ICT Based Diabetes Management System with Comprehensive Mobile Application: Clinical Usefulness Evaluation

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ABSTRACT
Objective of the presented study is to introduce telemedicine system that integrates all of the most implemented features that appear in different mobile diabetes applications in addition to blood glucose: tracking of insulin or other medications, communication, diet management, physical activity, weight, blood pressure, personal health record, education, social media, and alerts. Presented telemedicine system employs these features for management of Type 1 and Type 2 diabetes patients. Clinical evaluation after 3 months of intervention showed change of HbA1c in both patient groups was not only statistical significant but it had also a clinical dimension. The HbA1c decreased by 0,5% represents significant change for reduction of diabetic complications. Baseline for HbA1c in 29 T1DM patients: **8.1±1.5% versus 7.5±1.2% (P = 0.008).** Baseline for HbA1c in 26 T2DM patients: **7.4±1.2% versus 6.8±1.1% (p=0.001).** Results show statistically significant tendency to decrease in T2DM patients in weight 93.2±13.6kg compared to 91.9±14.2kg (P=0.08); and BMI 30.7±4.1 kg/m2 compared to 30.2±4.2 kg/m2 (P=0.08).

Categories and Subject Descriptors
J. [Computer Applications]: J. 3. Life and Medical Sciences - *Medical information systems*

General Terms
Measurement, Design, **Human Factors**, **Verification**.

Keywords
mhealth, telemedicine, telehealth, wearable, diabetes, study

1. INTRODUCTION
It is estimated that total 382 million people are living with diabetes, which represents 8.5% of the world's population. Unfortunately this is not a final number as 175 million people have undiagnosed Type 2 diabetes. Global prevalence on diabetes is estimated to reach 592 million by 2035. Daily healthcare represents a pressing challenge due to the dominance of chronic diseases that will become even more critical with ongoing demographic developments towards ageing society. Disruptive technological innovations have facilitated seamless monitoring of physiological data in a daily life. To support more effective healthcare these solutions provide increased data collection rates, interpretation of physiological significance, ease of use for untrained users with less interference with their daily activities. This enables tight glycaemic control and support that are essential for prevention and minimization of acute events and long-term complications in diabetes care [1]. Medical personnel should recognize the potential of ongoing shift towards home-based daily monitoring and play essential role in promoting health and not merely treating disease. To support medical doctors and healthcare workers in facilitating this shift in medical paradigm there should be supplied accurate and reliable evidence that seamless monitoring in daily life support complex management of diabetic chronic conditions with favourable impact on metabolic control in patients.

In this context objective of the presented study is to introduce telemedicine system that integrates all of the most implemented features in reviewed mobile diabetes applications [2] and to evaluate impact in clinical outcomes related to the glycated hemoglobin (HbA1c) and set of metabolic parameters (weight, BMI). The system is designed for self-monitoring of T1DM and T2DM patients and supported in patient management for healthcare providers. In section II we present the trial design and

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telemedicine system for management of diabetic patients. Section III introduces results of 3-months period from ongoing 6 months-study. In section IV we discuss the factors leading to presented results. Section V concludes on the results and introduces directions for future research and development by our research team.

2. TRIAL DESIGN AND METHODS

2.1 Participants

The inclusion criteria define group of patients diagnosed with Type 1 or Type 2 diabetes mellitus (DM) at least 1 year prior to this study, 18–50 years of age, suitable for home monitoring of blood glucose and blood pressure with necessary level of technical skills, as well as the willingness to work with information and communication technologies (ICT). The patients had been on stable therapy preceding the last 6 months before inclusion in the study and no change of treatment for the next six months is planned. Treatment of DM included insulin therapy, oral antidiabetic drugs (OAD), combination of OAD with insulin treatment, and diet. Exclusion criteria included pregnancy and lactation; lack of appointment compliance; psychiatric disorders; severe comorbidities that would render participation unethical or medically challenging. All the patients provided written informed consent. Total of 400 patients were included into the study (150 with Type 1 diabetes and 243 with Type 2 diabetes; 5 patients are not included into evaluation due to incomplete health profiles; 2 patients dropped out of the study due to non-compliance to treatment).

