded in the general practice records, so the individual is not contacted again.

Follow-up on non-responders

The GP clinician will record potential participants who do not respond to the information message (Appendix 3), hereafter referred to as 'non-responders, in a list.

Likewise, the GP clinician record a list of decliners. Decliners are potential participants who have either declined participation or further information about the study or failed to respond after three contact attempts by the GP clinician (see section below).

Also, general practice will keep a record of participants.

Maintaining a record of participants, individuals who decline or do not respond ensures the integrity of the recruitment process and participant follow-up.

Non-responders will receive a follow-up message two weeks after the initial contact;

If there is still no response after a further two weeks, general practice will send a final follow-up message.

If the potential participant still has not replied within an additional fortnight, they will be classified as a decliner.

After giving consent, the participants next annual follow-up will be conducted digitally.

1.3.5/ Digital follow-up intervention

The overall aim of the Digital Annual follow-up is to ensure ongoing optimal disease monitoring and metabolic control to reduce short- and long-term diabetes complications.

The digital annual follow-up is preceded with a preliminary examination.
The participant will have blood test taken to measure HbA1c, total cholesterol, HDL and LDL cholesterol, and eGFR, along with a urine sample to assess the urine albumin/creatinine ratio (UACR). The blood sample can be taken at the participant's general practitioner or at the affiliated hospital laboratory, following their usual procedure. Additionally, the participant will receive an electronic form with instructions for 3-day home blood pressure monitoring, recording weight (if feasible), and reporting lifestyle information (exercise, smoking, alcohol), as well as a questionnaire (Appendix 1). screening for signs of complications (Palpitations, shortness of breath, pressure or pain in the chest, altered or reduced sensation in the feet, ulcers on feet or legs, erectile dysfunction), addressing challenges with medication and any need for a consultation about diabetes.

When all test results are available, the responsible healthcare professional will perform a clinical evaluation of the results and communicate the evaluation to the participant by a message in the “My Doctor” app. The evaluation should be based on the participants Careplan, which presents results and target levels for HbA1c, LDL, and blood pressure, take into consideration the answers in the complication-screening questionnaire, reported lifestyle information and the participants medical record in general. If the participant indicates a need for a consultation about diabetes, an appointment will be arranged accordingly.

If the clinical evaluation raises concerns, the participant may be scheduled for an in-person-, telephone-, video-, or email consultation. The healthcare professional responsible will determine the most appropriate communication method.
Standardized responses will be used when all values are within target. These messages will state that measurements and goals are visible in the Careplan, remind participants to continue their current medications and that prescriptions remain available at the pharmacy, and prompt them to book their next routine annual follow-up one year ahead.

1.3.6/ Standard follow-up at the end of the study.

Eleven to thirteen months after the participants digital follow-up, the participant will attend a standard annual follow-up. The scheduling and execution of this follow-up will adhere to the standard procedures at the patient's general practitioner.

No in-between routine diabetes check-ups.
The study does not include routine 3- or 6-month diabetes checkups or HbA1c measurements. The population is expected to be well-controlled at enrollment, and one annual HbA1c testing, for the majority of participants, aligns with national guidelines for follow-up (9). If medically indicated, the clinician may order any relevant blood tests, including HbA1c, at any time during the study period. This will not affect participation in the study.

1.3.7/ Data material (outcome measures)

1.3.7.1/ Outcome

The primary outcome is HbA1c.
We hypothesize non-inferiority with respect to changes in HbA1c for the participant in the intervention group compared to the non-intervention group.

Furthermore, during the data collection period, the following information will be evaluated: number of HbA1c measurements in the study period, blood pressure, cholesterol levels, UACR, eGFR, contacts with the primary and secondary healthcare system, as well as medication and comorbidity.

1.3.7.2/ Paraclinical data material

All blood and urine samples must be sent to and analyzed at the local Department of Clinical Biochemistry. Analyses will follow the department's standardized and accredited procedures.
Point-of-care HbA1c measurements conducted in the GP clinic are not acceptable.
Blood pressure; arm cuff only, no wrist or finger devices. Home monitoring consists of three measurements each morning and three each evening for three consecutive days. Patients enter all readings into Webpatient.dk. Reported blood pressure is the average of all measurements.
Weight: patients self-record weight on their personal bathroom scale during the intervention, or weight recorded at the GP practice when blood samples are taken.

