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A COMPREHENSIVE ANALYSIS OF DIABETIC PATIENT DATA BEFORE AND DURING THE COVID-19 PANDEMIC: INSIGHTS FROM THE MÉRY DIABETES DATABASE (MDD)

PhD thesis

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LIST OF ABBREVIATIONS

ACE	Angiotensin-converting enzyme
AGP	Ambulatory glucose profile
BMI	Body mass index (Testtömeg index)
CAPISCO	CArdiometabolic Panel of International experts on Syndemic COvid-19
CD36	Cluster of differentiation 36
CGM	Continuous glucose monitoring
COVID-19 (=COVID)	Coronavirus disease of 2019
DCM	Diabetes care management
DKA	Diabetic ketoacidosis
DM	Diabetes mellitus
DPP-4	Dipeptidyl peptidase-4
EESZT	Hungarian National Electronic Health Service Space (Elektronikus Egészségügyi Szolgáltatási Tér)
eHealth	Electronic health
FDA	Food and Drug Administration
GDM	Gestational diabetes mellitus
GDPR	General data protection regulation
GLP-1	Glucagon-like peptide-1
GLUT	Glucose transporter
HAT	Hyperglycemia assessment tool
HbA_{1c}	Hemoglobin A1c
ICU	Intensive care unit
IMV	Invasive mechanical ventilation
IOS	iPhone Operating System
IQR	Interquartile range
IR	Insulin resistance
ISO	International Organization for Standardization
MDD	MÉRY Diabetes Database
MDT	Hungarian Diabetes Association (Magyar Diabetes Társaság)
mHealth	Mobile health
NDDM	Newly diagnosed diabetes mellitus
PC	Personal computer
PGC-1α	Peroxisome proliferator-activated receptor-γ coactivator 1-α
PPAR-γ	Peroxisome proliferator-activated receptor-gamma
RAAS	Renin-angiotensin-aldosterone system
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SGLT-2	Sodium-glucose cotransporter-2

Sirt	Sirtuin
SMBG	Self-monitoring of blood glucose levels
SREBP	Sterol regulatory element-binding protein
T1DM	Type 1 Diabetes mellitus
T2DM	Type 2 Diabetes mellitus
WHO	World Health Organization

1. INTRODUCTION

Thirty years ago, the establishment of home blood glucose monitoring marked a significant milestone in the management of diabetes care. This advancement eliminated the necessity for patient hospitalization, enabling individuals to receive real-time information about their blood glucose levels from the comfort of their homes and within the context of their daily lives. The digitalization of these blood glucose readings has not only brought substantial progress in individual patient outcomes but has also contributed significantly to the development of extensive databases formed from the numerous measurements of a large patient population.

1.1 The importance of self-monitoring of blood glucose levels (SMBG) and digital diaries

Prior to the widespread availability of self-monitoring devices, often patients with mild changes of blood glucose levels and carbohydrate metabolism required hospitalization. In contrast, contemporary medical practice reserves hospitalization for patients experiencing severe hypo- or hyperglycemia or those demonstrating inadequate compliance, with further treatment administered on an outpatient basis. This shift has been facilitated by the widespread accessibility of home blood glucose monitoring, which not only reduces healthcare costs and alleviates the social burden associated with frequent hospitalizations but also enhances patients' sense of security regarding hypoglycemia and enables real-time therapeutic interventions.

For the past two decades SMBG has become an essential part of diabetes mellitus (DM) care. Self-monitoring devices are easy to use, cost-effective, reliable and at the same time provide valid data directly from the patients’ home (1, 2, 3). The significance of measuring blood glucose levels frequently is that regular monitoring has been linked to better glycemic control (4, 5). Until the year 2000 SMBG was the most widespread method of regular glucose monitoring for DM patients; however, since the Food and Drug Administration (FDA) approved continuous glucose monitoring (CGM) in 1999, it has revolutionized the treatment of diabetes by providing blood glucose values every 5-10 minutes throughout the day (6).

However, SMBG and CGM systems are equally effective, both are able to provide valuable data and may also complement one another (7). In fact, when used together, diabetes care may be better overall (8, 9) and by monitoring their own blood glucose levels, patients may feel as an integral part of their own treatment. Self-monitoring of blood glucose through capillary glucose testing continues to be one of the most prevalent methods for monitoring glucose levels due to its relative accuracy, familiarity, and affordability. Although CGM systems offer a more comprehensive overview of blood glucose levels, their high cost and the need for regular calibration – along with concerns regarding the accuracy of earlier devices – currently limit CGM usage to specific patient groups (10).

The ROSSO study (11) published in 2006 drew attention to the importance of the relationship between regular self-monitoring and the complications of diabetes including myocardial infarction, stroke, blindness, amputation and overall mortality. The study has concluded that regular self-monitoring of blood glucose levels improves quality of life and enhances longevity. Among patients on insulin therapy using regular SMBG there was a 51% decrease in mortality and a 32% decrease in diabetes-related complications compared to patients who did not monitor their blood glucose levels on a regular basis. Similarly, data regarding type 2 diabetic patients in the ROSSO study also demonstrated a significant decrease in both mortality (42%) and the occurrence of complications (28%) including myocardial infarction, stroke, lower limb amputation, vision loss and dialysis.

It should also be noted that the blood glucose data recorded by patients in their monitoring diaries, if executed properly, can help the physician to recognize tendencies in blood glucose changes and may overall contribute to a more optimal treatment plan. It was also reported that SMBG results in better short term glycemic control in patients with type 2 diabetes mellitus (T2DM) (12). Pleus et al. (4) argued that currently used SMBG systems are advantageous as they are easy to use, small in size, require only small volumes of capillary blood sample and provide results within seconds. However, it has also been found that only around 50% of adult blood glucose diaries may be considered accurate due to both patients' failure to record blood glucose measurements and their random addition of values into the diaries (13). A recent study (14) concluded that patients' blood glucose diaries omit at least 50% of hypoglycemic events. Additionally, it was reported that data from one in six non-insulin-treated diabetic patients who use self-monitoring is lost (15). Consequently, neither the patients nor their physicians can make use of the results. This situation not only wastes resources but is also highly ineffective for both patients and the healthcare system.

The rationale behind the discrepancy, invalidity and lack of data lies in the difference between manual and digital blood glucose diaries. The data collected and stored by digital devices are based exclusively on valid measurements whereas manual diaries are easy to manipulate. Patients may enter improved blood glucose levels to impress their physician or they may even enter data without actual measurement because they want to avoid the pain caused by regular measurements. Digital blood glucose measuring devices and the underlying technology operate in a closed system; therefore, the devices forward valid data only to the digital blood sugar diaries, therefore this data cannot be modified or falsified. As a consequence, data validity is close to 100 percent as opposed to the 50 percent validity of manual diaries. Valid data collection and storage, patient education and increased compliance may all contribute to an improved carbohydrate metabolism and help to avoid the micro- (retinopathy, nephropathy and neuropathy) and macrovascular (ischemic heart disease, peripheral vascular and cerebrovascular disease) complications of diabetes.

A further advantage of SMBG devices is that they may easily be connected to personal computers (PCs), smart phones and other diabetes management technology tools to create digital diaries while they still remain the most wide-spread and most readily available self-monitoring devices. Nowadays the most modern blood glucose meters operate without any external supporting device and they send real-time patient data to a cloud based system.

Data clinicians receive from various blood glucose monitoring devices has also changed over the past few decades. HbA_{1c}, which has long been the standard for evaluating glucose profile as well as managing and following DM treatment, does not genuinely reflect individual patient blood glucose variability (16). Therefore, clinicians have also started to use ambulatory glucose profile (AGP) which allows doctors and patients to better understand DM management (17). The AGP report is easy to use and as opposed to HbA_{1c}, it also takes daily variations of blood glucose levels into account and allows clinicians to determine the main challenges of maintaining optimal blood sugar levels (18). AGP is a standardized value and may be calculated from both CGM and SMBG. All diabetic centers receive the patient AGP, which is advantageous as standardized values accelerate patient care, recording and interpreting blood glucose values and also promote research. In digital diaries the blood glucose values appear separately and individually in each individual patient AGP profile in a standardized form, which enhances the efficiency of patient care. Analyzing and processing all the structured digital blood glucose data is a quick and standardized method to provide an opportunity to make therapy related decisions and facilitate patient education.

1.2 The need for an optimal diabetes database

Integrating extensive data from blood glucometers into a centralized database is crucial for obtaining meaningful therapeutic insights. By compiling and analyzing this data, healthcare professionals can identify patterns and trends in glucose levels that might otherwise be overlooked. This comprehensive data analysis facilitates more accurate and personalized treatment plans, enhances the ability to predict and prevent complications, and supports ongoing monitoring and adjustments to therapy. Ultimately, this systematic approach leads to improved patient outcomes and more efficient management of diabetes.

A key question is how extensive blood glucose data collected by diabetic centers can be utilized for diabetes care. This digitally stored data may be analyzed in two ways: on an individual basis for a single patient or collectively for a large group of diabetic patients. The vast amounts of standardized blood glucose data from tens of thousands of patients present an opportunity for analyses that could significantly impact the treatment of the entire diabetic population.

Over the past few decades, numerous national and international efforts have been made to analyze large healthcare databases of blood glucose data (19-22). However, many of these databases have been facing limitations such as insufficient participant numbers, poor maintenance, and validity issues related to manual diaries. Big databases often lack sufficient data to represent the relevant population accurately. Nevertheless, there are methods to enhance data quality and create a well-designed database.

Through analysis of existing databases in the literature and our research team's three decades of experience in managing diabetes patients, we identified nine key characteristics essential for an optimal diabetes database (23). These characteristics are crucial for establishing a reliable platform for clinical research focused on enhancing diabetes care by maintaining target blood glucose levels, preventing hypoglycemic episodes and complications, and improving quality of life and longevity. First, a high-quality database should collect data that accurately represents the relevant population. Second, the data must be integrated into a unified, homogenous database. Third, consistent monitoring and maintenance are essential. Fourth, a sufficient volume of patient data, based on validated and digitally stored measurements is necessary. Fifth, it is crucial to record the type of therapy (e.g., oral antidiabetics or insulin) and correlate it with blood glucose levels. Sixth, the data pathway must be secure and traceable from initial collection to final analysis. Seventh, the data should be suitable for both cross-sectional and longitudinal research. Eighth, each patient should have a single set of data, with duplicates eliminated. Finally, the database must include qualitative details such as the time and date of blood glucose measurements, patient age, gender, geographic region, type of therapy, and type of diabetes (23).

1.3 The MÉRY Diabetes Database (MDD) - ensuring the gathering of large quantities of reliable data

By integrating the nine characteristics described above, an optimal diabetes database can serve as a solid foundation for clinical research in diabetes management and treatment. The MDD is distinguished as a unique database that closely matches the attributes of an optimal database. To our knowledge, no other research has utilized a database of similar size, regular maintenance, and continuous expansion as the MDD.

The selection of highly accurate blood glucose meters is essential. Data collection for the MDD utilizes MÉRYkék blood glucose meters, manufactured by Di-Care Zrt., located at Sáfrány Street 23, Budapest, 1116. The MÉRYkék device adheres to all international regulatory standards, providing precise blood glucose measurements with an accuracy of 10% within the normal range. A comprehensive international analysis of the precision of various blood glucose meters found that only 63% of devices meet the ISO 15197:2003 standards, and an even smaller percentage (42%) comply with ISO 15197:2013 standards (24). Since May 2016, blood glucose meters have been required to conform to ISO 15197:2003 criteria. The MÉRYkék device distinguishes itself by meeting all these international standards. Although the international standard permits a precision variation of +/- 20%, the MÉRYkék device exceeds this requirement with only a 10% deviation. This superior accuracy ensures that patients using the MÉRYkék device can depend on highly reliable blood glucose readings, surpassing the performance of many other devices on the market.

Data for the MDD is collected from four primary sources. The first source is MÉRY Online, a freely available software that patients can download to record and transmit their data. The second source is MÉRY Android, an application for Android devices equipped with Bluetooth, enabling patients to submit their data. The third source is the DiabManag system, utilized by specialized healthcare professionals in clinics. These professionals use self-downloading tools (KD1, KD2, KD2m) to gather patient data, currently serving as the predominant method of data collection with 270 sites across Hungary, ensuring extensive national coverage. The fourth source is the new IOS (iPhone Operating System) MÉRYkék device, designed for user-friendliness and capable of transmitting data globally without relying on an external support system. It is anticipated that this device will become the most widely adopted method for data collection in the future.

