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People living with type 1 diabetes point of view in COVID-19 times (COVIDT1 study): Disease impact, health system pitfalls and lessons for the future [☆]

Cristina Tejera- Perez ^{a,1}, Óscar Moreno-Pérez ^{b,c,1}, Jose Rios ^d, Rebeca Reyes-García ^{e,*}

^aUnidad de Endocrinología y Nutrición, Complejo Hospitalario Universitario de Ferrol, Spain

^bEndocrinology and Nutrition department, Alicante General University Hospital - Alicante Institute of Health and Biomedical Research (ISABIAL), Alicante, Spain

^cClinical Medicine department, Miguel Hernández University, Elche, Spain

^dMedical Statistics Core Facility, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS) and Hospital Clinic, Barcelona, Spain. Biostatistics Unit, Faculty of Medicine, Universitat Autònoma de Barcelona

^eUnidad de Endocrinología y Nutrición. Hospital Universitario Torrecárdenas, Almería, Spain. CIBERFES, Instituto de Salud Carlos III

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ABSTRACT

Aims: To analyse the effects of confinement among people with type 1 diabetes (T1D) and their caregivers over the course of the COVID-19 crisis and to evaluate contemporary changes in medical assistance and patient preferences.

Methods: An observational cross-sectional study designed as a self-reported web-based survey was conducted over the course of the COVID-19 pandemic.

Results: A total of 769 subjects participated in the survey (603 people with T1D and 166 caregivers). Changes in glycaemic control were reported in 66% of cases, weight gain in 40.4% of cases and decreased exercise levels in 65.4% of cases. Of the cohort, 53% maintained contact with the healthcare team, and 23% received specific information related to COVID-19. Emotional support was requested by 17% of respondents. Regarding telemedicine, 97.9% agreed with its use with the following preferences regarding the future: telephone call (84.5%), video-call (60.6%) and platform devices (39.7%).

Conclusions: Over the course of the COVID-19 pandemic, at least two-thirds of people with T1D underwent changes in the management of their condition. Almost all participants agreed with the concept of telemedicine, favouring telephone and video calls as their preferred means of communication.

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* Corresponding author.

E-mail addresses: cristina.tejera.perez@sergas.es (C. Tejera- Perez), omorenoperez@hotmail.es (Ó. Moreno-Pérez), jose.rios@uab.es (J. Rios), rebeca.reyes.garcia@gmail.com (R. Reyes-García).

¹ These authors contributed to the manuscript equally and share first authorship.

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1. Introduction

The rapid spread of the novel coronavirus disease 2019 (COVID-19), caused by SARS-CoV-2, throughout the world quickly turned into a pandemic. The COVID-19 outbreak caused a global health crisis with significant potential impact on people with chronic diseases [1]. It is well known that both people with type 1 diabetes mellitus (T1D) and those with type 2 diabetes mellitus (T2D) are exposed to an increased risk of infection and a greater number of associated complications. In the context of COVID-19, people living with diabetes (PLWD) are at risk of rapid progression and worse disease outcomes [2,3]. Recently, Barrón and colleagues published an adjusted odds ratio of dying of COVID-19 in hospital of 2.86 in people with T1D and 1.81 in those with T2D compared to those without diabetes [4]. Other major comorbidities related to COVID-19 severity are advanced age, hypertension, cardiovascular disease, smoking, and obesity [3].

However, conflicting evidence has emerged regarding the risk of SARS-CoV-2 infection among people with diabetes [2,5]. Adding to the confinement situation and the subsequent restriction of hospital visits, this conflicting health information has increased concerns among PLWD. Public health regulations and governmental measures adopted during the COVID-19 pandemic have enforced restrictions on day-to-day life, including isolation and home confinement. The impacts of these restrictions on health behaviour and lifestyle at home are as yet undefined. While we have increasing amounts of data on hospitalized diabetes patients, both in the general ward and in critical care units [1,6], the real impact of the pandemic on people with diabetes and their caregivers staying at home during the confinement period has not been fully defined.

