Development and evaluation of DiabeText, a personalized mHealth intervention to support medication adherence and lifestyle change behaviour in patients with type 2 diabetes in Spain: a mixed-methods phase II pragmatic randomized controlled clinical trial

Rocío Zamanillo-Campos[a,b], Maria Antonia Fiol-deRoque[a,b*], Maria Jesús Serrano-Ripoll[a,b,c], Sofía Mira-Martínez[a,b], Ignacio Ricci-Cabello[a,b,d]

a. Balearic Islands Health Research Institute (IdISBa). Carretera de Valldemossa, 79, Hospital Universitari Son Espases. Edifici S. 07120. Palma, Spain.

b. Primary Care Research Unit of Mallorca, Balearic Islands Health Service. Carrer de l'Escola Graduada, nº 3. 07002 Palma, Spain

c. Research Network on Chronicity, Primary Care and Health Promotion (RICAPPS, RD21/0016/0005). Gran Via de les Corts Catalanes, 587, 08007 Barcelona, Spain

d. CIBER de Epidemiología y Salud Pública (CIBERESP). Av. Monforte de Lemos, 3-5. Pabellón 11. Planta 0 28029 Madrid, Spain.

* Correspondence: Carrer de l'Escola Graduada, nº 3 07002 Palma, Illes Balears, Spain. mariaantonia.fiol@ibsalut.es +34 971 17 58 97

ABSTRACT

Background: Despite the increasing interest in text-messaging interventions to support healthcare delivery, the available evidence about their effectiveness is still limited.

Objectives: 1) to develop DiabeText, an intervention delivering automated, tailored brief text messages to support diabetes self-management; 2) to explore the potential impact of DiabeText on self-management behavior and glycaemic control, and; 3) to examine the feasibility of conducting a future phase III randomized clinical trial to evaluate the effectiveness of DiabeText.

Methods: 3-month, two-arm, randomized feasibility trial (ClinicalTrials.gov: NCT04738591) with patients with type 2 diabetes (HbA1c>8%). Participants were allocated to the control (usual care) or DiabeText group (usual care + five text messages per week). Outcomes were: recruitment rate; follow-up rate, missing data; medication adherence; adherence to Mediterranean diet; physical activity; and HbA1c. In addition, after delivering the intervention, we conducted a qualitative study involving 14 semi-structured interviews with participants allocated to the DiabeText group, to understand their views about the intervention.

Results: From 444 screened people, we recruited 207 participants (recruitment rate = 47%), of which 179 completed the post-intervention interview (follow-up rate = 86%). We sent 7,355 SMS during the intervention period, of which 99% successfully reached the participants. At post-intervention, DiabeText was associated with non-statistically significant ($p>0.05$) improvements in adherence to medication (OR=2.0; 95%CI 1.0 to 4.2), Mediterranean diet (1.7; 0.9 to 3.2), and physical activity (1.7; 0.9 to 3.1). No between-group differences were observed in mean HbA1c ($p=0.670$). The qualitative study indicated that participants perceived DiabeText as a helpful resource because it increased their awareness about the importance of adequate self-management and the sense of being cared for.

Conclusions: DiabeText is the first system in Spain to integrate patient-generated and routinely collected clinical data to deliver tailored text messages to support diabetes self-management. More robust trials are needed to determine its effectiveness and cost-efficacy.

Keywords

Randomized controlled trial; type 2 diabetes mellitus; mobile health; treatment adherence; mHealth; SMS; lifestyle behaviour; diabetes self-management; glycemic control

1. INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a frequent long-term condition affecting around 5 million people in Spain (1), with an adjusted incidence of 11.6 cases/1000 person-years (IC95% = 11.1–12.1) (2). People with T2DM are at high risk of developing serious complications (e.g., blindness, lower-limb amputations, kidney disease, cardiovascular disease), which reduce their quality of life and life expectancy. T2DM and its complications involve large expenditures to the Spanish National Health System (NHS): annually, these costs comprise €5.1 billion for direct costs (8% of the total NHS expenditure) and €1.5 billion for diabetes-related complications (3). T2DM complications affect not only the health status of the individual but also their ability to work during their productive life: labour productivity losses attributable to diabetes in Spain are around €2.8 billion (3). Alongside lifestyle changes, medicines are used to lower blood glucose, blood pressure, and lipids to prevent those complications. However, in Spain, adherence to oral antidiabetic medication is worryingly low, with non-adherence rates ranging from 45% to 52% (4-8).

A number of different factors influencing medication non-adherence have been identified (9-12). In some cases, non-adherence is a deliberate choice (e.g., when patients have concerns about medication side effects or are willing to minimise their intake of medicines). In other cases, medication non-adherence is related to logistical issues around collecting the medication or reminders to take it. In the case of diabetes medication, beliefs about treatment necessity can lead to patients stopping their treatment when they think they can successfully control diabetes through physical activity and diet (13).

There is an increasing interest in the use of interventions based on the use of SMS text messages (frequently called mobile Health (mHealth) interventions) to support healthcare delivery (14). They constitute a promising strategy to support medication adherence, as highlighted by the American Heart Association (15). Spain is the country with the highest mobile phone use rates in the world, with 99% of users (16). Therefore, a tool delivering short automated messages to support diabetes self-management has the potential to reach a very large proportion of the Spanish population.

