



# ASSESSING THE CLINICAL IMPACT OF SOCIALDIABETES MEDICAL DEVICE IN PATIENTS WITH TYPE 1 DIABETES MELLITUS

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# 1. ABSTRACT


**Background**

Diabetes mellitus is a chronic and prevalent disease that requires almost constant attention from the patient and regular evaluation by the clinician. However, in health care systems, physicians have some difficulties to provide optimal care for patients with diabetes due to the lack of patient involvement and poor communication. The rapid development of a variety of new technologies is making a huge impact on healthcare field because these new tools are helping to deal with those obstacles. The chance to automatically transfer data to clinicians and receive timely guidance in therapy adjustments through remote consults, can lead to an improvement of patients' diabetes self-management ability, which is directly related to an enhancement of blood glucose control, minor risk of long-term complications and better perception of quality of life and treatment satisfaction.

**Purpose**

The aim of this study is to determine the safety and the efficacy of SocialDiabetes mobile phone application in the management of the intensive insulin therapy of patients with type 1 diabetes mellitus in comparison to the management with current model of medical assistance.

**Design**

An open-label, controlled, randomized cluster sampling, non-inferiority clinical trial that will be executed at Hospital Universitari Doctor Josep Trueta of Girona with a follow-up period of 6 months.

**Participants**

The study will evaluate a total of 192 subjects. The sample will be composed by men and women (≥18-≤55 years old) who had been diagnosed of T1DM at least 1 year before the beginning of this study and at this moment are in treatment with intensive insulin therapy.

**Intervention**

SocialDiabetes intervention, involving the use of mobile devices and applications for remote patient monitoring and delivery of clinical feedback for self-management of diabetes, versus the current model of assistance through in-person hospital visits.

**Outcomes**

The main outcome will be changes in HbA1c and secondary outcomes will be perception of treatment satisfaction and quality of life.



**Key words**

HbA1c, mHealth, Type 1 diabetes mellitus, Self-management, SocialDiabetes, Treatment satisfaction, Quality of life.

# 2. ABBREVIATIONS

| | |
|---|---|
| **ADA** | American Diabetes Association |
| **BGM** | Blood glucose monitor |
| **CGM** | Continue glucose monitor |
| **CSII** | Continuous subcutaneous insulin infusion |
| **DM** | Diabetes Mellitus |
| **DTSQ** | Diabetes Treatment Satisfaction Questionnaire |
| **DTSQc** | Diabetes Treatment Satisfaction Questionnaire, change version |
| **DTSQs** | Diabetes Treatment Satisfaction Questionnaire, status version |
| **EHR** | Electronic health record |
| **EsDQOL** | Diabetes Quality of Life, Spanish version |
| **FPG** | Fasting plasma glucose |
| **HCP** | Health care provider |
| **HUDJT** | Hospital Universitari Doctor Josep Trueta |
| **Hb** | Hemoglobin |
| **HbA1c** | Glycated hemoglobin |
| **IIT** | Intensive insulin therapy |
| **mHealth** | Mobile health |
| **MDI** | Multiple daily injections |
| **NHS** | National Healthcare System |
| **NGSP** | National Glycohemoglobin Standardization Program |
| **OGTT** | Oral glucose tolerance test |
| **PG** | Plasma glucose |
| **SMBG** | Self-monitoring of blood glucose |
| **T1DM** | Type 1 diabetes mellitus |
| **T2DM** | Type 2 diabetes mellitus |

# 3. INTRODUCTION

## 3.1. Type 1 diabetes mellitus

Diabetes mellitus (DM) is a complex, chronic illness requiring lifelong medical assistance. In Spain, the total prevalence of diabetes mellitus (DM) adjusted for age and sex is 13,8% of the total population. (1)

Type 1 diabetes mellitus (T1DM) is one of the most common long-term conditions affecting children and young adults worldwide. It comprises 5-10% of all causes of diabetes and is one of the most frequent autoimmune diseases of early life (2). The pathophysiology of T1DM is characterized by beta-cell destruction, usually leading to an absolute insulin deficiency that produces a hyperglycemic status (3). Chronic hyperglycemia causes damage to blood vessels generating long-term diabetes complications. This damage can be macrovascular (causing ischemic heart disease, peripheral vascular disease and cerebrovascular disease) or microvascular (causing nephropathy, retinopathy and neuropathy which evolution can culminate in kidney failure, blindness and lower limb amputations) (4,5).

### 3.1.1 Diagnosis

Diabetes is diagnosed based on plasma glucose criteria:

- **Fasting plasma glucose (FPG**): Where "fasting" is defined as non-caloric intake for at least 8 hours.
- **2-h plasma glucose (2-h PG) value during a 75-g oral glucose tolerance test (OGTT).** OGTT should be performed using glucose load containing the equivalent of 75-g anhydrous glucose dissolved in water.
- **Glycated hemoglobin (HbA1c) testing** (6). HbA1c, also called A1C, is a measure of the amount of glucose attached to hemoglobin (Hb) in red blood cells. The higher the glucose levels over the previous 2-3 months, the higher the A1C. When using A1C to diagnose diabetes, it is important to recognize that it is an indirect measure of average blood glucose levels and other factors that may

affect hemoglobin glycation levels apart of glycaemia such as age, race/ethnicity and anemia/hemoglobinopathies might be considered (7).

The American Diabetes Association's (ADA) sets the same diagnostic criteria for both type 1 and type 2 diabetes (*Table 1*).

**Table 1.** Criteria for the diagnosis of diabetes. Adapted from(7)

| Criteria for the diagnosis of diabetes |
|---|
| FPG ≥ 126 mg/dL (7.0 mmol/L)* |
| OR |
| 2-h PG ≥200 mg/dL (11.1 mmol/L) during OGTT* |
| OR |
| HbA1C ≥6,5% (48mmol/mol)* |
| OR |
| In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200mg/dL (11.1 mmol/L) |
| *In absence of unequivocal hyperglycemia, results should be confirmed by repeat testing. |

Children with T1DM typically present with the hallmark symptoms of polyuria/polydipsia, and approximately one-third debut with diabetic ketoacidosis (8). On the other hand, the onset of type 1 diabetes may be more variable in adults due to a slower b-cell destruction, and it may not be present with the classic symptoms seen in children. So, unless there is a clear clinical diagnosis (e.g., patient in a hyperglycemic crisis or with classic symptoms of hyperglycemia and a random plasma glucose ≥200 mg/dL [11.1 mmol/L]), a second test is required for confirmation. It is recommended to repeat the same test or perform a different one using a new blood sample for disease confirmation. For example, if the A1C is 7.0% (53mmol/mol) and a second result is 6.8% (51 mmol/mol), the diagnosis of diabetes is confirmed. If two different tests (such as A1C and FPG) are both above the diagnostic threshold, this also confirms the diagnosis. On the other hand, if a patient has discordant results from two different tests, then the test result that is above the diagnostic threshold should be repeated, with consideration of the possibility of assay interference (7).

Most cases of type 1 diabetes represent an autoimmune disease, meaning patients often show features of an immunological contribution to disease pathogenesis.(9) Autoimmune destruction of b-cells is related to multiple genetic predispositions and is

influenced by environmental factors. We can also find several antibodies (autoantibodies of islet cells, autoantibodies against insulin, glutamic acid decarboxylase (GAD65), tyrosine phosphatases IA-2 and IA-2B and ZnT8) that act as markers of immune destruction. For this reason, ADA recommends to consider measurement of pancreatic autoantibodies to confirm the diagnosis of the disease (10). However, not all patients with type 1 diabetes have these characteristics, leading to proposed classifications of:

- **Type 1A** (autoimmune) diabetes, for the 70–90% of patients with type 1 disease that have self-reactive autoantibodies.
- **Type 1B** (idiopathic) diabetes, representing the remainder whose specific pathogenesis remains unclear (9).

### 3.1.2 Treatment

The treatment of the condition relies on supplementation of the deficient hormone. The aim of insulin therapy in T1DM is to mimic the physiological insulin secretion from a functional pancreas of a person without diabetes to maximize the chances of attaining normal blood glucose levels (11).

Evidence has shown that the more time a patient has blood glucose levels within the normal range, the lower the risk of long-term chronic complications (12,13). It has been seen that optimal glycemic control is best achieved by using an intensive insulin therapy (IIT) with a daily dose of basal insulin plus multiple daily injections (MDI) of prandial insulin (normally 3) or with continuous subcutaneous insulin infusion (CSII) using external pumps (4,14). Successful intensive insulin treatment also requires close self-monitoring of blood glucose (SMBG) with a blood glucose monitor (BGM) or a continue glucose monitor (CGM) to help to determine the amount of insulin needed so patients can adjust their insulin doses and behavior on the basis of the results (15) (See diabetes treatment tools in ANNEX 1). Measurement of blood glucose is especially important before main meals because the prandial insulin dose will vary with blood glucose level, planned carbohydrate consumption, and other factors (e.g. exercise or alcohol consumption) (16). However, an adjusted glycemic control increases the risk of hypoglycemia, so it is essential to find a balance between optimal glycemic control and avoid hypoglycemia (11,17).

### 3.1.3 Control

Diabetes mellitus, unlike most other chronic health conditions, requires almost constant attention from the patient and regular evaluation by the clinician (18). The medical evaluation includes the initial and follow-up evaluations, assessment of complications, psychosocial assessment, management of comorbid conditions, and engagement of the patient throughout the process.

Patients' SMBG or CGM and HbA1C help health care providers (HCP) and patients to assess the effectiveness and safety of a management plan on glycemic control. Specially, HbA1c reflects average glycaemia over approximately 3 months and has strong predictive value for diabetes complications (4). The United Kingdom Prospective Diabetes Study shows that every percentage point decrease in HbA1c reduces by 35% the risk of vascular complications (19). Thus, ADA recommends using HbA1c as a measurement of glycemic control for both diagnosis and treatment of diabetes (7).

### 3.1.4 Self-management

Diabetes self-management is essential for an effective treatment because it also plays an important role in the maintenance of good glycemic control and prevention of complications. Nevertheless, it is very complex because it forces patients to control permanently the amount of carbohydrates they ingest and to monitor blood glucose values several times a day to adapt insulin doses to the various situations of daily life. Diabetes self-management also includes preventing, detecting and treating acute and chronic complications; coping with psychosocial issues, and problem solving. (10) To carry out all this is not easy and patients often encounter various barriers in adhering to self-management programs. It is due to lack of knowledge and understanding of self-care activities, lack of individualized and coordinated care, inconvenient and costly education sessions and poor patient and HCP communication(20).

## 3.2. mHealth

The rapid development of a variety of new technologies is making a huge impact on healthcare fields. One of those technologies is mobile health (mHealth) systems. The Global Observatory for eHealth of the World Health Organization defines mHealth as "medical and public health practice supported by mobile devices such as mobile phones, patient monitoring devices, personal digital assistants and other wireless devices" (21,22)

According to the IQVIA institute for Human Data Science, there are more than 318,000 mHealth applications available to consumers (23) that can help people to improve the self-care of chronic pathologies through different behavior modification strategies, such as facilitating measurements, records, monitoring or management of their disease.

It also represents a good solution to collect and provide information about patient health and vital status to medical providers. Some examples of the benefits of mHealth are that it is able to enhance the continuity of care through better maintenance of patient medical records (24) and that patients are able to reduce their direct and indirect healthcare costs through reduction of the need for healthcare clinic visits or hospitalization (25).

### 3.2.1 mHealth and diabetes applications

According to the mHealth Economic 2017 study, the top 3 fields with the best market potential for digital health solutions are Diabetes, followed by Obesity and Depression (26). Diabetes apps accounted for 16% of the total number of disease-specific apps available to consumers. These apps vary in the functions they provide, including; tracking blood glucose measurements, nutrition database and carbohydrate tracking, physical activity and weight tracking, sharing data with clinicians or peers, social support, messaging and reminders (27). The use of these features could help patients adhere to diet, exercise and medication management plans, which could lead to improved diabetes-related outcomes (28).

### 3.2.2 Mobile diabetes self-management system

The basic functions of a smartphone-based diabetes self-management system adhere to the following principles:

1. To empower people with diabetes to self-monitor blood glucose or other variables when and as needed (e.g., blood pressure, weight, and diet);
2. To engage people in the management of their diabetes by promoting self-efficacy;
3. To achieve pre-set care targets and to provide interactive feedback between patients and physicians with respect to disease progress and adherence to therapy;
4. To allow physicians to facilitate patient self-care in order to improve outcomes with potential cost savings.