Regarding glycaemic control, in T1D, using flash glucose monitoring, glycaemic control improved in those who stopped working during the lockdown in Italy [7]. In Spain [8,9], despite the limitations of lockdown, glycaemic control improved in patients with T1D, suggesting that having more time for self-management may help improve glycaemic control in the short term.

The current COVID-19 pandemic provides an incentive to expand the use of telemedicine in relation to diabetes care, especially with regard to the management of T1D [10]. A better understanding of the barriers faced by digital diabetes care and the identification of unmet needs for PLWD may offer critically important approaches to improve this evolving technology in a safe, effective, and cost-efficient manner [11].

In recent months, many efforts and initiatives have been developed to adapt the care of PLWD to the current situation. As an example, in Italy, a joint telemedicine effort was made to have diabetologists available 7/7 days to take turn for online advice for drug dosage adaptation needs or any other remotely manageable medical emergencies. As the authors stated, “this crisis has to be taken as a real chance to rethink our own lives, thus turning into moral, social and scientific rebirth for the entire hard-hearted world of today” [12].

Moreover, in many diabetes clinics, there has been a rapid adaptation to telemedicine, about which individual experi-

ences have been communicated [13–15]. However, with current evidence, we believe that the effects of confinement, beyond glycaemic control, and in all PLWD (not just those using flash glucose monitoring) deserve to be better characterized. Furthermore, despite personal experiences having been published by various diabetes experts, the opinion of people with diabetes regarding these changes and their future wishes is also of undoubted interest.

The objective of this study was to analyse the effects of home confinement on PLWD type 1 and their caregivers. In addition, we evaluated medical assistance changes that have occurred during this sanitary crisis and patient preferences regarding the use of telemedicine in the near future. These lessons will help us turn this crisis into an opportunity by proposing efficient patient-centred care measures to scientific societies leading diabetes care and health systems to help people with diabetes.

2. Material and methods

2.1. Study design

This was an observational cross-sectional study designed as a web-based survey. The web-based survey was conducted in Spanish through social networks (Twitter, Instagram, Facebook and LinkedIn). People with any type of diabetes or their caregivers were invited to participate. All data were self-reported.

The survey was conducted between April 26th and May 3rd May 2020 during the COVID-19 pandemic (see Fig. 1 to place the timing of the survey in the context of the epidemiological curve). In Spain, the confinement period began on March 15th, during which only essential workers were allowed to work and basic-needs purchases could be made. On April 26th, children under the age of 14 were allowed to leave the house for 1 h each day provided they were accompanied by an adult, and from May 2, the entire population was allowed to go out for 1 h every day, staggered by age group.

2.2. Study population

The inclusion criteria were people with any type of diabetes (type 1 diabetes, type 2 diabetes, MODY, LADA, gestational diabetes, diabetes secondary to pancreatic insufficiency) or those caring for a person with any type of diabetes. A total of 898 PLWD and caregivers completed the survey. In this paper, we present data pertaining to people with T1D and their caregivers, representing the majority of the participants (85.6%).

The study protocol was in accordance with the Helsinki Declaration (October 2013) and the basic principles of Good Clinical Practice. Information about the survey was provided to potential participants, who were also offered the possibility of contacting the investigative team. The completion of the survey and return of the data were provided by implied consent. The participants did not receive any form of payment for their collaboration in the survey.

Given the prevalence of diabetes in Spain, for a confidence interval of 95% and a margin of error of 5%, we calculated that

