RESEARCH ARTICLE

Diabetes Management

Remote continuous data monitoring and personalized data-driven approach for managing diabetes in a virtual and physical setting

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ABSTRACT

Many factors have contributed to the global increase of Diabetes Mellitus (DM) and metabolic disorders worldwide. In the United Arab Emirates (UAE), the International rapid urbanization and socioeconomic development has led to an increased prevalence of diabetes, reaching 16.3%. In line with global patterns, adherence to recommended diabetes management in the UAE remains a challenge with low compliance. Clinical inertia, ineffective health system programs, lack of performance based reimbursement models, and outdated communication tools for physicians and patients are responsible for diabetes treatment failure over many years. Single-biomarker remote monitoring strategies, such as glucose monitoring, have demonstrated reduced medical spending due to lower mean glucose values.

The GluCare care model encompasses two components, a physical component and a continuous digital monitoring component termed Remote Continuous Data Monitoring (RCDM) as a standard methodology of care for patients with diabetes. Continuous real-time monitoring and analysis of numerous parameters, under the responsibility of the primary caregiver, such as glucose, sleep patterns, dietary choices, activity, weight, amongst others, allow for data-driven actionable insights by the care team.

Methods: A retrospective and observational 3 month study of the GluCare model of care was conducted. Primary and secondary outcomes were described. In addition, food logging and patient interactions and their correlations with the primary and secondary outcomes were analysed.

Results: Initial data (n=22) indicate that patient engagement via the GluCare model lead to significant improvement in HbA1c (-2.14% point, p=0.00013) and other metabolic parameters such as LDL-cholesterol (-17.25%, p=0.0071), body mass index (-4.55%, p=0.0003), triglycerides (-18.52%, p=0.0165) and uric acid (-20.4%, p=0.0052) within 90 days of program initiation.

Conclusion: These initial findings suggest that management of diabetes under the GluCare model of care has the potential to significantly improve diabetes outcomes.

Abbreviations: RCDM: Remote Continuous Data Monitoring; HbA1c: Glycosylated Hemoglobin; DM: Diabetes Mellitus; UAE: United Arab Emirates; IDF: International Diabetes Federation; CGM: Continuous Blood Glucose Monitor; BGM: Blood Glucose Monitor; EMR: Electronic Medical Record; NHANES: National Health and Nutrition Examination Survey; NAFLD: Nonalcoholic Fatty Liver Disease; NASH: Nonalcoholic Steatohepatitis; BG: Blood Glucose; HR: Heart Rate; HRV: Heart Rate Variability; RR: Respiratory Rate; BP: Blood Pressure; TIR: Time In Range; TG: Triglycerides; ALT: Liver Transaminase; hsCRP: High-Sensitivity C-Reactive Protein; LADA: Latent Autoimmune Diabetes in Adults; SPD: Steps Per Day; DPP: Diabetes Prevention Program.

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KEYWORDS

- remote continuous data monitoring
- diabetes
- continuous glucose monitoring
- data-driven personalized medicine
- virtual monitoring
- hba1c reduction
- glucare
- digital health
- digital therapeutics

Introduction

Many factors have contributed to the global increase of Diabetes Mellitus (DM) and metabolic disorders worldwide. In the United Arab Emirates (UAE), the International rapid urbanization and socioeconomic development has led to an increased prevalence of diabetes, reaching 16.3% [1,2]. In line with global patterns, adherence to recommended diabetes management in the UAE remains a challenge with low compliance [2,3]. Clinical inertia, ineffective health system programs, lack of performance based reimbursement models, and outdated communication tools for physicians and patients are responsible for diabetes treatment failure over many years [4]. Single-biomarker remote monitoring strategies, such as glucose monitoring, have demonstrated reduced medical spending due to lower mean glucose values [5]. It is well documented that strategies that reduce HbA1c can lead to significant reductions in both diabetes-related comorbidities and overall healthcare costs [6-8]. Beyond direct healthcare costs, diabetes and the associated complications lead to reduced productivity and increased absenteeism [9,10].