1.3.1 Developments in data transfer

Since its establishment in 2015, our database has undergone significant changes in data collection methods. Initially, data cables were used to connect blood glucose meters to personal computers, with later advancements transitioning to Bluetooth connectivity for data exchange between glucometers and smartphones or PCs. However, this shift required a basic level of computer literacy, presenting challenges for many elderly patients. The introduction of the Diabetes Care Management (DCM) hub device in August 2015 marked a notable advancement in data collection efficiency. The DCM hub system facilitated rapid data transmission, achieving widespread adoption in approximately 90 percent of diabetes centers across Hungary. By linking patients' blood glucose meters to the DCM hub, data could be swiftly transferred into digital formats within seconds.

In more recent developments, IOS device technology has been introduced, offering enhanced streamlining and acceleration of data transfer to the database. Equipped with integrated SIM cards, blood glucose data are immediately transmitted to a centralized data acquisition server, ensuring data integrity irrespective of geographical location. Furthermore, the device provides critical meal-related timing information essential for optimizing therapies. Technological advancements have empowered blood glucose meters to transmit individual patient data globally to a centralized database, eliminating the necessity for smartphone connections or additional fees. These devices have facilitated access to and utilization of measurement data, particularly benefiting older patients who may encounter challenges with smartphone applications or traditional PCs.

1.3.2 Applications

The integration of digital technologies into healthcare, coupled with the emergence of electronic health (eHealth) tools, has created new ways for tackling the challenges posed by the increasing prevalence of diabetes. Within this framework, mobile health (mHealth), a subset of eHealth, has been widely employed across various healthcare sectors. These applications encompass a diverse range of interventions, from promoting healthy lifestyles to facilitating the self-management of chronic conditions. Examples of such initiatives include mobile applications and wearable devices (25). Recent advancements have led to the development of diabetes-specific applications aimed at enhancing glycemic control and reducing HbA_{1c} levels. Studies conducted by Eberle et al. (26) have demonstrated the efficacy of these applications in improving overall diabetes management.

In addition to these advancements, MÉRY blood glucose meters are accompanied by a complementary application and support system known as DiabManage. Furthermore, through the MÉRY Online application, users can transfer data from MÉRY blood glucose meters to their personal computers. Certain models such as MÉRY PLUSZ, MÉRY PILLE, MÉRY ULTRA, MÉRYkék 1000, and MÉRYkék 800 allow users to set individual measurement limits. The downloaded data can be visually represented in graphs or charts, printed, or exported to an Excel file. If the patient's PC is connected to the internet while using the MÉRY Online Application, all data will automatically be saved and stored in a centralized database.

1.3.3 Data maintenance, updating and validity

The MÉRY Diabetes Database is supported by a specialized Call Center, which fulfills four primary roles. Firstly, it manages patient data, overseeing the establishment and maintenance of the patient-device relationship. Secondly, the Call Center conducts regular follow-up calls to remind patients to promptly update their data. Thirdly, on an annual basis (one year after the last contact), it proactively contacts all patients to ensure data accuracy, capturing any changes in therapy or personal information, and informing them about promotions and additional services. Lastly, the Call Center actively monitors and resolves any accidental data duplications. Additionally, healthcare professionals can adjust and update patient therapy data during face-to-face consultations, complementing the functions of the Call Center.

1.3.4 Recorded parameters and the size of the database

In the initial phase of our work, we began processing the data from the MDD, which incorporates diverse patient parameters, such as age, gender, geographic region, blood glucose records, measurement timestamps, therapy type (non-insulin/insulin), the daily administration frequency in the case of insulin and diabetes type (T1DM, T2DM, GDM). These parameters offer crucial data for conducting thorough analyses.

In the initial year of data collection (2015), a total of 1,443,171 blood glucose values were collected. However, as of December 2022, the MÉRY database had accumulated over 40 million registered blood glucose values. This substantial growth in data volume enables both cross-sectional and longitudinal analyses. In total, there were over 56 million records and after the cleaning process, we retained more than 43 million blood glucose data points available for analysis (see Section 3.2 below for more information on the cleaning process).

1.3.5 The MÉRY Diabetes Database as an optimal database

Our database exemplifies a high-quality diabetes database by incorporating nine essential characteristics. It collects representative data that accurately reflects the studied population and is sourced from a single, integrated database. With consistent monitoring and maintenance, the database ensures high data quality and integrity. The stored patient data comes from valid measurements, includes therapy-related information, and maintains data traceability to prevent manipulation. Furthermore, the database is secure and suitable for both cross-sectional and longitudinal research, uniquely identifies patients while eliminating duplicates, and includes qualitative data such as measurement details, patient demographics, and therapy types. By incorporating these nine characteristics, an ideal diabetes database can provide a robust foundation for clinical research in the field of diabetes management and treatment (23). The Méry Diabetes Database is distinguished by its close alignment with the ideal characteristics of a diabetes database and to our knowledge, no other research utilizes a database as extensive, regularly maintained, and continuously expanding as the MDD.

According to the IDF Diabetes Atlas (27), the global prevalence of diabetes is currently 10.5%. In Hungary, the reported prevalence is 8%, making it a representative Caucasian population in terms of diabetes. The prevalence of diabetes in other developed European countries is comparable to that in Hungary (Germany: 6.9%, UK: 6.3%, Poland: 6.8%). Therefore, our findings may be applicable and perhaps extrapolated to a broader context, potentially extending to neighboring countries with similar proportions of the diabetic population.

1.4 The intricate relationship between diabetes and COVID-19

According to the World Health Organization (WHO), as of October 2024, there have been over 776 million confirmed cases of COVID-19 since 2019, resulting in more than 7 million deaths globally (29). Similar to the experiences from the previous SARS and MERS outbreaks in 2002-2003 and 2013, respectively, comorbidities such as diabetes mellitus, obesity, and hypertension have been associated with a heightened predisposition to complications and an increased risk of mortality (30).

Diabetes is a prevalent comorbidity in COVID-19 with its incidence ranging from 7% to 30% (31). Initial reports from Wuhan, China revealed a disproportionately high prevalence of individuals with diabetes among COVID-19 fatalities, with T2DM being associated with nearly a threefold increase in mortality compared to non-diabetic individuals (32). Evidence indicates that patients with diabetes tend to experience a more severe course of COVID-19 infection and are more susceptible to long-term complications that are significantly impacting their overall health (33, 34). In a retrospective single-center study, diabetes and hyperglycemia were present in 30% of patients who died from COVID-19, with diabetes being an independent predictor of higher in-hospital mortality (35). Similarly, a large-scale clinical study reported that diabetic patients had a significantly increased likelihood of requiring admission to the intensive care unit (ICU) during their infection (36). Furthermore, the risk of hospitalization is tripled for individuals with diabetes or obesity who contract COVID-19, and this risk increases to 4.5 times for those with both conditions (37).

Accumulating experimental, clinical, and epidemiological data support the existence of a complex interplay between COVID-19 and diabetes emphasizing their bidirectional and reciprocal relationship (31, 38-43). It has been demonstrated that diabetes not only exacerbates the severity of COVID-19, but the virus itself also impairs glucose regulation through various mechanisms (44). On one hand, preexisting diabetes is linked to greater COVID-19 severity; on the other hand, cases of deteriorating metabolic control in diabetic patients – manifesting as diabetic ketoacidosis (DKA), hyperglycemic hyperosmolar syndrome, or new-onset hyperglycemia – have been documented during COVID-19 infection (40, 45) . It is plausible that COVID-19 may disrupt the glycometabolic system, leading to hyperglycemia and insulin resistance, which could not only exacerbate the pathophysiology of preexisting diabetes but also potentially trigger new-onset diabetes (46).

In addition, the incidence of diabetes has risen not only in adults but also in children following COVID-19 infection. The onset of the COVID-19 pandemic was associated with an increased incidence of type 1 diabetes and diabetic ketoacidosis (DKA) at diagnosis among children and adolescents compared to the pre-pandemic period (47). Moreover, a retrospective cohort study of 613,602 patients aged 10 to 19 years found a higher risk of new type 2 diabetes diagnoses within six months of a COVID-19 diagnosis, compared to other respiratory infections (48).

The Coronado study (49) emphasizes the importance of closely monitoring the weight and body mass index (BMI) of diabetic patients hospitalized with COVID-19. Additionally, age, treated obstructive sleep apnea, and both microvascular and macrovascular complications were independently associated with an increased risk of death by day 7. Notably, the Coronado study also reported that in diabetic patients, BMI—rather than long-term glucose control—was independently and positively correlated with the need for tracheal intubation and/or death within the first week (49). Given the importance of the link between COVID-19 and diabetes, Bornstein argues that people with diabetes who have not yet been infected with the SARS-CoV-2 virus should intensify their metabolic control as needed as means of primary prevention of COVID-19 disease and its complications (50).

1.4.1 The pathomechanism of COVID-19: Unraveling its role in exacerbating diabetes through insulin resistance

Various mechanisms have been identified by which SARS-CoV-2 can cause hyperglycemia, including direct damage to pancreatic β-cells due to the virus binding to angiotensin-converting enzyme 2 (ACE2) receptors on pancreatic islets, the stress response, which triggers elevated release of catecholamines and glucocorticoids, and heightened inflammatory activity, leading to increased insulin resistance (51). However, growing molecular evidence indicates that insulin resistance may be the primary factor contributing to the rapid metabolic deterioration observed in diabetes or the onset of new hyperglycemia during the course of COVID-19 (52-54). The COVID-19 pandemic is caused by the novel coronavirus SARS-CoV-2, which enters host cells via the angiotensin-converting enzyme 2. Beyond being an enzyme, ACE2 serves as a functional receptor expressed abundantly in the heart, kidneys, and lungs, and is released into the plasma and it plays a crucial role in regulating the renin-angiotensin-aldosterone system (RAAS). SARS-CoV-2 disrupts the ACE/ACE2 balance, leading to RAAS activation and contributing to the progression of COVID-19, particularly in individuals with comorbidities such as hypertension, diabetes mellitus, and cardiovascular disease (55-57).

Mahmudpoor et al. propose that the entry of SARS-CoV-2 via the ACE2 receptor initiates a range of molecular signaling pathways beyond the angiotensin II/ACE2-Ang-(1–7) axis (46). These include the downregulation of PGC-1α and irisin, increased activity of SREBP-1c, upregulation of CD36, and inhibition of Sirt1, all contributing to insulin resistance. Additionally, the viral hijacking and replication trigger further molecular disruptions in the host's metabolic processes, such as SREBP-2 upregulation, reduced Sirt1 expression, and dysregulation of PPAR-ɣ, ultimately leading to insulin resistance. The molecular effects triggered by SARS-CoV-2 entry through ACE2, along with viral replication and inflammatory responses, lead to insulin resistance (IR) by impairing insulin signaling, reducing GLUT4 translocation, disrupting glycometabolic control, and exacerbating adipokine imbalances (46).

During the COVID-19 pandemic, cases of hyperglycemia, diabetic ketoacidosis, and new-onset diabetes increased, suggesting that SARS-CoV-2 may trigger both insulin resistance, type 2 diabetes, and type 1 diabetes mellitus (58). T1DM typically arises from immune-mediated destruction of islet β cells, influenced by genetic and environmental factors. Wang presents evidence linking viral infections to the development and progression of T1DM (59). Possible mechanisms include virus-induced β-cell damage through immune-mediated cell death, infection of surrounding cells, and direct viral effects. SARS-CoV-2 may trigger T1DM via autoimmune processes like epitope spreading, molecular mimicry, and bystander activation (59).

1.4.2 Diabetes epidemic within a pandemic: COVID-19 as a trigger for new diagnoses of DM

New diagnoses of diabetes mellitus (NDDM) frequently coincided with COVID-19 diagnoses (60-62). A retrospective review of patients admitted with COVID-19 and NDDM revealed elevated inflammatory markers in those with NDDM and this condition was also linked to prolonged hospital stays and higher rates of intensive care unit admission (63).

Newly diagnosed diabetes appears to be particularly dangerous in the case of COVID-19 infection. Research has investigated the correlation between various levels of hyperglycemia and the risk of all-cause mortality among hospitalized COVID-19 patients (64). Newly diagnosed diabetic patients had the highest rates of ICU admission and invasive mechanical ventilation (IMV), followed by those with pre-existing diabetes and hyperglycemia, compared to individuals with normal glucose levels. Additionally, newly diagnosed diabetes was associated with the greatest risk of all-cause mortality (64). These findings highlight the importance of long-term blood glucose monitoring in COVID-19 survivors (65). A systematic review and meta-analysis of over 40 million participants further indicated an increased incidence and relative risk of newly diagnosed diabetes across all ages and genders post-COVID-19, emphasizing the need for close monitoring, especially during the first three months after infection (66). Since COVID-19 appears to be associated with a higher risk for developing new onset diabetes among survivors, active monitoring of glucose dysregulation after recovery from COVID infection is definitely warranted (67, 68). Without careful monitoring, the risk of adverse outcomes in the short to medium term is likely to increase, placing a substantial strain on the healthcare system (69).

