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"Predictive model-based decision support for diabetes patient empowerment"

D6.2: Description Quantification Campaign Dataset

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Dissemination Level		
PU	Public	X
PP	Restricted to other programme participants (including the Commission Services)	
RE	Restricted to a group specified by the consortium (including the Commission Services)	

CO	Confidential, only for members of the consortium (including the Commission Services)	

POWER2DM Consortium Partners

abbrev	Participant organization name	Country
LUMC	Leiden University Medical Center	Netherlands
IDK	Institute of Diabetes “Gerhardt Katsch” Karlsburg	Germany
SAS	SAS Servicio Andaluz de Salud	Spain
TNO	Nederlandse Organisatie voor Toegepast Natuurwetenschappelijk Onderzoek	Netherlands

Abbreviations

This section contains the abbreviations used in this deliverable.

Abbreviation	*Definition*
(S)AE	**(Serious) Adverse Event**
AE	**Adverse Event**
ASQ	**After-Scenario Questionnaire**
BMI	**Body mass index**
CGM	**Continuous Glucose Monitor**
CSV	**Comma-Separated Values file format**
DEPS-R	**Diabetes Eating Problem Survey-Revised**
D-FISQ	**Diabetes Fear of Injecting and Self-Testing Questionnaire**
DSMQ	**Diabetes Self-Management Questionnaire**
FCQ	**Fear of Complications Questionnaire**
FGM	**Flash Glucose Monitoring**
FSL	**FreeStyle Libre Flash Glucose Monitor**
GAD-7	**brief measure of Generalized Anxiety Disorder**
HbA1c	**Glycated hemoglobin**
HFS-II	**Hypoglycemia Fear Survey-II**
JSON	**JavaScript Object Notation**
KADIS	**Karlsburg Diabetes Management System**
mHealth	**Mobile Health**
MySQL	**Oracle MySQL database format**
PAID	**Problem Areas in Diabetes**
PHQ-9	**Patient Health Questionnaire**
PSS	**Perceived Stress Scale**
QC	**Quantification Campaign**
SPSS	**IBM SPSS Software**
T1DM	**Type 1 Diabetes Mellitus**
T2DM	**Type 2 Diabetes Mellitus**
WHO-5	**WHO-5 Well-Being Index**

Change procedure and history

This section contains the procedures for modifying the deliverable and maintaining a history of the changes.

Version	Date	Changes	From	Review
V1.0	July 5, 2017	First description of QC dataset	LUMC	LUMC, SAS, IDK, TNO
V1.1	July 20, 2017	Revisions to “First description of QC dataset”	SAS	LUMC, SAS, IDK, TNO
V1.2	July 20, 2017	Revisions to “First description of QC dataset”	TNO	LUMC, SAS, IDK, TNO
V1.3	July 20, 2017	Incorporated revisions to “First description of QC dataset”	LUMC	LUMC, SAS, IDK, TNO

SUMMARY

This deliverable provides a description of the experiences with data collection and the dataset of the Quantification Campaign. The study population consisted of 29 patients with T1DM and 31 with T2DM. Patients were recruited from outpatient clinics in Spain (SAS), the Netherlands (LUMC) and Germany (IDK). The lessons learned from the data collection by patients via mHealth devices and online questionnaires in the QC were that the FSL and Fitbit devices were appreciated by the patients and data collection worked quite well. In contrast, the Spire device garnered little positive feedback and its worse usability limited the data collection. In addition, the mobile diary used in the QC was not optimal and the patient feedback, including offline data entry and data review functionality should be taken into account with the design of the Power2DM app. This resulted in a QC dataset with high variations in data quality and missing value frequency within and between patients.

Task 6.2 involved the combination of the several data sources, including mHealth devices, online questionnaires and the preparation of the combined dataset for further analysis in T6.3. To that end the data from the mHealth devices and diary cards were merged into a single table with a 5 min epoch base. Each entry was characterised by a patient study id number, the day, hour and minute of follow-up, day of week and time of day. For each sensor signal, including blood glucose levels, heart rate, number of steps and respiratory rate, we estimated an average level per 5 min epochs over each day based on the smoothed raw data. These smoothed values will be used in the analyses and visual examination of trends in the individual patient data.