Despite increasing options for diabetes medication, lifestyle modification programs, and availability of new technologies for monitoring diabetes, most provider-reported outcomes have not improved significantly over time or led to sustainable cost reduction [11]. Digital models of care have yielded good results [12]; however, have remained siloed, and not fully integrated with traditional diabetes provider practices.

Few advances in diabetes technology have been used with traditional treatment programs. Research has shown that diabetes technology, when coupled with education and follow-up, can improve the lives and health of people with diabetes [13]. Coaching and increased frequency of communication and education have also shown improvement in outcomes for diabetes better than standard in-clinic visits [14].

Remote Continuous Data Monitoring (RCDM) is a relatively new category of personalized, preventative healthcare services that utilizes continuous health information from users combined with cloud based artificial intelligence (AI) tools that work alongside medical professionals to assist patients in self-management on a continual basis.

This report describes the RCDM approach of managing diabetes and the associated outcomes on preliminary clinical data and patient engagement at GluCare from the patient's initial visit through their 3 month follow up visit.

Methods

Overview of GluCare health program

GluCare is an end-to-end diabetes program that encompasses both a physical and virtual infrastructure to support care teams and patients in diabetes education and management. This allows patients to effectively self-manage their diabetes and reach their targets, controlling or delaying micro and macrovascular complications. The physical aspect of the program is a 10,000 sq.ft facility located in Dubai, UAE, focused on treating diabetes with supporting services including a laboratory, imaging services, and pharmacy co-located within the facility.

GluCare's program combines a proprietary, clinical-grade, multisensor band, a smartphone application (app), and a clinical platform. The program is managed through this innovative software platform, which includes a central dashboard for team management of patient profiles, health data and program engagement.

The platform is integrated with commercially available devices such as continuous glucose monitor (CGM), blood glucose monitor (BGM), weight scales, and blood pressure cuffs which are provided in the first consultation. These devices track a range of data including heart rate (HR), heart rate variability (HRV), respiration rate (RR), skin temperature and blood pressure. The app also displays glucose readings, insulin dosages, tracks activity and sleep, patient surveys and has the ability to log meals.

This band data, integrated with GluCare's Electronic Medical Record (EMR) data provides insightful real-time at risk-screening for several disease conditions. Data is further processed using an artificial intelligence platform and machine learning algorithms which allows predictive risk scores on 18 different, diabetes-related health conditions. This is done by using a probabilistic graphical modeling approach, Bayesian Network, to model the causal relationships of medical concepts related to the diseases of interest. These include demographic variables, disease risk factors, symptoms, biometrics, etc. Model parameters were largely learned from the National Health and Nutrition Examination Survey (NHANES) (Centers for Disease Control and Prevention, 2021).

This intervention program combines mobile app technology, live and remote personalized lifestyle coaching from GluCare health coaches, live consultations with a GluCare diabetes nurse educator, dietitians and board-certified endocrinologists for medication management and prescription. Regarding nutrition intervention, participants log their meals through the app and receive feedback from the dietitians to improve their knowledge regarding quality and quantity of macronutrients and carbohydrate counting. In addition, physician feedback or prescription modification occurs as needed, usually a few days into the program. Data is reviewed daily by the healthcare team.

Educational content is provided through GluCare's customized and accredited (QISMET, United Kingdom) program depending on the health condition in the form of visual and text cards, sent periodically over the course of 12 months via the app.

■ Enrollment and engagement

A retrospective and observational 3 months study of our model of care was conducted. Primary outcomes were glycosylated hemoglobin (HbA1c) and interstitial glucose time in range (TIR) between 70-180 mg/dl. Secondary outcomes included reduction in cardiovascular risk, weight, BMI, LDL-cholesterol, HDL-cholesterol, triglycerides (TG), liver transaminase (ALT), uric acid and high-sensitivity C-reactive protein (hsCRP). We also describe the number of CGM readings, food logs recorded and number of patient interactions with the healthcare team via the app and its correlations with the primary and secondary outcomes.