Although the impact of mHealth interventions has been assessed in a large number of recent trials (17-25), the available evidence base about the effectiveness of text messaging interventions is still limited: a non-condition specific systematic review about the use of SMS text messages to improve medication adherence identified 29 trials, 11 of which reported it was a not effective strategy (26). A recent Cochrane review concluded that there is low-certainty evidence on the effects of mobile phone-delivered interventions to increase adherence to medication prescribed for the primary prevention of cardiovascular diseases (27). In a diabetes-specific systematic review by members of our team (28), we identified 11 relevant trials examining the impact of interventions promoting brief messaging to support medication adherence, observing that, although these interventions have the potential to improve medication adherence in patients with diabetes, evidence of their efficacy is limited and additional, high-quality research is needed.

Also, text messaging interventions have been used to support not only medication adherence but also other key aspects of diabetes self-management, such as healthy diet and physical activity (29-31). A recent meta-analysis showed that SMS interventions can lead to clinically relevant improvements in HbA1c, with effect sizes similar to the ones produced by more complex forms

of digital interventions such as mobile apps (32). Available evidence also suggests that SMS interventions can produce positive impacts on healthy behaviours (33).

In Spain, up to now, no research has been conducted to evaluate the potential impact of mHealth interventions on diabetes self-management. Taking into account the potential for mHealth interventions to be cost-effective and highly scalable strategies to reduce diabetes-related mortality and complications, additional, and methodologically robust research is needed.

The aims of this study were threefold: 1) to develop DiabeText, an intervention based on the use of a mobile-device-based system delivering automated, tailored brief text messages to support medication adherence and lifestyle change behaviour to people with type 2 diabetes; 2) to examine the feasibility of conducting a future phase III randomized clinical trial to evaluate the effectiveness of DiabeText, and; 3) to explore the potential impact of DiabeText on medication adherence, self-management behaviour and glycaemic control.

2. METHODS

2.1. Intervention development

Based on the recommendations from the Medical Research Council for the development of Complex Interventions (34), we developed DiabeText in a process that involved three main stages (see Supplementary Material 1): i) intervention planning, ii) intervention design and development, and iii) intervention pretesting.

Throughout the entire design, development, and pretesting process, we applied the person-based approach framework (35), which emphasizes the importance of understanding and accommodating the perspectives of the people who will use the intervention.

2.2. Mixed-methods feasibility study

Between 18 January and 4 June 2021, we conducted a three-month, two-arm (1:1 allocation ratio), randomized, parallel-group feasibility trial. The study results are reported in accordance with the Consolidated Standards of Reporting Trials (CONSORT) 2010 statement (36).

2.2.1. Participants' eligibility criteria: we included primary care patients aged >18 years, with at least one prescription of antidiabetic medication, and with poorly controlled T2DM (defined as having an HbA1c level greater than 8% in their most recent registration). Patients who were taking insulin, had no HbA1c record in the previous six months or reported an inability to receive, read, and comprehend SMS text messages in Spanish via a mobile phone were excluded from the study.

2.2.2. Sample size: We calculated the sample size based on the follow-up rate, one of the key outcomes in our feasibility trial (see details in the “Outcomes” section, below). With 200 participants (100 in each group), this feasibility study was powered to estimate an 80% follow-up rate within 95% confidence intervals of 73.8% to 86.2% (i.e., with 200 participants there would be a 95% chance that the real follow-up value is within ±6.2% of the measured value).

2.2.3. Recruitment of participants: The IT unit from the Health Service of the Balearic Islands (see acknowledgments) extracted from electronic health records a list of patients potentially meeting the eligibility criteria. Using the messaging platform from the Health Service, we sent these patients a text message invitation containing a link to the patient information sheet. After 24-48 hours, we phoned them to request informed consent (audio-recorded) and collect baseline data (please refer to “Ethics approval and consent to participate” for further details).

2.2.4. Randomization and treatment allocation: Participants were randomly assigned to the intervention or control group using a computer-generated sequence of random numbers. Randomization was not stratified. The outcome data collectors and trial statisticians were unaware of the treatment allocation. The three-month follow-up period did not start at the same time for all the patients. Rather, the participants were gradually entering the follow-up period when successfully recruited and all their baseline data had been collected (i.e., rolling enrolment approach).

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time for all the patients. Rather, the participants were gradually entering in the follow-up period when successfully recruited and all their baseline data had been collected (i.e., rolling enrolment approach).
During the three months follow-up period, all the participants continued with their usual diabetes care including all medical visits, tests, and diabetes support program. In addition, the intervention group received the DiabeText intervention, consisting of five text messages per week (intervention details available below, and in the TIDieR Checklist in Supplementary material 2).

2.2.6 Description of the DiabeText intervention: DiabeText is a theory-driven mobile-device-based system that integrates data from electronic health records and patient-generated data to deliver automated, tailored, brief text messages to support medication adherence. The results from our formative work (qualitative focus groups with patients) indicated the need for DiabeText to support not only medication adherence, but also lifestyle change behaviour (37). Therefore, in addition to messages related to diabetes medication, DiabeText also sends messages with generic information about diabetes and its complications, dietary and nutritional guidance, tips on physical activity, and motivational messages for changing lifestyle behaviour. It also includes messages on various topics such as wound healing, sexual health, caregiver support, myths about diabetes, psychobehavioral support, sleep hygiene, social support, reminders for regular check-ups, diabetic foot care, and smoking, among others. Additionally, DiabeText includes messages about upcoming appointments, upcoming medication available to be dispensed from the pharmacy, and notifications about improvements or worsening of HbA1c results. Table 1 shows a sample of the messages part of the DiabeText intervention.
These messages, mapped into Behaviour Change Techniques (38), address the needs of different patient profiles, which are established based on patient-generated data (behavioural questionnaires administered at baseline – see section "2.2.6. Outcomes" for additional details). Around 50% of the messages are generic (suitable for all patients), whereas the rest are specific according to specific data registered in electronic health records, including the type of antidiabetic drugs prescribed, and presence of hypercholesterolemia, diabetic retinopathy, hypertension, diabetic foot, neuropathy, kidney disease, obesity, and smoking behaviour.