The general architecture of m-Health diabetes self-management and care systems consist of these modules (*Figure 1*):

- **Patient's device**
- **Remote data servers or clouds**, which host the patient electronic health record (EHR)
- **HCP**

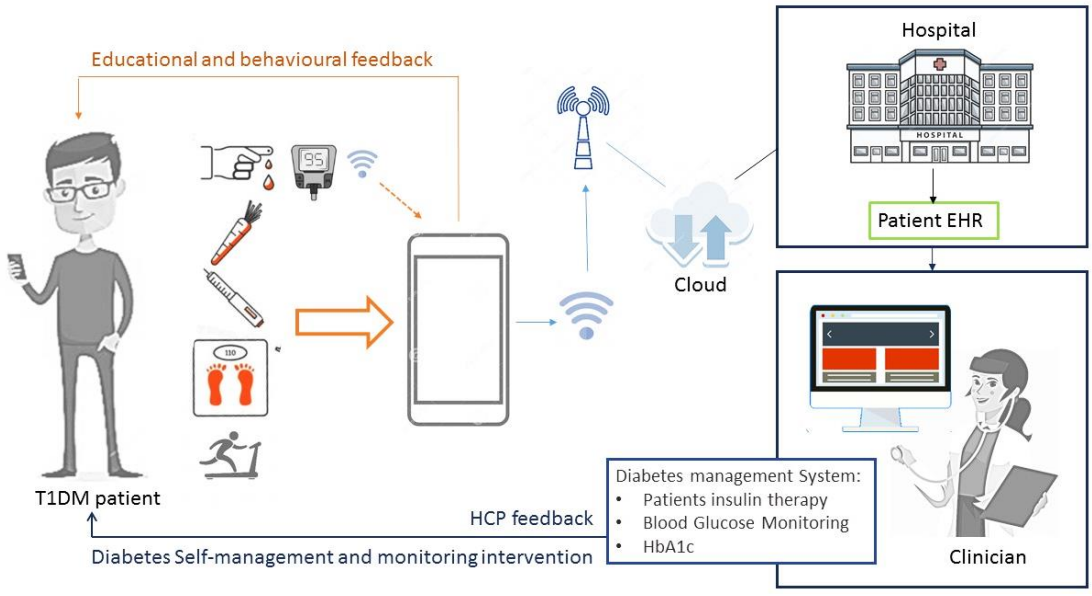


Figure 1. Diabetes mHealth application system

The patient's device consists of a smartphone equipped with a special diabetes app connected wirelessly via Bluetooth to a BGM, that is used for tracking and storing the patient's daily blood glucose data. The patient can also load more other data of interest (exercise, food, weight…) and store even more information about the disease management in the app. The acquired data is transmitted wirelessly via the individual patient's smart phone and stored in a remote portal hosted in a health clinic or hospital. This portal consists of the patient's EHR, supported with intelligent data analytic tools that can process the data and produce simple illustrative graphics. These can be accessed and viewed by the patient and physician via two separate web portals, each designed and developed for separate access. The graphics provide information and decision support messages, such as lifestyle change, educational notes, and medication required to improve the patient's daily management routine.

Smart devices, such as some CGM and CSII can also communicate wirelessly to their smartphones for monitoring purposes and some applications can administrate their information.

The adaptation of any medication and treatment plans required for individual patients is based on their self-management history, daily blood glucose and HbA1c profiles, treatment progress and other information. In addition, with some of the new diabetes apps, the HCP can communicate with the patient through the mobile phone and make treatment modifications or solve doubts when the patient requires it (29).

### 3.3. Social Diabetes app

Between all mhealth applications available in Spanish developed with the purpose of assisting patients in the self-management of T1DM, SocialDiabetes was the one that reached the best punctuation for its functionalities (30). It has the CE mark and has been downloaded more than 350,000 times.

The functionalities of SocialDiabetes mhealth app are: (See User's Manual in ANNEX 2)

- **For patients**:
    - A free app that includes (*Figures 2-3*):
        - Registers: Glycemic, food, medication, activity, HbA1c (with a minimum of 3 blood glucose logs daily for 3 months, it is able to calculate the estimated HbA1c), weight, heart pressure, ketones.
        - Bolus calculator: rapid insulin dose recommendations.
        - Digital diary that includes all the registered controls
        - Carb Calculator: the patient can calculate the number of carbs he is going to eat by grams or rations.
        - Nutritional database
        - Graphs to visualize the evolution of glucose level, estimated HbA1c and ranges.
        - Bluetooth connection with patients' blood glucose meter. The compatible devices are:
            - GlucoMen Areo 2K (only with Android), GlucoCard SM.
            - Accu-chek Aviva Connect, Accu-Chek Guide.
            - Contour Next ONE.
            - CareSens Dua
            - AgaMatrix Jazz
            - Abbott: FreeStyle Libre (available only in EU)
        - Reminders: taking medication, realization of controls…
        - Reports generation: on screen or download them.
        - Text messaging: to establish connection with HCP
    - SocialDiabetes web-platform that allows patient to access to the information and his digital logbook to analyze his data in different charts.


**Figure 2.** Glucose monitoring with Social Diabetes app. From SocialDiabetes website

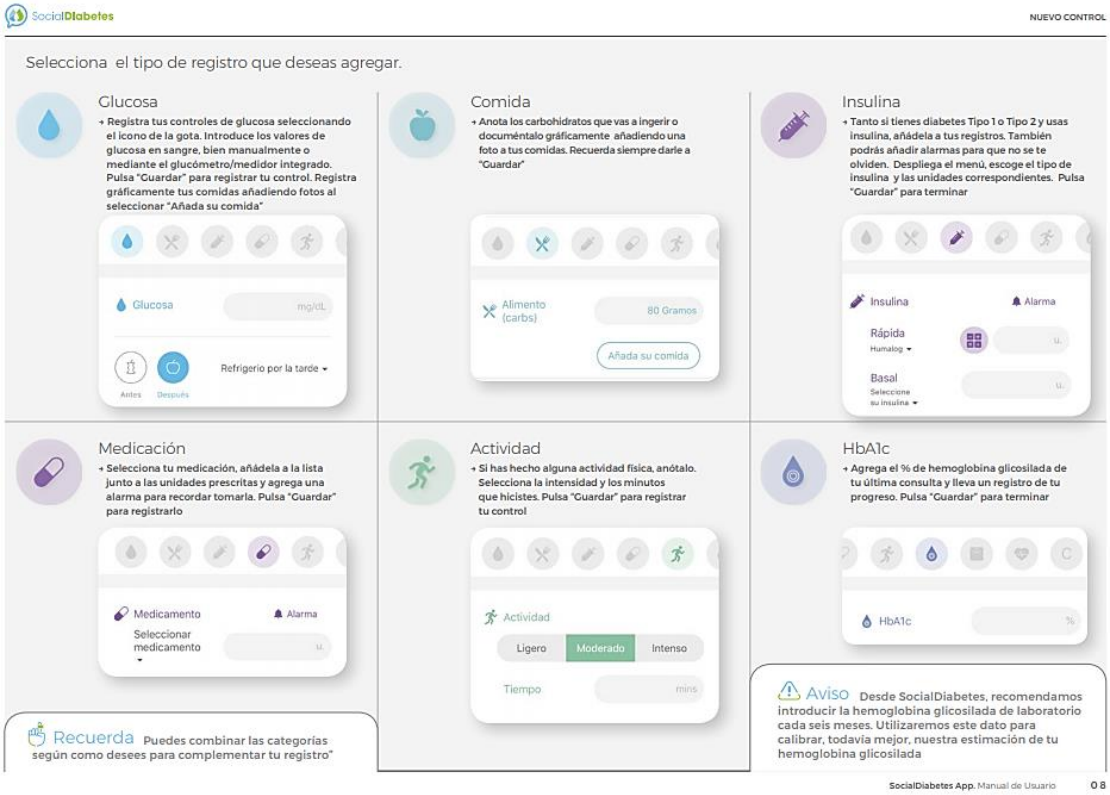


**Figure 3**. Diabetes control items of SocialDiabetes app. From SocialDiabetes website

- **For the HCP and sanitary organizations,** SocialDiabetes offers a:
    - SocialDiabetes Web platform permits a remote patients monitoring trough a control panel that substitutes common control visits. This tool may allow them to track patients' records, to prioritize the most urgent cases and implement remote treatment changes. The platform includes:
        - Searcher and filters
        - Communication with the patient through the platform
        - Real-time data of all the activity recorded by the patient (glucose, HbA1c, weight, self-reported feeding through photography, medication, exercise)
        - Remote configuration of the bolus calculator with automatic update of the treatment in the patient's app
        - Reports generation. On screen or download them.
        - Differentiated assignment of patients
        - Automated alerts

# 4. JUSTIFICATION

The burden of diabetes mellitus–associated complications worldwide is a major healthcare problem that we urgently need to find solutions to. It is definitely one of the main causes of mortality and major morbidities, including cardiovascular disease, kidney failure, amputations and blindness. However, health care systems and providers have the following obstacles to provide optimal care for diabetic patients in outpatient clinics: inconvenience because of time and space limitations, limited ability to gain diabetes self-management knowledge in a short period of time and poor compliance with a diabetes diary. (31) All this impediments together prevent doctors from providing effective treatment guidance.

In order to reduce diabetes-related complications, HCPs want to encourage patients to self-manage their health and provide them with tools to help achieve optimal glucose control (27). Scientific evidence exists that demonstrates the efficacy and safety of mHealth apps in the management of diabetes mellitus. Studies relate the use of this tool with different outcomes of interest like a decreased HbA1c during a follow-up period or an improved quality of life (32). In addition, it has also been seen that mobile phone-based interventions with clinical feedback with the HCP have better results than stand-alone mobile apps (33,34). For this reason, more and more clinicians and patients have started to use mHealth to assist diabetes self-management (35). However, current studies are mostly focused on type 2 diabetes mellitus (T2DM) patients and results are stronger and more significantly in the management of T2DM, (34,36,37) so it is necessary to perform more robust clinical studies about mhealth interventions in patients with T1DM.

There are many mobile diabetes apps which have no evidence about their safety and usability and patients who use these apps are essentially experimenting on themselves. It is also important to present evidence on commercially available apps for diabetes self-management including evidence of efficacy and information about app function, cost, and usability to help patients, clinicians and professional societies make informed choices.

Enhancement of patients' self-efficacy and timely disease monitoring by the HCP is possible thanks to a variety of diabetes control tools offered by Social Diabetes app. Due to this reason, we think that T1DM patients with IIT, who must control their blood glucose values and insulin doses strictly, could decrease the risk of long-term diabetes-related complications by using this medical device. In addition, well-controlled patients would not have to come to unnecessary planned visits, because the HCP would be able to assess his disease in the distance.

Consequently, this study aims to evaluate the safety and efficacy of the SocialDiabetes medical device in the management of patients with T1DM with IIT within the public healthcare system. In order to assess the safety of the device, first we propose to study if the use of this tool does not mean a deterioration of HbA1c of T1DM patients with IIT. Then, to evaluate the efficacy of the platform we will study if the same patients even achieve to improve the HbA1c levels using the app. However, the efficacy of diabetes treatment should not be evaluated solely by HbA1c level. They should also focus on patient-reported outcomes: patient satisfaction, wellbeing and quality of life (38). The importance of assessing patient's treatment satisfaction rests in its correlation with a best self-management adherence and, in consequence, its positive effect on metabolic control (39). For these reasons, we will also evaluate the changes in patient's treatment satisfaction and in his quality of life by using validated questionnaires.

# 5. HYPOTHESES

## 5.1. General hypothesis

The SocialDiabetes application is a safe and effective tool that helps improving T1DM self-management abilities and gives a better medical assistance in comparison with the current sanitary assistance model.

### 5.1.1 Main hypothesis

- The utilization of SocialDiabetes mHealth system by the HCP and T1DM patients does not suppose a worsening of the glycemic control measured by HbA1c levels.

### 5.1.2. Secondary hypotheses

- The use of SocialDiabetes tool by HCP and patients offers other advantages in the disease's management:
  - Enhancement of glycemic control in patients with T1DM.
  - Improvement of the treatment satisfaction of the patients.
  - Increment of their quality of life.

# 6. OBJECTIVES

## 6.1. General objective

Evaluate the safety and the efficacy of SocialDiabetes intervention, involving the use of mobile devices and applications for remote patient monitoring and delivery of clinical feedback for self-management of diabetes, in the management of IIT of T1DM patients in comparison to the current model of assistance with in-person visits.

### 6.1.1. Main objective

- The main aim of the study is to prove if sanitary assistance through the SocialDiabetes medical device is safe and comparable to the current model of assistance with in-person visits. An HbA1c difference of -0.35% will be accepted as the non-inferiority threshold.

### 6.1.2. Secondary objectives

- Evaluate the advantages of the implementation of this new tool at the healthcare assistance:
  - Assess if there is an improvement of glycemic control considering clinically significant an HbA1c difference greater than 0.5%.
  - Establish by means of questionnaires, whether patients experience an improvement in treatment satisfaction after using the mHealth platform.
  - Determinate if the use of this tool generates positive changes in the perception of quality of life of patients using a questionnaire.

# 7. METHODS

## 7.1. Study design

The study will be carried out through an open-label, controlled, randomized, non-inferiority clinical trial that compares the safety and efficacy of SocialDiabetes platform in patients with T1DM. It will be done in the Hospital Universitari Doctor Josep Trueta (HUDJT) with a follow-up period of 6 months.

## 7.2. Study population

The subjects of the study will be patients with T1DM and IIT of the HUDJT of Girona.

The estimated time of recruitment is about 3 months. Subjects will be recruited when they visit outpatient clinic of one of the monographic consultations of IIT of the hospital if they fulfill all the following inclusion and exclusion criteria:

### 7.2.1. Inclusion criteria

- Patients diagnosed of Type 1 Diabetes Mellitus with, at least, more than 1 year since its diagnosis.
- Age between 18 and 55 years
- In treatment with MDI or CSII at least in the 6 previous months.
- HbA1c between 6-9%.
- With a stable HbA1c value in the last 6 months (variations less than 0.75%).
- Patients with BGM or CGM with Bluetooth connectivity and compatible with SocialDiabetes app.
    - GlucoMen Areo 2K (only with Android), GlucoCard SM.
    - Accu-chek Aviva Connect, Accu-Chek Guide.
    - Contour Next ONE.
    - CareSens Dua
    - AgaMatrix Jazz
    - Abbott: FreeStyle Libre (available only in EU)
- Owners of a smart mobile phone (with Android or IOS software) with internet connection on a regular basis and compatible with SocialDiabetes app.
- Signed informed consent.