2.2 Trial Design

We are presenting preliminary results after 3 months of total 6-month ongoing prospective, non interventional, observational, multicentre study conducted in 26 Outpatient Slovak Centres for Diabetes. The local Ethics Committee, which follows the Helsinki Protocol has accepted design of the presented study. Standard management of diabetic patients includes personal visits to diabetic centres every three months for regular checkups. During the study patients will make three visits: initial meeting at the clinic (M0) and two regular visits after three and six months (M3 and M6). At every visit basic laboratory tests including the determination of laboratory parameters (total serum cholesterol, HDL, LDL cholesterol, triglycerides, FPG, glycosylated hemoglobin HbA1c) are performed. The anthropometrics measurements - height (meters), weight (kg) and blood pressure (mmHg) is measured and BMI (kg/m2) is calculated.
Patients were trained in usage of telemedicine system. At the initial meeting (M0) personalized telemedicine intervention was created for each patient based on patient's health profile. Intervention was defined as minimal number and type of required measurements per month (standard and monitoring days). Standard day included minimum one glucose measurement before any meal, blood pressure and weight measurement. Monitoring day included extended set of physiological parameters acquisition: 7x glucose measurements (before each main meal and 90-120 minutes after the meal), blood pressure, weight, 3x food intake (recording each major meal of the day in the morning, at noon and in the evening), physical activity, medication intake (insulin doses, OAD), waist circumference and general health conditions (mood, feelings, energy, and quality of sleep).

2.3 Telemedicine System for Diabetes Monitoring

Advances in sensor and information and communication technologies facilitates perception of diabetes as a disease of numbers. Results of published review reveals the most implemented features in mobile diabetes applications in addition to blood glucose [2] are tracking of insulin or other medications (in 65% of reviewed applications), communication (59%), diet management (52%), physical activity (40%), weight (39%), blood pressure (32%), personal health record (PHR, 29%), education (20%), social media (15%) and alerts (12%). Presented telemedicine system employs these features with respect to management of both Type 1 and Type 2 diabetes patients.
The schematic in Fig. 1 illustrates components and interactions that comprise overall telemedicine system architecture. Components are related to physiological sensors (off-the-shelf medical devices), mobile technologies, server, and patient and healthcare provider (HCP) applications.

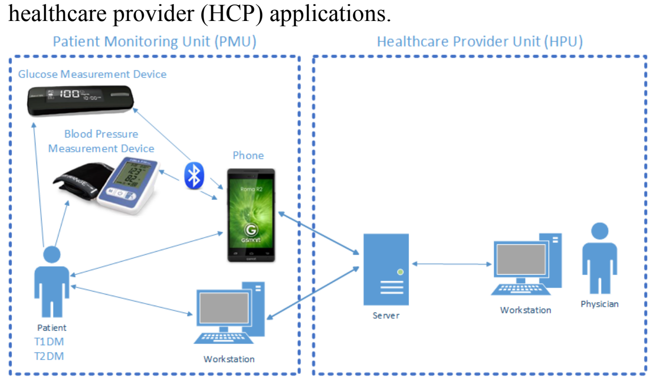

Figure 1. Telemedicine system architecture combining components and interactions related to patients and healthcare providers

Patient monitoring unit (PMU): patient devices with mobile and web applications are used for obtaining the physiological data from sensors, recording parameters related to self-management of disease, receiving messages from healthcare personnel on therapy adjustments, receiving reminders, alarms and reviewing development of health in tabular form and graphical historic trends (Fig. 2).

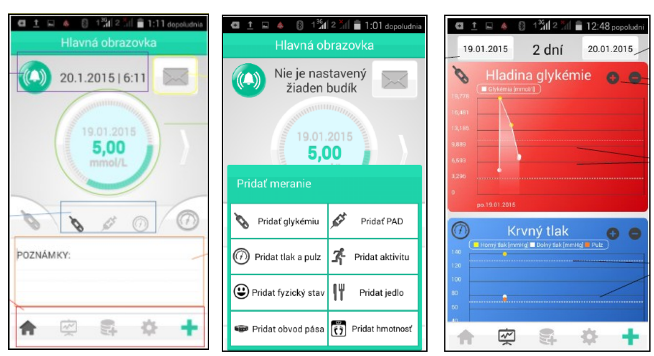

Figure 2. Mobile phone displaying the main screen with basic information and options, measurements and data entry menu, and graphical historic trends

Mobile terminals were provided to patients by research and development team (R&D). As reported in [3] patients generally preferred to use their own mobile phones. Mobile terminal provided in this study (GSmart Roma R2 with OS Android 4.4.2) had two SIM slots and patients could use their own SIM card in addition to one with data package provided by the R&D team.