Despite the issues encountered, the QC has actually been a big success in that we produced a valuable dataset containing large amounts of continuous data for further analyses and that it has provided valuable insights into monitoring issues and the user experience of mHealth devices by patients with type 1 and type 2 diabetes. Detected problems have been an excellent source for anticipating and avoiding possible problems during EC and in making choices for the devices and the design of the Power2DM system.

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1. INTRODUCTION

The purpose of the Quantification Campaign (QC) was to ground and calibrate the predictive models with experimental data and fine tune the developed computational patient models and clinical state prediction framework. Essentially, the QC was designed to see how we could gather data necessary for predictive models using current norms of mobile health (mHealth) technologies along with traditional forms of data collection.

This deliverable provides a description of the gained experiences concerning data collection by patients via mHealth devices and online questionnaires during Power2DM's QC. We provide an overview of the dataset that was collected at the 3 study sites in Spain (SAS), Germany (IDK) and The Netherlands (LUMC). The full process lasted from February 2016 (preparation and literature review) to July 2017 (data compilation and management). Task 6.2 involved the combination of the several data sources, including mHealth devices, online questionnaires, etc. and the preparation of the combined dataset for further analysis in T6.3.

The experience with data collection in the QC and the resulting dataset will allow us to assess:

- the usability, stability, and predictive ability of the KADIS and MARVEL models
- whether new technologies can improve the usability, stability, and predictive ability of the KADIS model
- whether psychosocial barriers to self-management to guide action plan development can be identified by (standard) questionnaires
- and highlight potential data collection issues that may impede implementation of POWER2DM

2. PREPARATION OF THE QUANTIFICATION CAMPAIGN

Preparation for writing of the protocol began in February 2016 at the LUMC. At this time, the requirements of the predictive models were identified and a literature search was used to identify possible mHealth technologies and techniques that had been previously shown to be effective in tracking of these data parameters. An initial protocol was delivered to the consortium in May 2016 and a final version was agreed upon by the clinical sites and parties responsible for the predictive model aspects of Power2DM in July 2016. The original planned start date was the end of September 2016.

3. QUANTIFICATION CAMPAIGN DESIGN

The QC was an observational cohort study of three months of involvement from each participant. In this three month period there were two periods of continuous data collection: an initial four week active period (Phase 1), a six week down period with no data collection, and a follow-up two week active period (Phase 2). During the two active periods, the patients were asked to continuously gather the data required by the KADIS model as described above. Baseline measures included lab tests, and a medical history. In Phase 1, study participants performed continuous glucose monitoring using the Freestyle Libre flash glucose monitor (Abbott,USA). Other mHealth devices used were the Spire (www.spire.io) that measures stress levels based on respiratory rate and the Fitbit wristband (www.fitbit.com) which measures physical activity and sleep quality (Figure 1). In addition, daily tracking of diet, physical activity, diabetes medication usage, sleep, mood, and stress using a dedicated app developed by Power2DM partner iHealth (Table 1). Additionally, during the first 72 hours the patients conducted blood glucose monitoring using finger pricks (8/day). In addition, participants completed psychosocial evaluations related to quality of life, psychosocial barriers to self-management, emotional and disease related (dis)stress at baseline, end of week 4, and end of week 12 to identify psychosocial factors that may influence successful self-management, assess the relationship between continuous stress and glucose, and validated new translations of pre-existing questionnaires for use in the evaluation campaign. Finally, during the debrief final lab tests were taken for pre-post analysis.

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Figure 1. mHealth devices. Left: FreeStyle Libre; middle: Spire and right: Fitbit.