### 7.2.2. Exclusion criteria

- Type 2 DM, LADA diabetes, MODY and other types of diabetes.
- Patients who have recently (<6 months) changed the insulin regimen (changes in the basal insulin prescription, withdrawal / initiation of some type of insulin)
- Patients who have been in a labile state of glycemic control (variations of HbA1c ≥ 0.75%) in the last 6 months.
- HbA1c < 6% or HbA1c >9%.
- Pregnant women or with intention to be pregnant in the following 6 months.
- Patients with severe diabetes long-term complications or occurrence of chronic hyperglycemic complication during the study.
- Patients with comorbidities that can effect blood glucose levels:
  - Cardiac insufficiency.
  - Other endocrine disease: Hypo/Hyperthyroidism, Addison's disease, GH deficiency, hypopituitarism.
  - Renal failure.
  - Severe hepatic dysfunction/ Hepatic failure.
  - Cancer.
- Current acute comorbidity: sepsis, burns.
- Factors that can modify HbA1c values.
  - Ethnicity: African American will be excluded because their hemoglobin variants can interfere with the measurement of HbA1c.
  - Conditions that affect red blood cell turnover
    - Anemias.
    - Pregnancy (second and third trimesters).
    - Hemodialysis.
    - Recent blood loss or transfusion.
    - Erythropoietin therapy.
    - End stage kidney disease.
    - Splenectomy.
- Use of other drugs that can affect the glycemic control (corticoids, beta-blockers, diuretics, adrenalin, estrogens, sulfonylureas, thyroid substitute hormones...).
- Use of illicit drugs.
- Psychiatric disease (diagnosed at clinical history).
- Alcohol consumption (not more than 3-4 units of alcohol/day for men and 1-2 units of alcohol/day for women).
- Low sociocultural level.
- Language barriers: patients must speak and understand Catalan or Spanish.
- Homelessness or food insecurity.

### 7.2.3. Withdrawal criteria

1. Patient decision: withdrawal of patients from this study is not predicted to be huge because of the short study duration and the interventions seems to be not much difficult for patients who live with diabetes every day. However, the subject can withdraw his/her consent to participate in this study at any time and for any reason. At patient request, all previously added data will be destroyed from the study database. Finally, subjects withdrawn from the trial will not be replaced.
2. Protocol withdrawal criteria:
    - Belatedly identified violation of the inclusion and/or exclusion criteria.
    - Any severe adverse event, unacceptable health risk or consequence for the participant derived from this study (for example, appearance of episodes of hypoglycemia, extreme glucose excursions, etc.).
    - Apparition of intolerable clinical symptoms that cannot be explained by DM (onset of a new disease, comorbidity, etc.)
    - No collaboration of the patient (not willing to attend appointments or answer questionnaires).

## 7.3. Sample size and collection

### 7.3.1. Sample size

In a bilateral contrast with an α significance level of 5% and a power of 80%, assuming that the effect of the intervention will be moderate, we need a sample of 87 people per consultation / cluster. Considering a loss of a 10% during the study, we will require a total of 192 patients.

The computations were carried out with the professor Marc Saez' software based on the library "PWR" of the free statistical environment R (version 3:5.1).

### 7.3.2. Sample collection

The sample collection will be performed with a non-probabilistic sampling method according to the 4 monographic consultations of T1DM with IIT of the HUDJT. The HCP of each external consultation will select subjects who fulfill inclusion criteria and have no exclusion criteria listed in the above sections. Those patients will be invited to participate in the study and will be informed about its requirements. Finally, those who agree to participate in the study will be asked to sign the informed consent sheet.

The recruitment phase will take about a total three months. At the end of the process, each HCP will have had selected 48 patients, making a total sample of 192 subjects.

We will use an intention to-treat analysis. If a patient leaves the study or his follow-up is lost, data will not be excluded. As said before, subjects withdrawn from the trial will not be replaced.

## 7.4. Randomization and masking

### 7.4.1. Randomization

The randomization of the subjects to the control group or to the intervention one will be done through a randomization by clusters corresponding to the 4 consultations: 2 consultations will be randomized to management with SocialDiabetes and the other 2 will be randomized to routine management with in-person visit with the HCP (control group). The randomization will be made by raffle by an statistical specialist and the information will arrive to each HCP by a sealed envelope.

### 7.4.2. Masking

Due to the characteristics of the study, it must be open because is not possible to hide the intervention to patients neither to HCPs. However, it will be an observer-blind study, where the analyst will not know if the patient was a SocialDiabetes user or not.

## 7.5. Variables

### 7.5.1. Independent variable

The independent variable of this study is a qualitative dichotomous variable that consists in the utilization or not utilization of SocialDiabetes tool by patients and their physician.

### 7.5.2. Dependent variables

- **HbA1c:** It is a quantitative continue variable. It will be measured by a sample of venous blood, which will be processed in the HUDJT clinical laboratory with a high performance liquid chromatography method. The technique is based on separation of Hb species according to load differences and HbA1c will be estimated through a quantitative analysis of total Hb and HbA1c. The relationship between both measurements will be made according to the National Glycohemoglobin Standardization Program (NGSP) and standardized with the specifications of the DCCT (Diabetes Control and Complications Trial) (6,40). Finally, it will be expressed as a percentage.

  To evaluate the main objective, we will assess HbA1c changes accepting as the non-inferiority threshold an HbA1c difference of <0,35%. Then, for the first secondary objective, we will consider clinically significant an HbA1c difference greater than 0.5%.

- **Treatment satisfaction**: It will be evaluated with the Diabetes Treatment Satisfaction Questionnaires (DTSQ) consisting of the DTSQ status version (DTSQs) and the change version (DTSQc) (42). Both of them are quantitative discrete variables and they will be measured as means.
  - DTSQs: it will be administrated to all patients at baseline to determine patient treatment satisfaction before intervention. It is calculated as the sum of all the items (except items 2 and 3, which will be evaluated separately)

- DTSQc: it will be administered to all patients in the last visit to assess changes in treatment satisfaction and to evaluate patient preference for the system compared with their previous technology or diabetes treatment process.

- **Quality of life**: It will be evaluated with EsDQOL questionnaire (Spanish version of Diabetes Quality of Life questionnaire). We will administrate it to patients of all groups at the first and last visits. It is a quantitative discrete variable and it will be measured as a mean. (43)

  In the *ANNEXES* section you will find all the questionnaires and the description of its evaluation. (See ANNEXES 3-6)

### 7.5.3. Co-variables

- **Age:** 18 or above years old. It is a discrete quantitative variable. It will be measured in years.

- **Gender**: is a dichotomous nominal qualitative variable. It will be assessed by male/female.

- **Body mass index (BMI):** Is a continuous quantitative variable. It will be expressed in kg/m2.

- **Diabetes duration:** Is a nominal qualitative variable because we measure it as intervals (year intervals: ≥1 year, ≥5 years, ≥10 years). We will know it by the information in the clinical history.

- **CMG usage**: it is a dichotomous nominal qualitative variable. It will be assessed by Yes/No.

- **CSII usage**: as in the previous item, it is also a dichotomous nominal qualitative variable. Also assessed by the options: Yes/No.

- **Clusters (HCP):** the four HCP are different exercising the profession so it is convenient to study the results according to the professional / medical

consultation (clusters) to see how this can have affected them. It is a nominal qualitative variable because we will distribute them in consultation number 1, 2, 3 or 4.

- **Presence of micro/macroangiopathic complications:** is a dichotomous nominal qualitative variable. It will be assessed by Yes/No.

- **Severe hypoglycemic events during the study:** Severe hypoglycemia is an event requiring assistance of another person to actively administer carbohydrates, glucagon, or take other corrective actions. Plasma glucose concentrations may not be available during an event, but neurological recovery following the return of plasma glucose to normal is considered sufficient evidence that the event was induced by a low plasma glucose concentration (41). The information will be collected from "*patient's data collection sheet*" (See ANNEX 12) delivered by the patient in the final visit. It is a discrete quantitative variable that will be measured as numbers (1, 2, 3, etc.).

- **Number of consultations with HCP during the study**
    - **Number of in-person visits**: is a discrete quantitative variable. It will be measured as numbers (1, 2, 3, etc.). That number will be taken from "*patient's record sheet*" which will be given to physician at final visit.
    - **Number of remote consultations trough SocialDiabetes app:** This will be only evaluated in the intervention group as a discrete quantitative variable. It will be measured as numbers (1, 2, 3, etc.). That number will be taken from "*patient's record sheet*" which will be given to physician at final visit.

## 7.6. Study procedures and visit schedule

Participation in this study implies, in the intervention group, the substitution of face-to-face visits for visits through the Social Diabetes platform, while in the control group in-person visits will be maintained.

To evaluate the impact in glucose control we will extract venous blood samples to determine if there are difference in the HbA1c laboratory results between the baseline visit (before using the app) and the final visit (after using the app) in patients of the experimental group. To assess if there is clinical significance those results will be compared with the ones obtained from the control group.

To establish differences in the quality of life or treatment satisfaction we will give the three questionnaires (DTSQs, DTSQc and EuroQol-5D) to all the participants in order to compare differences in the results of both groups. The DTSQs will serve to benchmark current levels of treatment satisfaction at the baseline visit. Then the DTSQc will be given at the end to assess changes in treatment satisfaction and to evaluate patient preference for the system compared with their previous diabetes treatment process. The EsDQOL questionnaire will be given at the first and last visits to establish also comparisons between the perception of quality of life at the start and the end of the intervention in both groups.

In hospital visits and during the study some data of interest will be collected, which will be used as co-variables. Those data will be registered through three "data collection sheets". In those sheets, we will also include some information that may be useful for future studies but that we will not use as variables in the present study (e.g. average glycemia of the month prior to the visit, number of capillary blood glucose controls performed per day, etc.).

### 7.6.1. Study procedures

1) **Screening visit**: Patients will come to Endocrine outpatient consultation routinely to check-out DM control. There: (*Figure 4*)

1. The physician will make to the patient a good anamnesis, a physical examination and will collect information of registered blood glucose values and treatment.

2. If a patient is recognized as a possible partaker into the study (because he seems to complete the study conditions), the physician will explain briefly the argument of the study and its design. It is important to aware the patients about the possibility to not be chosen for the study (because of inclusion or exclusion criteria).

3. If patient wants to take part of the study, the physician will meticulously check if the he/she fulfills the selection criteria to enter into the study by using information contained in the clinical history and information obtained through anamnesis and physical examination.

4. If the patient is finally selected and he definitely want to participate, physician will give him an information sheet (See ANNEXES 7 and 9) which explains in a more completed but understandable way the study procedures. The physician will also answer to all the doubts and questions of the patient to be sure that patient has understood all the process.

5. The physician will be the responsible for decide if the patient complete all the requirements of the study. He can notify to the patient that he or she can join the study during that visit (and the informed consent (See ANNEXES 8 and 10) will be signed) or during the following days with a call (if there is no time during the visit, the informed consent will be signed the first day of the study). If the patient cannot take part because he/she does not complete the criteria, the physician will explain it to him in the most respectful way.

6. In order to reduce biases, participants must be selected before the randomization of the conglomerates and the person who make the assignment must be different from those who made the recruitment. (44) Thus, a different specialist will proceed to make the randomization of the consultations, once the sample has been chosen.

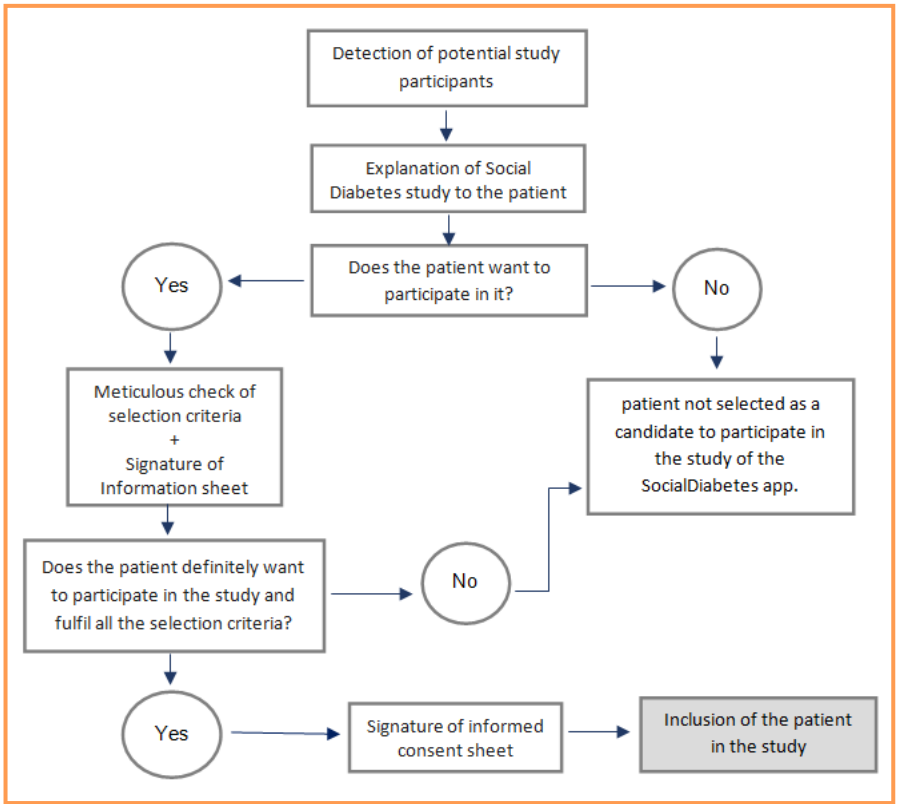


**Figure 4.** Screening process

2) **Starting the study**:

- **Baseline visit:** during the following month, patients will be cited at Endocrinology Day Hospital of HUDJT for the baseline visit of the study. In this visit:
  - Patients who have not signed the informed consent will do it. They must know that they can quit the study at any time although they have signed the informed consent.
  - A nurse will perform a blood test to the patient and the sample will be given to the clinical laboratory.
  - Then, the physician will fill out the data collection sheet of the baseline visit (See ANNEX 11) of all participants, taking information from the medical history, physical examination, data from blood glucose diary or CGM and through anamnesis.