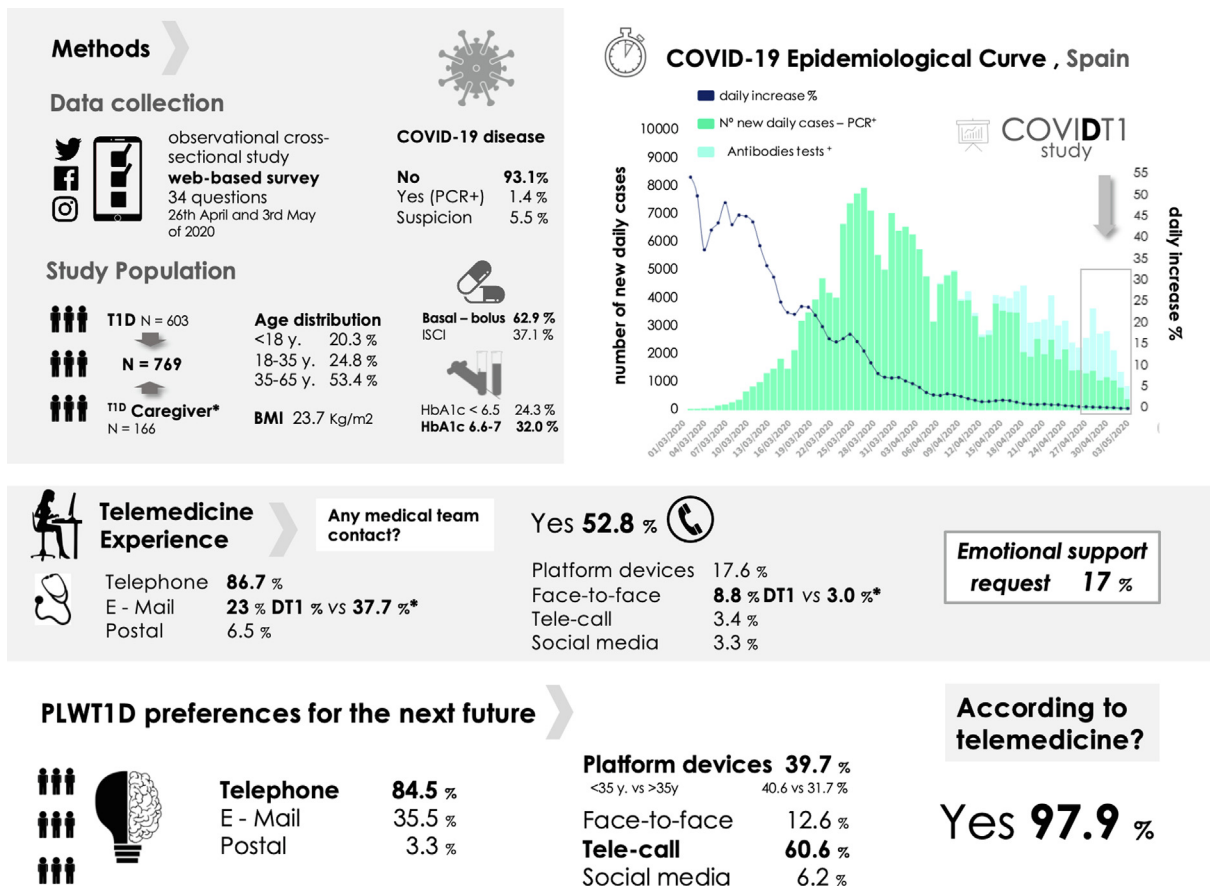


Fig. 1 – Healthcare and telemedicine experience. PLWT1D, people living with type 1 diabetes; *, T1D Caregiver.

the sample size should be at least 385 people. Considering the Spanish T1D population, which stands at 90,000 individuals, the sample size for the PLWD type 1 subpopulation would have to be at least 383.

2.3. Survey development

The investigators developed a survey comprising 34 questions (Appendix 1). The estimated time to complete the survey was approximately 15 min, and no personal data were requested to identify the participants. Pursuant to current European legislation (General Data Protection Regulation (EU) 2016/679 (GDPR)), no identifying data such as date of birth or gender were requested.

The survey items were devised to evaluate demographic information, type of diabetes, data about treatment and glycaemic control, changes in diabetes management and healthcare assistance changes and pitfalls identified over the course of the COVID-19 pandemic, telehealth preferences for the near future, knowledge about diabetes and COVID-19, and sources of information. A section on the effects of confinement in diabetes and an open participants' comments section were also included. All participant data and replies were anonymous.

2.4. Data analysis

The sample size was calculated based on the analysis plan and to ensure that comparisons could be made across groups. Continuous variables were expressed as means and standard deviations, and categorical variables were expressed as percentages. The T-test was used to compare means between two groups. An association study was performed between categorical variables using the chi-square test. The magnitude of the association between the variables explaining weight variations and requests for emotional support among the T1D subpopulation were analysed using a univariate logistic regression model.