1.4.3 Integrating perspectives: The CAPISCO initiative and a holistic approach to COVID-19 and diabetes

As of Oct 2024, over 16,800 articles have been published on PubMed examining the relationship between COVID-19 and diabetes mellitus. This growing body of research highlights the intricate relationship between the two conditions, where diabetes exacerbates COVID-19 severity, and the virus, in turn, worsens glucose control, creating a complex and mutually reinforcing cycle. Understanding this dynamic is crucial for effective management and treatment, emphasizing the need to address both diabetes and COVID-19 in a comprehensive and holistic approach.

In 2021, a global multidisciplinary team of researchers called for a syndemic approach to managing cardiometabolic diseases during the COVID-19 pandemic. As part of this effort, the CAPISCO (CArdiometabolic Panel of International experts on Syndemic COvid-19) expert panel was formed with the aim to provide evidence-based recommendations to the global medical and scientific community to enhance patient care during and after the pandemic (70). The CAPISCO initiative emphasizes that physicians should consider their patients' social, economic, and environmental contexts while utilizing available healthcare resources to enhance access to care.

In response to challenges posed by the COVID-19 pandemic, the CAPISCO expert panel brought together a diverse multidisciplinary team of international researchers and clinicians from various disciplines, including diabetology, endocrinology, cardiology, lipidology, internal medicine, radiology, preventive medicine, public health, and biochemistry, representing a novel approach to addressing COVID-19. Geographical diversity was also prioritized to encourage collaboration and knowledge-sharing among experts from different continents facing varied challenges during the pandemic. The members of CAPISCO aim to collaboratively explore several key areas, including how patients with cardiometabolic diseases are currently managed, why COVID-19 mortality rates differ across countries, whether telemedicine can reliably provide high-quality care based on pandemic experiences, and how to evaluate the long-term consequences of delayed management of cardiometabolic and other diseases due to COVID-19 (70).

The focus on social distancing and minimizing close contact during the COVID pandemic posed challenges in providing medications and medical supplies to diabetes patients, leading to a greater reliance on telemedicine for diabetes management (71). As part of the CAPISCO initiative, Rosta and Menyhárt (72) conducted a review of telemedicine solutions in diabetes care during COVID-19 across Hungary, the US, Turkey, and Poland. Their review highlights the significance of employing telemedicine solutions for glucose self-monitoring and weight control to mitigate the risk of cardiovascular events and hypoglycemia in diabetic patients affected by COVID-19. Smartphone applications have demonstrated the potential to assist individuals with diabetes in reducing their HbA_{1c}

levels by an average of 0.33% (73). Furthermore, through appropriate patient education and the effective utilization of telemedicine tools, it is possible to achieve a reduction of over 1% in HbA_{1c} levels among patients with diabetes (74). There is an urgent necessity to enhance awareness regarding the efficacy of telemedicine tools in facilitating effective diabetes management, particularly during challenging circumstances such as an ongoing pandemic.

The type of diabetes therapy patients receive during COVID-19 is also significant. Notably, prior use of metformin was associated with a threefold reduction in mortality following a COVID-19 diagnosis (75). This finding was further supported by the CAPISCO expert panel. In a recent review (76), they summarized current knowledge on glucometabolic disturbances in patients with type 2 diabetes during acute COVID-19 infection and potential strategies to address them with novel antidiabetic therapies. Observational data suggest that the use of metformin, GLP-1 receptor agonists, and SGLT-2 inhibitors prior to hospital admission is linked to lower mortality rates, whereas the use of DPP-4 inhibitors is associated with increased in-hospital mortality in T2DM patients with COVID-19. However, this higher mortality risk among DPP-4 inhibitor users should be interpreted with caution, as these medications are often prescribed to older, frail patients and those with multiple comorbidities (76).

The CAPISCO panel also reinforced the bidirectional relationship between COVID-19 and diabetes, emphasizing that COVID-19 can trigger acute complications such as diabetic ketoacidosis (DKA) in both new-onset and preexisting type 1 diabetes, or a hyperosmolar hyperglycemic state in those with type 2 diabetes. These complications arise due to hyperglycemia and limited access to healthcare during critical moments. The panel stressed the importance of closely monitoring patients with SARS-CoV-2 infection and hyperglycemia, as they are at high risk for both mortality and long-term complications resulting from the infection (77). Patient follow-up was also highlighted because the negative effects of COVID-19 can persist even after recovery. Unfortunately, the post-acute phase of the illness may be characterized by a range of symptoms, collectively known as "Long COVID" or "Post-COVID Syndrome", which is thought to involve a chronic, low-grade inflammatory and immunologic state that can persist for weeks or even months (78). Consequently, active monitoring of glucose metabolism is recommended in patients who have recovered from SARS-CoV-2 infection (77).

1.4.4 Telemedicine in action - Safeguarding diabetes care during health emergencies

Based on evidence, it seems justified that during health emergencies like the COVID-19 pandemic, continuous monitoring of diabetic patients is critical, as diabetes management can be severely disrupted by restricted access to healthcare, increasing the risk of complications such as diabetic ketoacidosis and worsening glycemic control. During the COVID-19 pandemic, patients with diabetes and obesity experienced reduced contact with healthcare providers, leading to a general decline in the quality of disease management (79). In such situations, telemedicine plays a pivotal role by ensuring that patients continue to receive timely care and guidance, regardless of physical limitations. By facilitating remote consultations, monitoring and medication adjustments, automatic uploads of sensor or glucometer data, telemedicine may help to decrease the risks and maintain a steady line of communication between patients and healthcare providers - ultimately improving outcomes and reducing the strain on overburdened healthcare systems. The COVID-19 pandemic has accelerated the advancement, innovation and regulation of various digital tools for the remote management of diabetes, such as technologies for physiological monitoring, data analysis, and communication, which are expected to have a lasting positive impact on diabetes care in the future (80).

Telemedicine and technology, which are vital during a pandemic, should continue alongside in-person visits in the post-pandemic era to ensure timely care and reduce strain on healthcare systems (72, 81-83). Digital tools, such as online education and smartphones, can improve disease management, particularly in glucose monitoring and treatment are as crucial as raising awareness about weight gain and cardiovascular risks through digital platforms (81).

Sarveswaran et al. suggest that teleconsultations for individuals with diabetes mellitus should encompass lifestyle modifications (such as exercise, nutrition, maintaining a healthy body weight, and stress management), blood glucose monitoring (including the frequency of self-monitoring blood glucose and target blood glucose levels), guidance on insulin administration (covering preferred injection sites and techniques), recognition of hypoglycemia symptoms and strategies for preventing diabetes-related complications (81). Utilizing telemedicine tools during health crises allows for continuous monitoring and timely medical interventions for diabetic patients, even when face-to-face visits are limited. These digital platforms enable healthcare providers to manage glucose levels, adjust treatments, and offer guidance remotely, reducing the risk of complications. By integrating telemedicine, we can help maintain effective disease management while minimizing disruptions to care during emergencies like the COVID-19 pandemic.

During health emergencies, such as the COVID-19 pandemic, the management of diabetes requires heightened attention due to increased risks of complications and challenges in accessing routine care. Blood glucose levels can fluctuate significantly in times of crisis due to disruptions in daily routines, stress, and reduced contact with healthcare providers. Regular monitoring and analysis of blood glucose data become essential tools in detecting these changes and adjusting treatment regimens promptly. As a consequence, data collection not only provides insights into patients' glycemic control but also enables healthcare providers to identify trends and patterns that may signal the need for additional support. This approach is critical for minimizing risks associated with poor glycemic control, such as diabetic ketoacidosis or severe hyperglycemia, thereby helping to maintain stability in diabetic patients even in the most challenging healthcare environments.

2. OBJECTIVES

Building on the need for close monitoring of diabetic patients during health emergencies (31, 38-43), this study aims to analyze the impact of the COVID-19 pandemic on blood glucose management among diabetic patients. Specifically, we focus on examining and comparing patient data from before and during the COVID-19 period to identify any significant changes in glycemic control and management patterns. The study’s timing during the COVID-19 pandemic offers a unique opportunity to assess the influence of a major health crisis on diabetes care, motivated by well-established correlations between diabetes and adverse COVID-19 outcomes. Through this analysis, we hope to better understand how health crises affect blood glucose management and to inform future strategies for diabetes care in similar situations.

Diabetic patient data in the MDD before and during the COVID-19 pandemic was compared, covering 126 weeks in each period. To enhance our comparison, we also divided these intervals into 20-week segments. The analysis was centered on three key areas:

(1) weekly average blood glucose levels
(2) daily average blood glucose measurements and
(3) frequency of blood glucose data uploads.

We eventually sought to identify changes in patient characteristics, measurement patterns, and glycemic control. The ultimate aim of was to facilitate more effective diabetes care in similar health emergencies.

3. METHODS

3.1 Participants

3.1.1 Age, gender and geographical distribution of patients

The MÉRY Diabetes Database covers a significant portion of the national diabetic population, including data from over 4% of Hungary's total diabetic patients (32,775 out of 800,000 DM patients). This substantial sample size enhances the database's credibility and representativeness. Moreover, the database captures information from approximately 40% of all test strips sold for blood glucose meters, further underscoring its comprehensive coverage. In terms of gender distribution, the database shows a balanced representation, with 48.15% male participants and 51.85% female participants, aligning with global gender distribution trends in diabetes (27).

The database also provides notable representation across age groups, encompassing data that closely reflects the distribution among diabetic patients. Particularly noteworthy is the significant representation of data from the over-65 age group, which comprises the largest proportion of diabetic patients in Hungary and globally (19, 28). Additionally, the database exhibits representative regional distribution, encompassing data from various regions across Hungary. This extensive regional coverage enhances the overall representativeness of the database, facilitating comprehensive analyses and insights into diabetes management.

3.1.2 Types of therapy among diabetic patients in the database

The MÉRY Diabetes Database features an analysis of the therapies administered to patients, with a specific focus on insulin treatment frequency and the types of diabetes (T1DM, T2DM, GDM) present. Additionally, the analysis includes the examination of average blood glucose levels. The patient population within the database is representative of the various types of diabetes treatment, including oral antidiabetic medications (8.71% of all patients in the database) as well as different frequencies of insulin administration – once (11,16%), twice (9,76%), three times (7,3%), four times (53,12%), and more than four times a day (9,95%). It is important to note that patients receiving insulin four times a day are overrepresented in the database. This overrepresentation is anticipated because this group constitutes the largest subset of insulin-treated patients who generally monitor their blood glucose levels more frequently.

3.2 Data collection and data cleaning

Data collection for the MÉRY Diabetes Database began in 2015 and continues to date, with a significant increase in the accumulation of blood glucose data. The qualitative data collection process involves collecting several essential parameters, including the exact timing and date of measurements, age, gender, address, social security number, therapy type (non-insulin/insulin), frequency of insulin administration (if applicable), and diabetes type (T1DM, T2DM, GDM). Table 1 provides a breakdown of the number of blood glucose records received before and after the data cleaning procedure.

Table 1 Total number of blood glucose records in the MÉRY Diabetes Database before and after the cleaning process (23)

Action	Queries in order	Removed	Number of blood glucose records after the query
Check count	Count all records	0	56,494,451
Cleaning	Remove records that are not linked to a patient	7,474,415	49,020,036
	Remove records of excluded patients	5,633,354	43,386,682
Total			**43,386,682**

A key part of data cleaning involved establishing the inclusion criteria for participants. First, records that were not linked to any patient were removed. Second, when analyzing and comparing data from before and during the COVID period, we included only those patients who had complete demographic information. Additionally, patients were required to use the Méry device for a minimum of 30 days and perform at least one measurement every 10 days to be eligible for inclusion. This criterion ensured the exclusion of individuals who measured sporadically or with long intervals between measurements, thereby reducing potential biases. Patients with gestational diabetes were excluded and they were saved for potential future analysis. Table 2 summarizes the inclusion and exclusion criteria for patients in the analysis. Importantly, all patients included in the study were ambulatory and managed as outpatients, ensuring the data reflects non-hospitalized individuals.In total, there were over 56 million records, and after this cleaning process, we retained more than 43 million blood glucose data points available for analysis.