- At this moment of the study, the randomization of the groups will have already taken place so patients will have already been assigned to the control or intervention group:
    a. Patients assigned to the remote consultation through SocialDiabetes
        - Will be trained in the management of the platform, by a worker from SocialDiabetes team, to pass the glycemic data to the cloud and be able to use the different functionalities of the app. We will give them a "User's SocialDiabetes manual" (See ANNEX 2) so they can consult any doubt about the operation of the cell phone application.
        - The alarm parameters / alerts will be agreed with each individual.
    b. Patients assigned to the face-to-face consultation:
        - Will have to record in a diary their blood glucose levels (See ANNEX 1) or with the CMG as they normally do for the regular reviews with the endocrinologist.
- At the end of the visit all the participants:
    a. Will be asked to complete the two questionnaires required in the start visit ( DTSQs and EsDQOL) by themselves.
    b. Finally, the physician will give them a record sheet ("*patient's record sheet*") (see ANNEX 12) that they will have to compete during the following 6 months with this information:
        - Number of severe hypoglycemia events experimented during the study.
        - Number of face-to-face visits with their endocrinologist and number of visits to medical emergencies during the 6 months follow-up period. It also includes a section of "remote consultations" for participants of the experimental group, where they will have to register the number of consultations they do through the SocialDiabetes app too.

- **Follow-up study period**: During the study:
  - Patients of the control group will continue to manage their illness in the same way as they did before with SMBG and IIT, and planning visits with the specialist when required.
  - Patients in the experimental group will have access to the application and to all their functionalities explained in the introduction (Log register, bolus calculator, digital diary, carb calculator…) and will be able to consult their concerns and doubts with the doctor when necessary (trying to be coherent with the time). In case that they prefer a consultation through a face-to-face visit, they will also be able to request visits with their endocrinologist (as well as the other group) as this will help us verify if the remote consultations are useful or futile.

- **Final visit:** after 6 months, all the patients will be cited to come again to the hospital where:
  - At the Endocrinology Day Hospital, the same nurse will do another blood test to the patient and the sample will we given again to the clinical laboratory.
  - The physician will fill out the data collection sheet of o the final visit (See ANNEX 13) of all the patients (with information from the record sheet given, the anamnesis and from devices) and will do them a physical examination.
  - The physician will access to glucose through SocialDiabetes app, glucose diaries or CMG of patients.
  - Patients will be asked deliver the "record sheet" and to complete DTSQc and EsDQOL questionnaires by themselves.
  - The number of hypoglycemia events will be registered in the data collection sheet to take them in consideration for the statistical analysis.

- **Unscheduled visits**. Throughout the study, clinicians will be instructed to monitor the clinician web portal homepage once a week to identify high-risk patients who may require an unscheduled visit to address the concern. Those unscheduled visits will be recorded and taken in consideration together with the registered visits in the "patient's record sheet".

### 7.6.2. Visits schedule

| Schedule of visits in the HUDJT | | Screening visit | Study | |
|---|---|---|---|---|
| | | | Baseline visit | Final visit |
| **Information sheet** | | ✓ | | |
| **Informed consent sheet** | | ✓ | | |
| **Data collection** | | ✓ | | |
| **Anamnesis** | | ✓ | ✓ | ✓ |
| **Physical examination** | | ✓ | ✓ | ✓ |
| **Blood test** | | | ✓ | ✓ |
| **Creation of users of SocialDiabetes app** | Only in intervention group | | ✓ | |
| **Social Diabetes Training** | | | ✓ | |
| **"Baseline visit "data collection sheet** | | | ✓ | |
| **Patient's record sheet** | Delivery | | ✓ | |
| | Collection | | | ✓ |
| **"Final visit" data collection sheet** | | | | ✓ |
| **Questionnaires** | DTSQs | | ✓ | |
| | DTSQc | | | ✓ |
| | EsDQOL | | ✓ | ✓ |

# 8. STATISTICAL ANALYSIS

The statistical analysis will be performed using Statistical Package for Social Sciences (SPSS©) and Microsoft Excel Windows to manage computed data. We will perform an intention to treat analysis and differences with levels of $p < 0.05$ will be assumed as statistically significant.

For the main objective we will accept as the non-inferiority threshold an HbA1c difference of -0.35%. Then, to assess the superiority of SocialDiabetes application in comparison with current model of assistance we will consider clinically significant differences of the HbA1c greater than 0.5%.

## 8.1. Descriptive analysis

We will summarize the quantitative variables in means, standard deviation, medians and interquartile ranges, stratifying by intervention and control groups.

On the other hand, the qualitative variables will be summed up in proportions expressed in percentages, stratifying again by intervention and control group.

## 8.2. Bivariate inference

We will compare means and medians of the quantitative variables between the control and intervention groups by using T-Student and V Mann-Whitney respectively. Our main and secondary response variables of interest are: HbA1c, DTSQ and EsDQOL results.

The proportions of the qualitative variables will be compared using $chi^2$ or Fisher's exact test.

## 8.3. Multivariate analysis

To assess the interventions efficacy we will estimate linear regression models where the response variable will be the HbA1c variations and the independent variable will be the intervention/control group. Adjusting it according to the co-variables, which include: age, gender, IMC, diabetes duration, CMG usage, CSII usage, HCP (clusters), presence of micro or macroangiopathia, number of severe hypoglycemia during the study and number of HCP visits/consultations.

# 9. ETHICAL CONSIDERATIONS

This research protocol will be valued by the Comitè Ètic d'Investigació Clínica (CEIC) from Hospital Universitari Doctor Josep Trueta and will start once they give their approval.

All basics ethics principles will be respected according to Worlds Medical Association Declaration of Helsinki about ethical principles for medical research involving human subjects.

SocialDiabetes is a software designed for self-management of type 1 and type 2 diabetes, which facilitates the calculation of the insulin dose of bolus and provides tools for glucose control to the users. The European Commission (CE) has certified the Social Diabetes app as a medical product, according also to the Spanish law (Real Decreto 1090/2015 del 4 de Diciembre ). At the moment, the CE marking is Class I which means the application is providing only "recommendations" that can be accepted (or not) by the user and it does not serve for medical diagnosis. The information provided by the services or by the Platform from the data entered by the user is for informational purposes only and does not replace the medical criteria. For any decision related to medication, users must previously obtain the opinion, prescription, or supervision of a physician. This study guarantees that physicians who will be registered in the Platform are qualified doctors legally allowed to practice the profession.

By registering and using the website or the application, the user consents and expresses his agreement with the terms and conditions of the application and its privacy and security policy.

Due to CE certificate, this study does not need to ask for the approval of the Agencia Española de Medicamentos y Productos Sanitarios (AEMPS) and does not require the contract of an insurance policy.

Every single patient will be properly informed and an information sheet concerning the study protocol (See ANNEXES 7 and 9) will be given for that purpose. Then, patients will sign voluntarily the informed consent (See ANNEXES 9 and 10). Participants have the right to withdraw the consent without having a negative effect on the relationship with

their assigned doctor or treatment received. The principle of autonomy will be respected in all the process.

Patients will not be identified by their names, but by their unique identification numeric code. The patients data collected will follow the Spanish data protection law (Ley Orgánica 15/1999, de 13 de Diciembre, de protección de datos de carácter personal), in order to protect the patients' confidentiality.

# 10. STUDY LIMITATIONS

## 10.1. Study design

### 10.1.1. Internal validity

The main limitation of the study consists of being a controlled trial randomized by clusters because this type of study design can be more exposed to bias than a simple randomized design. Furthermore, many studies by conglomerates, due to the complexity of their interventions, are impossible or very difficult to maintain a double blind. Under these circumstances, the risk of selection bias is high and this could affect the internal validity of the study (45).

However, in certain circumstances, it is the only or the best existing design option. In this study, making a randomization by clusters would be justified due to the following reasons:

1. We want to study the implementation of a new tool to improve the quality of healthcare assistance in the public health system and studies confirm that in this case, it would be justified to use a study of these characteristics.(44) This is because the clinical trials carried out by conglomerates are more efficient from the administrative point of view and the compliance of the participants is usually better.
2. Patients usually talk in the waiting room, and in general, they sit close to other patients treated by the same physician. There, they can share information about their treatments and talk about individual experiences. What we want to avoid, is that the ones assigned to the control group use SocialDiabetes app after interact with another patient. Social Diabetes app is free and anyone can access to it so it is impossible to control. We want avoid that this situation could finish contaminating the sampling and altering the results of the study.

   It is known that the risk of contamination is very high in a clinical trial with randomization of individuals (44,45) so we think that is more convenient to opt for a design in conglomerates where all the patients of the same consultation will be assigned to the same control/intervention group. This will make more

difficult that interactions between patients lead them to change their treatment management.

3. In our study, the intervention involves the training and education of HCP on the use of the SocialDiabetes platform. Randomizing the groups according to the consultations decreases the number of doctors that have to be trained.

Taking into consideration the limitations exposed above and considering that it is impossible to main the double blind (we cannot hide the use of the mobile application), patients will be selected before randomization. This will help reducing the risk of bias selection because will avoid that recruitment be influenced by the assigned intervention.

### 10.1.2. External validity

To determine whether the generalization of the results across heterogeneous populations is feasible, we have to say that the study contains a large number of inclusion and exclusion criteria and the results may not be representative for all the population. In addition, although the app is free, the phone and data service may provide a barrier to care for patients who are unable to afford these extra costs.

### 10.1.3. Variables

The HbA1c test is an indirect measure of average glycemia and, as such, is subject to limitations. As with any laboratory test, there is variability in the measurement of HbA1c. Although such variability is less on an intraindividual basis than at blood glucose measurements, clinicians should exercise judgment when using HbA1c as the sole basis for assessing glycemic control. Nevertheless, the significance of HbA1c as the central parameter for assessing the quality of glycemic control achieved over time is undisputed (7). Due to this reason, we decided to use it as the main variable. To reduce the variability with laboratory test or manipulation, all blood samples will be taken by the same nurse and they will be analyzed in the same laboratory with the same analytic method.

HbA1c does not provide a measure of glycemic variability or hypoglycemia. For patients prone to glycemic variability, especially patients with T1DM, glycemic control is best evaluated by the combination of results from HbA1c and SMBG or CGM. Also, it is known that among patients with type 1 diabetes, there is a correlation between greater SMBG frequency and lower HbA1c. Considering all this, we think that not analyzing other parameters of blood glucose control such as SMBG frequency could represent a limitation. However, we will collect some of that information in the collection sheets in order to be able to use them in further investigations.

## 10.2. Patients participation

Participants enrolled in these studies may be more highly motivated to improve blood sugar control, which adds to selection bias mentioned before.

# 11. WORK PLAN AND CHRONOGRAM

## 11.1. Work plan

The general coordinator of the study (GC), four endochrinologists (EC), a technical expert from SocialDiabetes (SDT), and a statistical specialist (SS) will compose the research team (RT). A computer engineer (CE) and a data manager (DM) will help in the database elaboration and data register.

### STAGE 0: Preparation – 1 month

- **Activity 1:** Protocol processing. It will be reviewed in order to identify possible misspellings, statistical errors or other mistakes. The GC will be in charge of it.
- **Activity 2:** Presentation of the protocol to the Comitè Ètic d'Investigació Clínica (CEIC) for approval. The GC will be the responsible for this activity.
- **Activity 3:** Presentation of the protocol to the director of the Hospital by the GC. His approval is required prior to starting the study.

### SAGE 1: Coordination – 1 month

- **Activity 4:** Informative meeting. This meeting will help us to conduct the study adequately. It is an all-member meeting where the GC will explain the working plan, schedule and methods to the rest of the professionals.
- **Activity 5:** Database elaboration. It will be done by a CE.

### STAGE 2: Patients recruitment and intervention – 12 months

- **Activity 6:** Each of four EC will recruit 48 patients, who will follow the selection criteria mentioned previously and will have signed the informed consent, by a consecutive non-probabilistic sampling. The estimated time of recruitment will be 3 months. Then, a SS will randomize the patients of the four consultations.
- **Activity 7:** Training in the use of SocialDiabetes app of the two ECs that will assist the patients randomized to intervention group.

- **Activity 8**: The four ECs will do the data collection of all the patients. The subjects of the consultations assigned to the intervention group, will have a training lesson of the app by the SDT, who will attend any problem with the app during the study. At the end of the intervention period, the ECs will return to collect data of all the patients. The DM will be the responsible for register all the sheets information in the database.

### STAGE 3: Data analysis and interpretation – 1 month

- **Activity 9**: The SS will analyze data with the appropriate statistical test.
- **Activity 10**: Results will be discussed and interpreted by the whole RT.

### STAGE 4: Publication and dissemination of the research finding – 5 months

- **Activity 10:** Publication. The GC will send the articles to different journals for their publication.
- **Activity 11:** Dissemination of the findings. We will attempt to display our results in conferences and congresses related to technologies and Type 1 Diabetes Mellitus management.