The qualitative study:
Data from the qualitative study will consist of recorded and transcribed interviews and written fieldnotes. Data material will be pseudonymised, coded and analyzed anthropologically and provide contextual knowledge to the understanding of the primary outcomes.

1.3.7.3/ Data period

Prospective follow-up study with intervention

- Cholesterol, HbA1c, eGFR, UACR, smoking status, weight, blood pressure, secondary care contacts, number of HbA1C measurements, morbidity, and diabetes relevant medication (appendix 13): September 2025– December 2028.
- Number of consultations at the general practitioner: September 2024–December 2028.

The qualitative study

- Data collection: September 2026–December 2028.

1.3.7.4/ Data source

By consenting, the participant authorizes the principal investigator, the study team, the sponsor and the sponsor's representatives, and any relevant regulatory authority direct access to obtain information from the patient's medical records, including electronic records, in order to view the trial participant's health information necessary for conducting the research project and for oversight purposes, including internal control, quality control and monitoring, as required of them.

To evaluate treatment quality against a matched control group, we will collect the following data after consent is given:

From GP record the following data are collected:
At time of inclusion:

- Year of diabetes onset.
- Recent recorded blood pressure measurement.
- Recent recorded weight.
- Recent recorded smoking status.

At the time of the digital annual follow-up and at the following standard annual follow-up (at the end of the study):

- blood pressure measurement.
- Weight.
- smoking status.

By linking these records for the identified patient group with BI Data Warehouse and DPA_Praksissektor, we obtain:

- HbA1c.
- UACR.
- eGFR.
- Total cholesterol.
- LDL cholesterol.
- Total number of consultations (face-to-face, telephone, video, or email) to the GP.
- Contacts with secondary healthcare.
- Diabetes relevant medication (appendix 13)
- Comorbidities.

Transferred from the GP clinic to the project in anonymized form and subsequently aggregated

Anonymized data (individuals assigned consecutive ID numbers instead of names or CPR numbers) on potential participants who meet the inclusion criteria for HbA1c, LDL cholesterol, kidney function and urinary albumin but either fail the communication requirements or are excluded due to comorbidity.
If a practice has fewer than five individuals in this category, it must not submit these data.
The purpose of collecting these data is to characterize people with well-controlled type 2 diabetes who are nonetheless unsuitable for digital annual follow-up because of comorbidities or language/digital barriers.
The data provided to the project in according to this is (appendix 10):

- Age
- Gender.
- Psychiatric/mental illness
- Limited linguistic, verbal, or digital proficiency
- Coexisting Somatic Disease
- Other (optional short free-text)

No biological material is stored for a biobank in this study.

1.3.8/ Analysis

The follow-up study:

1.3.7.1 Sample and power calculation

In Denmark, a typical GP has about 1,500 registered patients; with a T2D prevalence of 7.1%, this equates to 100 people with type 2 diabetes per GP. According to regional registry data, about 30% of people with type 2 diabetes have normal values HbA1c, LDL cholesterol, UACR and eGFR, thereby meeting a substantial portion of the inclusion criteria.

To be eligible, participants must be able to use digital tools, understand Danish, and be judged suitable by their GP for a digital annual follow-up. We estimate each GP will have about 15 potential participants and expect roughly two out of three to accept participation, corresponding to about 10 participants per GP.
Based on publicly available data, a Danish clinic on average consists of 2.4 GPs with about 24 potentially eligible patients per clinic (10).
We estimate statistical precision for the primary outcome as follows. The SD for individual patient changes in Hba1c is assumed to be 9.4 mmol/mol (15). To account for the cluster effect due to patients being affiliated with the same clinic, we used an ICC of 0.01. By recruiting 25 clinics with 60 GPs and 600 patients, the expected Standard Error (SE) for the change in Hba1c is then 0.0174 mmol/mol. The corresponding SE for the difference between intervention and the matched control group is 0.0246 mmol/mol. The latter will thus have an expected width of the 95% confidence interval (CI) of less than 0.10 mmol/mol. If only 20 clinics are recruited, the 95% CI for the difference in average changes will instead have a width of 0.12 mmol/mol. As we consider a difference of 3 mmol/mol to be the limit for clinically relevant changes, the study will be able to identify if the intervention group has a larger increase than this when compared to the control group. As we match on relevant confounders (age, sex, baseline Hba1c), the SE of the difference in changes the calculation above is conservative, as matching can be expected to improve precision.