Table 2 Inclusion and exclusion criteria for participants

CRITERIA TYPE	DETAILS
Inclusion criteria	
Patient status	Outpatients or ambulatory patients only
Linked records	Blood glucose records must be linked to identifiable patients
Complete demographics	Patients must have complete demographic information
Device usage	Patients must use the Méry device for at least 30 days
Measurement frequency	At least one measurement every 10 days
Exclusion criteria	
Unlinked records	Blood glucose records not linked to any patient were excluded
Hospitalized status	Records from hospitalized (inpatient) individuals were excluded
Sporadic measurement	Patients with sporadic measurements or long intervals between measurements were excluded
Gestational diabetes	Patients with gestational diabetes were excluded (saved for potential future analysis)

In the MÉRY Diabetes Database, there were 26,655 patients during the pre-COVID period, with 19,649,098 corresponding records. In the COVID period, the participant count decreased to 20,936, accompanied by 16,184,106 records (Table 3).

Table 3. Number of patients and records after the cleaning steps (Hermányi et al, 2024, 84)

	Pre-Covid time	Covid time
Number of patients after cleaning	26,655	20,936
Number of records after cleaning	19,649,098	16,184,106

There was a marked decrease in the number of patients contributing data during the COVID period, specifically a reduction of 5715 patients (Table 3). This decline predominantly affected elderly patients, indicating they were likely most impacted by the pandemic, resulting in discontinued measurements, data reporting and missed routine check-ups. Another important factor might have been that data collection concluded on July 30, 2022. However, supposedly some patients, out of COVID related fear and anxiety, visited their healthcare provider after the data collection period ended, and thus, these data were not included in the analysis.

3.3 Anonymity, security and GDPR

When acquiring a MÉRYkék device, patients are required to provide informed consent by completing a form attached to the device. This consent authorizes access, storage, and processing of their data in an anonymous manner. Consequently, only the device's manufacturing number is linked to the patient, ensuring confidentiality of their personal information. To manage this extensive volume of anonymized data in compliance with the General Data Protection Regulation (GDPR), a separate database is established. This database facilitates analysis of data from tens of thousands of patients while preserving anonymity and adhering to GDPR guidelines.

The management of the MDD followed the principles outlined in the Declaration of Helsinki (2013) by the World Medical Association (85). The study protocol was approved

(71-IK/2024) by the Regional and Institutional Committee of Science and Research Ethics at Uzsoki Hospital, Budapest, the teaching hospital of Semmelweis University.

3.4 Data analysis before and during the COVID-19 pandemic

We analyzed patient data related to the periods before and during the COVID pandemic to gain insights into the measurement and data upload habits of diabetic patients, as well as the changes in blood glucose levels before and during the pandemic. The comparison involved results from a 126-week pre-COVID period (1 October 2017 - 29 February 2020) and a 126-week period during the COVID-19 pandemic (1 March 2020 - 30 July 2022). We evaluated the recorded values and the rate of change in data uploads during both periods. To further emphasize the dynamic nature of the pandemic, we also analyzed the data in 20-week periods. Firstly, we analyzed the last 20 weeks of the pre-COVID period in comparison to the first 20 weeks of the COVID period to assess the immediate changes at the onset of the pandemic. Secondly, we compared data from the first 20 weeks of the COVID period to the subsequent 20 weeks. Lastly, we compared data from the last 20 weeks of the pre-COVID period to the second 20 weeks of the COVID period to determine if the results were largely similar (Figure 1).

	Pre-COVID time	**COVID time**
(1)	All weeks	All weeks
(2)	Last 20 weeks	First 20 weeks
(3)		First 20 weeks & second 20 weeks
(4)	Last 20 weeks	Second 20 weeks

Figure 1 The different ranges of data analysis in the pre-COVID and COVID times (84)

We retrieved weekly data uploads over a span of 882 days (126 weeks) for both the pre-COVID and COVID periods. The aim was to determine the statistical significance of the COVID results compared to the pre-COVID data. Due to the unequal number of patients across the two periods, a t-test for two independent samples assuming unequal variances was used. The analysis was performed using R software version 4.2.1 (2022-06-23 ucrt). Four distinct data ranges were compared in our analysis, as shown in Figure 1:

(1) between 126 weeks of pre-COVID time and 126 weeks of COVID time

(2) between the last 20 weeks of the pre-COVID period and the first 20 weeks of the COVID period to assess immediate changes

(3) between the first 20 weeks of the COVID period and the subsequent 20 weeks to examine any potential return to normalcy

(4) between the last 20 weeks of the pre-COVID period and the second 20 weeks of the COVID period to assess the similarity of results.

We established a null hypothesis asserting that there is no statistically significant difference between the pre-COVID and COVID periods. Conversely, the alternative hypothesis proposed that there is a significant difference between these two periods. A p-value of less than or equal to 0.05 was considered statistically significant.

4 RESULTS

4.1 Population statistics in the dataset: Age, gender, regional characteristic before and during the pandemic

There was no statistical difference in age distribution among participants between the two periods. In both periods, the largest age group comprised patients over 66 years old, accounting for 59.23% before COVID and 57.96% during COVID (Figures 2a and 2b, Hermányi et al, 2024, 84).. The age group of 51-65 years old represented 27.24% before COVID and 27.64% during COVID. The gender distribution was also very similar in both periods; before COVID, 48.03% of patients were male and 51.97% were female. During the COVID period, these figures were 48.13% male and 51.87% female.

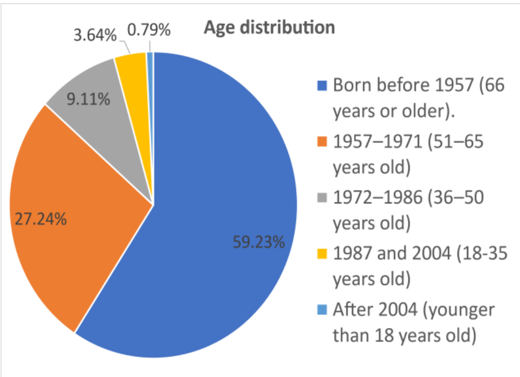

Figure 2a Age distribution of patients before COVID

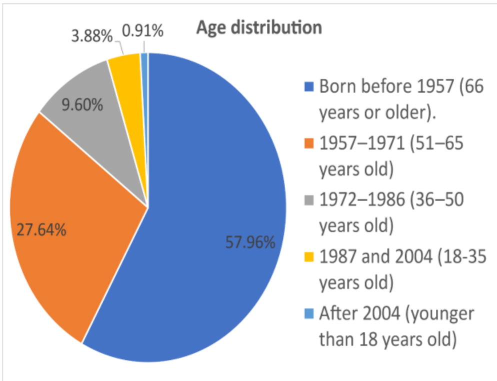

Figure 2b Age distribution of patients during COVID

To illustrate the geographic distribution of the dataset both before and during the COVID pandemic, the study area was divided into seven regions (as color-coded in Figure 3): three in the western part of Hungary, three in the eastern part, and one in the middle comprising Budapest, the capital. Figure 3 displays the percentage of participants contributing data from each region in both periods. No significant differences in the regional distribution of data contributors were found between the pre-COVID and COVID periods. Overall, when comparing the pre-COVID and during-COVID periods, it was found that patients providing data in both periods were very similar in terms of age, gender, and geographical distribution.

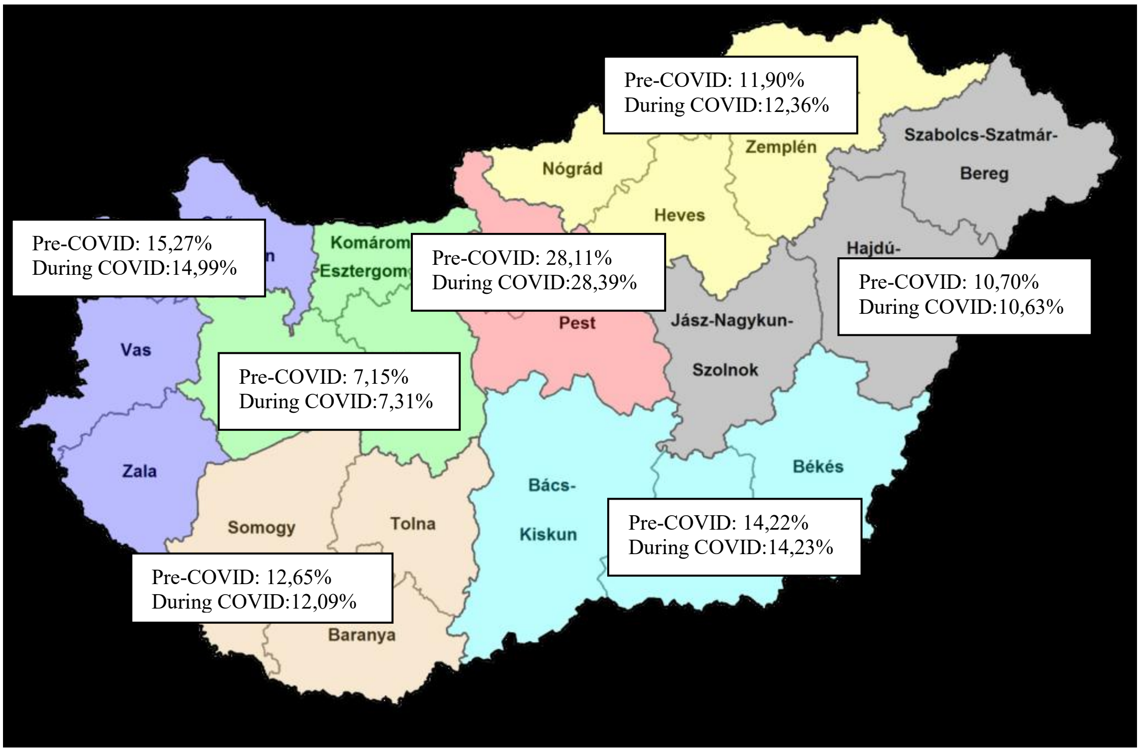

Figure 3 Regional distribution of participants before and during the COVID pandemic (Hermányi et al. 2024, 84)

4.2 Number of patients and frequency of blood glucose measurements by treatment modalities before- and during COVID-19

Table 4a and 4b illustrate the shifts in the distribution of patients using different antidiabetic treatment modalities within the database, comparing the periods before and during the COVID-19 pandemic. The data show that before the COVID-19 pandemic, the proportion of all patients on oral antidiabetics was 8.8%, while during COVID-19 it was 8.7%. The proportion of measurement data in this patient group was 3.21% vs. 2.85% of all measurements. The proportion of patients receiving once-daily insulin therapy was 11.18% both before and during COVID-19, with their measurement rate being 5.92% (pre-COVID-19) and 6.41% (during COVID-19). The proportion of patients treated with insulin twice a day changed from 9.59% (pre-COVID) to 9.76% (during COVID-19), while their measurement data decreased slightly from 6.35% (pre-COVID-19) to 6.05% (during COVID-19). The proportion of patients receiving insulin three times a day was 7.73% both before and during COVID-19, while their measurement data decreased from 7.19% (pre- COVID-19) to 6.58% (during COVID-19). Patients receiving insulin four times a day, who comprised the largest portion of the database in both time periods at 53.1%, contributed measurement data at a rate of 65.1% before COVID-19 and 65.96% during COVID-19. The last group consisted of patients receiving insulin more than four times a day, who were present in the database at a rate of 9.86% before COVID-19 and 9.95% during COVID-19, with their measurement rate being 12.15% in both time periods.

Tables 4a and 4b demonstrate that the percentage change in patient groups regarding treatment is minimal, with no statistically significant differences observed. However, it is noteworthy that the number of patients undergoing four daily insulin treatments increased in the pandemic period. Concerning the number of measurements, it is important to highlight that there was a decrease across all groups. Specifically, patients using insulin four times daily recorded a total of 816 measurements before the pandemic, whereas this number declined to 600 during the COVID-19 period, demonstrating a signifiicant 26% reduction.

Table 4a Number of patients and number of blood glucose measurements **pre-COVID-19** according to the type of therapy received (84)

	Number of patients	Patient ratio	Number of measurements	Measurement ratio
Oral antidiabetics	2590	8,82%	628443	3,21%
Insulin once a day	3286	11,18%	1158991	5,92%
Insulin twice a day	2819	9,59%	1243132	6,35%
Insulin 3 times a day	2166	7,37%	1406826	7,19%
Insulin 4 times a day	15627	53,18%	12759025	65,18%
Insulin more than 4 times a day	2897	9,86%	2377963	12,15%
Total	29385	100%	19574380	100%

Table 4.b Number of patients and number of blood glucose measurements **during COVID-19** according to the type of therapy received (84)

	Number of patients	Patient ratio	Number of measurements	Measurement ratio
Oral antidiabetics	2848	8,70%	451502	2,85%
Insulin once a day	3657	11,18%	1013822	6,41%
Insulin twice a day	3195	9,76%	957804	6,05%
Insulin 3 times a day	2388	7,30%	1040926	6,58%
Insulin 4 times a day	17380	53,11%	10435213	65,96%
Insulin more than 4 times a day	3256	9,95%	1922251	12,15%
Total	32724	100%	15821518	100%

4.3 Patient distribution across treatment modalities by quartiles

Patients receiving various treatment modalities were further divided into subgroups based on their measurement frequency (average number of measurements per day) using the statistical method of IQR (InterQuartile Range). In the upper and lower quartiles, we highlighted the 25% of patients who performed self-monitoring most and least frequently, respectively. The remaining "middle" group represents 50% of the patients.