## 11.2. Chronogram

| ACTIVITY | PERS | 2019 | | | | | | 2020 | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Jan - Feb | March- April | May-June | July-August | Sept- Oct | Nov- Dec | Jan- Feb | March- April | May-June | July-August |
| **STAGE 0:** Preparation | | | | | | | | | | | |
| Protocol processing | GC | | | | | | | | | | |
| Ethical approval | GC | | | | | | | | | | |
| Hospital's approval | GC | | | | | | | | | | |
| **STAGE 1:** Coordination | | | | | | | | | | | |
| Informative meeting | RT | | | | | | | | | | |
| Database elaboration | CE | | | | | | | | | | |
| **STAGE 2**: Patients recruitment and intervention | | | | | | | | | | | |
| Recruitment | EC | | | | | | | | | | |
| EC training | SST | | | | | | | | | | |
| Data collection and Intervention | EC DM | | | | | | | | | | |
| **STAGE 3:** Data analysis and interpretation | | | | | | | | | | | |
| Statistical analysis | SS | | | | | | | | | | |
| Discussion | RT | | | | | | | | | | |
| **STAGE 4:** Publication and dissemination of the research finding | | | | | | | | | | | |
| Publication | RT | | | | | | | | | | |
| Dissemination | GC | | | | | | | | | | |

# 12. FEASIBILITY

This trial will take place exclusively in the Endocrinology and Nutrition Service of the HUDJT, which is the reference center of endocrinology for the Girona region. The Hospital belongs to Institut Català de Salut (ICS) and has an assigned population of 800,000 inhabitants. It has a team specialized in type 1 diabetes that is responsible for monitoring the treatment of a total of 1,800 patients with this disease, most of whom are under intensified insulin treatment. Therefore, its specialized team and the access to a large number of patients with T1DM make it an ideal center to assess the security and efficacy of a diabetes mHealth app.

The endocrinologists, the nurse and laboratory personnel will receive their habitual salaries in the hospital. The only works that will be paid will be the ones conducted by the SocialDiabetes app expert, data manager and engineer and the one done by the statistical specialist.

The material required for this trial is the standard material used in the management of patients with diabetes. We only have to add the questionnaires licenses and the data collection sheets, which represent an essential extra tool that will be useful for data analysis. The most important elements of this investigation are the SocialDiabetes app, which is free, and the HbA1c testing, which is considered as a routine control.

The adoption and use of smartphones and other mobile devices is widespread so learning about the usage of the application will not represent a problem for patients neither for physicians. The only challenge that physicians will have to face is that patients might contact them out of their working hours and they will have to learn to administrate their time to deal with SocialDiabetes platform requirements.

In conclusion, this project seems to be an economically feasible study, which can be performed in a reference hospital with the necessary amount of patients. Morover, the study can become the first step to completely change the sanitary assistance related to diabetic patients treatment.

# 13. BUDGET

## 13.1. Cost division

In order to calculate accurately the needed budget for this trial we have divided the costs in personnel, materials and services and publication results costs (*Table 2*).

### 13.1.1. Personnel

Most of the activities will be performed by professionals of the HUDJT. The personnel of the study will consist of the four physicians of the 4 monographic consultations of IIT, a nurse that will help with data collection and Hba1c testing and personnel from the clinical laboratory. The physician outpatient visits are not included in the budget; neither the nurse nor laboratory work because HbA1c testing is considered patient routine analytical control so its performance will not represent an extra expense.

The study will have to contract a coworker from SocialDiabetes team that will help with clinicians and patients' training in the diabetes app.

A skilled staff is required to be in charge with data monitoring and quality control data. We will have to hire a computer engineer to create the database and then, a data manager will be needed for the uploading of clinical data to the database. The same person will also have to carry out the evaluation of the questionnaires and will have to pass all the information obtained to the database. Finally, the study will also need a qualified statistician in order to randomize patients and to analyze statistically data collected. He or she will give a code number to patients too.

### 13.1.2. Materials and services

Regarding to our study variables, we will have to pay the license to perform the treatment satisfaction questionnaires and the quality of life questionnaire but HbA1c testing, as said before, is considered patient normal analytic control.

SocialDiabetes app is free and it will not suppose an extra cost because physicians and patients will be able to access to it after downloading it in Google Play for Android devices and in Apple App Store for iOS mobile phones. However, we will give a "User's SocialDiabetes manual" to all users so they can consult any doubt about the operation of the application. Thus, we will have to assume a minor cost for printing the manuals and all the other sheets required for the study (information sheets for patients, informed consent forms, data collection sheets and questionnaires).

The budget does not include material office supplies and software such as SPSS© and Microsoft Windows© software, because our participating center hold the correspondent licenses.

Finally, it is important to remind that patients will be covered by the hospital liability insurance and that contracting any other insurance policy will not be necessary because the SocialDiabetes app has de CE certification.

### 13.1.3. Publication and dissemination of the results

After the study, an important part is the publication and the dissemination of the results. For the publication in national and international journals, we have assigned 1000€. The dissemination includes the registration in two congresses; the Congreso Nacional de la Sociedad Española de Diabetes (SED) and the Meeting of the European Association for the Study of Diabetes (EASD). We have to assume expenses in registration of two people and costs of travelling, accommodation and food.

**Table 2.** Study budget

| PERSONNEL COSTS | | | | |
|---|---|---|---|---|
| **PERSONNEL** | **FUNCTIONS TO BE PERFORMED** | **NUMBER OF PEOPLE** | **ESTIMATED TIME** | **COST** |
| **INVESTIGATORS** | Selection of participants according to inclusion and exclusion criteria and clinical characteristics of person.<br>Information of the patients included in the study<br>Revision of the clinician web portal homepage once a week to identify high-risk patients | 4 people | Provided by the National Health System (NHS) | |
| **NURSE** | Extraction of venous blood sample | 1 person | | |
| **CLINICAL LAB.** | Analysis of venous blood samples | 1 person | | |
| **SOCIALDIABETES COWORKER** | Training in Socialdiabetes app | 1 person | 20h | 20€/h |
| **COMPUTER ENGINEER** | Design and creation of databases and analysis software. | 1 person | 20 h | 12€/h |
| **DATA MANAGER** | Evaluation of questionnaires<br>Passing clinical data and questionnaires information to the database. | 1 person | 1 year | 20.000€/ year |
| **STATISTICAL SPECIALIST** | Randomization of patients and statistical analysis of data | 1 person | 50h | 25€/h |
| The cost has been calculated in relation to the estimated hours each professional will be doing. | | | | |
| | | | **Total personnel cost** | **21.890€** |

| MATERIAL AND SERVICES | | |
|---|---|---|
| **MATERIAL** | **DESCRIPTION** | **TOTAL** |
| **SOCIALDIABETES APP** | Free | 0 |
| **HBA1C** | It is considered a routine analytical control of diabetic patient. | 0 |
| **QUESTIONNAIRES LICENSE** | License of DTSQs-DTSQc and EsDQOL | 1000€ |
| **USER'S SOCIALDIABETES MANNUAL** | Manual copy for each user | 200 € |
| **PRINTED SHEETS** | Information, data collection and informed consent sheets. + Questionnaires. | 90 € |
| | **Total of material and services cost** | **1.290 €** |

| PUBLICATION AND DISSEMINATION OF THE RESULTS | | | |
|---|---|---|---|
| **ITEM** | **APPROXIMATE PRICE** | **QUANTITY OR PEOPLE** | **TOTAL** |
| **PUBLICATION EXPENSES** | 1000 | 1 | 1.000€ |
| **REGISTRATION IN SED NATIONAL CONGRES** | 570€/person | 2 people | 1.140€ |
| **REGISTRATION IN EASD MEETING** | 600€/person | 2 people | 1.200€ |
| **TRAVELLING, ACCOMMODATION AND FOOD EXPENSES FOR THE TWO CONGRESSES** | 700€/person | 2 people | 1.400€ |
| | **Total of publication and dissemination of the results expenses** | | **4.740€** |
| | | **TOTAL** | **27.920€** |

# 14. IMPACT ON THE NATIONAL HEALTH SYSTEM

Diabetes mellitus is a leading health problem globally. DM is one of the main causes of mortality and major morbidities, including cardiovascular disease, kidney failure, amputations and blindness (1). The risk of developing these conditions is higher for diabetic patients compared with non-diabetic patients in the same age-group. (46)

Working towards diabetes prevention as well as prevention of diabetes-related complications is a real goal. Our study aims to verify if SocialDiabetes application can really help to achieve a best blood glycemic control by enhancing diabetes self-management. However, not only is important to reduce long-term diabetes complications. In addition, this app may also help improving satisfaction with treatment and perceptions of the quality of patient's care, which are also important outcomes related with patient's life.

Regarding to diabetes care, Spain offers a good health coverage system with well-developed care. All diabetes expenses are fully covered by the NHS. The annual cost per diabetic patients averages close to €1,660 for direct costs and €916 for productivity losses, with significant differences between patients with and without micro and macrovascular complications.(47) In the near future, the use of the application would lead to a greater reduction of long-term complications in patients with T1DM and would generate fewer expenses in public health system.

Finally, we also believe that the use of this platform by professionals can cover the healthcare needs of patients with DM1 of the 21st century. It will represent a significant reduction in indirect costs for the patient and society with fewer trips and less loss of working hours. For professionals, it will mean an increasing time devoted to the review of the most problematic or complex DM1 cases to the detriment of routine in-person visits of well-controlled patients, a condition that will add value to healthcare activity.

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# 16. ANNEXES

## 16.1. Diabetes treatment

### 16.1.1. **ANNEX 1** – Diabetes treatment tools

Blood Glucose Monitor (BMG)

Continuous Glucose Monitor (CMG)

Multiple Daily injections (MDI)


Long-Acting Insulin = Lantus, Levemir
Rapid-Acting Insulin = Humalog, Novolog, Apidra

Continuous subcutaneous insulin infusion (CSII)

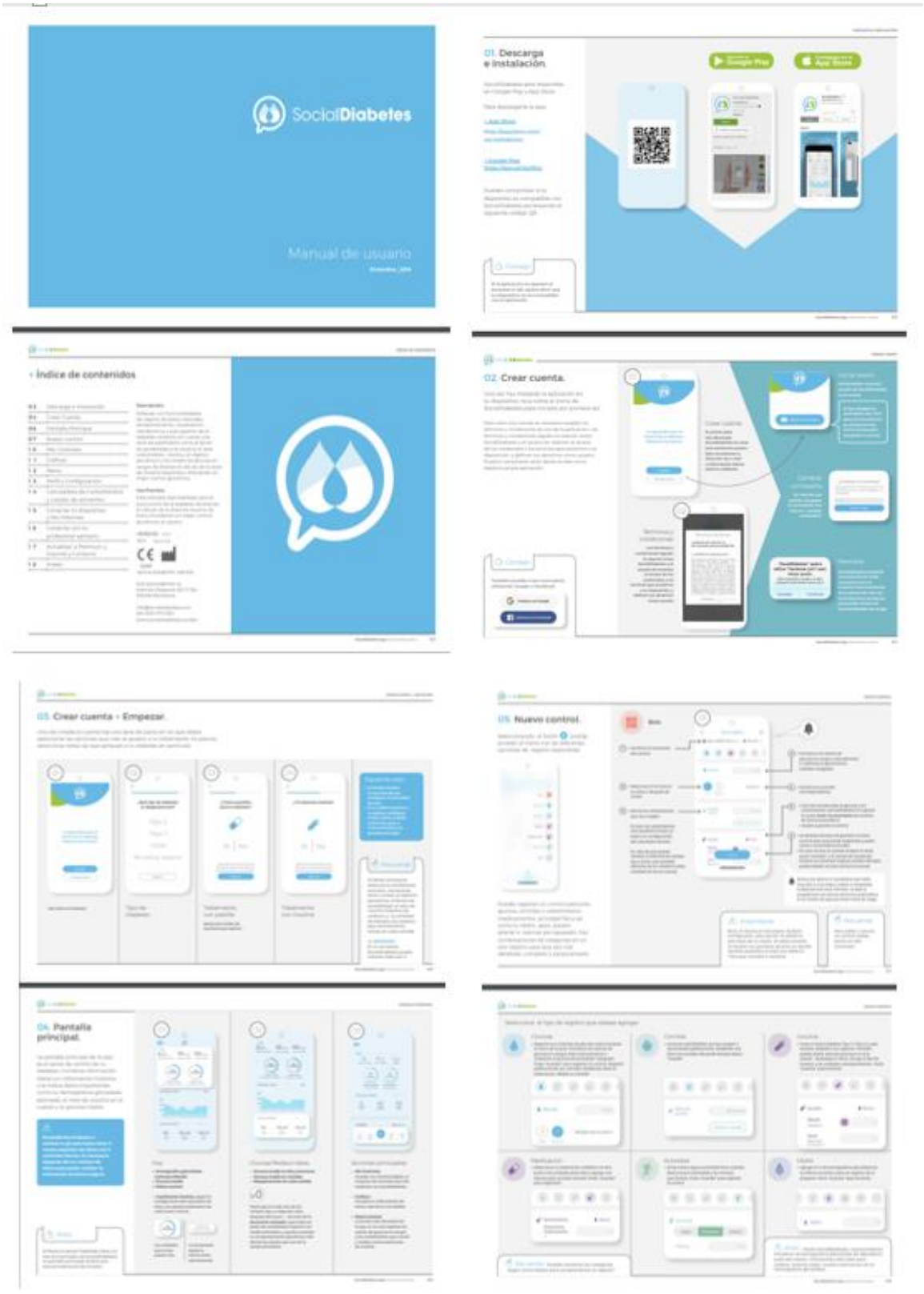

Insulin Pumps use only Rapid-Acting Insulins:
Humalog, Novolog, Apidra

Blood glucose diary

| MES | NIVEL DE GLUCOSA EN LA SANGRE | | | | | | | DOSIS INSULINA/PASTILLAS | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Días | Antes del desayuno | Después del desayuno | Antes de la comida | Después de la comida | Antes de la cena | Después de la cena | Nocturno | Desayuno | Comida | Cena | Antes de ir a dormir |
| Lunes | | | | | | | | | | | |
| Martes | | | | | | | | | | | |
| Miércoles | | | | | | | | | | | |
| Jueves | | | | | | | | | | | |
| Viernes | | | | | | | | | | | |
| Sábado | | | | | | | | | | | |
| Domingo | | | | | | | | | | | |