To evaluate the changes in primary and secondary outcomes (as defined above), we apply a matched difference in difference analysis. This method applies a two-step identification strategy first matching a control group and secondly accounting for changes over time in the difference in difference analysis. In the matching step, we match a control group to the intervention group. This is done one-to-one so that each individual in the control group has one matched control. The matching is carried out using propensity score matching using available sociodemographic and clinical parameters from the BI Data Warehouse including but not limited to: Sex, age and baseline HbA1c. The matching is evaluated using Chi-2-test or t-test for categorial and continuous variables, respectively, as well as via Standardized Mean Difference. P-values less than 0.05 is treated as statistically insignificant, and a standardized mean difference measured in % bias of less than 20 % is treated as a success full match.
In the difference in difference step, we calculate the changes from baseline to follow-up in the intervention and matched control group respectively. The difference between these changes is then the effect attributable to the intervention.

The Qualitative study:
The data analysis will be abductively performed in dialogue with relevant literature and concurrently with data collection. The analytical process includes coding, memo-writing, case descriptions, synthesizing, theorizing, and contextualizing. The analysis will provide contextual understanding of the implications and characteristic patterns of patients and health professionals experience of “Digital annual follow-up”.

1.4/ Ethic and safety
The processing and storage of personal data in the study complies with the General Data Protection Regulation (GDPR). The Data Protection Act is complied with.
No information will be disclosed to the study team before a participant has provided written consent.
An application to The Regional Committee on Health Research Ethics for Central Denmark is sent.
Approval is required before the study begins.
The study is registered in the internal register of the Central Denmark Region.

The study does not transfer personal data abroad.

All participants will be informed orally and in writing about the form, the aim of the study, and possible side effects.
The information will state that participation is voluntary, and refusal to participate will involve no loss of benefits to which the subject is otherwise entitled. Furthermore, participants may discontinue participation at any time without penalty or loss of benefits, to which the subject is otherwise entitled.

Participants are informed that, apart from the annual diabetes follow-up, they should always contact their GP as they normally would. This means that if they experience any symptoms or signs that would usually prompt medical advice, they should still seek care while participating in the study. Likewise, they should continue their routine diabetic screenings (foot- or eye screening) if they fall in the study period.
Because participants are well controlled at enrollment and continue to receive annual screening to ensure ongoing monitoring and metabolic control, the risks of participating in the study are expected to be very low.
There is a small risk that increases in HbA1c, elevated blood pressure, or declines in kidney function or symptoms could have been detected earlier with more frequent measurements and follow-ups. These risks are nevertheless considered acceptable, as they fall within normal clinical practice, in which people with type 2 diabetes should be followed 1–4 times per year. Because the study includes only persons with well-controlled type 2 diabetes, one annual monitoring is considered consistent with current guidelines.
Participants accustomed to more frequent HbA1c testing may find one annual monitoring unsettling. Participation in the study is compatible with additional HbA1c tests if the clinician deems them medically indicated.
A change in how the annual follow-up is communicated — including the absence of an in-person consultation — may feel unsafe or psychologically burdensome for some participants.
Participants who are offered interviews may experience that the interview can bring up thoughts or feelings that are uncomfortable to address.

The risks associated with participation in the study are considered minimal and acceptable, as they are consistent with ordinary clinical practice and current guidelines. Ultimately, the study is expected to contribute to greater health equity by generating knowledge in the areas listed in Section 1.5.

The participants in the study are insured by the Danish Patient Compensation.