The measurement patterns and blood glucose values of patients on oral antidiabetic therapy are shown in Table 5. Patients in the highest percentile of measurement frequency recorded measurements 6.8 times more frequently than those in the lowest percentile during the pre-COVID-19 period, while in the COVID-19 period the former group measured 6.2 times more frequently than the least frequent measurers. There is a correlation between measurement frequency and blood glucose levels, as the most frequent measurers exhibited lower blood glucose values compared to the least frequent measurers ($p<0.05$).

Table 5 Measurement frequency and blood glucose levels in patients on **oral antidiabetic agents**

	Number of patients	Average number of measurements	Average blood glucose level (mmol/l)
Patients belonging to the most requently measured quartile	Pre-COVID: 566 COVID: 398	Pre-COVID: 332 COVID:346	Pre-COVID: 8,15 COVID:7,91
Patients belonging to the middle two quartiles	Pre-COVID: 1124 COVID:782	Pre-COVID: 139 COVID:144	Pre-COVID: 8,07 COVID:8,18
Patients belonging to the quartile who measure their glucose levels the least frequently	Pre-COVID: 572 COVID:397	Pre-COVID: 49 COVID:55	Pre-COVID: 8,35 COVID:8,05
Total number of patients on oral antidiabetics	Pre-COVID:2262 COVID:1577	Pre-COVID: 277 COVID:284	Pre-COVID: 8,13 COVID:8,00

Table 6 displays the measurement patterns and blood glucose values of patients receiving once-daily insulin injections. Patients in the highest percentile of measurement frequency exhibited a significantly higher frequency of measurements, approximately 7 times more often than those in the lowest percentile during the pre-COVID period. Similarly, in the COVID period, the former group measured approximately 6.1 times more frequently than the least frequent measurers. Additionally, patients in the highest quartile of measurement frequency demonstrated improved blood glucose values compared to those in the lowest quartile of measurement frequency ($p<0.05$).

Table 6 Measurement frequency and blood glucose levels in patients receiving **once-daily insulin** injection

	Number of patients	Average number of measurements	Average blood glucose level (mmol/l)
Patients belonging to the most frequently measured quartile	Pre-COVID: 776 COVID: 606	Pre-COVID: 517 COVID:611	Pre-COVID: 8,23 COVID:8,07
Patients belonging to the middle two quartiles	Pre-COVID: 1544 COVID:1193	Pre-COVID: 206 COVID:247	Pre-COVID: 8,39 COVID:8,17
Patients belonging to the quartile who measure their glucose levels the least frequently	Pre-COVID: 778 COVID:607	Pre-COVID: 74 COVID:99	Pre-COVID: 8,64 COVID:8,39
Total number of patients insulin therapy once a day	Pre-COVID:3098 COVID:2406	Pre-COVID: 374 COVID:420	Pre-COVID: 8,29 COVID:8,11

Among patients receiving twice-daily insulin treatment (Table 7), there was also a significant difference in measurement frequency, with the highest and lowest quartiles exhibiting nearly a 7-fold difference. However, within this subgroup, it is noteworthy that patients in the middle quartile demonstrated the lowest blood glucose values ($p<0.05$).

Table 7 Measurement frequency and blood glucose levels in patients receiving **twice-daily insulin** injection

	Number of patients	Average number of measurements	Average blood glucose level (mmol/l)
Patients belonging to the most frequently measured quartile	Pre-COVID: 664 COVID: 507	Pre-COVID: 697 COVID:675	Pre-COVID: 9,17 COVID:9,12
Patients belonging to the middle two quartiles	Pre-COVID: 1280 COVID:1008	Pre-COVID: 316 COVID:299	Pre-COVID: 8,98 COVID:8,78
Patients belonging to the quartile who measure their glucose levels the least frequently	Pre-COVID: 647 COVID:509	Pre-COVID:115 COVID:108	Pre-COVID:9,43 COVID:9,7
Total number of patients on insulin therapy two times a day	Pre-COVID:2571 COVID:2024	Pre-COVID:483 COVID:470	Pre-COVID:9,11 COVID:9,00

Patients receiving three times daily (Table 8) insulin treatment also showed a remarkable difference in measurement frequency, with the most frequent measurers measuring approximately 7 times more often compared to the least frequent measurers. In this subgroup those in the highest measurement frequency quartile exhibited the lowest blood glucose values ($p<0.05$).

Table 8 Measurement frequency and blood glucose levels in patients receiving **three times daily insulin** injection.

	Number of patients	Average number of measurements	Average blood glucose level (mmol/l)
Patients belonging to the most frequently measured quartile	Pre-COVID: 494 COVID: 359	Pre-COVID: 996 COVID:1000	Pre-COVID: 9,4 COVID:9,1
Patients belonging to the middle two quartiles	Pre-COVID: 979 COVID:710	Pre-COVID: 465 COVID:495	Pre-COVID: 9,5 COVID:9,19
Patients belonging to the quartile who measure their glucose levels the least frequently	Pre-COVID:499 COVID:357	Pre-COVID:150 COVID:169	Pre-COVID:10,13 COVID:10,10
Total number of patients on insulin therapy three times a day	Pre-COVID:1972 COVID:1426	Pre-COVID:713 COVID:726	Pre-COVID:9,45 COVID:9,16

The most frequent data-providing group were the patients receiving 4 times daily insulin injection. The blood glucose values improved both before and during COVID in the highest quartile of measurement frequency, indicating better control in patients receiving four times daily insulin treatment ($p<0.05$). Additionally, the improvement in blood glucose values was also pronounced in this subgroup as measurement frequency increased (Table 9).

Table 9 Measurement frequency and blood glucose levels in patients receiving **four times daily insulin** injection.

	Number of patients	Average number of measurements	Average blood glucose level (mmol/l)
Patients belonging to the most frequently measured quartile	Pre-COVID: 3543 COVID: 2854	Pre-COVID: 1307 COVID:1271	Pre-COVID: 9,21 COVID:9,12
Patients belonging to the middle two quartiles	Pre-COVID: 7069 COVID:5707	Pre-COVID: 601 COVID:687	Pre-COVID: 9,4 COVID:9,25
Patients belonging to the quartile who measure their glucose levels the least frequently	Pre-COVID:3545 COVID:2854	Pre-COVID:189 COVID:236	Pre-COVID:9,73 COVID:9,78
Total number of patients on insulin therapy four times a day	Pre-COVID:14157 COVID:11415	Pre-COVID:900 COVID:903	Pre-COVID:9,29 COVID:9,19

Similarly to most subgroups, differences in blood glucose values were also observed between the least frequent and most frequent measurers among patients receiving more than 4 insulin injections per day ($p<0.05$) (Table 10).

Table 10 Measurement frequency and blood glucose levels in patients receiving **more than four times daily insulin** injection

	Number of patients	Average number of measurements	Average blood glucose level (mmol/l)
Patients belonging to the most frequently measured quartile	Pre-COVID: 652 COVID: 525	Pre-COVID: 1315 COVID:1276	Pre-COVID: 9,4 COVID:9,5
Patients belonging to the middle two quartiles	Pre-COVID: 1299 COVID:1046	Pre-COVID: 609 COVID:699	Pre-COVID: 9,53 COVID:9,33
Patients belonging to the quartile who measure their glucose levels the least frequently	Pre-COVID: 651 COVID:526	Pre-COVID:193 COVID:226	Pre-COVID:9,86 COVID:9,73
Total number of patients on insulin therapy more than four times a day	Pre-COVID:2602 COVID:2097	Pre-COVID:914 COVID:903	Pre-COVID:9,46 COVID:9,45

4.4 Weekly average of mean glucose levels in the pre-COVID and COVID periods

Our initial analysis covered the entire measurement period, spanning 2 x 126 weeks (1764 days), to examine the average blood glucose values over the pre-COVID and COVID periods. During the 126 weeks of the pre-COVID period, the average blood glucose level was 9.19 mmol/L ± 0.1721mmol/L. This value decreased to 8.97 mmol/L ± 0.1418 mmol/L during the corresponding COVID period. The p-value was less than 0.001, indicating statistical significance.

Subsequently, we analyzed the changes in blood glucose values over two consecutive periods, comparing the first 20 weeks before COVID to the initial 20 weeks of the COVID period. In the 20 weeks preceding COVID, the average blood glucose level was 9.08 mmol/L ± 0.1575 mmol/L. During the first 20 weeks of COVID, this value decreased to 8.96 mmol/L ± 0.0997 mmol/L. The p-value was 0.004, indicating a statistically significant difference in the average blood glucose levels between these two periods.

Next, we compared the measurements taken at the beginning of the pandemic, specifically the average blood glucose levels during the first and second 20 weeks of COVID. In the first 20 weeks of COVID, the average blood glucose level was 8.96 mmol/L ± 0.0997 mmol/L, while in the second 20 weeks of COVID, it was 9.04 mmol/L ± 0.0634 mmol/L. The p-value of 0.002 indicates a significant difference in the average blood glucose levels between these two periods.

Lastly, when comparing the last 20 weeks of the pre-COVID period to the second 20 weeks of the COVID period, we observed the following results for average blood glucose levels. In the last 20 weeks before COVID, the average blood glucose level was 9.08 mmol/L ± 0.1575 mmol/L, whereas in the second 20 weeks during COVID, it was 9.04 mmol/L ± 0.0634 mmol/L. The p-value of 0.19 indicates that the null hypothesis is correct, suggesting no significant difference in the average blood glucose levels between these two periods.

Figure 4 depicts the trends in blood glucose levels in the studied population during the pre-COVID and COVID periods. Notably, there are significant spikes in blood glucose levels during year-end holidays (Christmas and New Year's) each year, as well as during summer vacations. We should note that data collection began in different months for the two periods: in the pre-COVID period, data collection started on October 1, 2017, while for the COVID period, it commenced on March 1, 2020. Consequently, in the pre-COVID data (orange), an elevated blood glucose peak reflecting the Christmas holiday period appears around week 13. In contrast, in the COVID-period data (green), this same end-of-year peak appears around week 41. Therefore, these two peaks correspond to the same seasonal period of each year (Christmas and New Year’s). This pattern suggests that patients may be less attentive to dietary management during holiday seasons.

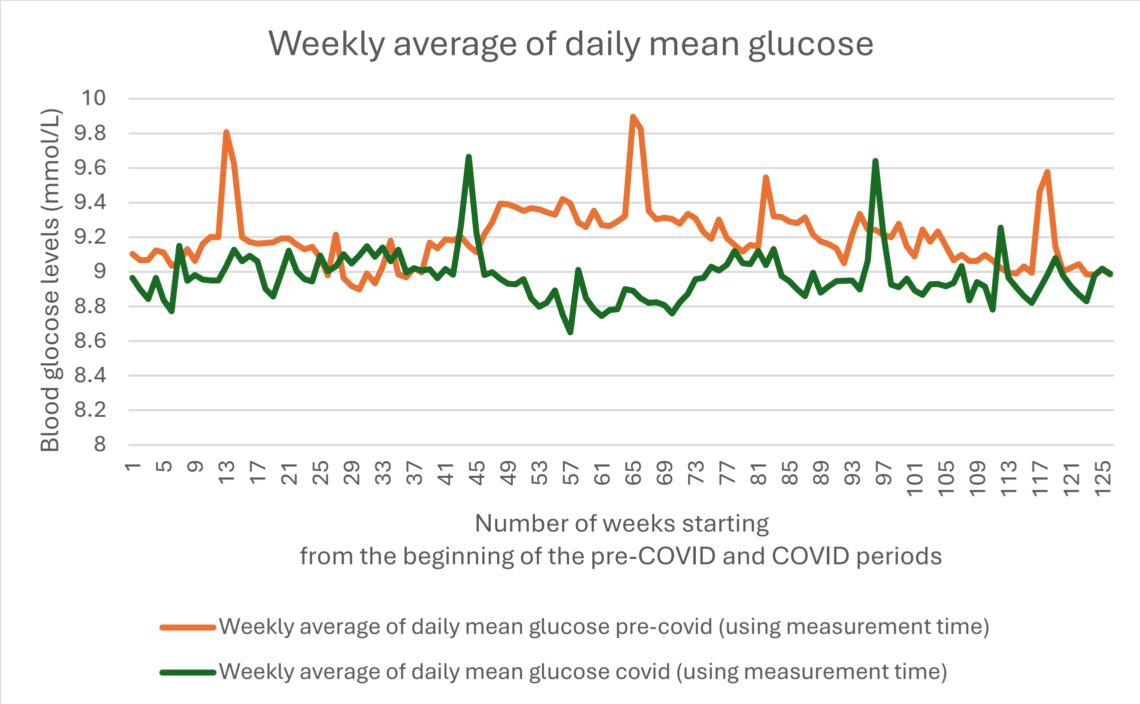

Figure 4 Weekly average of mean glucose levels before and during COVID

4.5 Daily average number of blood glucose measurements in the pre-COVID and COVID periods

Comparing the overall pre-COVID and COVID periods, significant differences were observed in the daily number of blood glucose measurements. In the pre-COVID period, the daily average measurement count was 0.83 ± 0.0708, whereas during the COVID period, this figure increased to 0.87 ± 0.2028, displaying a statistically significant difference ($p=0.01$). Additionally, comparing the last 20 weeks of pre-COVID to the first 20 weeks of COVID revealed significant differences in measurement counts. While the daily average count was 0.82 ± 0.0372 in the immediate pre-COVID 20 weeks, it rose to 0.99 ± 0.0462 in the first 20 weeks of COVID ($p<0.001$). The daily average count of 0.99 ± 0.0462 in the first 20 weeks of COVID showed a significant difference compared to the subsequent, that is, the second 20 weeks of COVID, where it decreased to 0.95 ± 0.0440 ($p<0.001$). Finally, comparing the last 20 weeks of pre-COVID (0.82 ± 0.0372) to the second 20 weeks of COVID (0.95 ± 0.0440) also revealed significant differences ($p<0.001$).