## 16.2. mHealth

### 16.2.1. **ANNEX 2** - User's SocialDiabetes Mannual




07. Gráficas.


06. Mis controles.


08. Menú.


09. Perfil y configuración.

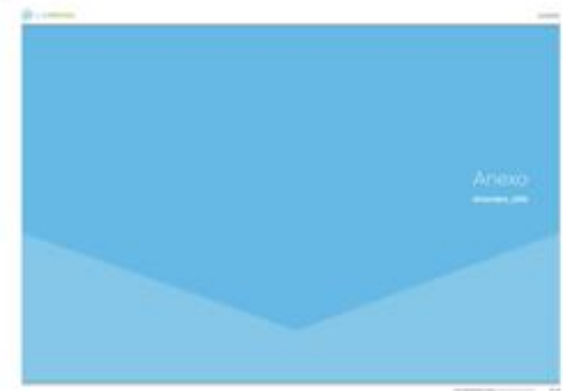

12. Conecta tu dispositivo.
13. Mis informes.


10. Calculadora de carbohidratos.
11. Listado de alimentos.


14. Conectar con tu profesional sanitario.


15. Actualizar a Premium
16. Soporte y contacto


I. Notificaciones, iconos, colores


Anexo


II. Terminología


III. FreeStyle Libre


SocialDiabetes

## 16.3. Questionnaires

### 16.3.1. **ANNEX 3** - DTSQs

**CUESTIONARIO DTSQs**

Por favor, conteste cada pregunta haciendo **un círculo** en un número de cada una de las escalas, para indicar la extensión de cómo Ud. ha experimentado los cambios.
**Si no ha experimentado ningún cambio, marque con un círculo "0".**
En comparación con su experiencia con el tratamiento en los últimos tres meses,

1. ¿En qué medida está Ud. satisfecho/a con su tratamiento actual?

Muy satisfecho/a 6 5 4 3 2 1 0 Muy insatisfecho/a

2. Últimamente, ¿con qué frecuencia ha considerado que su nivel de azúcar es inaceptablemente alto?

La mayoría del tiempo 6 5 4 3 2 1 0 Nunca

3. Últimamente, ¿con qué frecuencia ha considerado que su nivel de azúcar es inaceptablemente bajo?

La mayoría del tiempo 6 5 4 3 2 1 0 Nunca

4. Últimamente, ¿en qué medida considera Ud. que su tratamiento resulta fácil/cómodo?

Muy fácil/muy cómodo 6 5 4 3 2 1 0 Muy difícil/muy incómodo

5. Últimamente, ¿en qué medida considera Ud. que su tratamiento se adapta a su vida?

Se adapta muy fácilmente 6 5 4 3 2 1 0 No se adapta a mi vida

6. ¿En qué medida está satisfecho/a con su grado de conocimiento acerca de su diabetes?

Muy satisfecho/a 6 5 4 3 2 1 0 Muy insatisfecho/a

7. ¿Recomendaría esta forma de tratamiento a alguien con una diabetes similar a la suya?

Sí, sin duda 6 5 4 3 2 1 0 No, no en absoluto

8. ¿Hasta qué punto estaría satisfecho/a de continuar con su tratamiento actual?

Muy satisfecho/a 6 5 4 3 2 1 0 Muy insatisfecho/a

## 16.3.2. **ANNEX 4** - DTSQc

**CUESTIONARIO DTSQc**

Por favor, conteste cada pregunta haciendo **un círculo** en un número de cada una de las escalas, para indicar la extensión de cómo Ud. ha experimentado los cambios.
**Si no ha experimentado ningún cambio, marque con un círculo "0".**
En comparación con su experiencia con el tratamiento en los últimos tres meses,

1. ¿En qué medida está Ud. satisfecho/a con su tratamiento actual?

Mucho más satisfecho/a ahora 3 2 1 0 – 1 – 2 – 3 Mucho menos satisfecho/a ahora

2. Últimamente, ¿con qué frecuencia ha considerado que su nivel de azúcar es inaceptablemente alto?

Mucho más frecuente ahora 3 2 1 0 – 1 – 2 – 3 Mucho menos frecuente ahora

3. Últimamente, ¿con qué frecuencia ha considerado que su nivel de azúcar es inaceptablemente bajo?

Mucho más frecuente ahora 3 2 1 0 – 1 – 2 – 3 Mucho menos frecuente ahora

4. Últimamente, ¿en qué medida considera Ud. que su tratamiento resulta práctico/cómodo?

Mucho más práctico/cómodo ahora 3 2 1 0 1 – 2 – 3 Mucho menos práctico/cómodo ahora

5. Últimamente, ¿en qué medida considera Ud. que su tratamiento es flexible?

Mucho más flexible ahora 3 2 1 0 – 1 – 2 – 3 Mucho menos flexible ahora

6. ¿En qué medida está satisfecho/a con su grado de conocimiento acerca de su diabetes?

Mucho más satisfecho/a ahora 3 2 1 0 – 1 – 2 – 3 Mucho menos satisfecho/a ahora

7. ¿Recomendaría esta forma de tratamiento a alguien con una diabetes similar a la suya?

Probablemente, recomendaría 3 2 1 0 – 1 – 2 – 3 Probablemente, recomendaría
mucho más el tratamiento ahora mucho menos el tratamiento ahora

8. ¿Hasta qué punto estaría satisfecho/a de continuar con su tratamiento actual?

Mucho más satisfecho/a ahora 3 2 1 0 – 1 – 2 – 3 Mucho menos satisfecho/a ahora

## 16.3.3. **ANNEX 5** - EsDQOL questionnaire

**ANEXO 1** **EsDQOL modificado**

| |
|---|
| **Satisfacción** |
| 1. ¿Está usted satisfecho con la cantidad de tiempo que tarda en controlar su diabetes? |
| 2. ¿Está usted satisfecho con la cantidad de tiempo que ocupa en revisiones? |
| 3. ¿Está usted satisfecho con el tiempo que tarda en determinar su nivel de azúcar? |
| 4. ¿Está usted satisfecho con su tratamiento actual? |
| 5. ¿Está usted satisfecho con la flexibilidad que tiene en su dieta? |
| 6. ¿Está usted satisfecho con la carga que supone su diabetes en su familia? |
| 7. ¿Está usted satisfecho con su conocimiento sobre la diabetes? |
| 8. ¿Está usted satisfecho con su sueño? |
| 9. ¿Está usted satisfecho con sus relaciones sociales y amistades? |
| 10. ¿Está usted satisfecho con su vida sexual? |
| 11. ¿Está usted satisfecho con sus actividades en el trabajo, colegio u hogar? |
| 12. ¿Está usted satisfecho con la apariencia de su cuerpo? |
| 13. ¿Está usted satisfecho con el tiempo que emplea haciendo ejercicio? |
| 14. ¿Está usted satisfecho con su tiempo libre? |
| 15. ¿Está usted satisfecho con su vida en general? |
| **Impacto** |
| 16. ¿Con qué frecuencia siente dolor asociado con el tratamiento de su diabetes? |
| 17. ¿Con qué frecuencia se siente avergonzado por tener que tratar su diabetes en público? |
| 18. ¿Con qué frecuencia se siente físicamente enfermo? |
| 19. ¿Con qué frecuencia su diabetes interfiere en su vida familiar? |
| 20. ¿Con qué frecuencia tiene problemas para dormir? |
| 21. ¿Con qué frecuencia encuentra que su diabetes limita sus relaciones sociales y amistades? |
| 22. ¿Con qué frecuencia se siente restringido por su dieta? |
| 23. ¿Con qué frecuencia su diabetes interfiere en su vida sexual? |
| 24. ¿Con qué frecuencia su diabetes le impide conducir o usar una máquina (p. ej., máquina de escribir)? |
| 25. ¿Con qué frecuencia su diabetes interfiere en la realización de ejercicio? |
| 26. ¿Con qué frecuencia abandona sus tareas en el trabajo, colegio o casa por su diabetes? |
| 27. ¿Con qué frecuencia se encuentra usted mismo explicándose qué significa tener diabetes? |
| 28. ¿Con qué frecuencia cree que su diabetes interrumpe sus actividades de tiempo libre? |
| 29. ¿Con qué frecuencia bromean con usted por causa de su diabetes? |
| 30. ¿Con qué frecuencia siente que por su diabetes va al cuarto de baño más que los demás? |
| 31. ¿Con qué frecuencia come algo que no debe antes de decirle a alguien que tiene diabetes? |
| 32. ¿Con qué frecuencia esconde a los demás el hecho de que usted está teniendo una reacción insulínica? |
| **Preocupación: social/vocacional** |
| 33. ¿Con qué frecuencia le preocupa si se casará? |
| 34. ¿Con qué frecuencia le preocupa si tendrá hijos? |
| 35. ¿Con qué frecuencia le preocupa si conseguirá el trabajo que desea? |
| 36. ¿Con qué frecuencia le preocupa si le será denegado un seguro? |
| 37. ¿Con qué frecuencia le preocupa si será capaz de completar su educación? |
| 38. ¿Con qué frecuencia le preocupa si perderá el empleo? |
| 39. ¿Con qué frecuencia le preocupa si podrá ir de vacaciones o de viaje? |
| **Preocupación relacionada con la diabetes** |
| 40. ¿Con qué frecuencia le preocupa si perderá el conocimiento? |
| 41. ¿Con qué frecuencia le preocupa que su cuerpo parezca diferente a causa de su diabetes? |
| 42. ¿Con qué frecuencia le preocupa si tendrá complicaciones debidas a su diabetes? |
| 43. ¿Con qué frecuencia le preocupa si alguien no saldrá con usted a causa de su diabetes? |

## 16.3.4. **ANNEXE 6** - Questionnaires' measurement

1. **Diabetes Treatment Satisfaction Questionnaire (DTSQ)**: Is a validated questionnaire now widely used. It is used particularly in clinical trials but it also could be used for routine clinical monitoring. The original DTSQ is now referred to as the status version (DTSQs) in order to distinguish it from the DTSQ change version (DTSQc), which has been developed to overcome potential ceiling effects (i.e. where respondents score maximum or near-maximum satisfaction at baseline and can show little or no improvement at follow-up). They are available in more than 100 languages, including Catalan and Spanish. Both forms of the DTSQ are suitable for use by people with type 1 or type 2 diabetes (42).
    a. **DTSQs:** DTSQs contains 8 items scored on 7-point scales ( from 6 -= *very satisfied* to 0 =very dissatisfied:
        - Six items (Qs.1 and 4–8) measure Treatment Satisfaction (dealing with: satisfaction with current treatment; convenience of the treatment; flexibility; satisfaction with own understanding of their diabetes; how likely to recommend their present treatment; and how satisfied to continue with their present treatment). These are summed to produce a total Treatment Satisfaction score.
        - Questions 2 and 3, concerning Perceived Frequency of Hyperglycemia ('Perceived Hyperglycemia')/Perceived Frequency of Hypoglycemia ('Perceived Hypoglycemia') respectively, are treated separately from the satisfaction items and from each other [5,16]. On these two items, low scores represent good perceived blood glucose control.
    b. **DTSQc:** Like the DTSQs, the DTSQc contains eight items scored on 7-point scales with the same questions. The differences are that:
        - In the DTSQc, the wording of item 7 (recommending the treatment) directs the respondent to compare their experience of the current treatment with their experience of treatment before the study began,
        - DTSQc scores from +3 = much more satisfied now to -3 = much less satisfied now, with 0 (midpoint), representing no change.

    We will obtain the results of the questionnaires dividing the questions in two groups: all the Satisfaction items loading together on factor 1 and the Perceived Hyper- and Hypoglycemia items (items 2 and 3) loads together on factor 2.

- A high score in factor 1 in DTSQs implies that the patient feels a high satisfaction with the treatment and low punctuations show dissatisfaction. In DTSQc a high score means that now he or she is more satisfied with the recent treatment than with the previous one. A punctuation of 0 means no change and a negative punctuation represent a change into worse.
- In factor 2, in DTSQs, low scores represent good perceived blood glucose control and high punctuations, a bad perception. In DTQSc, low scores represent a better perception of blood glucose control in comparison with the previous treatment; a score of 0 mans no change and a high punctuation a worsening of perceived blood glucose control.

2. **Diabetes Quality of Life (EsDQOL; Spanish version)**: this questionnaire has 43 questions distributed into 4 subcategories: "Satisfaction" (15 questions), "Impact" (17 questions), "Social/vocational concern" (7 questions) and "Diabetes worry" (4 questions). Every question has to be quantified with a 5-point Likert scale:
    a. "Satisfaction": the 5 options are *Very satisfied* [1], *Quite satisfied* [2], *Somewhat satisfied* [3], *little satisfied* [4], *Not satisfied* [5]. For example, if in all questions are very satisfied, the patient will have a punctuation of 15.
    b. "Impact", "Social/vocational concern" and "Diabetes worry": the 5 possible answers are *Never* [1], *Almost never* [2], *Sometimes* [3], *Almost always* [4], *Always* [5]. The minimum punctuations of those subcategories are 17, 7 and 4 respectively, which means diabetes performs low impact and little worry into life of diabetes patients.