Table 1. Sample of short text messages delivered by the DiabeText intervention

Target	**Personalization**	**Behaviour Change Technique applied**	**Text**
Diabetes knowledge	Generic (for all patients)	Information on health consequences	The symptoms of poorly controlled diabetes are increased thirst, frequent urination, constant hunger, fatigue, and weight loss.
Diabetes knowledge	Patients with internet access through their phones	Information about others' approval	Woody Allen has type 2 diabetes and has recorded a message for people with diabetes in Spain: https://www.youtube.com/watch?v=QuiI19m4OGQ
Medication	Generic (for all patients)	Problem solving	When traveling, it is a good strategy to duplicate the medications that we are going to need during the holidays and distribute them in different pieces of luggage.
Medication	Patients in treatment with glimepiride	Instruction on how to perform a behavior	Take your glimepiride medication as instructed by your doctor. It is important not to skip any meals when you are taking glimepiride

Physical activity	Physical inactive patients (according to IPAQ score)	Instruction on how to perform a behavior	If you have been having a sedentary lifestyle and want to start exercising, do it progressively to avoid injuries.
Physical activity	Generic (for all patients)	Verbal persuasion about capability	5,000 steps a day is the minimum you should get. For sure you can get it and even do more some days with more time!
Healthy diet	Generic (for all patients)	Instruction on how to perform a behavior	Controlling blood sugar and avoiding complications is possible by following a Mediterranean diet rich in vegetables, legumes, whole grains and fruit
Healthy diet - Conscious eating	Generic (for all patients)	Problem solving	Do you prepare two kinds of meals at home? Needless! Following a healthy and Mediterranean diet is also beneficial for your family
Prevention of overweight	Obese patients (according to BMI)	Salience of consequences	Small changes are important. Just by losing a few kilograms or improving your diet, you already improve your health
Healthy diet	Generic (for all patients)	Instruction on how to perform a behavior	Go shopping sticking to a shopping list and always after eating, it will help you not to make food transgressions
Reminder	Patients with medication withdrawal in the pharmacy available	Instruction on how to perform a behavior	Starting today, you can withdraw the medicine that contains [name of "*active ingredient*"] at your pharmacy. If you don't take it, see your doctor to check it out.

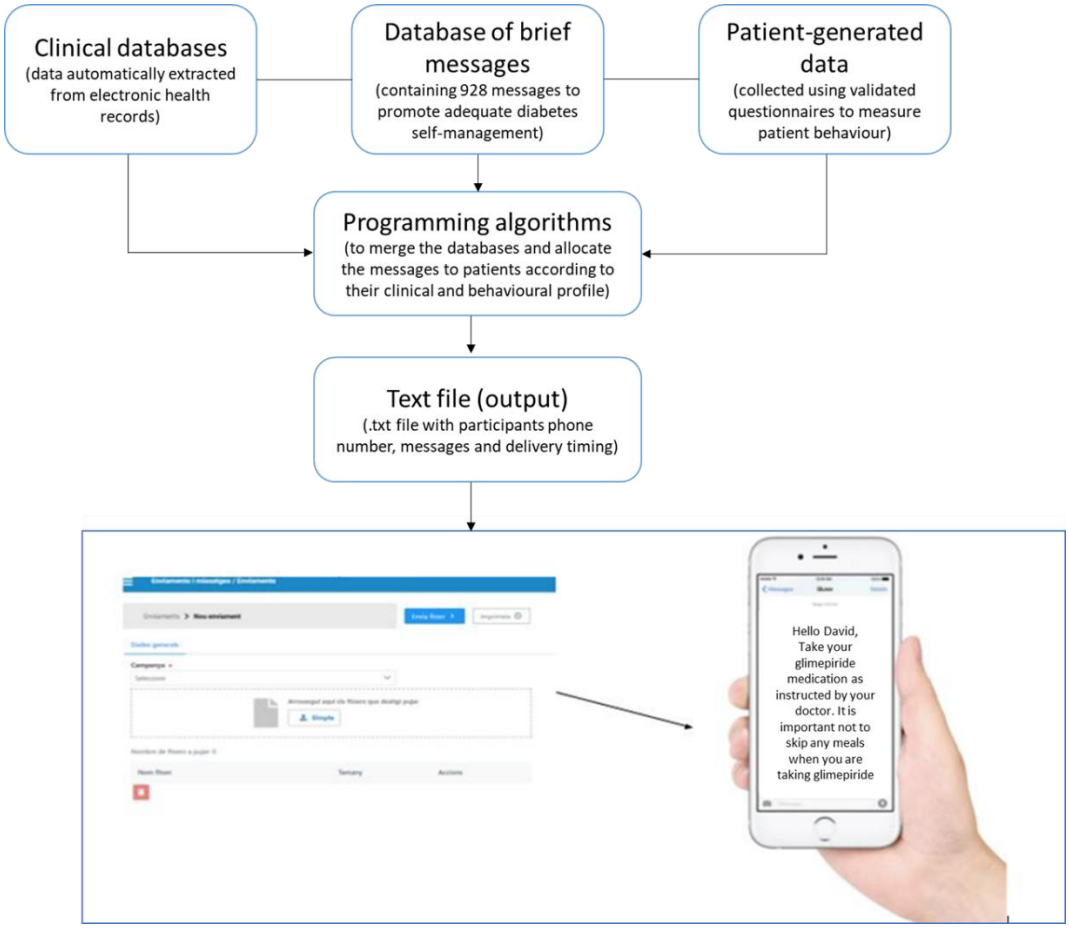
The architecture of the DiabeText system is described in Figure 1. The system is based on input from three different sources:

1) data from electronic health records, extracted using specific queries designed by a medical computer programmer from PRISIB (Health Information Research Platform from the IdISBa Research Institute – see acknowledgements) to extract relevant data from four clinical databases: the Primary Care database (eSIAP), the Hospital database (HCIS) (both including data about diagnoses, treatments and, appointments), the laboratory database (GESLAB – including laboratory test results data), and the pharmacy database (RELE – prescription and dispensation data). The queries are automatically launched fortnightly, and a single linked database is automatically stored in a secured server behind the firewall of the Health Service of the Balearic Islands.

2) patient-elicited data, collected by trained interviewers at baseline, measuring lifestyle behaviour and medication adherence – see details above. This information is used to generate the user profiles and to personalize the content of the message.

3) database of 928 text messages. The messages cover the three key areas of diabetes self-management: healthy diet (257 messages), physical activity (152 messages), and diabetes medication (297 messages). It also includes 222 messages with general information about T2DM.

Figure 1. System architecture of the DiabeText intervention*



* The DiabeText system is based on a set of algorithms that merge three input sources (clinical databases, database of brief messages, and patient-reported data) to generate text files (outputs) containing the text messages that each patient would receive on a certain day based on their clinical and behavioural data. The resulting .txt files are then manually uploaded to the SMS platform of the Balearic Islands Health Service which sends them to the patients.

2.2.7. Data collection: Trained evaluators administered via telephone structured self-management behaviour questionnaires to all the patients that had provided informed consent. These questionnaires were administered at baseline and at 3 months follow-up.

In addition, we securely extracted HbA1c data from participants' electronic health records. In the Balearic Islands, patients with HbA1c > 8% are requested an HbA1c measurement every three months as part of routine primary care. For the baseline measure, we extracted the most recent HbA1c values recorded before enrolling in the study. For the post-intervention measure, we extracted the most recent HbA1c value recorded after the three months follow-up. When needed (i.e., when no HbA1c was available during the three months after the intervention), we contacted the patients and healthcare professionals to arrange laboratory tests. In addition, we extracted the following baseline characteristics: diabetes duration, number of antidiabetic prescriptions, number of overall prescriptions, body mass index, and diagnosis of hypertension, retinopathy, chronic kidney disease, neuropathy, diabetic foot, and depression.

We extracted from the messaging platform the meta-data concerning the number of SMS uploaded to be sent, and the number of messages successfully delivered that reached participants' phones.

2.2.8. Outcomes: We included outcomes related to the feasibility of the trial and the impact of the intervention.

The feasibility outcomes included:

- Total number of patients meeting our eligibility criteria that can be identified from available data from electronic health records.
- Recruitment rate: number of patients successfully recruited (numerator) out of the total number of patients invited who confirmed meeting the eligibility criteria (denominator).
- Follow-up rate: number of patients retained during the follow-up (i.e., not withdrawing from the study (numerator)), out of the total number of patients recruited (denominator).
- Proportion of missing data: number of patients with incomplete outcome data (numerator) out of the total number of patients recruited (denominator).

The impact outcomes included:

- Adherence to diabetes medication: 7-item *ad hoc* questionnaire adapted from Jiménez et al. (39): adherent = 7 points; non-adherent <7 points.
- Adherence to the Mediterranean diet: 14-point Mediterranean diet adherence screener (MEDAS-14) (40): non-adherent ≤7 points; adherent >7 points.
- Physical activity: 6-item International Physical Activity Questionnaire (IPAQ) (41, 42): low activity ≤ 3.3 metabolic equivalent tasks; moderate/ high activity> 3.3 metabolic equivalent tasks.
- Glycated hemoglobin (% HbA1c), based on data registered in participants' electronic health records (see details in the "Data collection" section, above).
- Intervention acceptance (only post-intervention): *ad hoc* questionnaire based on the Technology Acceptance Model (TAM) (43) to measure perceived utility, ease of access and general satisfaction with the DiabeText intervention.
    - Perceived utility was measured through the question: "From your experience, do you find receiving informative text messages about diabetes on your mobile phone to be a helpful tool in managing your diabetes? On a scale of 1 to 10, with 1 being not helpful at all and 10 being extremely helpful, what rating would you give it?"
    - Ease of access: "Have you found it easy to access the messages you've received? Please rate your experience on a scale of 1 to 10, where 1 means it's not easy at all and 10 means it's very easy."
    - Satisfaction: "Have you found it enjoyable to receive information through your mobile phone during this time? Please rate your experience on a scale of 1 to 10, where 1 means you haven't enjoyed it at all and 10 means you have enjoyed it very much."

2.2.9. Statistical analysis: We used descriptive statistics to calculate recruitment and retention rates, and to examine the sociodemographic and clinical characteristics of the participants (overall and by group – using chi-squared and t-tests to examine potential differences between the control and intervention groups and between intervention completers and noncompleters). We built regression models to examine between groups difference in the outcome measures at post-intervention (linear regression for HbA1c, and logistic regression for the behavioural

outcomes), adjusting for the baseline score. All the analysis were carried out on the basis of intention-to-treat (i.e., all participants were included in the analyses, regardless of whether they received any exposure to the assigned study treatment). We did not apply any method for handling missing data from attrition or from incomplete post-intervention measures for this feasibility trial. All analyses were carried out in Stata 15 (StataCorp) and we used an α of 5% throughout.