Healthcare provider unit (HPU): web application enables healthcare professionals to overview and manage evolution of patient's health based on data from telemonitoring, modify treatments and communicate through text messages with patients. Overview of laboratory tests results taken at regular check up visits at diabetic centres enable evaluation of patient's health. Longitudinal and comprehensive health data records provide simple and functional PHR system (Fig. 3).

Server: is used for hosting communication and analytic functionalities, security and integrity of medical data. Communication between mobile terminals and web applications use HTTPS protocol and transferred electronic data are encrypted through AES. Web and database servers are hosted on separate virtual servers. All stored data are anonymised, patients are represented through predefined codes. Mapping codes to real patients is known only to healthcare providers and is not stored in the system. Mobile data privacy is secured through SQLCipher that encrypts local database.

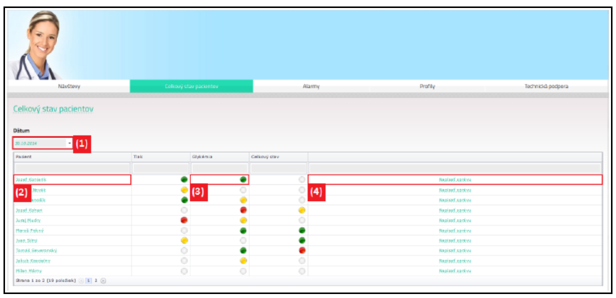

Figure 3. HPU web interface with status preview of recorded health parameters (red color indicating alarming thresholds; yellow - borderline values; green - good health conditions; white - no measurements)

Blood glucose data are wirelessly transmitted from a meter (Fora Diamond Mini) to a mobile terminal using Bluetooth interface. Data can be recorded also manually however in case of more than three successive manual entries patient would receive warning to prefer automatic transmission via Bluetooth. This is due to minimization of transcription errors from display of the meter. Patient can add details about type of meal and record notes with any relevant information about measurement or specific health conditions. This latter functionality is available for all data entries. Fig. 4 shows graphical overview of blood glucose development through PMU web interface.

Most people with Type 2 diabetes do not use insulin but take oral medication or apply lifestyle changes such as diet and physical activity. Tracking of **insulin** and **oral medications** includes information about type, manufacturer, and/or dose. Concerning the impact of **food** on blood glucose development patient can select food/drink type, enter quantity and type of meal (breakfast, lunch, etc.). Applications calculate amount of carbohydrate for the selection. To support diet recording not only for highly motivated patients there is also possibility for a less demanding data entry by a) creating predefined food menus that patient often consume and b) input directly amount of carbohydrates contained in a meal. **Weight and waist circumference** is recorded to easily quantify effectiveness of diet adherence. Measurements of **blood pressure** were done by Fora P30 Bluetooth meter. **Physical activity** together with blood glucose levels, medication and nutrition habits are the four main elements that influence personal diabetes management. Patient's mobile provides built in accelerometer for quantification of activity level from predefined types of different exercises and sports. To assess the **overall wellbeing** patient can enter status of four general health conditions related to mood, feelings, energy, and quality of sleep. Severity of each condition is recorded through selection of five states ranged from normal to worsened. In case values of glycaemia are out of predefined range patient will be automatically asked to enter information about overall wellbeing.