The multiple correspondence analysis (MCA) method was conducted using SAS software. MCA is a non-supervised method for a multivariate description of qualitative variables. The objective of the use of MCA analysis was to explore the responses of patients from a self-administered survey aimed to assign a definition to the new dimensions to facilitate clustering the responses than suppose similar characteristics of the subjects in a reasonable number of groups [16].

We performed two different MCA approaches from two sets of variables. For the selection of these variables, their relevance and clinical implications have been taken into consideration. The MCA output shows a calculation of the weight of each category of each qualitative variable to the possible

explanation of total variability explained in the dimensional axis, named Dim. This dimensional method allows for each category to evaluate in which dimension is best represented, facilitating the definition of this dimension.

Based on these descriptions, a tentative interpretation of the observed clusters of T1D and caregiver response conditions was drafted.

IBM SPSS Statistics v25 (Armonk, NY, USA) and SAS v9.4 (SAS Institute, Cary, NC, USA) were used for analyses. All statistical analyses were performed using a two-sided type I error of 5%. Since this was an observational study with the aim of describing an approach to the possible relation of factors to weight changes and emotional support requests, all p-values were considered for descriptive purposes.

3. Results

3.1. Study population

A total of 769 subjects completed the survey, 603 PLWD type 1 and 166 caregivers. General characteristics of the survey cohort are shown in Table 1, including employment status and usual healthcare. Basic purchases during lockdown were

carried out by PLWD themselves in 46.2% of cases (56.7% of people with T1D and 7.8% by caregivers).

3.2. Impact of quarantine in diabetes control

Changes in glycaemic control, physical activity and other diabetes-related aspects and difficulties during lockdown are summarized in Table 2. Changes in glycaemic control were reported in 66% of cases, with 40.4% reporting an increase in weight, 19.2% exercising more, and 58.8% exercising <30 min a day or not at all. Weight changes were associated with increased food intake (related to stress) (OR 2.29, CI 95% 1.73–3.04) and limited physical activity (<30 min/no exercise) (OR 1.45, CI 95% 1.40–1.91), whereas an increase in regular physical activity exerted a protective effect (OR 0.46, CI 95% 0.32–0.67).

When analysing these items, certain differences were identified between people with T1D and their caregivers. During the quarantine period, caregivers reported higher glycaemic control than usual, higher insulin requirements and less exercise. Furthermore, no weight changes were reported for a higher percentage of caregivers when compared to people with T1D.

Table 1 – Baseline characteristics of participants.

	Total n = 769	T1D n = 603	Caregiver n = 166
BMI (kg/m²)	23.7 ± 6.1	24.9 ± 6.1	19.4 ± 3.9
Age-group (years)			
< 18	156 (20.3)	13 (2.2)	143 (86.1)
18–35	191 (24.8)	182 (30.2)	9 (5.4)
36–65	411 (53.4)	401 (66.5)	10 (6.0)
66–75	7 (0.9)	5 (0.8)	2 (1.2)
>75	4 (0.5)	2 (0.3)	2 (1.2)
Pharmacological treatment (%)			
Insulin infusion	285 (37.1)	229 (38)	56 (33.7)
Basal bolus therapy	484 (62.9)	374 (62)	100 (66.3)
Last HbA_{1c} (%)			
<6.5	187 (24.3)	149 (24.7)	38 (22.9)
6.6–7	246 (32)	194 (32.2)	52 (31.3)
7.1–8	218 (28.3)	168 (27.9)	50 (30.1)
8.1–9	71 (9.2)	60 (10)	11 (6.6)
9.1–10	15 (2)	10 (1.7)	5 (3)
>10	5 (0.7)	5 (0.8)	0
Don't know	27 (3.5)	17 (2.8)	10 (6)
Occupation (%)			
Temporary employment regulation file	86 (11.2)	83 (13.9)	3 (1.8)
Telecommuting from home	162 (21.2)	156 (26.0)	6 (3.6)
Sick leave due to risk	74 (9.7)	73 (12.2)	1 (0.6)
No occupation out of home in that moment	134 (17.5)	115 (19.2)	19 (11.5)
Student	184 (24.1)	53 (8.8)	131 (79.4)
Habitual occupation with adaptations	14 (1.8)	13 (2.2)	1 (0.6)
Essential workers	110 (14.4)	106 (17.7)	4 (2.4)
Regular healthcare			
Primary Care	22 (14.4)	15 (2.5)	7 (4.2)
Endocrinology	180 (14.4)	447 (74.1)	112 (67.5)
Both, Primary Care and Endocrinology	180 (23.4)	134 (22.2)	46 (27.7)
Others	8 (1)	7 (1.2)	1 (0.6)

Data are expressed as mean standard deviation or as n (%).