Table 1. Measurement schedule

Measure Name or Type (# items)	Code	Introduction visit (Baseline)	Period 1 (Week 1-4)	Period 2 (Week 11-12)
Lifestyle and Daily Monitoring	LDM			
Blood glucose level	1	Once	Continuous	Continuous
Dietary intake	2	Once	Continuous	Continuous
Physical Activity	3	Once	Continuous	Continuous
Sleep- quantity	4	Once	Continuous	Continuous
Sleep- quality (1)	5	Once	Daily	Daily
Stress-physiological	6	Once	Continuous	Continuous
Stress-perceived (1)	7	Once	6/day	6/day
Mood (1)	8	Once	6/day	6/day
Diabetes medication treatment- type/dosage/ frequency	9	Once	Daily	Daily
Questionnaires (# items)	**Q**			
WHO-5 (5)	1	Once		Once
PHQ-9 (9)	2	Once		Once
GAD-7 (7)	3	Once		Once
PSS (10)	4	Once	End week 4	Once
PAID (20)	5	Once	End week 4	Once
DSMQ-R (20)	6	Once	End week 4	Once
HFS-II (33)*	7	Once		
DEPS-R (14)*	8	Once		
FCQ (15)*	9	Once		
D-FISQ (21)*	10	Once		
ASQ (3)	11		End of Week 1 and 4	
Clinical/Lab Tests	**CLT**			
HbA1c	1	Once		Once
Fasting Glucose	2	Once		
Triglycerides	3	Once		
Cholesterol	4	Once		
HDL Cholesterol	5	Once		
LDL Cholesterol	6	Once		
Cholesterol Ratio	7	Once		
Urine-Albumin	8	Once		
Creatinine	9	Once		
Fasting insulin	10	Once		
Cortisol (hair sample)	11			Once
Patient Characteristics	**PC**			

Measure Name or Type (# items)	Code	Introduction visit (Baseline)	Period 1 (Week 1-4)	Period 2 (Week 11-12)
Anamneses: Age/ Gender/Height/Type of Diabetes /Medical History (Time since diagnosis/ Complications/ Physical examination/Comorbidities)/AS4	1	Once		
Weight	2	Once		Once
BMI (calculated from Weight and Height)	3	Once		Once
Waist	4	Once		Once
Blood pressure	5	Once		

4. STUDY POPULATION

The study population consisted of patients with T1DM (N=29) and T2DM (N=31). Patients were recruited from outpatient clinics in Spain (SAS), the Netherlands (LUMC) and Germany (IDK). To be eligible to participate in this study, a subject needed to be able to self-monitor and work with a computer and smart phone with internet connections (as assessed by researcher). Patient characteristics are shown in table 2.

Table 2. Patient characteristics

	T1DM	**T2DM**
General Descriptives		
N	29	31
Age: M (SD, range)	53 (11.89, 23-70)	59.83 (7.32, 41-73)
Sex (% Female)	41.4	41.9
Civil Status (%)		
Single	10.3	6.5
In a relationship	0	6.5
Married/In long term relationship	86.2	77.4
Separated	0	6.5
Divorced	3.4	3.2
Medical History		
Years since DM diagnosis: M (SD, range)	28.9 (16.0, 0-51)	12.07 (8.3, 1-31)
% Insulin dependent	96.6	38.7
% Using oral medication for diabetes	0	87.1

% Self-monitor glucose part of diabetes care	93.1	67.7
Reported frequency of monitoring per day M (SD, range)	1.5 (2.5, 0-7)	1.6 (3.0, 0-7)
% with Diabetes related Retinopathy	55.2	12.9
% with Diabetes related Neuropathy	31.0	6.5
% with Diabetes related Nephropathy	20.7	6.5
% with Diabetes related Macroangiopathy	24.1	3.2
% with other relevant medical conditions	51.7	12.9
% prescribed other medications	55.2	61.3
% who experience hypoglycemic events	65.5	25.8
% with intact hypo awareness	51.7	25.8

5. MHEALTH DATA COLLECTION

5.1 Data collection applications

The original data collection plan was to use the PatientCoach system for daily tracking of self-management. Upon further testing, the PatientCoach system was unable to provide the functionality for a mobile diary card. iHealth agreed to assist the project by building a data mobile diary card for the QC. The initial application was delivered in December 2016. A major revision followed in February 2017 (Figure 2). When major technical difficulties were encountered by patients they continued their data collection on paper. The data collection via the online questionnaires and the Fitbit and Spire devices could be monitored by the PatientCoach researcher portal (Figure 3). With the PatientCoach researcher portal we could also monitor the intraday variations in physical activity (steps and heart rate) with Fitbit and respiratory rate by the Spire device in individual patients.