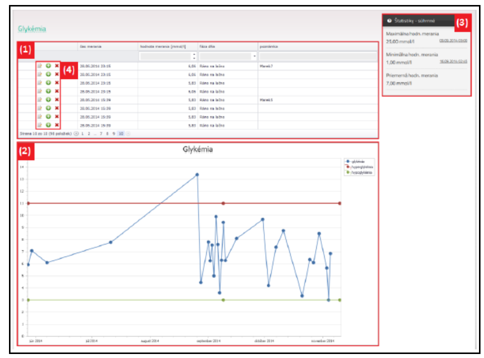

Figure 4. PMU web interface displaying development of blood glucose

Mobile and web applications serve as a **communication platform** between patients and HCPs. Healthcare providers send text messages and provide manual feedback through HPU web application interface to patient's mobile terminal. It can be used to adjust therapy, ask for further information about patient's health status, invitation for unscheduled health check at diabetic centre, etc. This functionality also influence positive impact on relationship between HCPs and patients due to feeling of being taken care of and security [4]. Patient's web application facilitates adherence to therapy through reminders about missing data entries and measurements and enables patient to access **blogs** and join **discussion forums** with other users of telemedicine system. **Educational** functionality of the system is reflected through simple analytics and graphical output of development of recorded data and enables its role as a coach in facilitating the patients to keep their health under control. It actively monitors individual health status, and sends out alerts when e.g. blood glucose exceeds an alarming threshold. This analytics functionality is implemented at patient's mobile application and both PMU and HPU web applications.

3. RESULTS

Total 29 patients with type 1 DM and 26 patients with type 2 DM were evaluated. This is due to the fact that up to June 2015 only these patients had completed M3 visits and laboratory examinations. Rest of the 400 patients still haven't completed three months in the study or visited diabetic centre for regular check-up. We presume this was because of enrolment process that lasted from January to April 2015. The average age of patients with type 1 DM was 35.1 ± 11.5 years, compared to 47.2 ± 3.4 years patients with type 2 DM ($p<0.01$). There was significant difference between the groups in terms of weight and BMI as shown in table 1.

Table 1. Description of baseline characteristics (mean ± SD)

Parameter	DM type 1 (n=29)	DM type 2 (n=26)	p value
Mean age (years)	35.1±11.5	47.2±3.4	<0.01
Height (cm)	172.9±9	174.4±7.8	NS
Weight (kg)	76.2±14.4	93.23±13.6	<0.01
BMI (kg/m^2)	25.29±3.2	30.7±4.1	<0.01
Number of standard days measurements per month	8.52±1.94	8.88±2.55	NS
Number of monitoring days measurements per month	4.52±1.40	4.32±1.77	NS

MAP – mean arterial pressure

Considering the period of 3 months during telemedicine intervention the average blood glucose in patients with type 1 DM was 8.1 ± 1.5 mmol/l compared to 8.4 ± 2.1 mmol /l in type 2 DM (p=0,62). The mean systolic BP in patients with type 1 DM was 124.1± 11.1, diastolic BP 81.2 ± 8.2, MAP 95.5 ± 7.9 and mean systolic BP in patients with type 2 DM was 132.3± 8.8, diastolic BP 83.6 ± 6.2, MAP 99.8 ± 6.3 (p<0.01, 0.23 and 0.03 respectively).

Both groups were tested at first visit (M0) and then after 3 months (M3) of telemetric measurements (tables 2 and 3).

Table 2. Description of characteristics (mean ± SD) in DM type 1 participants before (M0) and 3 months (M3) after start using telemedicine

Parameter	DM type 1 M0	DM type 1 M3	p value
HbA1C % DCCT	**8.1±1.5**	**7.5±1.2**	**0.008**
total cholesterol (mmol/l)	4.6±0.7	4.5±0.9	NS
LDL cholesterol (mmol/l)	3±0.7	2.8±0.8	NS
HDL cholesterol (mmol/l)	1.5±0.3	1.6±0.3	NS
Triglycerides (mmol/l)	1±0.7	1.1±0.8	NS
Systolic BP (mmHg)	127.7±14.6	125.3±16.5	NS
Diastolic BP (mmHg)	79.4±8.0	80.3±10.28	NS
Weight (kg)	76.2±14.4	75.7±14	NS
BMI (kg/m2)	25.3±3.2	25.1±2.9	NS

The results reveals significant reduction in HbA1C level in both groups 3 months since starting to use telemedicine system. Initial mean HbA1C was 8.1±1.5 % DCCT in the group of patients with type 1 DM and 7.4±1.2 % DCCT in patients with type 2 diabetes mellitus, whereas HbA1C in 3 months decreased to level 7.5±1.2 % DCCT in the first group and to level of 6.8±1.1 % DCCT in the second group (p value between M0 and M3 0.008 and 0.001). Patients did not have significant changes in lipoprotein panel after 3 months. Nevertheless, there was a tendency to decrease in weight of patients in type 2 group as well as in patients' BMI (p= 0.08).