BMI: body mass index; T1D: type 1 diabetes.

Table 2 – Impact of confinement and public health normative in diabetes control and diabetes-related aspects.

	T1DM (n = 603)	Caregiver (n = 166)	p value
	n = 603	n = 166	
Glycaemic control (%)			<0.0001
Higher than usual	117 (19.4)	58 (34.9)	
Lower than usual	69 (11.4)	11 (6.6)	
Unstable	210 (34.8)	41 (24.6)	
No changes	207 (34.3)	56 (33.7)	
Changes in treatment (%)			0.006
No changes	200 (33.1)	46 (27.7)	
Increased	279 (46.2)	101 (60.8)	
Decreased	119 (19.7)	18 (10.8)	
No changes but maybe necessary	4 (0.6)	1 (0.6)	
Physical activity (%)			0.250
30 min or less	213 (35.3)	69 (41.5)	
30 to 60 min	193 (32.0)	48 (28.9)	
>60 min	65 (10.7)	11 (6.6)	
None	132 (21.8)	38 (22.8)	
Exercise in quarantine versus previous exercise (%)			<0.0001
Similar	98 (16.2)	20 (12.0)	
Less than usual	374 (62.0)	129 (77.7)	
More than usual	131 (21.7)	17 (10.2)	
Type of exercise during quarantine, in %			0.023
None	146 (24.2)	39 (23.4)	
Aerobics	208 (34.4)	77 (46.3)	
Resistance	50 (12)	12 (7.2)	
Both	199 (38)	38 (22.8)	
Body weight changes, in kg			<0.0001
No changes	279 (46.2)	97 (58.4)	
1–3 kg increase	226 (37.4)	46 (27.7)	
3–5 kg increase	33 (5.4)	0	
> 5 kg increase	6 (0.9)	0	
Not known	59 (9.7)	23 (13.8)	
Food patterns			<0.0001
Higher intake due to anxiety	216 (35.8)	33 (19.8)	
Healthy cooking	127 (21)	13 (7.8)	<0.0001
Still working, difficulty for healthy eating	67 (11.1)	7 (4.2)	0.008
Healthy diet most days, an occasional extra	368 (61)	120 (72.2)	0.026
Any difficulties (%)			
Pharmacy, prescriptions	126 (20.8)	30 (18)	0.812
Therapy doubts	37 (6.1)	11 (6.6)	0.814
Overwhelmed with Glycemic control impact	242 (40.1)	47 (28.3)	0.005
None	238 (39.4)	80 (48.1)	0.039
Request for emotional support	102 (16.9)	24(14.4)	0.451

Data are expressed as n (%). Differences were evaluated by Chi-Square test.

When queried about difficulties during lockdown, more people with T1D reported having had difficulties with glycaemic control when compared to caregivers (Table 2).

3.3. Sources of information

Only 23% of survey participants expressed having received information related to COVID-19 from their healthcare providers. By contrast, 79% of the sample expressed an interest in receiving this information.

In order of relevance, non-healthcare information channels used were as follows: television (49.1%), press (41.7%), and the internet (38.8%). The preferred healthcare sources of information were as follows: (43%), Ministry of Health (40.6%), physicians and scientific societies web sites (39.9%), web-based (37.8%), and patient associations (36.0%).