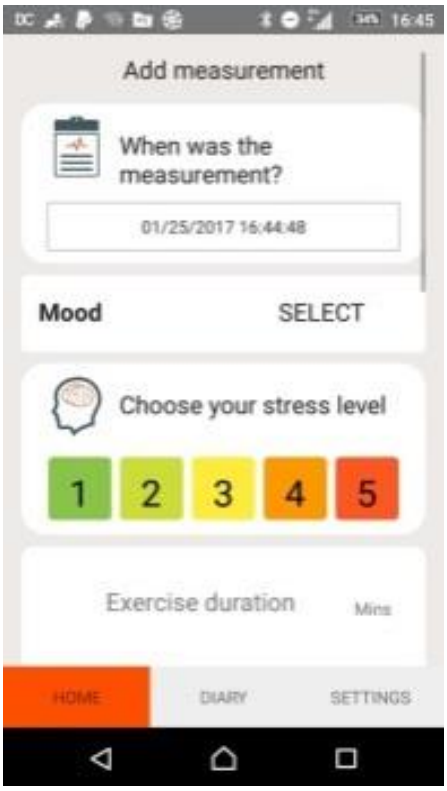

Figure 2. iHealth mobile diary app

Figure 3. PatientCoach researcher portal: overview patients

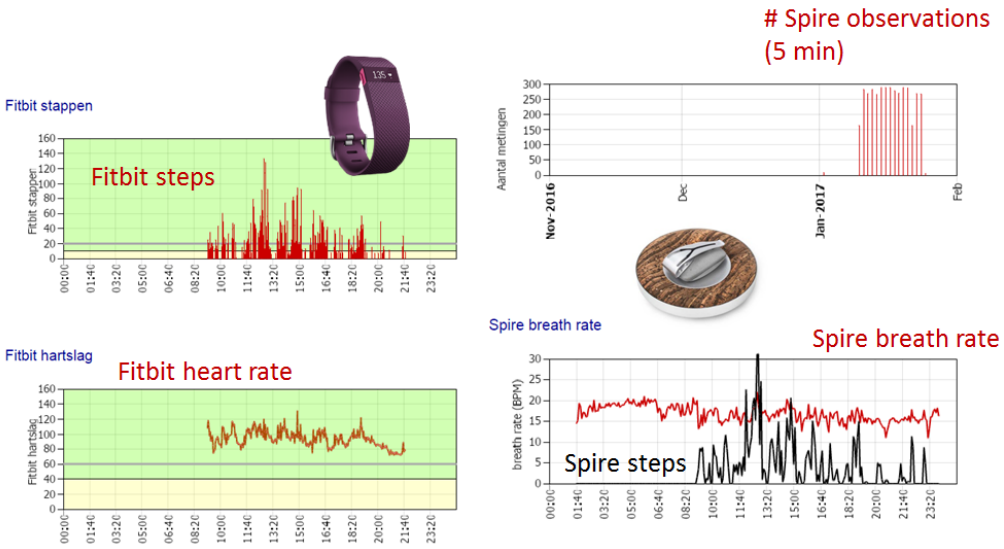

Figure 4. PatientCoach researcher portal: intraday monitoring of physical activity (steps and heart rate) with Fitbit and respiratory rate by the Spire device.

5.2 Study Site Experiences

The following section is a brief review of the experiences reported by each clinical site and the experience of the LUMC as QC organizer in working with these sites. The LUMC provided instructions for professionals and patients and provided helpdesk and backup support. At each site professionals guided, examined, and revised the progress of the study for each patient, evaluating if they had correctly used the system, and the results of the program. This allowed us to collect and evaluate user feedback on the usability and usefulness of the components patients' empowerment.

5.2.1 Patient identification and start

Patient identification began in the end of 2016 and went through March 2017. Potential participants were identified the patients' treating physicians. Patients were provided with information regarding the study and asked if they would like to come in for an information session. A typical initial intake session lasted around 2.5 hours in which the patients signed an informed consent letter, completed the CRF and baseline questionnaires, a full physical examination was conducted, and blood samples were taken. Additionally, patients (when technically capable) or researchers set up all devices on the mobile phone of the participant and the participant received instruction on their use. At some points, multiple patients were included during the same session.

5.2.2 Phases review

Phase 1: Initial problems regarding difficulties setting up the patients and connecting all the devices to the PatientCoach platform were resolved in real-time by researchers at SAS, LUMC and IDK. One of the major obstacles encountered was that the mobile devices of the participants were not always compatible with the mHealth devices and applications being used in the study. Some difficulties related to language issues were encountered by the researchers when explaining what the patients would have to do during the study. To overcome this issue, LUMC patients with non-compatible mobile phones were given an iPod for use during the study. Beyond this, no serious issues were encountered related to the requirements of the study.