Table 3. Description of characteristics (mean ± SD) in DM type 2 participants before (M0) and 3 months (M3) after start using telemedicine

Parameter	DM type 2 M0	DM type 2 M3	p value
HbA1C % DCCT	**7.4±1.2**	**6.8±1.1**	**0.001**
total cholesterol (mmol/l)	4.5±1	4.7±1.5	NS
LDL cholesterol (mmol/l)	2.7±0.8	2.5±1.4	NS
HDL cholesterol (mmol/l)	1.2±0.3	1.3±0.4	NS
Triglycerides (mmol/l)	1.8±1.2	1.8±1	NS
Systolic BP (mmHg)	135±9.8	132.1±13.8	NS
Diastolic BP (mmHg)	80.6±8.7	80.7±9.3	NS
Weight (kg)	93.2±13.6	91.9±14.2	0.08
BMI (kg/m2)	30.7±4.1	30.2±4.2	0.08

4. DISCUSSION

Telemedicine programs can impact various aspects of patient care, including informational, clinical, behavioural, structural, and economic [5]. The informational impact delivers better quality of information than handwritten records that may be incomplete or inadvertently forgotten at home on appointment days. The clinical impact is a more frequent communication of information and instructions, which can lead to improved outcomes with lower HbA1c levels or fewer adverse events of the therapy. Ultimately, the success of a program must be judged on its clinical outcomes. The surrogate marker for long-term complications is HbA1c. A program that can consistently lower (or at least not rise) the HbA1c level is considered by most diabetes experts to be better (or no worse) than existing care in terms of the risks of long-term microvascular complications of diabetes. Many short-term programs (especially when the patients are not blinded) look better during the first year than base case treatment because of initial patient enthusiasm, which may or may not be able to sustain beyond the study period or because of maldistribution of prognostic variables [6]. We showed that both groups of patients improved the glycaemic compensation measured by HbA1c levels. The change of HbA1c was not only statistical significant but it had also a clinical dimension. The level decreased by 0.5% and it is a significant change for reduction of diabetic complications. Many effective antidiabetic drugs have the effectiveness to reduce the HbA1c level by 0.3-0.6 %. We believe this good result can be due to more frequent self-monitoring of glucose (SMBG) and stricter compliance with a diabetic regime. Major clinical trials of people with insulin-treated diabetes demonstrating improvements in diabetic complications from intensive glycaemic control have included SMBG as part of a multifactorial intervention. SMBG is thus an integral component of effective therapy for type 1 diabetes [7]. Therefore the use of telemedicine for the improvement of SMBG is very important. The reduction in T2DM patient can be due the more frequent glucose testing but also stricter eating habits.

5. CONCLUSIONS

Findings from various studies of SMBG used in non-insulin-treated T2DM have been inconsistent due to differences in study designs, populations, and interventions used [8]. However, the data available from randomized controlled trials (RCTs) suggest that SMBG is likely to be an effective self-management tool only when results are reviewed and acted upon by healthcare providers and/or people with diabetes to actively modify behaviour and/or adjust treatment [9]. Still, optimal use of SMBG for people with non-insulin treated type 2 diabetes remains unclear [10]. A recent meta-analysis of non-insulin treated people with type 2 diabetes concluded that SMBG was associated with a reduction in HbA1c of 0.2% / 2 mmol/mol [11]. We demonstrated in our group of patients that the impact of telemedicine can result to higher reduction of HbA1c. Very interesting is the statistical significant reduction of weight and also BMI in T2DM patients. This may indicate that the telemedicine system motivated the patients to more consistent compliance (diet meal, physical activity etc).

It has to be noted that we presented only preliminary data and only in a small group of patients. Nevertheless, we showed that the telemedicine system is an effective tool for management of diabetes. There was an improvement of HbA1c levels by 0.5% during the first 3 months. The study is ongoing; we expect the data from more patients and comparison of results will be done after 6 months of using the system. Very interesting will be evaluation of the telemedicine system by the patients and the care providers to estimate impact of implemented set of features.

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