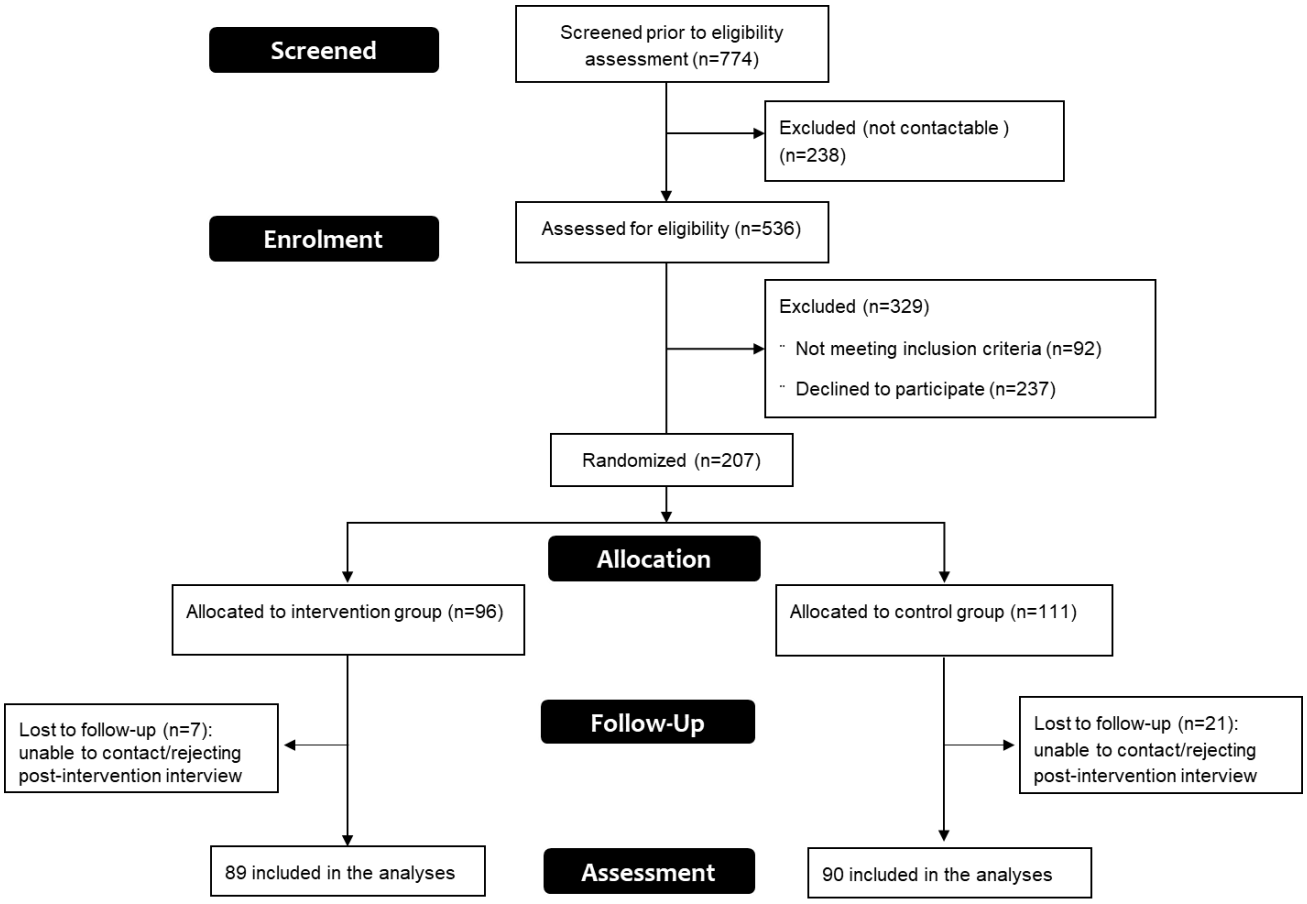
2.2.10. Embedded qualitative study: Within one month after delivering the intervention, we conducted 14 semi-structured interviews with a sample of participants allocated to the intervention group, to understand the way the messages were perceived. These interviews took place between day 2 and day 12 after the participants completed the intervention period. We used purposeful sampling to recruit a diverse group of participants in terms of age, gender, comorbidity, and medication use. We used an interview guide (Supplementary Material 3) that was flexible in order to elicit perceptions, suggestions, and opinions related to the proposed intervention. The interviews were carried out by telephone during May-June 2021. They were recorded and manually analysed by one researcher (RZC) using thematic analysis (44). We conducted 14 interviews because we considered that with this number we had successfully reached data saturation (45). The results were discussed with the rest of the team to identify the main issues to be addressed to improve DiabeText intervention prior to its evaluation as part of a full-scale phase III trial.

3. RESULTS

3.1. Recruitment and baseline characteristics

A CONSORT flowchart from patient invitation to data analysis is available in Figure 2. Based on data extracted from electronic health records, we identified 774 patients a priori meeting our eligibility criteria and sent all of them an SMS invitation to participate in the study. Among the 444 patients that were successfully contacted via telephone, and who confirmed meeting the eligibility criteria, 207 agreed to participate (recruitment rate = 47%). At three months follow-up, 28 patients declined to participate in the follow-up interview or were not reachable over the phone (follow-up rate = 86%). There were no significant differences between groups in sociodemographic and clinical characteristics at baseline or between those who completed and did not complete the follow-up interview (see Table 1).
The remaining 179 patients (90 in the control and 89 in the intervention group) completed the post-intervention assessment interview (complete data registered for all the patients). Follow-up HbA1c data were successfully obtained from 156 of the 179 participants (87%).