4.6 Weekly uploads of blood glucose data in the pre-COVID and COVID periods

Throughout the entire period under investigation, the average number of blood glucose data uploads per week was 155,945 ± 47104.0612 during the pre-COVID period and 128,445 ± 52868.8681 during the COVID period, indicating a significant difference ($p<0.001$). When comparing the last 20 weeks of pre-COVID to the first 20 weeks of COVID, the weekly data upload counts were 181,901/week ± 74522.1392 and 92,013/week ± 74522.1392, respectively, also showing a significant difference ($p<0.001$). Furthermore, comparing the first 20 weeks of COVID (average uploads: 92,013 ± 74522.1392) to the second 20 weeks of COVID (average uploads: 171,417± 48928.0553) revealed a significant difference ($p<0.001$). Finally, comparing the uploads from the last 20 weeks pre-COVID (181,901 per week ± 60952.2065) to the second 20 weeks of the pandemic (171,417 ± 48928.0553) indicated that the differences are not significant (p>,005), therefore the null hypothesis is the correct one, meaning there is no significant difference in data uploads between the pre-COVID last 20 weeks and the COVID second 20 weeks.

In summary, Table 11 presents the results of the statistical analysis and the corresponding p-values, focusing on the three main parameters: weekly average glucose levels, daily average number of blood glucose measurements, and weekly uploads of blood glucose data in the four different ranges of comparison.

Table 11 Statistical analysis summary of MDD data results (84)

Time/ Parameter	**Weekly average of mean glucose levels (mmol/L)**	**Daily average number of blood glucose measurements**	**Weekly uploads of blood glucose data**
Precovid/ Covid	9,19/8,97 p<0.001	0,83/0,87 p=0.01	155,945/128,445 p<0.001
Precovid last 20 weeks/ Covid first 20 weeks	9,08/8,96 p=0,01	0.82/0.99 p<0.001	181,901/92,013 p<0.001
Covid first 20 weeks/ Covid second 20 weeks	8,96/9,04 p=0,01	0.99/0.95 p<0.001	92,013/171,417 p<0.001
Precovid last 20 weeks/ Covid second 20 weeks	9,08/9,04 p= 0,19	0.82/0.95 p<0.001	181,901/171,417 p>0.05

4.7 Peculiarities in the process of data collection

During the pre-COVID period, approximately 2% of patient blood glucose data was consistently uploaded from home, as depicted by the red line in Figure 5a. The vast majority, 98%, of blood glucose data were collected at healthcare facilities. Data upload patterns remained stable throughout the year, except during specific periods such as Christmas, Easter, All Saints' Day, and the beginning of August, which coincide with typical times for summer vacations, resulting in reduced patient data uploads.

Figure 5b illustrates the data uploaded from blood glucose meters at healthcare facilities during COVID-19. There were noticeable declines in data uploads during national and religious holidays, and most remarkably a sharp decrease during peaks of the first COVID-19 waves in Hungary.

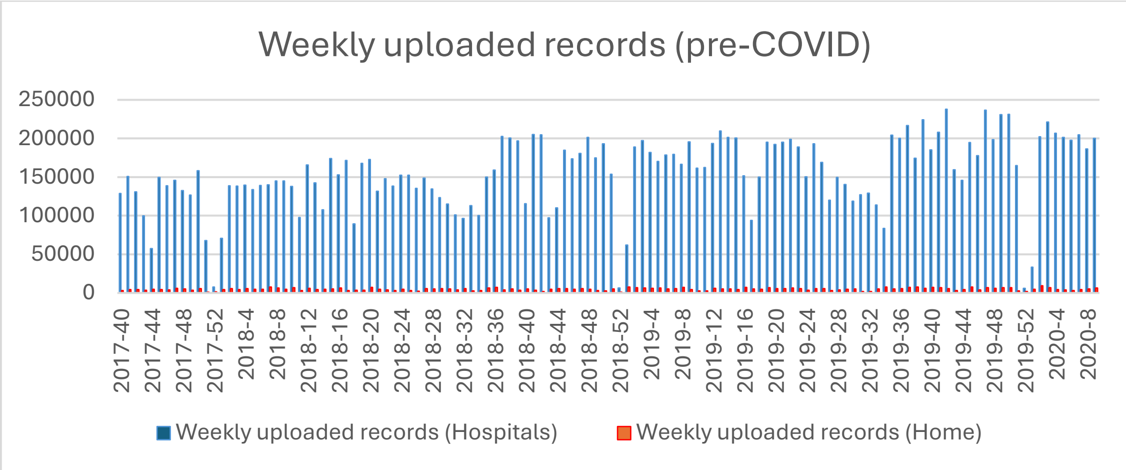

Figure 5a Data uploaded from blood glucose meters at healthcare facilities and from home (indicated in red) in the pre-COVID period (84)

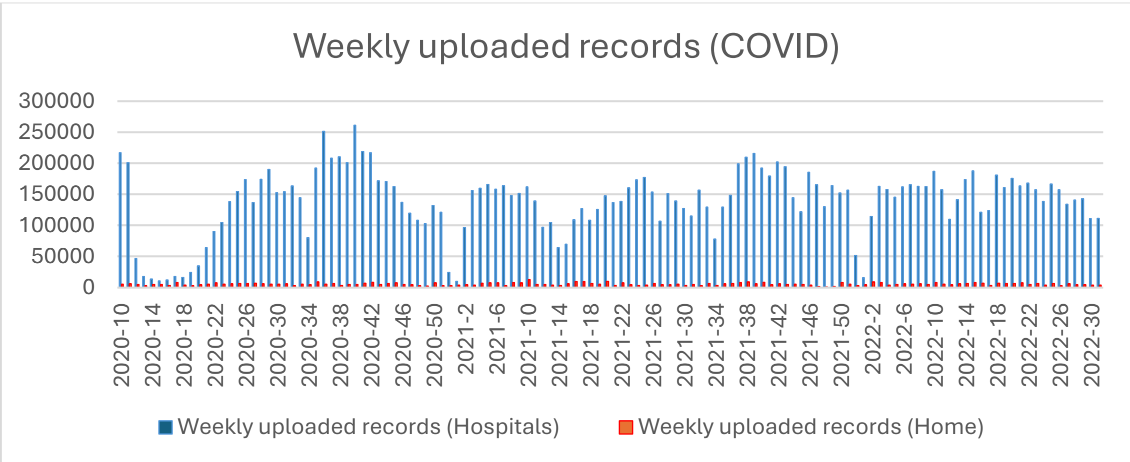

Figure 5b Data uploaded from blood glucose meters at healthcare facilities and from home (indicated in red) during the COVID period (84)

Figure 6 illustrates the average weekly uploads across the three 20-week periods. In the last 20 weeks of pre-COVID, an average of 181,901 records were uploaded, while during the first 20 weeks of COVID, this figure dropped to 92,013 indicating a significant decrease ($p=8,6x10^{-5}$), nearly halving in uploads immediately following the onset of the pandemic and the ensuing healthcare system limitations. It also underscores the time it took, an additional 20 weeks, for the healthcare system to begin its recovery, allowing for increased data uploads as in the second 20 weeks of COVID when the average uploads rose to 171,417.

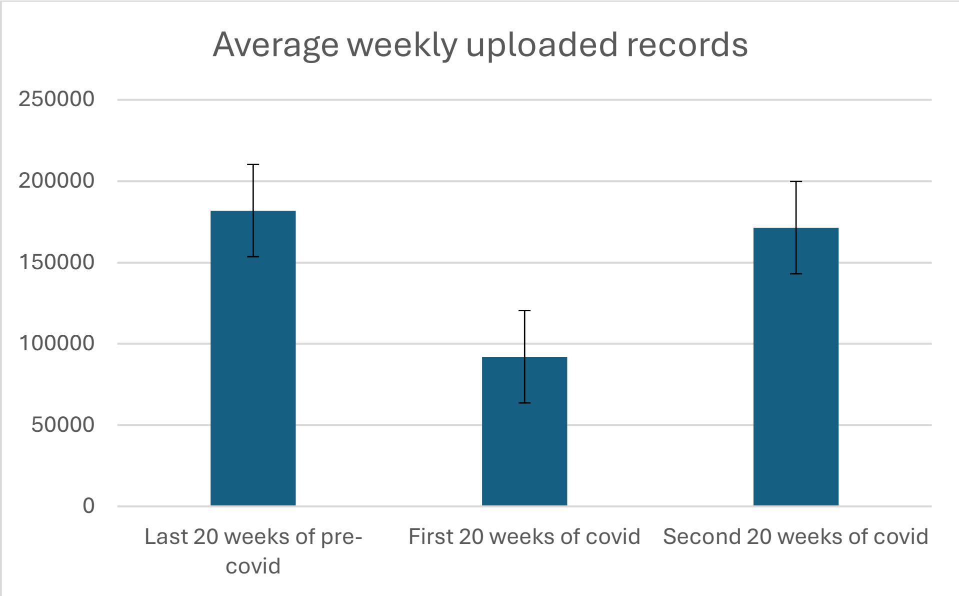

Figure 6 Average weekly uploads in the three 20-week periods (84)

Figure 6 also demonstrates the average number of uploads along with the standard deviation in the three 20-week-long periods. In the last 20 weeks of pre-COVID standard deviation was substantial (60,952), indicating variability in upload activity. In the first 20 weeks of COVID, standard deviation is the highest (74,522) of all three periods whereas in the last 20 weeks of the COVID period standard deviation was the lowest (48,928) indicating relatively consistent uploads week-to-week.

We also illustrated the data uploads for the examined three 20-week periods on a weekly basis to better highlight the temporal differences and the impact of the COVID waves. Figure 7 shows the changes in weekly upload data over the three examined 20-week periods: the last 20 weeks of pre-COVID (indicated in blue), the first 20 weeks of COVID (indicated in red), and the second 20 weeks of COVID (indicated in green). What stands out immediately is the significant drop in upload numbers around the midpoint of the last 20 weeks of the pre-COVID period, specifically in the 117th week. This period coincided with the Christmas and New Year holidays, indicating that patients uploaded significantly fewer data during this time, likely due to reduced clinic visits, where a substantial portion of data uploads typically occur. During the first 20 weeks of COVID, we also observed a dramatic decrease in data uploads, attributable to the pandemic-associated healthcare restrictions. In the second 20 weeks of COVID, this decline in data uploads is no longer observed, indicating that data reporting and healthcare service delivery regained stability after the initial shock of the first 20 weeks.