This study took place in Dubai, UAE, during 2020/2021 and enrolled 22 participants from 20-71 years old with a diagnosis of type 1 DM, LADA (Latent Autoimmune Diabetes in Adults) and type 2 DM for at least one month prior to the first consultation. Patients gave consent to share their data. All 22 GluCare program-adherent participants met at least one of the metrics below plus a HbA1c ≥ 6.5 within one month prior to the first consultation. Blood tests were conducted as close as possible to 90 days from the initial visit and results were labelled as follow up results.

■ Metrics for participants' GluCare adherence

The following metrics were used to measure patient compliance:

1. Communication with a coach/care team at least once every 2 weeks

2. A minimum of 1 weight reading received every 30 day period

3. A minimum of 22 blood pressure readings received every 30 day period

4. A minimum of 45 days of receiving data from the wearable band over a 90 days period

5. CGM/BGM readings over 90 days

■ Demographic and clinical covariates

Data collected during the consultations from the physician medical reports included: year of diabetes diagnosis, current diabetes treatment, diet, physical activity, diabetes management perception, assessment of diabetes complications and comorbidities with retinal scan, ECG, body composition analysis, blood and urine tests. The EMR was used to extract this information.

Retrospective and observational analyses were performed by linking data from the GluCare app and data from other devices: the Dexcom G6 CGMs (Dexcom Clarity), Accu Chek Meter (Roche), Weight Scale (Mefit), and Blood Pressure (Omron) into the GluCare portal linked with the EMR. Blood tests were collected and analysed inside our facility. GluCare's HbA1c assay was conducted on the Roche Cobas Integra 400. Lipids, liver transaminases, and hsCRP assays were conducted on the Roche Cobas c501. The body composition scans (Seca) were performed during the live consultations. The cardiovascular risk was assessed using the UKPDS cardiac risk calculator [15].

Statistical analysis was performed by Microsoft Excel and presented as a mean. Correlations between the analysed variables were assessed by Pearson's product - moment correlation ($r>0.5$). A paired t-test was used to compare pre and post-intervention outcomes ($p<0.05$).

Anthropometric characteristics of the 22 participants are shown in TABLE 1. The overall population was predominantly male, 72%, and the average age was 45.27 years. Regarding the type classification of DM: one participant was classified as LADA, 4 participants type 1 DM and 17 participants type 2 DM. The mean diabetes duration for type 1 patients was 17.6 years, 8 years for the LADA patient, and 7.6 years for the type 2 DM patients. In the first visit, 50 % of type 1 patients, 23 % of type DM2 patients, and the LADA patient had retinopathy with elevated urinary albumin-to-creatinine ratio (30-299 mg/g creatinine) but normal estimated glomerular filtration rate. Only one type 2 DM had neuropathy with Charcot Foot with a history of toe amputation. Of all 22 participants, 19 were using sensors for continuous monitoring of glucose. Two had previous use before arriving at GluCare, both were type 1 DM patients, female and under 30 years old. Regarding the treatment of type 1 and LADA patients, all were in insulin basal-bolus therapy with multiple dose injections. The antihyperglycemic agent therapy in type 2 DM, is outlined in TABLE 2.

TABLE 1: Demographic and baseline clinical characteristics.

Parameter	HbA1c Evaluation Cohort (n=22)
Age, y	45.27
Male, # (%)	16 (72.73)
Body mass index	27.87
Baseline HbA1c, %	8.86
Weight, kg	80.06
Waist circumference, cm	97.47

TABLE 2: Drugs combination used in type 2 DM therapy.

Antihyperglycemic agents	Type 2 DM (n=17)
Metformin only	3
GLP-1Ra only	1
Metformin + DDP4i	2
Metformin + GLP-1Ra + SGLT-2i	9
Metformin + GLP-1Ra + SGLT-2i+ insulin	2

DPP 4 inhibitors , dipeptidyl peptidase-4; GLP1-Ra, glucagon-like peptide 1 receptor agonist; SGLT2i, sodium glucose cotransporter-2 inhibitor

Results

Overall patient characteristics

The primary endpoint average HbA1c reduction from baseline to 3 month follow-up was 2.14% points (p=0.00013). The average HbA1c baseline was 8.86%. Seven participants who had an initial HbA1c of over 9% dropped an average of 4.58% points.