Figure 2. Participant CONSORT flow diagram



The baseline sociodemographic and clinical characteristics of the 207 participants are shown in Table 2. Around a third were women (72/207; 34.8%), with a median (sd) age of 62 (11) years. Approximately half of them (103, 49.8%) presented obesity (BMI >30), and two-thirds (137, 66.2%) had hypertension. The mean (sd) number of active antidiabetic prescriptions was 1.8 (0.7). Mean (sd) HbA1c was 9.0% (1.2%).

Table 2. Sociodemographic and clinical characteristics of the study participants

	Overall (n=207)	**Control (n=111)**	**Intervention (n=96)**	**Between-group differences at baseline *p*-value**	**Differences between completers (n=179) and noncompleters (n=28)**
Sociodemographic characteristics					
Female, n (%)	72 (34.8%)	37 (33.3%)	35 (36.5%)	0.638	0.591
Age (years), mean (sd)	62 (11)	61 (12)	63 (10)	0.204	0.113
Clinical characteristics*					
Diabetes duration (years), mean (sd)	8.4 (5.1)	8.2 (5.1)	8.7 (5.1)	0.555	0.086
HbA1c (%), mean (sd)	9.0 (1.2)	9.1 (1.3)	9.0 (1.0)	0.734	0.779
Number of antidiabetic prescriptions, mean (sd)	1.8 (0.7)	1.8 (0.7)	1.8 (0.7)	0.946	0.155
Number of overall prescriptions, mean (sd)	6.3 (3.5)	6.4 (3.6)	6.3 (3.5)	0.796	0.349
Hypertension, n (%)	137 (66.2%)	74 (66.7%)	63 (65.6%)	0.874	0.129
Obesity (BMI>30) n (%)	103 (49.8%)	59 (53.2%)	44 (45.8)	0.190	0.146
Depression, n (%)	29 (14.0%)	18 (16.2%)	11 (11.5%)	0.325	0.528
Diabetic foot, n (%)	23 (11.1%)	9 (8.1%)	14 (14.6%)	0.139	0.472
Chronic kidney disease, n (%)	14 (6.8%)	8 (7.2%)	6 (6.3%)	0.784	0.931
Diabetic retinopathy, n (%)	4 (1.9%)	1 (0.9%)	3 (3.1%)	0.246	0.498
Diabetic neuropathy, n (%)	4 (1.9%)	1 (0.9%)	3 (3.1%)	0.426	0.424

* data regarding participants' clinical characteristics were extracted from electronic health records

BMI, body mass index; sd, standard deviation; HbA1c, glycated haemoglobin; n, number of participants; %, percentage

3.2. Reach, acceptability, and perceived utility of the DiabeText intervention

Over the course of the 3-month follow-up period, the intervention group participants received a total of 60 text messages each (20 per week). In addition, we sent an average of 17 additional messages per participant, which were only sent under specific circumstances, such as appointment reminders, updates on laboratory test results, notifications about medication availability for dispensing, and birthday messages. According to the meta-data extracted from the messaging platform, of the 7,355 SMS uploaded to the platform to be sent during the 3-month intervention period, 6,940 (94.4%) immediately reached participants' phones, 342 (4.6%) were put on hold (mostly due to poor mobile coverage) and delivered later, and 73 (1.0%) were not delivered (mostly due to wrong number or because the operator was not able to send them).

In the post-intervention interview, 85 out of 89 participants (95.6%) in the intervention group reported that they received the DiabeText SMSs properly, and 78 out of 89 participants (87.6%) were able to confirm that they received the complete set of messages offered as part of the intervention.

In relation to its perceived utility, participants in the intervention group rated DiabeText as a useful resource to help them manage their diabetes (mean (sd) perceived utility score 8.9/10 points (1.49)). The ease of access to the messages was highly rated, with a mean (sd) score of 9.5 out of 10 points (0.95). In general, participants were very satisfied with the DiabeText intervention (mean satisfaction score 9.0/10 (1.42)).

3.3. Impact of DiabeText on self-management behaviour

Table 3 shows the outcome measures between the DiabeText intervention and the control groups at baseline and at three months follow-up. Follow-up data regarding self-management behaviour was successfully collected for the 179 patients completing the trial. At baseline, no significant differences were observed between the intervention and control groups in terms of the proportion of patients not adherent to their antidiabetic medication (25.0% vs 31.5% in the intervention and control group respectively), not adherent to the Mediterranean diet (49.0% and 50.5%), and with low levels of physical activity (41.7% vs 50.5%). Over the 3-month period, the DiabeText group was associated with non-statistically significant ($p>0.05$) improvements in adherence to Mediterranean diet (OR = 1.70; 95%CI 0.89 to 3.23), higher levels of physical activity (1.69; 0.90 to 3.18), and higher adherence to antidiabetic medication (2.04; 0.99 to 4.21).

3.4. Impact of DiabeText on glycaemic control

Follow-up HbA1c data was successfully collected from 156 of the 179 patients completing the trial (87.2%). At baseline, no significant differences were observed between the intervention and control groups. Over the 3-month period, there was a significant drop in HbA1c values in both groups: from 9.0% and 9.1% at baseline to 7.6% and 7.7% at 3 months in the control and intervention group, respectively ($P < 0.001$ in both groups). No significant differences between groups were observed post-intervention (Table 3).

Table 3. Comparison of outcome measures between the DiabeText intervention and the control groups at baseline and at three months follow-up. Data represent Odds Ratio with 95% CIs in parentheses.