3.4. Impact on daily life

Regarding COVID-19 infection issues, 1.4% of subjects reported having tested positive for reverse transcriptase–polymerase chain reaction (RT-PCR) for SARS-CoV-2, and 5.5% suspected having contracted COVID-19. When asked about fear of infection, 39.1% reported being rather worried, 44% mildly worried, and 16.9% were not concerned at all. Thirty-five percent were considered to be at a higher risk of infection, and 65.9% suffered from poorer outcomes if infected. A total of 41.5% of people with T1D and 29.3% of caregivers declared being overwhelmed by confinement ($p = 0.005$).

Emotional support was requested by 17% of respondents; these requests were associated with unhealthy eating behaviour related to anxiety (OR 2.94 [CI 95% 2.07–3.04]), changes in metabolic control due to feeling overwhelmed (OR 1.74

(CI 95% 1.23–2.47)) and the absence of COVID-19-specific information by their usual healthcare team (OR 2.14 [CI 95% 1.17–3.90]).

3.5. Healthcare and telemedicine experience

Telemedicine results and preferences for the near future are summarized in Fig. 1. Fifty-three percent of the survey cohort had contact with the healthcare team during the COVID-19 crisis. The communication channels used were as follows: telephone (86.7%), e-mail (14.3%), platform devices (17.6%), face-to-face visits (4.03%), postal (6.5%), video calls (3.4%) and social media (3.3%). A higher proportion of caregivers used e-mail, while more people with T1D used face-to-face visits.

The majority of subjects were open to the possibility of using telemedicine (97.9%). The preferred means of communication chosen were as follows: telephone, video-call and platform devices. When analysing responses by age, the only difference identified was a greater preference for platform devices among PLWD type 1 under 35 years old.

Multiple correspondence analysis MCAs in the PLWD type 1 subpopulation are summarized in Fig. 2. The multifactorial analysis shows some internal consistency due to the grouping of categories into already known variables (changes in glucose/changes in treatment) (grey arrows). From a multifactorial point of view, contact during confinement with the medical team (yes, green spot) entailed the absence of greater stress, weight gain and request for psychological support (green area Fig. 2A), while an increase in regular stress (red spot) was associated with higher weight gain, mainly in patients with obesity (red area Fig. 2A). In the second MCA

approach, the absence of contact with the medical team during the crisis (orange spot) was associated with the presence of greater stress (red spot), changes in metabolic control, the need for changes in therapy and requests for psychological support (red area Fig. 2B).

Dimension 2 of the second MCA model is not shown, because it is clearly polarized between “telematic agree” and the remaining categories, making it impossible to search for groupings in this plane of dimension 1 against 2.

4. Discussion

We present the results of a web-based survey that was developed to learn about concerns and behavioural changes among people with diabetes during the COVID-19 pandemic. COVIDT1 study findings contribute to arriving at a better definition of the COVID-19/diabetes tandem picture from the point of view of PLWD type 1. Two-thirds of the people surveyed reported deteriorated glycaemic control, and 4 out of 10 gained weight. Almost all people with T1D and their caregivers declared being in agreement with telemedicine, with telephone and video calls as their preferred options.

To the best of our knowledge, there has been a scarcity of initiatives addressing the feelings and attitudes of PLWD during the SARS-CoV-2 pandemic. Upon closure of this study, we found just two surveys addressing issues related to diabetes and COVID-19, one from Insel Hospital (Bern, Switzerland) aimed at people with T1D requesting a weekly response and another from Diabetes UK, restricted to people from the United Kingdom. No data regarding the results of these surveys have been reported.