    The total punctuation of every subject is the sum of all punctuations. There are not a cutoff score. The lower the total punctuation is, the lesser the impact to quality of life exercise diabetes.(43)

## 16.4. Information and informed consent sheets

### 16.4.1. **ANNEX 7** - Information sheet for participants. Catalan version.

**FULL D'INFORMACIÓ AL PACIENT**

**Títol de l'estudi:** Avaluació de l'impacte clínic de l'eina tecnològica SocialDiabetes en pacients amb Diabetis Mellitus tipus 1

**Investigadors:** _____

**Centre:** _____

**1. Introducció**

Ens dirigim a vostè per informar-la sobre un estudi d'investigació en el que se la convida a participar. Aquest estudi ha sigut aprovat pel Comitè Ètic d'Investigació Clínica (CEIC)

La nostra intenció es tan sols que vostè rebi la informació correcta i suficient per a que pugui avaluar i jutjar si vol o no participar en aquest estudi. Per dur-ho a terme llegeixi aquest full d'informació amb atenció i nosaltres li aclarirem els dubtes que li puguin sorgir després de l'explicació. A més, pot consultar amb les persones que consideri oportú.

**2. Participació voluntària**

Ha de saber que la seva participació en aquest estudi és voluntària i que pot decidir NO participar o canviar la seva decisió i retirar el consentiment en qualsevol moment, sense que això alteri la relació amb el seu metge ni es produeixi cap perjudici en la seva atenció sanitària.

**3. Objectius de l'estudi**

Aquest estudi vol avaluar la seguretat i l'eficàcia de l'aplicació per a telèfons mòbil SocialDiabetes en el maneig de la diabetis. És una App lliure que inclou: Registre de controls (glucosa, carbohidrats, exercici, alimentació), Calculador de bolus per la recomanació automàtica de la dosi d'insulina ràpida, llibreta digital que inclou tots els controls registrats, calculadora de carbohidrats i base d'aliments, gràfiques per visualitzar l'evolució del nivell de glucosa, estimació de l'hemoglobina glicosilada, i els rangs, Connexió amb una varietat de glucòmetres Bluetooth i amb LibreLink (Abbott), Recordatoris (presa de medicaments, realització de controls, etc.), informes exportables, connexió amb el professional. Es preveu una millora en la potenciació de l'autogestió que fan de la seva malaltia i possibilita la intervenció dels professionals de la salut

mitjançant l'opció d'un monitoratge a distància com a activitat integrada en la història clínica electrònica.

**4. Descripció de l'estudi**

L'estudi té una durada de 6 mesos i la primera fase consisteix en seleccionar els pacients que s'inclouran en l'estudi. Això dependrà del compliment d'uns criteris de selecció i de la voluntat del pacient a participar en aquest. Durant aquesta primera fase seran informats sobre els procediments de l'estudi i se'ls demanarà que signin els fulls d'informació i de consentiment informat.

Durant els propers dies els pacients finalment inclosos en l'estudi seran citats per una primera visita. En aquesta visita es dividirà els pacients en dos grups; un grup serà assignat al grup "intervenció", i seran els pacients usuaris de l'aplicació i per altra banda, els pacients assignats al grup "control" continuaran amb les consultes presencials amb el seu metge habitual. Durant la primera visita, es crearà l'usuari en l'aplicació dels pacients assignats al grup intervenció . També rebran una formació sobre el funcionament de l'app i un "manual de l'usuari" per consultar cap dubte que se'ls presenti. També, en col·laboració amb el metge, s'acordarà amb vostè uns paràmetres d'alarma/alertes que posaran en marxa la plataforma de SocialDiabetes per part dels professionals sanitaris. Els pacients assignats a consulta presencial hauran de continuar amb l'assistència sanitària habitual. En aquesta primera visita, a tots els pacients (usuaris o no de l'app) se'ls realitzarà una exploració física i diverses qüestions amb l'objectiu d'omplir un full de recol·lecció de dades necessari per portar a terme l'estudi. A més a més se'ls farà una anàlisi de sang i se'ls demanarà que emplenin dos qüestionaris relacionats amb la satisfacció amb el tractament i la percepció de qualitat de vida. Finalment a tots els pacients se'ls proporcionarà un full de registre perquè apuntin el número d'hipoglucèmies greus que experimentin mensualment i les consultes presencials i remotes que realitzin amb el seu metge.

Tornaran a ser citats 6 mesos després d'aquesta primera visita per una segona avaluació. El metge/metgessa tornarà a emplenar un full de registre amb dades seves i un infermer o infermera els tornarà a treure una mostra de sang per a una analítica. Finalment se'ls demanarà que entreguin el full de registre que se'ls havia proporcionat en la primera visita i que emplenin de nou dos qüestionaris.

A part de les visites programades, vostè pot rebre totes les visites de seguiment que consideri oportú o necessari.

Si vostè accepta participar en l'estudi implica que adquirirà les responsabilitats necessàries per assistir en els procediments de l'estudi, igual com seguir les instruccions del protocol i notificar qualsevol esdeveniment advers que li passi o si ha tingut canvis en la seva medicació (advertint que, excepte en cas d'urgència, no modifiqui la medicació que està prenent ni prengui altres medicaments o "plantes medicinals" sense consultar abans amb el metge de l'estudi.
Finalment, també accepta emplenar els qüestionaris de forma veraç i amb el temps requerit per contestar-los durant les seves visites a consulta.

**5. Beneficis i riscs derivats de la seva participació en l'estudi**

És possible que no obtingui cap benefici immediat derivat de la seva participació en l'estudi, però si en la seva assistència i maneig de la malaltia en un futur pròxim. No es preveuen riscs ni inconvenients per a participar en aquest estudi.

**6. Assegurança**

Per a la participació en aquest estudi , vostè estarà cobert per la pòlissa d'assegurança de l'Hospital Doctor Josep Trueta que s'ajusta a la legislació vigent i que li proporcionarà la compensació i indemnització en cas de menyscabament de la seva salut o de lesions que puguin produir-se en relació amb la seva participació en l'estudi

**7. Confidencialitat/Protecció de dades personals**

El promotor es compromet al compliment de la Llei Orgànica 15/1999, de 13 de desembre de protecció de dades de caràcter personal i al Reial Decret que la desenvolupa (RD 1720/2007) i el reglament (UE) 2016/679 del Parlament Europeu i del Consell de 27 d'abril de 2016 Protecció de Dades (RGPD). Les dades recollides a l'estudi estaran identificades mitjançant un codi, de manera que no inclogui informació que pugui identificar-lo, i només el seu metge de l'estudi / col·laboradors podran relacionar aquestes dades amb vostè i amb la seva història clínica. Per tant, la seva identitat no serà revelada a cap persona llevat d'excepcions en cas d'urgència mèdica o requeriment legal. El tractament, la comunicació i la cessió de les dades de caràcter personal de tots els participants s'han d'ajustar al que disposa aquesta llei.

L'accés a la seva informació personal identificada quedarà restringit al metge de l'estudi / col·laboradors, autoritats sanitàries (Agència Espanyola de Medicaments i Productes Sanitaris, autoritats sanitàries estrangeres), al Comitè d'Ètica de la Investigació i personal autoritzat pel promotor (monitors de l'estudi, auditors), quan ho necessitin per comprovar les dades i procediments de l'estudi, però sempre mantenint la confidencialitat dels mateixos d'acord amb la legislació vigent.

Les dades es recolliran en un fitxer de recerca responsabilitat de la institució i es tractaran en el marc de la seva participació en aquest estudi. Les dades del present estudi es poden utilitzar per a futures investigacions relacionades amb l'estudi. El promotor ha d'adoptar les mesures pertinents per a garantir la protecció de la seva privacitat i no permetrà que les seves dades es creuin amb altres bases de dades que poguessin permetre la seva identificació.

D'acord al que estableix la legislació de protecció de dades, vostè pot exercir els drets d'accés, modificació, oposició i cancel·lació de dades. Amb la legislació actual pot limitar el tractament de dades que sigui incorrecte, sol·licitar una còpia o demanar que es traslladin a tercers (portabilitat) les vostres dades personals cedides per l'estudi.

Per a això haurà de dirigir al seu metge de l'estudi: _____

Si vostè decideix retirar el consentiment per participar en aquest estudi, cap dada nova serà afegida a la base de dades.

Les dades codificades poden ser transmeses a tercers i a altres països però en cap cas han de contenir informació que el puguin identificar directament, com nom i cognoms, inicials, adreça, número de la seguretat social, etc. En el cas que es produeixi aquesta cessió, serà per als mateixos objectius de l'estudi descrit o per al seu ús en publicacions científiques però sempre mantenint la confidencialitat dels mateixos d'acord amb la legislació vigent. La confidencialitat de les dades es garantirà mitjançant contractes o convenis específics
Les dades recollides durant l'estudi es guardaran almenys durant 25 anys, passat aquest temps les dades es poden continuar guardant sempre que vostè autoritzi altres finalitats d'investigació biomèdica

**8. Despeses i compensació econòmica**

En cas de que participi en l'estudi, no tindrà cap despesa ocasionada per participar-hi. No està prevista cap compensació econòmica per participar en l'estudi.

**9. Altra informació rellevant**

També ha de saber que pot ser exclòs de l'estudi si l'investigador ho considera oportú, ja sigui per motius de seguretat, per qualsevol esdeveniment advers que es produeixi per la intervenció en l'estudi o perquè consideri que no està complint amb els procediments establerts. En qualsevol dels casos, vostè rebrà una explicació adequada del motiu que ha ocasionat la retirada de l'estudi.

**10. Telèfon de contacte en cas de dubtes.**

Si durant la seva participació té algun dubte o necessita obtenir més informació, poseu-vos en contacte amb Dr/Dra _____Tel:_____
correu electrònic:_____

Al signar el full de consentiment informat adjunt, es compromet a complir amb tots els procediments de l'estudi que s'han exposat.

## 16.4.2. **ANNEX 8** - Informed consent sheet for participants. Catalan version.

**CONSETIMENT INFORMAT PER ESCRIT PEL PACIENT**

**Títol de l'assaig clínic:** Avaluació de l'impacte clínic de l'eina tecnològica SocialDiabetes en pacients amb Diabetis Mellitus tipus 1

**Investigador principal:**_____

**Centre/Servei:** _____

Jo (Nom i Cognoms): _____

He llegit el full d'informació que se m'ha entregat.

He pogut fer preguntes sobre l'estudi

He rebut suficient informació sobre l'estudi.

He parlat amb: _____ (nom de l'investigador)

Comprenc que la meva participació és voluntària

Comprenc que puc retirar-me de l'estudi:

1. Quan vulgui
2. Sense haver de donar explicacions
3. Sense que això repercuteixi en el tracte mèdic.

Rebré una còpia signada I datada d'aquest consentiment informat. Dono lliurement de la meva conformitat per participar en l'estudi I dono el meu consentiment per l'accés i utilització de les meves dades en les condicions detallades en el full d'informació.

Firma del pacient:

Nom i cognoms: _____
DNI: _ _ _ _ _ _ _ _ - _
Data: __/__/_____

Firma de l'investigador:

Nom i cognoms:_____
DNI: _ _ _ _ _ _ _ _ - _
Data: __/__/___

## 16.4.3. **ANNEX 9** - Information sheet for participants. Spanish version.

**HOJA DE INFORMACIÓN AL PACIENTE**

**Título del estudio:** Evaluación del impacto clínico de la herramienta tecnológica SocialDiabetes en pacientes con diabetes mellitus tipo 1.

**Investigadores:** _____

**Centro:** _____

**1. Introducción**

Nos dirigimos a usted para informarle sobre un estudio de investigación en el que se le invita a participar. El estudio ha sido aprobado por el Comité de Ética e Investigación Clínica (CEIC).

Nuestra intención es que usted reciba la información correcta y suficiente para que pueda decidir si quiere o no participar en este estudio. Por ello lea esta hoja informativa con atención y nosotros le aclararemos las dudas que le puedan surgir después de la explicación. Además, puede consultar con las personas que considere oportuno.

**2. Participación voluntaria**

Ha de saber que su participación en este estudio es voluntaria y que puede decidir NO participar o cambiar su decisión y retirar el consentimiento en cualquier momento, sin que eso altere la relación con su médico ni perjudique su atención sanitaria.

**3. Objetivos del estudio**

Este estudio quiere evaluar la seguridad y la eficacia de la aplicación para telefonía móvil SocialDiabetes en el manejo de la diabetes. Es una aplicación libre que incluye: Registro de controles (glucosa, carbohidratos, ejercicio, alimentación), calculador de bolo por la recomendación automática de la dosis de insulina rápida, libreta digital que incluye todos los controles registrados, calculadora de carbohidratos y base de alimentos, gráficas para visualizar la evolución del nivel de glucosa, la estimación de la hemoglobina glicosilada y los rangos, conexión con una variedad de glucómetros Bluetooth y con LibreLink (Abbott), recordatorios (toma de medicamentos, realización de controles, etc.), informes exportables, conexión con el profesional. Se prevé una mejora en la potenciación de la autogestión que hacen los pacientes de su enfermedad y posibilita la intervención de los profesionales de la salud mediante la opción de una monitorización a distancia como actividad integrada en la historia clínica electrónica

**4. Descripción del estudio**

El estudio tiene una duración de 6 meses y la primera fase consiste en seleccionar a los pacientes que serán incluidos. Esto dependerá del cumplimento de unos criterios de selección y de la voluntad del paciente a participar en el estudio. Durante esta primera fase los pacientes serán informados sobre los procedimientos de este y se les pedirá que firmen las hojas de información al paciente y de consentimiento informado

Durante los días siguientes, los pacientes finalmente incluidos en el estudio serán citados para una primera visita. En esta los pacientes serán divididos en dos grupos; un grupo será asignado al grupo "intervención" y serán aquellos pacientes usuarios de la aplicación; por otro lado, los pacientes asignados al grupo "control" continuarán con las consultas presenciales con su médico habitual. Los primeros recibirán una formación sobre el funcionamiento de la aplicación y un "manual del usuario" para consultar cualquier duda que se les presente. También, en colaboración con el médico, se acordará con usted unos parámetros de alarma/alertas que pondrán en marcha la plataforma SocialDiabetes por parte del médico. En esta primera visita los pacientes asignados al grupo de "consulta presencial - control" serán informados de que deberán seguir con las visitas habituales y con el manejo habitual de su diabetes. También, a todos los pacientes (usuarios o no de la aplicación) se les realizará una exploración física y varias preguntas con el objetivo de llenar una hoja de recolección de datos necesaria para llevar a cabo el estudio. Además, se les realizará un análisis de sangre y se les pedirá que rellenen dos cuestionarios relacionados con la satisfacción con el tratamiento y la percepción de calidad de vida. Finalmente, a todos los pacientes se les proporcionará una hoja de registro para que anoten el número de hipoglucemias graves que experimenten mensualmente y el número de consultas presenciales y remotas (a través de la app) que realicen con su médico.