The study manager, the research team and Steno Diabetes Center Aarhus declares to have no economic interest in the study.

1.5/ Measurement of success and publication

The study's success criteria are to generate knowledge and directions for ways to reframe and differentiate the future management of diabetes care.
This knowledge includes:

- Evidence-based indicators for safe stratifying follow-up of persons with well-controlled type 2 diabetes.
- Safe protocols for replacing an annual face-to-face diabetes review with a digital review every second year for this group.
- Personalized and effective care for persons with type 2 diabetes.
- Patient priorities and preferences for planning diabetes care.
- Factors influencing patients' experiences of digital annual follow-ups.

- Ways digital communication between patients and healthcare providers can support differentiation and treatment.

Positive, negative, and inconclusive results will be published. The results are expected to be published in national and international journals. The study results will also be communicated to general practitioners in Denmark via articles in professional journals and at national meetings for general practitioners and may contribute to updates of clinical guidelines.

The study will result in minimum two peer-reviewed articles with the preliminary titles:
• Can patients with well-regulated type 2 diabetes have digital annual check-ups, a prospective follow-up study.
• Systematizing differentiated diabetes care in general practice. A qualitative study of implications and experiences.

1.6/ Initiation and funding of the study

Initiation to conduct the study was taken by Kirsten Christensen, senior physician at Steno Diabetes Center Aarhus and professor, head of unit, Annelli Sandbæk at Steno Diabetes Center Aarhus.
The investigator is employed by the sponsor.

Steno Diabetes Center Aarhus funds the study.
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A detailed budget is outlined in Appendix 12.

1.7/ Research Team

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1.8/ Abbreviations and definitions

T2D, type 2 diabetes.
GP, general practitioner.
ESC, European Society of Cardiology.
ASCVD, Atherosclerotic cardiovascular disease. Defined as coronary heart disease, cerebrovascular disease and periphery vascular disease presumed to be of atherosclerotic origin.
HbA1c, glycated hemoglobin.
CVD, cardiovascular disease.
eGFR, estimated glomerular filtration rate in mL/min/1.73 m2.
SCORE2-Diabetes, type 2 diabetes-specific 10-year CVD risk score.
T2DM, type 2 diabetes mellitus.

TOD, target-organ damage.
UACR, urinary albumin-to-creatinine ratio in mg/g.
RAS-blokade, Renin-Angiotensin-System-blokade.
SGLT-2i, Sodium–glucose cotransporter 2 inhibitor.
GLP-1, Glucagon-Like Peptide-1 receptor agonist.
ARB, angiotensin II receptor blocker.
ACE-I, Angiotensin-converting enzyme inhibitor.
Proteinuria, UACR >300 mg/g.
Microalbuminuria, UACR 30-300 mg/g.
KiAP, Kvalitet I Almen Praksis. Quality in General Practice.
SCORE2-diabetes, Algorithm which uses the T2D patient's sex, age at diabetes diagnosis, smoking status, systolic blood pressure, total cholesterol, HDL cholesterol, HbA1c and eGFR to calculate the risk for CVD within the next ten years (6). Validated only for patients aged 40–69 without ischemic heart disease. The score divides the patients into four risk groups, low: <5%, middle 5-<10%, high 10-<20%, very high: ≥20%.

1.9/ References

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Appendix

1. **Spørgeskemaer. Symptomscreening+KRAM.**
2. **Procedure for mundtlig deltagerinformation.**
3. **Rekrutteringsbesked 1.**
4. **Rekrutteringsbesked 2.**
5. **Skriftlig deltagerinformation.**
6. **Samtykkeerklæring.**
7. **Skriftlig information til almen praksis.**
8. **Procedure til almen praksis.**
9. **Rekrutteringsmateriale til almen praksis.**
10. **Deltagerlisten inkl. årsager til at patienter findes uegnet til digital årskontrol.**
11. **Forsøgspersoners rettigheder i et sundhedsvidenskabeligt forskningsprojekt.**
12. **Budget.**
13. **Diabetes relevant medicin på ATC-koder.**
14. **Auditskema.**
15. **Samarbejdsaftale almen praksis.**