Phase 2: No major issues as all problems related to the data collection were resolved or anticipated after Phase 1. All SAS and LUMC patients in this stage collected their self-management information on paper and the final review went well. However, there were difficulties in data collection by patients at IDK due to the availability of supporting personnel and logistic issues.

5.2.3 Device acceptance and usage

FreeStyle Libre (FSL): The FSL was almost universally accepted and praised by the participants. Many reported that they liked how easy it made self-monitoring of glucose levels in their daily management. Three patients reported losing the sensors. Two reported the loss as having occurred during or after manual labour when they believed sweat loosened the sensor and physical contact knocked it off. One patient lost three sensors in Phase 1. He believes this is due to the frequency with which he showers. One patient reported that it did not add much to their self-management as they did not check often before and felt that having the sensor on made him feel that he had to check more often then he would have liked to. This frequent checking and better insight into his glucose level was distressing as before he could say that if he felt fine then that was good enough but now he was inclined to see what his glucose levels actually were when he normally would not have checked. Many type 2 diabetic patients reported that this device helped them to have a better insight of their disease, and to engage to a healthier lifestyle.

Fitbit: The Fitbit device was well received by the patients. Most patients found it interesting to receive the feedback on activity that the Fitbit provided. Two Fitbits had to be replaced due to issues regarding connectivity. SAS reported little issue in connecting this device to the mobile phones of the patients. Issues were reported regarding connecting the accounts to PatientCoach to allow for data aggregation but these were resolved in cooperation with LUMC.

Spire: The Spire garnered little positive feedback from the participants. Many viewed it as a nuisance or didn't regard it at all outside of putting it on their clothing. Three participants lost the device due to the rubber grip falling off after repeated use. The devices did not connect well initially to the smartphone and later issues related to connectivity were repeatedly experienced. The patients reported finding the device annoying.

Data collection app: Many technical issues were reported regarding the mobile application, including repeated log-in failures or that it simply did not work in some of the worst cases. Additionally, patients reported not being able to save data or see an overview of the data that they had already filled in. Connectivity errors in reaching the network were frustrating and a frequent reason for participants to contact the researchers to inquire as to what should happen. Therefore, the mobile diary should also facilitate offline data entry with later synchronisation. When the application did not work the patients were instructed to track their self-management on paper using a provided logbook. All SAS and LUMC patients used on the paper diary during Phase 2. There were difficulties in data collection on a paper diary in

patients at IDK. One IDK patient wrote a letter to communicate his dislike with the Project, finding it useless and annoying as a part of his treatment. Patients found data collection very time intensive. Data quality ranges from minimum notations to highly detailed reports. Still, patients seemed to find tracking beneficial and in general liked it.

Follow up-questionnaires: The automatic links that were sent to deliver follow-up questionnaires did not work in some instances or were missed by the patients. Therefore, the researchers still had to deliver the questionnaires on paper to many patients.

5.2.4 Dropouts, (Serious) Adverse events

SAS reported no adverse events, serious or otherwise. They did have three patient dropouts. Two patients dropped out during Phase 1 (one due to relocation, one due to severe depression), and lost one patient to follow-up in Phase 2. At the LUMC, one patient reported an adverse reaction to the strap of the Fitbit activity trackers. A rash was experienced where the strap contacted the skin. The patient was able to resolve this issue through the use of over-the-counter medications. The LUMC also lost one-patient to follow-up in Phase 1. At IDK one patient passed away prior to the completion of Phase 2 due to a stroke.

6. DATA MANAGEMENT

Task 6.2 involved the combination of the several data sources, including mHealth devices, online questionnaires, etc. and the preparation of the combined dataset for further analysis in Task 6.3. Data from the anonymous FSL accounts were exported to ".csv" files at each site and transferred to LUMC. Other online data that were collected using anonymous accounts at the 3 study sites (Spain, Germany and The Netherlands) were stored on PatientCoach servers at LUMC. Paper diaries and questionnaires were transferred to LUMC and data entry is ongoing. The next step was the transformation of the different data formats (e.g. MySQL, csv, SPSS) using StatTransfer (www.stattransfer.com) to a single format to enable combination of the different tables in STATA 14.0 (software for statistical analysis and data management www.stata.com) for further analyses. The syntaxes for data cleaning and merging of the tables from various sources and tables were developed using STATA. This resulted in a number of tables that can be used in further statistical analyses.