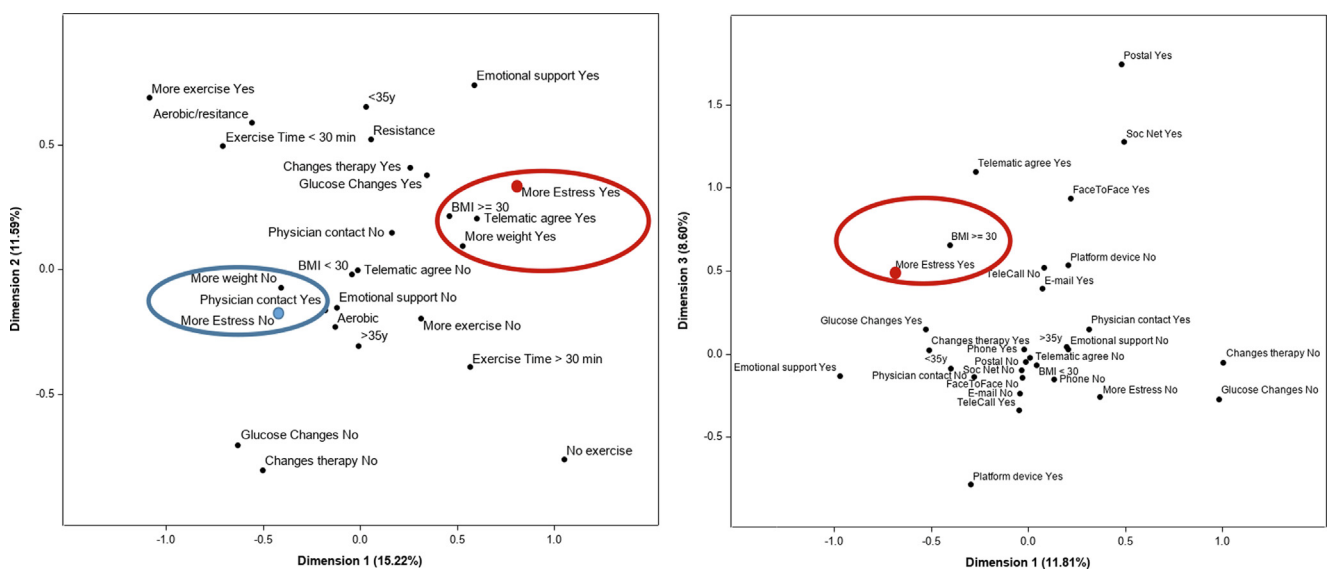


Fig. 2 – Multiple Correspondence Analysis. A. Set variable includes: metabolic, exercise, estres (more, red spot), therapy and weight changes; contact with the medical team during the crisis (yes, green spot), telematic agree, emotional request, age, and body mass index (BMI). **B.** Set variables include: metabolic, estres (more, red spot) and therapy changes; contact with the medical team during the crisis (no, orange spot), telematic agree and preference channels, emotional request, age, and BMI. The multifactorial analysis shows internal consistency due to the grouping of categories into already known variables (changes in glucose / changes in treatment) (gray arrows). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Unfavourable changes in lifestyle habits play an important role in the COVID-19/diabetes tandem because they are associated with a worsening of metabolic control and other major comorbidities, such as obesity and hypertension, which negatively influence the possibility of infection [17]. The increase in food intake (one-third), a higher proportion of less physical activity than usual (two-thirds) and the high prevalence of increased weight may explain the high percentage of people with T1D reporting a worsening of glycaemic control during confinement. Two recent studies in Spain in PLWT1D using FGM reported no deterioration in glycaemic control resulting from the lockdown enforced as a result of the COVID-19 pandemic [8,9]. However, this study was conducted using a smaller portion of the population using FGM; therefore, the results may not be applicable to the global population of people with T1D.

Emotional support was requested by 17% of the individuals surveyed. Considering a unique pathological entity, diabetes-related distress is frequently linked to diabetes (18–45%), and therefore, its routine evaluation is recommended in caring for PLWD [18]. In the second Diabetes Attitudes, Wishes and Needs (DAWN2) study, while significant diabetes-related distress was reported among 45% of participants, just 24% had been asked about how it affected their lives by healthcare professionals [19]. According to the COVIDT1 study results, high diabetes-related distress exerts a negative impact on medication adherence, as well as being linked to poor glycaemic control, lower self-efficacy, and poorer dietary and exercising behaviour [20]. Specific factors related to the COVID-19 crisis, such as fear of infection, a higher risk of poor outcome, becoming overwhelmed by confinement and treatment problems related to lockdown were identified as factors that may determine higher diabetes-related distress. The identification of specific distress factors during this pandemic, such as its close relationship with the lack of detailed information provided by the usual medical team as reported here, might allow us to better define interventions aimed at reducing diabetes-related distress in the near future.