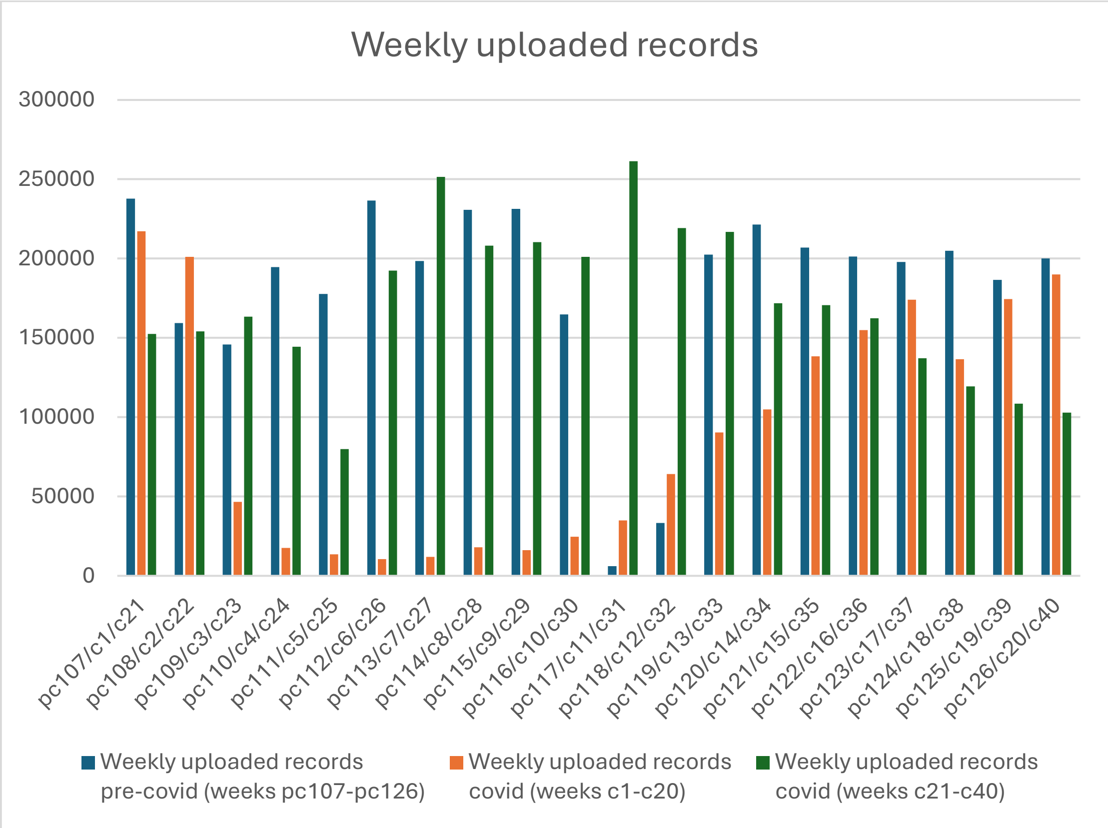

Figure 7 Weekly uploaded records in the last 20 weeks of pre-COVID, the first 20 weeks of COVID and the second 20 weeks of COVID (pc=pre-COVID, c=COVID; the numbers refer to the number of the week in the given period) (84)

5. DISCUSSION

The MÉRY Diabetes Database offers a uniquely comprehensive, nationwide dataset, encompassing over 40 million blood glucose readings from more than 32,000 diabetic patients in Hungary. To our knowledge, no other national database in this field achieves the same breadth and continuous data collection, making it a particularly valuable resource for monitoring diabetes management trends. For comparison, a similar database involved 8,190 patients, nearly 10 million capillary blood glucose readings, and centered primarily on the prevalence of nocturnal hypoglycemia, emphasizing the challenges of managing nighttime glucose levels (20). This dataset, though informative, covered a shorter period, and patients used a variety of glucometers, potentially affecting consistency. Another study involving a large database, the HAT (Hyperglycemia Assessment Tool) study, provided another substantial international dataset from 27,585 adults across 24 countries (21). However, limitations in the HAT database include its reliance on self-reported data, absence of electronic glucose measurements, and its primary focus on hypoglycemia. Additionally, unlike the MDD, the HAT study lacks continuous updates and broad epidemiological data, such as treatment types or regional or demographic information. Some studies, such as a recent German analysis, investigated HbA_{1c} trends across pre-pandemic and pandemic periods, finding that HbA_{1c} levels remained mostly stable (22). However, none of these investigations offered the longitudinal scope and range of data points captured in the MÉRY Diabetes Database, which facilitates a broader analysis of diabetes management over time.

Our investigation sought to compare different aspects of diabetic patient data in the MDD before and during the COVID-19 pandemic. These aspects included demographic statistics, average weekly glucose levels, weekly uploads of blood glucose data and the daily average number of blood glucose measurements. We also conducted analyses using data spanning 882 days and examined data in 20-week intervals to compare trends before and during the COVID-19 period (84). The demographic characteristics, including age, gender, and geographical distribution of participants showed significant similarities between the two periods, suggesting a consistent representation of the population. There was no significant change in the treatment modalities between the pre-COVID and

COVID periods. However, it is noteworthy that the number of patients undergoing four daily insulin treatments increased during the pandemic, which suggests that many patients were initiated on insulin therapy during COVID; moreover, in numerous cases, the management of already insulin-dependent diabetic patients also required intensification. Further investigations are required to determine at which stage of the pandemic the intensification occurred and whether patients increased the frequency of insulin administration on their own initiative or based on medical advice

Considering the different treatment modalities, we observed a strong association between an increase in the frequency of glucose measurements and lower blood glucose values in patients receiving oral antidiabetic agents, once-, three-times, four-times and more than four-times-daily insulin therapy. It seems rational that more frequent monitoring would correlate with improved results. Patients who measure more frequently tend to achieve lower blood glucose values, likely due to better adherence to treatment plans and more timely adjustments in their insulin dosage and lifestyle factors (12). The recorded values in these groups of patients reflect a proactive approach toward managing their condition, suggesting that they are more likely to adhere to dietary and exercise recommendations. This indicates that increased engagement with self-monitoring can support better blood glucose regulation, which may help reduce the risk of diabetes complications in the long term.

Among patients using once-daily insulin, those in the highest percentile of measurement frequency monitored their blood glucose approximately seven times more than those in the lowest percentile pre-COVID and six times more during the pandemic. These individuals demonstrated better glycemic control, likely due to a proactive approach to diabetes management, including adherence to dietary and exercise recommendations and behavioral adjustments informed by glucose readings.

For patients on twice-daily insulin therapy, there was a notable seven-fold difference in monitoring frequency between the highest and lowest quartiles. Interestingly, patients in the middle quartile achieved the best glycemic control, suggesting they struck a balance between adequate monitoring and stable management. Over-monitoring in the highest

quartile might reflect more severe diabetes or inconsistent management, whereas moderate but consistent monitoring, as seen in the middle quartile, appears to support optimal glucose levels without the need for excessive testing.
In patients receiving four daily insulin injections, those in the highest quartile of measurement frequency achieved improved glycemic control during both the pre-COVID and COVID periods. This finding indicates that more frequent monitoring may enhance glucose regulation in individuals on intensive insulin regimens. However, while these differences were statistically significant, their clinical relevance remained minimal, suggesting that the practical benefits of frequent monitoring in these subgroups are limited. Overall, the findings emphasize the potential advantage of moderate and consistent monitoring, particularly for patients on less intensive insulin regimens, in achieving effective glycemic management. It should be noted that the number of patients in this group increased during the COVID period compared to the pre-COVID period. The reasons behind this increase remain unclear and warrant further investigation. It is uncertain whether these patients independently began administering insulin more frequently at the onset of the pandemic or if this change was influenced by medical advice received during the later stages of the pandemic as access to healthcare services was restored.

The weekly average of mean glucose levels during the pre-COVID and COVID periods showed statistical significance; however, this difference was not considered clinically significant. Nevertheless, it was observed that the average blood glucose level of 9.19 mmol/L in the pre-COVID period was notably higher than the recommended range, potentially increasing susceptibility to infections like COVID-19 (30, 36). It must also be noted that the pre-COVID average blood glucose level of 9.3 mmol/L highlights that the carbohydrate metabolism of diabetic patients was far from ideal even at the onset of the pandemic. To reduce the risk of both short- and long-term complications, it is crucial to reduce patients' blood glucose levels into the target range appropriate for their age. Given the heightened risk for the diabetic population during the pandemic, effective blood glucose management becomes critical to enhance their protection against such health threats (33, 34).

When observing patients' blood glucose values throughout the pre-COVID and COVID periods, a significant increase can be noted during the end-of-year holiday season and summer vacation periods. These trends likely indicate that patients tend to pay less attention to maintaining a suitable diet during holiday times. These seasonal fluctuations in blood glucose values highlight the clinical importance of consistent dietary management for diabetes patients, especially during holiday periods when routine and eating habits may be disrupted. The COVID-19 pandemic has further exacerbated this issue by altering daily routines and limiting access to healthcare, making it crucial for healthcare providers to pay even closer attention to their patients during such medical emergencies. Elevated glucose levels during holidays can lead to worsening glycemic control, increasing the risk of both acute and chronic complications. Therefore, proactive counseling on maintaining dietary and lifestyle consistency during these critical times is essential to mitigate potential health risks associated with these disruptions (86).

Concerning the daily average number of blood glucose measurements in the pre-COVID and COVID periods, although significant differences were observed statistically, these differences did not deem clinically significant. Patients showed an initial increase in blood glucose measurements during the first 20 weeks of COVID-19, possibly driven by heightened awareness of diabetes risks amidst the pandemic. However, measurement frequency declined in the subsequent 20 weeks. The shift to remote work ("home office") aimed at preventing COVID-19 spread may have disrupted routines, impacting factors such as eating habits, physical activity, and access to healthcare. In an international survey involving European, African and Asian participants Ammar et al. (87) examined the impact of COVID-19 home confinement on physical activity levels noting significant reductions in all intensity levels of physical activity (vigorous, moderate, walking, and overall). Additionally, daily sitting time rose markedly from 5 to 8 hours per day and confinement also led to poorer dietary habits, with increased consumption of unhealthy foods and altered meal patterns, including more frequent snacking and reduced control over eating behavior (87). Additionally, social isolation and associated mental health effects might have contributed to this trend. El-Malky (79) maintains that during the COVID-19 pandemic, patients with diabetes and obesity have had reduced contact with healthcare providers, leading to a noticeable decline in disease management. Under such conditions, it has become increasingly difficult for patients to adhere to treatment regimens, maintain regular glucose monitoring, follow healthy eating habits, and engage in sufficient physical activity (79). This disruption in daily management increases the risk of complications and worsening health outcomes for these vulnerable populations.

Finally, the comparison of data uploads between the pre-COVID and COVID periods showed significant differences, both statistically and clinically. During the initial onset of the COVID pandemic the outpatient clinics experienced limitations in patient visits. As a result, weekly uploads, predominantly conducted at healthcare clinics, saw a significant decline due to imposed restrictions. The standard deviation was the highest during the first 20 weeks of COVID-19, indicating more variability in the weekly uploaded records. This heightened also reflects the initial disruptions and adjustments in healthcare practices and patient behaviors in the initial weeks of the pandemic. Factors such as restricted access to clinics, the rapid shift to remote care, and changes in patients' routines may have led to inconsistent data upload patterns. Essentially, it suggests a period of instability and adaptation as both patients and healthcare providers navigated the new circumstances. However, in the second 20 weeks of COVID, a sharp and dramatic increase was noted, suggesting that healthcare services adapted, regained stability after the initial shock and shifted towards telemedicine approaches for patient care to regain efficiency comparable to the pre-COVID era. Ye et al. (88) found a similar pattern in Canada when they aimed to assess how the COVID-19 pandemic affected essential healthcare services for diabetes patients, focusing on hospitalizations, emergency department visits, and primary care appointments. Their findings indicated that during the first wave of the pandemic, the rates of these healthcare services significantly dropped by 79.4%, 93.2%, and 65.7%, respectively (88). In the second wave, healthcare usage continued to decline, although emergency department visits rebounded slightly during a period when public health restrictions were temporarily eased. These results highlight the detrimental impact of COVID-19 on healthcare access for diabetic patients and underscore the need to strengthen healthcare systems in future public health crises. Similarly, In the United States, emergency department visits declined by 25.7% from April to December 2020 compared to the same months in 2019 (89). The CAPISCO expert panel also emphasized reduced frequency of healthcare visits in contributing to the worsening of chronic diabetic complications during the COVID-19 pandemic, in addition to increased physical inactivity, heightened anxiety and disrupted eating habits (77).

Both national and international data demonstrate that patients had limited access to healthcare services during the COVID-19 pandemic and were also less consistent in uploading home-monitored blood glucose readings. According to our findings, data uploads fell to nearly half of pre-COVID levels during the pandemic's first 20 weeks. In future health emergencies, it would be crucial for healthcare providers to receive timely information on patients' health status to make necessary adjustments in therapy. Addressing this gap could involve enhanced patient education to stress the importance of timely glucose data uploads. Alternatively, implementing glucose monitoring systems that automatically transmit data directly to healthcare providers could offer a practical solution, ensuring continuous monitoring and supporting informed, proactive treatment decisions.