	Baseline		3 months follow-up			
	Control (n=111)	Intervention (n=96)	Control (n=90)	Intervention (n=89)	OR (95% CI)*	p-value
Adherence to Mediterranean diet, n (%)						
Adherent	55 (49.5%)	49 (51.0%)	43 (47.8%)	53 (59.5%)	1	
Non-adherent	56 (50.5%)	47 (49.0%)	47 (52.2%)	36 (40.5%)	1.70 (0.89 to 3.23)	0.107
Adherence to physical activity, n (%)						
Adherent	55 (49.5%)	56 (57.2%)	52 (57.8%)	62 (69.7%)	1	
Non-adherent	56 (50.5%)	40 (41.7%)	38 (42.2%)	27 (30.3%)	1.69 (0.90 to 3.19)	0.105
Adherence to medication, n (%)						
Adherent	76 (51.4%)	72 (48.7%)	62 (68.9%)	73 (82.0%)	1	
Non-adherent	35 (31.5%)	24 (25.0%)	28 (31.1%)	16 (18.0%)	2.04 (0.99 to 4.21)	0.053
Glycemic control (Hba1c (%))**, mean (sd; range)	9.1 (1.3; 6.8 to 15.5)	9.0 (1.0; 7.4 to 12.1)	7.6 (1.2; 5.8 to 9.9)	7.7 (1.3; 5.7 to 10.6)	0.08 (-0.28 to 0.44)	0.670

sd, standard deviation; HbA1c, glycated haemoglobin; OR, Odds Ratio; CI, confidence interval

* Adjusted by baseline values, using multivariate logistic regression models for the three binary outcomes ("adherence to Mediterranean diet"; "adherence to physical activity", and "adherence to medication"), and lineal regression model for the continuous outcome variable (HbA1c).

** Between groups mean differences (HbA1c at post intervention available for 79 patients in the control group and 77 in the intervention group)

3.5. Embedded qualitative study

Results from the 14 semi-structured individual interviews with participants in the DiabeText group (7 males and 7 females) indicated that the participants perceived the intervention as a helpful resource for diabetes self-management. Some participants perceived they had improved medication taking, whereas others reported having increased their physical activity. Messages about nutritional education (e.g., how to prepare a healthier diet, or avoiding sweet and processed foods such as breakfast cereals) were positively regarded, although some participants missed more detailed information about healthy food.

In general, participants perceived that, although they previously knew most of the information provided by DiabeText, receiving the information through short but frequent SMSs helped them remember important aspects related to the management of their condition. Increased awareness about the importance of adequate diabetes self-management emerged as one of the key benefits of receiving the intervention, as well as the sense of being cared for.

Although in general participants perceived that the tone of the messages was adequate, for some of them the messages about the potential complications from T2DM were too blunt. Although this was perceived as a positive aspect by most participants, one participant reported feeling emotionally distressed about the possibility of suffering those complications. Most participants perceived the messages were easy to be understood, but some proposed the use of a more accessible language for some of them. The frequency of the messages delivered (five per week) was generally perceived as adequate (only one participant felt that the messages were too frequent). Most participants reported that they enjoyed and re-read the messages several times.

As a result of this qualitative study, we identified a number of areas for improvement of the intervention, which concerned the frequency, content, and tone of the messages, as well as the trial procedures (outlined in Box 1).

Box 1 Improvements in the DiabeText intervention identified as a result of the qualitative study with end-users

Frequency of the messages: start the intervention with 5 SMS per week, and gradually decrease the frequency, up to 2 SMS per week.

Tone of the messages: framed as offering a positive idea, to avoid generating fear, or anxiety (e.g., about complications from diabetes).

Content of the messages:

- create new messages and/or adapt the existing ones so they are adequate for patients with reduced mobility
- Include messages with more detailed and specific information about nutrition (e.g., food labelling information system).
- Include messages about recent advances regarding diabetes medication (e.g., results from new studies)
- Include messages about diabetes, medication and sexual health.

Sender/message signature: to include at the end of the SMS a signature to allow participants to easily recognize the sender.

Trial procedures: to inform participants the group they have been allocated to (intervention or control), so they know in advanced if they will receive or not the DiabeText intervention.

4. DISCUSSION

In this study, we developed DiabeText, a theory-based mHealth intervention to support medication adherence and lifestyle change behaviour in people with T2DM. We observed that it was feasible to integrate DiabeText with routinely recorded data from electronic health records and with patient-generated data, allowing the intervention to reach a high level of personalization and patient-centredness. DiabeText presented high end-user acceptability and perceived utility. A phase II clinical trial with 207 patients suggested that DiabeText may be effective in supporting lifestyle change behaviour and medication adherence.

4.1. Discussion of findings in relation to previous literature

4.1.1. Discussion of the findings concerning the feasibility of the DiabeText intervention

This study showed that it was feasible to develop a mHealth intervention integrated with data from electronic health records and with patient-generated data. The participants in our study were predominantly men, which is consistent with current epidemiological data of type 2 diabetes in our country (2) - which shows an OR of developing diabetes around 3-fold higher among men than among women (OR = 2.7 (1.6–4.5)).

Most of the previous interventions offer more limited personalization features and are not always integrated with clinical data. For example, a recent trial in New Zealand evaluated SMS4BG, a text messaging program to support diabetes self-management, which was personalized and tailored by demographic factors as well as personal goals and preferences (17). The Text4HeartII intervention (aimed to support medication adherence in people with heart disease) delivered text messages personalized based on the suboptimal behavior participants wanted to modify (e.g., physical activity, heart-healthy diet, stress management, and stop smoking).(18) In England, the SuMMiT-D trial evaluated theory-based messages including limited personalized content based on data from electronic health records (19).