During the 3 months follow up, the average number of CGM readings from Dexcom G6 per patient was 12,301 per month. For participants who had data transmitted (68.4%), 76.9% achieved a TIR average above 70% over the 3 month-period. The average TIR for these participants was 83.62% over the 3 month-period.

Secondary outcomes

Analysis of change in clinical outcomes among the participants from baseline to 3 months follow up is described in TABLE 3. We found reductions in UKPDS cardiovascular risk (39.03%, p=0.0006), BMI (4.55%, p=0.0003), Weight (4.49%, p=0.0003), Waist circumference (6.15% , p<0.0010), TG (18.52%, p=0.0165), LDL (17.25%, p=0.0071), HDL increment (5.19%, p=0.0630), ALT (9.44%, p=0.1198), Uric Acid (20.4%, p=0.0052), and hsCRP (6.19%, p=0.1973).

TABLE 3: Description of secondary outcomes improvement.

Clinical parameter	% Improvement	p
UKPDS CV Risk	39.03	0.0006
BMI	4.55	0.0003
Weight	4.49	0.0003
Waist circumference	6.15	< 0.0001
Triglycerides	18.52	0.0165
LDL	17.25	0.0071
HDL increment	5.19	0.0630
ALT	9.44	0.1198
Uric Acid	20.4	0.0052
hsCRP	6.19	0.1973

Remote data

The average meals recorded per participant per month was 9.22. The average number of messages exchanged was 24.05 per month per participant and the total exchanged messages for all participants in 3 months were 529. The number of steps per day (SPD) obtained from the wearable band were recorded as an average of 5.844 across all participants.

Correlations

Interesting correlations were observed between daily steps (SPD) and the TIR (r: 0.524, p=0.0805) and between hsCRP with the TIR, ALT and LDL-cholesterol (r: 0.667, r: 0.633, r: 0.544 and p = 0.0499, p = 0.015, p= 0.0443, respectively).

Discussion

Remote Continuous Data Monitoring, despite its field being young within the digital health space, can be effectively used by providers to drive evidence-based therapeutic interventions in real-time or near real-time. Similar to the positive results for digital therapeutic solutions, RCDM can be used independently or alongside medications, devices or other therapies to optimize patient´s care and health outcomes [16]. Since the beginning of the 2000s, applications that support healthy eating habits were suggested to be integrated with applications for managing blood glucose data and physical activity data [17]. Medical literature shows that mobile health care via cell phone technology is a promising tool for improving the results and efficiency of diabetes management and education [4], and can be useful to avoid clinical inertia.

This initial study by GluCare found that RCDM practiced within a provider setting is effective in lowering HbA1c and improving cardiovascular risk and comorbidities such as dyslipidemia and hyperuricemia in a 3 month period. Historically, it is well documented that 1% reduction in HbA1c with an intensive treatment can lead to reductions in end-point disease, death, heart attack and microvascular complications (21%, 21%, 14%, 37% respectively) [15,18,19]. In addition to HbA1c, the application of CGM has become mainstream in diabetes clinical practice, and TIR has become a useful tool to guide diabetes [13] treatment in patients using CGM. Effective TIR is associated with lower risk of microvascular complications, has become an accepTABLE endpoint for clinical studies and can be used for assessment of glycemic control [20-22].

Our results showed an HbA1c average reduction of 2.14% points, and data from 13 CGM using participants, 76.9% achieved TIR average above 70% over the follow-up period. This is a relevant outcome considering that the intervention occurred over a 3 month period, despite being a small and heterogeneous sample.

One of the aims of this study was to demonstrate improvements in other metabolic parameters beyond glucose control such as LDL-cholesterol, triglycerides and inflammation status linked with higher BMI and hsCRP. LDL reduction plays a critical role to prevent incident CVD and some data has also shown the role of reduced TG in CVD prevention in T2DM [23]. Hyperuricemia is a potential risk factor for CHD [24]. Therefore, lowering these variables is crucial in the prevention and treatment of CVD. Our study shows a reduction of 17.3%, 18.5% and 20.4% in LDL, TG and Uric Acid respectively. We also observed an increase of 5.19% in HDL, although this did not reach statistical significance.