Hungary benefitted during the COVID from the introduction of several digital and telemedical initiatives. The implementation of the Hungarian National Electronic Health Service Space (EESZT) facilitated the digital transmission of prescriptions from physicians to a cloud, streamlining retrieval for patients. Moreover, specialist recommendations and other healthcare documents could be conveniently uploaded to EESZT, ensuring easy access for other healthcare providers involved in patient care.

Rosta and Menyhárt (72) highlight various global healthcare sector initiatives aimed at utilizing technology and telemedicine to address challenges posed by the COVID-19 pandemic. They particularly emphasize the role of the Hungarian Diabetes Association (MDT) and diabetologists in maintaining essential diabetes care services during this period. The MDT actively engaged with the government to provide guidance on the safe delivery of medical services. From April 2020 onward, the MDT collaborated with its Primary Care Work Group to establish an online consultation platform on their website (www.diabet.hu), primarily benefiting primary care practitioners. The rise and widespread acceptance of online doctor-patient consultations also became apparent during this time. This initiative not only provided valuable experience but also contributed to the successful implementation of a fully funded online visit and consultation service by the National Insurance. Notably, on 29 April 2020, the Hungarian government issued a decree formally recognizing, regulating, and reimbursing telemedicine services.

The adoption of telemedicine in patient care was significantly boosted by the restrictions imposed on outpatient clinics during successive waves of the pandemic. This shift is clearly illustrated by the waveform pattern observed in the uploaded blood glucose data during the COVID period. The fluctuations in COVID waves are mirrored in the temporary decrease in uploads from healthcare providers, whereas during the pre-COVID period, uploads from healthcare providers were comparatively stable and consistent.

Despite the transition to telemedicine, the frequency of blood glucose data uploads from home remained consistent with pre-COVID levels, contrary to our expectations of an increase. There is a critical need to develop devices capable of automatically uploading real-time measurements, which would alleviate the burden on patients. Moreover, it is imperative to educate and motivate patients to regularly upload their data from home. In the event of future healthcare emergencies, greater emphasis should be placed on educating patients about the importance of monitoring and uploading their data, even in the absence of in-person visits to doctors or outpatient clinics. Modern blood glucose monitoring devices will play a pivotal role in facilitating this process.

Telemedicine and technology, which proved invaluable during the pandemic, should be integrated with in-person visits as we move into the post-pandemic era. This combination will ensure timely access to care while also alleviating pressure on healthcare systems, helping to improve patient outcomes and maintain continuity in care delivery (81). Furthermore Giorgino (2021) argues that exchanging valuable clinical experience among countries is now even more critical during the COVID-19 era than before as this collaboration can help mitigate the rise in severe hypoglycemia episodes and improve hyperglycemia management, often exacerbated by unhealthy lifestyles or poor adherence to therapy. It plays a vital role in identifying risk factors for unfavorable COVID-19 outcomes, as the virus impacts patients differently – some remaining asymptomatic while others face severe complications (81).

Years of experience show that patients are more likely to successfully transition to digital systems when they are required to do less in terms of data extraction and transmission (90). From the perspective of the older population, it would be even more beneficial to enable automatic data transmission using digital tools. Rapid and seamless data transfer would facilitate earlier therapeutic decisions by healthcare providers, helping to achieve target blood glucose levels more effectively. The introduction of blood glucose meters capable of automatic data transmission is further supported by the observation that, even when outpatient clinics were suspended, there was no increase in the number of home data uploads, a phenomenon attributable to patient-dependent factors.

Additionally, the forced lack of physical activity due to quarantine, combined with increased dietary intake, might lead to weight gain and further deterioration in carbohydrate metabolism. This situation underscores the need for continuous education regarding diet and exercise. Furthermore, there is a critical need to enhance education efforts targeting the vulnerable population aged 65 and above. Education should promote continuous at-home monitoring and health-conscious behaviors, aiming to reduce the duration and intensity of the initial shock phase observed during the first 20 weeks of future health crises.

However, the healthcare system must also be equipped to handle, process, and interpret the large volume of data, using it to make therapeutic adjustments. These modifications must then be communicated in a way that is clear and understandable to the patient. Expanding the capabilities of the EESZT in the future to manage both static and dynamic blood glucose data would represent a significant advancement, as being able to continuously receive and manage real-time blood glucose data would greatly improve diabetes care in Hungary. In the future, physicians, healthcare professionals, and health policy organizers at individual specialized care centers must pay increased attention to the broader dissemination of digital tools and the effective utilization of the data derived from them.

If we approach the results with a positive perspective, we can assert that the previously mentioned digital solutions facilitated the maintenance of diabetes care during the public health emergency. This means that blood glucose levels did not deteriorate, and patients continued to have access to both therapeutic measures and medical devices. This represents a significant advancement globally. Considering that diabetes is one of the most common comorbidities associated with COVID-19, we can conclude that we achieved a statistically significant even though clinically less relevant improvement by slightly decreasing blood glucose levels. However, due to the decrease in measurement frequency, it was not possible to maintain blood glucose levels within the target range, which could in fact influence the severity of COVID-19 progression. Additionally, the drastic reduction in the number of uploads at specialized care centers, coupled with the lack of compensatory or noticeable increases in uploads at home, hindered timely and effective treatment modifications that would have been essential to reduce COVID-19 complications as well.

While our study leveraged a nationwide database with comprehensive patient and measurement data, it is not without limitations. A notable issue was the exclusion of a significant number of patients during the COVID period due to incomplete data, suggesting a need for improvements in the call center's operations. Additionally, while many differences between the pre-COVID and COVID periods were statistically significant, they may not be considered clinically relevant. Also we had no data on patient HbA_{1c} or any additional therapy they received. Future studies could benefit from analyzing patients based on diabetes type and treatment, which could yield more refined conclusions.

6. CONCLUSIONS

In the contemporary realm of research, databases have emerged as the cornerstone of knowledge accumulation and synthesis. They play a crucial role in linking different aspects of academic research, creating a favorable environment for discovering truths and gaining insights. The Méry Diabetes Database (MDD) is a close to optimal collection of 40 million meticulously complied, regularly maintained, current and anonymized data of over 32000 diabetic patients in Hungary. It is a reliable and continuously expanding database that serves as a solid foundation for extensive clinical investigations and is positioned to significantly impact the field of diabetes care by improving targeted blood glucose levels and potentially enhancing patient compliance and quality of life.

In light of the critical need for continuous monitoring of diabetic patients during health emergencies, this study sought to examine the impact of the COVID-19 pandemic on blood glucose management among these patients. We analyzed and compared data from before and during the pandemic to identify significant shifts in glycemic control and management trends. We compared data from two 126-week periods, pre-COVID and COVID, enhancing this analysis by segmenting each period into 20-week intervals. This approach allowed for detailed examination of patterns over time in three main areas: weekly average blood glucose levels, daily average measurement frequencies, and the frequency of blood glucose data uploads. Ultimately, the insights gained from this analysis aim to inform more effective diabetes management strategies for future health emergencies, emphasizing the importance of adaptability in patient monitoring and data collection methods.

Although blood glucose levels measured during the pre-COVID and COVID periods showed statistically significant differences, these were not deemed clinically relevant. However, there were consistent spikes in blood glucose levels during the year-end holidays (Christmas and New Year's) and summer vacations each year. This pattern indicates that patients may be less attentive to dietary management during holiday seasons, highlighting the need for targeted patient education. Proactive counseling to encourage dietary and lifestyle consistency during these periods is essential for minimizing health risks associated with these disruptions. Moreover, the pre-COVID mean blood glucose level of 9.3 mmol/L underscores that diabetic patients' carbohydrate metabolism was suboptimal even before the pandemic began. To mitigate both immediate and long-term complications, it is essential to bring patients' blood glucose within a target range tailored to their age group. This approach could not only improve their overall metabolic control but also reduce the likelihood of adverse outcomes associated with prolonged hyperglycemia, such as cardiovascular and microvascular complications.

During the first 20 weeks of COVID-19, patients increased their daily blood glucose measurements, likely due to heightened awareness of diabetes risks amid the pandemic. However, in the following 20 weeks, measurement frequency declined. This shift may reflect the disruptions caused by remote work and home office measures intended to reduce COVID-19 transmission, which could have altered routines, affected eating patterns, decreased physical activity, and limited healthcare access. These changes highlight the impact of pandemic-induced lifestyle adjustments on diabetes self-management, emphasizing the need for sustained support for diabetic patients in adapting to evolving circumstances.

One of the most importent findings of the study was the dramatic reduction in data uploads during the first 20 weeks of COVID-19, which effectively halved compared to the pre-COVID period. This decline in uploads—typically conducted at healthcare facilities—highlights the critical impact of restricted patient visits during the onset of the pandemic. Prior to COVID-19, nearly 98% of glucose data uploads were performed in clinical settings, with only 2% being uploaded from patients' home. However, as healthcare facilities limited in-person appointments, weekly uploads dropped sharply, emphasizing the vulnerability of traditional data collection methods in emergency settings. After 20 weeks, data uploads began to recover sharply as healthcare systems adapted by integrating telemedicine and remote monitoring solutions. This highlights a key area for improvement in future health crises: ensuring that healthcare providers have rapid access to patient data to make timely therapy adjustments.

Another notable finding in our analysis is the pronounced reduction in data uploads around the 117th week, near the end of the pre-COVID period, which corresponds with the Christmas and New Year holidays. During this time, we observed a substantial decrease in upload frequency, likely due to reduced clinic visits when patients typically upload most of their blood glucose data. This seasonal pattern of reduced data reporting emphasizes how holiday periods can significantly impact routine diabetes monitoring. Consistently observed peaks in blood glucose levels during the year-end holidays and summer vacations further underscore this pattern, supporting the fact that holidays can significantly interfere with the maintenance of optimal glycemic control.

These observations underscore the need for robust telemedicine solutions and streamlined data reporting systems that can maintain stability during both predictable disruptions, such as holidays, and unforeseen health emergencies. The adoption of telemedicine for diabetes management accelerated significantly during the COVID-19 pandemic, especially as restrictions limited in-person visits to outpatient clinics. This shift is evident in the fluctuating pattern of blood glucose data uploads observed during COVID waves, where the frequency of uploads from healthcare providers temporarily declined in line with COVID wave peaks. In contrast, data uploads from healthcare providers during the pre-COVID period were relatively stable, highlighting the impact of pandemic restrictions on conventional healthcare delivery.

Despite the shift to telemedicine, home uploads of blood glucose data did not increase as expected, remaining at levels consistent with pre-COVID rates. This finding points to the need for improvements in remote monitoring technologies. Developing devices capable of real-time, automatic data uploads would reduce the burden on patients to manually submit their results. It is equally essential to strengthen patient education, emphasizing the importance of consistent data monitoring and upload from home, especially when access to in-person visits is restricted. In anticipation of future health emergencies, modernizing blood glucose monitoring devices and reinforcing patient engagement with remote health data submission could to a great extent enhance continuity in diabetes management.

7. SUMMARY

The Méry Diabetes Database (MDD) offers a robust, well-maintained dataset ideal for advancing diabetes care, focusing on achieving optimal blood glucose levels, and enhancing patient compliance and quality of life. This study utilized MDD data to assess trends in diabetic care before and during the COVID-19 pandemic, examining demographic statistics, weekly average blood glucose, frequency of data uploads, and daily glucose measurements. Data was analyzed over 882 days, with comparisons made in 20-week segments across pre- and mid-pandemic periods.

Demographic data revealed consistent representation across age, gender, and location in both periods, supporting the comparability of the two datasets. Among patients using different diabetes treatments, increased measurement frequency correlated with lower blood glucose levels, particularly among those receiving oral medications and once-, three-times-, four-times- and more than four-times-daily insulin regimens.

Although statistically significant differences in blood glucose and measurement frequency were identified between the pre-COVID and COVID periods, they were not considered clinically relevant. A pre-pandemic average blood glucose of 9.3 mmol/L underscored existing metabolic challenges among diabetic patients. Reducing glucose levels to age-adjusted targets remains essential to prevent both acute and chronic complications.

Initially, daily glucose measurements rose during the first 20 weeks of COVID-19, likely due to heightened health concerns. However, this increase waned in the subsequent 20 weeks. However, data uploads saw a substantial decrease, dropping by half during the first 20 weeks of COVID-19 as in-person clinic visits were restricted. Prior to COVID-19, 98% of uploads occurred in healthcare settings, with only 2% from home. The pandemic-driven shift to telemedicine allowed uploads to rebound in the later weeks, as healthcare adapted to remote monitoring. This shift underscores the need for better digital integration and patient education in diabetes care, particularly to enable swift therapy adjustments in future health crises.

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