4.1.2. Discussion of the findings concerning the acceptability and impact of the DiabeText intervention

Text messages have the advantage over more complex technologies that are familiar to most people (20). Our process evaluation indicated that ease of accessing the messages was highly rated, with a mean score of 9.5/10 points. Both ease of access (21) and ease of use (46) have been found to be important determinants of acceptance of mHealth interventions. However, familiarity with text messages does not necessarily imply that a text message-based intervention would be acceptable to the target population as a way of promoting behaviour change. Message personalization (22) and delivering messages through a trusted source are also important drivers of acceptability and perceived utility (23).

The DiabeText intervention was associated with non-statistically significant improvements in adherence to the Mediterranean diet, physical activity, and medication adherence. Despite not reaching the pre-established threshold of statistical significance (which could be attributed to the relatively small sample size in this feasibility study), the central estimates of effect sizes are clinically relevant – especially for a low-intensity intervention that could be implemented at the

population level at a low cost. We did not observe any effect on HbA1c, with similar large reductions in the intervention and control groups. This lack of effect could be attributed to the brief follow-up period of only three months. Usually, changes in behaviour take longer to manifest into better HbA1c levels, which reflect the average blood glucose levels over the preceding three months. Therefore, extended periods are generally required for such changes to produce improvements in HbA1c levels (47).

4.2. Practice and research implications

DiabeText provides a novel approach to self-management support for individuals with type 2 diabetes in Spain, which is both practical and cost-effective for primary care settings. Results from a qualitative study indicated that patients highly accept the intervention, and provided valuable recommendations for improvement. However, further robust trials are required to determine the effectiveness and cost-effectiveness of the intervention. Currently, a phase III trial with 740 patients is underway (NCT03936660), which will be conducted over 12 months and will provide a comprehensive evaluation of DiabeText's potential benefits across a range of clinical and behavioural outcomes. This trial will contribute to strengthening the available evidence base for the effectiveness of DiabeText.

4.3. Strengths and limitations

We followed a comprehensive approach to developing the intervention, following the Medical Research Council guidelines for the development of complex interventions. In our trial, although it was not possible to blind participants to group allocation, outcome data collectors and statisticians were blinded.
In terms of limitations, first, rather than ordering laboratory tests to measure HbA1c, we followed a more pragmatic approach, extracting this data from electronic clinical records. When the information was not available, we contacted doctors and patients to arrange laboratory tests. However, this delayed the collection of post-intervention HbA1c for some of the patients. Second, the use of an *ad hoc* questionnaire to measure medication adherence, as well as the short follow-up period need to be taken into account when interpreting our results. These shortcomings will be addressed by a fully powered (ongoing) trial, which will include a larger sample size (740 patients) followed up over 12 months, and which will measure adherence to antidiabetic medication based on medication possession rate (prescription/dispensation data from pharmacy health records). Finally, although 99% of the SMS messages were successfully delivered, and 96% of the participants stated that they received and read the messages as intended, we were not able to track the number of messages actually opened by the participants. Since reading the messages is a key requisite for the intervention to produce its intended benefits, future studies should closely monitor this aspect.

4.4. Conclusion

DiabeText is the first mobile-device based system in Spain integrating data from electronic health records and patient-generated data to deliver automated, tailored, brief text messages to support diabetes self-management. The intervention is feasible to be delivered, and well

accepted by the target population. Although the available evidence suggests that DiabeText may represent a helpful strategy to support medication adherence and lifestyle change, more robust trials are needed to determine its potential effectiveness and cost-efficacy before its widespread implementation in our context.

Declaration of Competing Interest
The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Ethics approval and consent to participate
The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board (or Ethics Committee) of Balearic Islands (protocol code IB4320-20PI in November 2020).

The extraction and treatment of personal and clinical data from participants was conducted by the externally by the Information Technology Unit of the Public Health Service of the Balearic Islands after being evaluated and approved by the Data Protection Service from the Public Health Service of the Balearic Islands (C/ de la Reina Esclaramunda, 9 07003 Palma. Tel. 971175600 www.ibsalut.es), who granted us permission to contact the patients to invite them to the study. The complete report from the Data Protection Service is available on request (in Spanish).All the procedures used in this trial, including patient recruitment, were evaluated and approved by the Research Ethics Committee of the Balearic Islands (CEI-IB) in June 2020 (IB4105-20 PI) and November 2020 (IB4320-20PI) respectively. Informed consent was obtained from all subjects involved in the study.

Consent for publication

Publication of the manuscript was approved by all authors.

Other information
Registration

ClinicalTrials.gov ID: NCT04738591 Official Title “Feasibility Study Through a Phase II Randomized Clinical Trial of an Intervention Based on Short Message System (SMS) to Promote Adherence to Antidiabetic Medication and Healthy Lifestyles in Patients With type 2 Diabetes Mellitus” https://clinicaltrials.gov/ct2/show/NCT04738591

Author contributions

Conceptualization, I.R.-C; methodology, I.R.-C., R.Z.-C.; data analysis, R.Z.-C., I.R.-C., M.A.F.-d., M.J.S.-R; data curation, R.Z.-C; writing—original draft preparation, R.Z.-C. and I.R.-C.; writing—review and editing, R.Z.-C., I.R.-C., A.-M.B., M.A.F.-d., M.J.S.-R; supervision, I.R.-C; project administration, I.R.-C. and R.Z.-C.; funding acquisition, I.R.-C. All authors have read and agreed to the published version of the manuscript.

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