Volverán a ser citados 6 meses después de esta primera visita para una segunda evaluación y se volverá a rellenar una hoja de recolección de datos. Un enfermero o enfermera les volverá a sacar una muestra de sangre para analizar y finalmente, se les pedirá que entreguen la hoja de registro que se les había proporcionado en la primera visita y que rellenen de nuevo dos cuestionarios más.

A parte de las visitas programadas, usted puede recibir todas las visitas de seguimiento que considere oportunas o necesarias.

Si usted acepta participar en el estudio implica que adquirirá las responsabilidades necesarias para asistir en los procedimientos del estudio, igual como seguir las instrucciones del protocolo y

notificar cualquier evento adverso que le pase o si ha tenido cambios en su medicación (advirtiendo que, salvo en caso de urgencia, no modifique la medicación que está tomando ni tome otros medicamentos o "plantas medicinales" sin consultar antes con el médico del estudio)

También acepta rellenar los cuestionarios de forma veraz y con el tiempo requerido para contestarlos durante sus visitas a consulta.

**5. Beneficios y riesgos derivados de su participación en el estudio.**

Es posible que no obtenga ningún beneficio inmediato derivado de su participación en el estudio, pero si en su asistencia y manejo de la enfermedad en un futuro próximo. No se prevén riesgos ni inconvenientes por participar en este estudio.

**6. Seguro**

Durante su participación en este estudio, usted estará cubierto por la póliza de seguro del Hospital Doctor Josep Trueta que se ajusta a la legislación vigente y que le proporcionará la compensación e indemnización en caso de menoscabo de su salud o de lesiones que puedan producirse en relación con su participación en el estudio.

**7. Confidencialidad/Protección de datos personales**

El promotor se compromete al cumplimiento de la Ley Orgánica 15/1999, de 13 de diciembre de protección de datos de carácter personal y el Real Decreto que la desarrolla (RD 1720/2007) y el reglamento (UE) 2016/679 del Parlamento Europeo y del Consejo de 27 de abril de 2016 Protección de Datos (RGPD). Los datos recogidos en el estudio estarán identificadas mediante un código, por lo que no incluya información que pueda identificarlo, y sólo su médico del estudio / colaboradores podrán relacionar estos datos con usted y con su historia clínica. Por lo tanto, su identidad no será revelada a ninguna persona salvo excepciones en caso de urgencia médica o requerimiento legal. El tratamiento, la comunicación y la cesión de los datos de carácter personal de todos los participantes se ajustarán a lo dispuesto en esta ley.

El acceso a su información personal identificada quedará restringido al médico del estudio / colaboradores, autoridades sanitarias (Agencia Española de Medicamentos y Productos Sanitarios, autoridades sanitarias extranjeras), el Comité de Ética de la Investigación y personal autorizado por promotor (monitores del estudio, auditores), cuando lo necesiten para comprobar los datos y procedimientos del estudio, pero siempre manteniendo la confidencialidad de los mismos de acuerdo con la legislación vigente.

Los datos se recogerán en un fichero de investigación responsabilidad de la institución y se tratarán en el marco de su participación en este estudio. Los datos del presente estudio se pueden utilizar para futuras investigaciones relacionadas con el estudio. El promotor debe adoptar las medidas pertinentes para garantizar la protección de su privacidad y no permitirá que sus datos se crucen con otras bases de datos que pudieran permitir su identificación.

De acuerdo a lo establecido en la legislación de protección de datos, usted puede ejercer los derechos de acceso, modificación, oposición y cancelación de datos. Con la legislación actual puede limitar el tratamiento de datos que sea incorrecto, solicitar una copia o pedir que se trasladen a terceros (portabilidad) sus datos personales cedidos por el estudio.

Para ello deberá dirigirse a su médico del estudio: _____

Si usted decide retirar el consentimiento para participar en este estudio, ningún dato nuevo será añadida a la base de datos.

Los datos codificados pueden ser transmitidas a terceros y en otros países, pero en ningún caso deben contener información que lo puedan identificar directamente, como nombre y apellidos, iniciales, dirección, número de la seguridad social, etc. En caso de que se produzca esta cesión, será para los mismos objetivos del estudio descrito o para su uso en publicaciones científicas, pero siempre manteniendo la confidencialidad de los mismos de acuerdo con la legislación vigente. La confidencialidad de los datos se garantizará mediante contratos o convenios específicos

Los datos recogidos durante el estudio se guardarán al menos durante 25 años, pasado este tiempo los datos se pueden seguir guardando siempre que usted autorice otros fines de investigación biomédica.

**8. Gastos y compensación económica**

En caso de que participe en el estudio, no tendrá ningún gasto ocasionado por participar. No está prevista ninguna compensación económica para participar en el estudio.

**9. Otra información relevante**

También debe saber que puede ser excluido del estudio si el investigador lo considera oportuna, ya sea por motivos de seguridad, por cualquier evento adverso que se produzca por la intervención en el estudio o porque se considere que no está cumpliendo con los procedimientos establecidos. En cualquiera de los casos, usted recibirá una explicación adecuada del motivo que ha ocasionado la retirada del estudio.

**10. Teléfono de contacte en caso de dudas**

Si durante su participación tiene alguna duda o necesita más información, póngase en contacto con Dr/Dra _____Tel: _____ correo electrónico:_____

Al firmar la hoja de consentimiento adjunta, se comprometa a cumplir con los procedimientos del estudio que se le ha expuesto.

## 16.4.4. **ANNEX 10** - Informed consent sheet for participants. Spanish version

**CONSETIMENTO INFORMADO POR ESCRITO PARA EL PACIENTE**

**Título del ensayo clínico:** Evaluación del impacto clínico de la herramienta tecnológica SocialDiabetes en pacientes con diabetes mellitus tipo 1.

**Investigador principal:** _____

**Centro/Servicio:** _____

Yo (Nombre y apellidos): _____

He leído la hoja de información que se me ha entregado.

He podido hacer preguntas sobre el estudio.

He recibido suficiente información sobre el estudio.

He hablado con: _____ (nombre del investigador)

Comprendo que mi participación es voluntaria.

Comprendo que puedo retirarme del estudio:

1. Cuando quiera
2. Sin tener que dar explicaciones
3. Sin que esto repercuta en el trato médico.

Recibiré una copia firmada y fechada de este consentimiento informado. Doy libremente mi conformidad para participar en el estudio y doy mi consentimiento para el acceso y la utilización de mis datos en las condiciones detalladas en la hoja de información.

Firma del paciente:

Nombre y apellidos: _____
DNI: _ _ _ _ _ _ _ _ - _
Fecha: __/__/_____

Firma del investigador:

Nombre y apellidos: _____
DNI: _ _ _ _ _ _ _ _ - _
Fecha: __/__/___

## 16.5. Data collection sheets

### 16.5.1. **ANNEX 11** - Baseline visit data collection sheet

**HOJA DE RECOGIDA DE DATOS VISITA INICIAL**

| DATOS DE FILIACIÓN | | |
|---|---|---|
| NHC | | |
| Género | Femenino | Masculino |
| Año de nacimiento | | |
| Año de diagnóstico de la diabetes | | |
| Nivel de estudios | | |
| Actividad laboral | | |
| Código postal domicilio | | |
| **DATOS CLÍNICOS** | | |
| Años de duración de la diabetes tras diagnóstico | | |
| IMC | | |
| Portador/a de monitor contínuo de glucosa (CGM) | SÍ | NO |
| Usuario/a de bomba de insulina (ISCI) | Sí | NO |
| Presencia de complicaciones micro/macroangiopáticas | SÍ | NO |
| HbA1c venosa actual | | |
| HbA1c promedio en el último año | | |
| Glucemia promedio del mes previo a la visita | | |
| Desviación estandar de la glucosa | | |
| Fecha ultima hipoglucemia grave | | |
| Nº de hipoglucemias graves en los últimos 6 meses* | | |
| Nº de hipoglucemias graves en el último mes* | | |
| Nºde controles de glucemia capilar que se realiza al día | | |
| Nºde controles de glucemia capilar que se realiza al mes | | |
| **CUESTIONARIOS REALIZADOS** | | |
| DTSQs | SÍ | NO |
| EsDQOL | SÍ | NO |

** Se considera hipoglucemia grave al evento que requiere la asistencia de otra persona para administrar activamente carbohidratos, glucagón o tomar otras medidas correctivas. Es posible que las concentraciones de glucosa en plasma no estén disponibles durante un evento, pero la recuperación neurológica después del retorno de la glucosa en plasma a la normalidad se considera evidencia suficiente de que el evento fue inducido por una baja concentración de glucosa en plasma.*

## 16.5.2. **ANNEX 12** - Patient's data collection sheet.

### HOJA DE RECOGIDA DE DATOS PARA EL PACIENTE

| A RELLENAR POR EL ESPECIALISTA EN LA VISITA FINAL | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Datos del paciente | NHC | | | | | | | | | |
| | Usuario SocialDiabetes | | | | | | | SÍ | | NO |
| Marcar con una **X** el número de veces que se ha **contactado con los pacientes** usuarios de la aplicación SocialDiabetes a través de la **plataforma virtual** durante el estudio | | | | | | | | | | |
| **Mes 1** | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| **Mes 2** | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| **Mes 3** | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| **Mes 4** | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| **Mes 5** | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| **Mes 6** | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| **A RELLENAR POR EL PACIENTE** | | | | | | | | | | |
| Marque con una **X** el número de **hipoglucemias graves*** experimentadas cada mes | | | | | | | | | | |
| **Mes 1** | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| **Mes 2** | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| **Mes 3** | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| **Mes 4** | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| **Mes 5** | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| **Mes 6** | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| Marque con una **X** el número de **consultas presenciales** que realice con el/la **especialista** o a **urgencias** en relación con su **Diabetes** cada mes. | | | | | | | | | | |
| **Mes 1** | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| **Mes 2** | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| **Mes 3** | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| **Mes 4** | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| **Mes 5** | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| **Mes 6** | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| **SI ES USTED USUARIO DE SOCIAL DIABETES** | | | | | | | | | | |
| Marque con una **X** el número de **consultas telemáticas** que realice con el/la especialista a través de la aplicación **SocialDiabetes** en relación con su Diabetes cada mes. | | | | | | | | | | |
| **Mes 1** | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| **Mes 2** | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| **Mes 3** | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| **Mes 4** | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| **Mes 5** | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| **Mes 6** | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |

** Se considera hipoglucemia grave al evento que requiere la asistencia de otra persona para administrar activamente carbohidratos, glucagón o tomar otras medidas correctivas. Es posible que las concentraciones de glucosa en plasma no estén disponibles durante un evento, pero la recuperación neurológica después del retorno de la glucosa en plasma a la normalidad se considera evidencia suficiente de que el evento fue inducido por una baja concentración de glucosa en plasma.*

## 16.5.3. **ANNEX 13** - Final visit data collection sheet

**HOJA DE RECOGIDA DE DATOS VISITA FINAL**

| DATOS DEL PACIENTE | | |
|---|---|---|
| NHC | | |
| Usuario SocialDiabetes | SÍ | NO |
| Entrega hoja recogida de datos | SÍ | NO |

| DATOS CLÍNICOS | | |
|---|---|---|
| IMC | | |
| Portador/a de monitor contínuo de glucosa (CGM) | SÍ | NO |
| Usuario/a de bomba de insulina (ISCI) | Sí | NO |
| Presencia de complicaciones micro/macroangiopáticas | SÍ | NO |
| HbA1c venosa | | |
| Glucemia promedio del mes previo a la visita | | |
| Desviación estándar de la glucosa | | |
| Fecha ultima hipoglucemia grave | | |
| Nº de hipoglucemias graves en los últimos 6 meses* | | |
| Nº de hipoglucemias graves en el último mes* | | |
| Nºde controles de glucemia capilar que se realiza al día | | |
| Nºde controles de glucemia capilar que se realiza al mes | | |

| CUESTIONARIOS REALIZADOS | | |
|---|---|---|
| DTSQc | SÍ | NO |
| EsDQOL | SÍ | NO |

** Se considera hipoglucemia grave al evento que requiere la asistencia de otra persona para administrar activamente carbohidratos, glucagón o tomar otras medidas correctivas. Es posible que las concentraciones de glucosa en plasma no estén disponibles durante un evento, pero la recuperación neurológica después del retorno de la glucosa en plasma a la normalidad se considera evidencia suficiente de que el evento fue inducido por una baja concentración de glucosa en plasma.*