Telehealth may make the delivery of diabetes care more patient-driven and patient-centred. Telemedicine in diabetes has shown to improve self-management, to provide educational requirements and to improve patient health-related quality of life [21], as well as to reduce diabetes-related distress among young people with T1D [22]. Additionally, it may reduce costs and improve access to the healthcare system [23]. Where glycaemic control is concerned, a meta-analysis of randomized controlled trials showed few changes in glycaemic control [21,24,25] and no effects related to an increased risk of hypoglycaemia [21]. Studies carried out over a more extended period of time (>6 months) were associated with more serious effects [24].

Furthermore, previous results regarding telemedicine may not be applicable to the current situation. The deep changes undergone not only in terms of medical assistance but also by society as a whole may bring about improvements in the performance of telemedicine within this new context. Additionally, the implementation of telehealth reduces overcrowding in health centres, consequently lowering infection and death rates.

Almost all survey subjects agreed with the possibility of using telemedicine. Telephone contact was frequently used during this crisis and turned out to be the preferred method for telemedicine. However, video calls were seldom used during the health crisis, despite being selected as the second preferred option. Similarly, platform devices were used in less than one in five telemedicine visits, this option ranking third by respondents. Nevertheless, the preferences and expectations of users represent key aspects for success in terms of the future development of telemedicine related to diabetes.

The COVID-19 crisis has brought to light a number of challenges and opportunities regarding global health management and, more specifically, the management of diabetes. We are faced with the opportunity to adopt digital technologies to improve the quality and reduce the costs of healthcare services and perhaps even to improve access to healthcare while increasing adherence to medical visits [26]. The identification of patient preferences regarding telemedicine may improve adherence.

Over the course of the crisis, we were able to identify certain pitfalls in diabetes care, one of the main learnings derived from the COVIDT1 study. First, the majority of people with T1D expressed their interest in receiving information related to COVID-19 from their healthcare providers. That being said, a low percentage of PLWD received information during this period, and this had a clear impact on stress levels. Second, despite having been requested by a fifth of respondents, there was a reported lack of emotional support and neglect on the part of healthcare professionals. Last, while widely underused during the management of the health crisis, the video-call method has, by a large margin, been pointed to by users as the second preferred communication channel. These three items may constitute future areas of improvement in the development of strategic tools and future new clinical models of PLWD type 1 care. Furthermore, the results of the present study highlight the need for a more stringent customization of therapy and education in PLWD.

The strengths of this nationwide study are the large number of people with T1D who participated in the survey, with representation from different regions within the country. In addition, the anonymity of the responses comes as a guarantee of the reliability of the thoughts and concerns expressed by people with T1D and their caregivers.

This study presents certain limitations that should be taken into consideration. First, all survey data were self-reported, so reporting accuracy could be a concern, as recall bias may have influenced the results. Second, according to the Spanish official data protection law, no data about sex were recorded, and thus, potential differences according to sex could not be evaluated. In addition, as with most studies based on internet surveys, data may be affected by selection bias. People who had access to the internet survey were more likely to present higher intellectual levels, access to the internet and to be more concerned about their disease. Finally, the respondents' diabetes diagnoses were not confirmed by a physician, and some of the respondents might have inaccurately reported a diabetes diagnosis, diabetes type, etc. However, due to differences in access to resources and educational programmes between T1DM and T2DM in Spain, incorrect identification of PLWT1D is unlikely.

5. Conclusion

Over the course of the COVID-19 pandemic, people with T1D suffered from diabetes management issues that affected their daily lives. Lockdown caused significant consequences affecting their weight, eating habits and exercise and glycaemic control, negatively impacting the health of PLWD. Almost all respondents agreed with the concept of telemedicine, with telephone and video calls being the preferred means of communication.

We anticipate many opportunities for further developing the virtual care model. PLWD type 1 reported their acceptance of and brought to light a need for telemedicine-enabled solutions, which has opened a window to further deploy the model in a system that has traditionally preferred face-to-face contact. The identification of PLWD type 1 preferences regarding a telemedicine health strategy in the COVIDT1 study has laid the groundwork for improved diabetes management in a safe, effective, and cost-efficient manner in the near future.

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Declaration of Competing Interest

The authors declared that there is no conflict of interest.

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