Since 1992, literature has described excess body fat and its distribution related to risk for T2D and CVD [23]. Improvement of excess body fat and its distribution with reduction of visceral tissue, BMI (4.55%, $p=0.0003$), weight (4.49%, $p=0.0003$), waist circumference (6.15%, $p<0.001$) were statistically significant in our retrospective study.

As part of determining the risk of heart disease, we included hsCRP as a routine parameter endorsed by the American Heart Association and Center of Disease Control [25] for patients with diabetes. However due to our small sample size, p-values for hsCRP were not statistically significant. Nevertheless, we observed a correlation between hsCRP and other metabolic parameters such as LDL-cholesterol, TIR over 70% and ALT, but hsCRP were not correlated with HbA1c improvement. These reductions found in correlation confirm the inflammation reduction process that participants had in a very short period of time.

Important meta-analysis about behavioral support with studies published between 2003 and 2016 described the Diabetes Prevention Program (DPP) based lifestyle intervention delivery via eHealth communication and its magnitude on weight loss showed the efficacy of interventions on weight loss can be greater when a provider is both involved in person and remotely [26]. At GluCare, the application of both remote and in-person coaching permits the care team to suggest any corrective actions required based on the information received or trends observed (sleep hygiene, activity, food logging, glucose readings, compliance criteria, etcetera). The engagement level was near daily per month (24.05 messages per month per participants). The food logging feature allowed the care team to also overlay CGM or BGM data received with dietary choices via the GluCare portal and drive further patient engagement and education about glycemic variability and compliance. Whilst an average of 9.22 meals per participant per month was recorded, the trend seen was an uptake of this feature early into the program with more meals logged, and a tapering off in the number of meals later on as feedback was received.

▪ Virtual disease management programs *vs* provider led remote continuous data monitoring

The success of virtual disease management programs is well documented [27] with HbA1c reductions ranging from 0.3-1.3% point over a similar time period (12-26 weeks). Many of these studies have not reported other clinical parameter reductions due to the fact that such programs have not been part of the primary care providers' management plans, but act as an additional management/engagement tool used to assist patients.

In comparison to pure digital solutions, primarily measuring blood glucose and weight with remote coaching, the GluCare approach is distinct due to:

1. Measurement of a range of parameters remotely (sleep, glucose, activity, HRV, dietary choices, HR, BG, RR, pulse oximetry), many of which have an effect on glycemic variability.

2. Use of machine learning algorithms to actively predict risk factors.

3. Inclusion of an in-person component of care management.

4. Utilization of the same care team for in-person and remote management.

These additional features added into a diabetes management solution may result in better HbA1c control perhaps due to a more holistic end-to-end approach and engagement as shown in this study. Allowing the same care team to access both remote and EMR data allows for a more integrated, continuous model of care, improving patient engagement and behavioral change. The data-driven behavioral nudges or precision engagement allows for better interventions to promote the desired commitment which is crucial for diabetes management.

Despite the study's few participants, non-randomized nature and lack of a control group, indications are that the program can support DM patients by enhancing the primary provider's role as effectively as, and in many cases much better than, a virtual management program working siloed from a patient's primary provider.

Conclusion

The GluCare model of care for the treatment and management of diabetes mellitus showed, over a 3 month period, a significant improvement in HbA1c levels, time in range, and other metabolic parameters. This report describes the RCDM approach of managing diabetes and the associated outcomes on preliminary clinical data and patient engagement at GluCare from the patient's initial visit through their 3 month follow up visit.

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None

Conflicts of interest

The following authors declared the following potential conflicts of interest: The following authors are full-time employees/interns at GluCare: Milena Caccelli, Yousef Said, Joena Mojado, Carolyn Palsky, Ihsan Almarzooqi, Ali Hashemi.

The following authors have affiliations with organizations with direct or indirect financial interest in the subject matter discussed in the manuscript: Ali Hashemi, Ihsan AlMarzooqi.

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