These tables include the baseline data (Clinical/Lab Tests) and questionnaire data from baseline and follow-up. The data from the mHealth devices and diary cards were merged into a single table with a 5 min epoch base. Each entry was characterised by a patient study id, the day, hour and minute of follow-up, day of week and time of day. For each sensor signal, including blood glucose levels, heart rate, number of steps and respiratory rate, we estimated

an average level per 5 min epochs over each day based on the smoothed raw data. These smoothed values will be used in the analyses and visual examination of trends in the individual patient data. To that end, we created graphs per patient per day showing blood glucose levels with medication usage, physical activity (heart rate and number of steps) and respiratory rate (Figure 5). In addition, this table forms the basis for the generation of JSON output by STATA syntax that can be directly fed into the KADIS model by IDK to run the model with different inputs, including exercise data from Fitbit or manually registered diary card data (Figure 6 & 7).

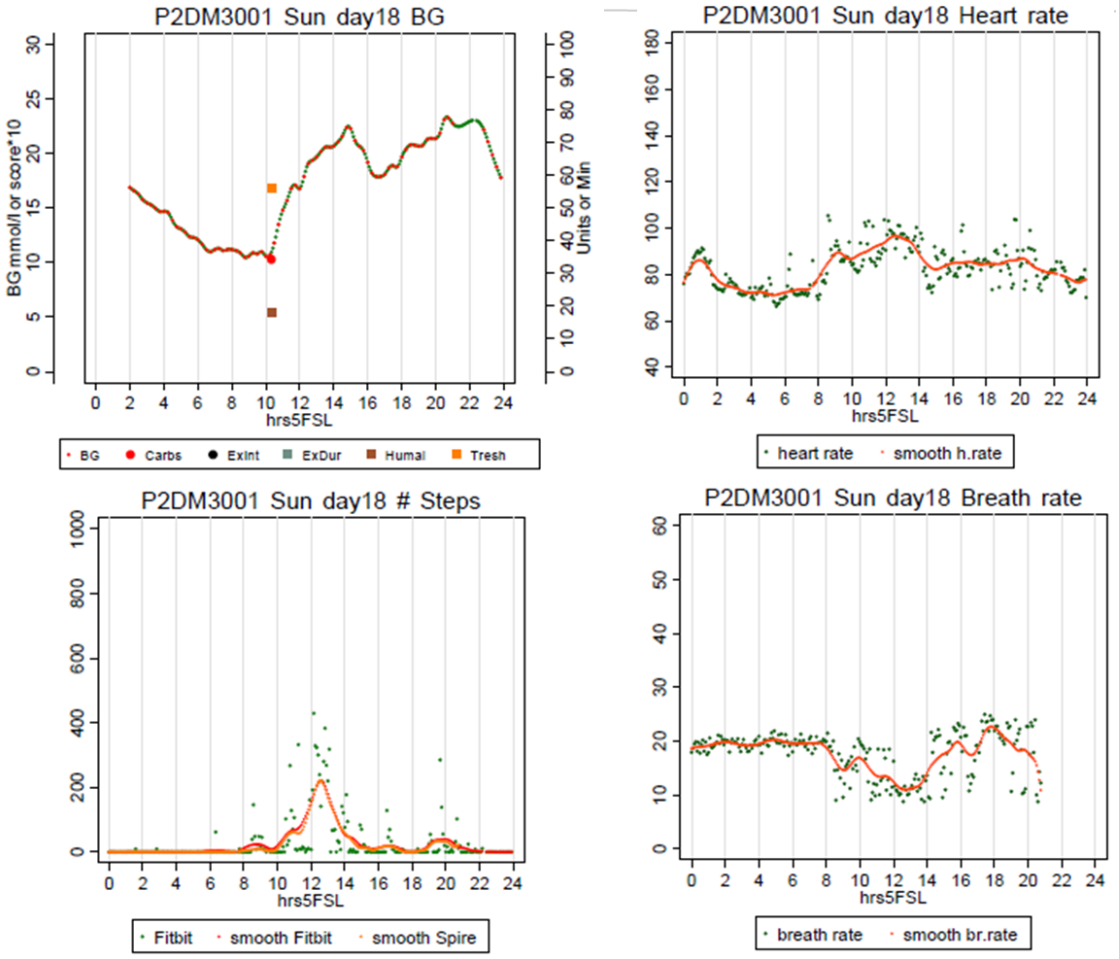

Figure 5. Visual examination of trends in individual patient data: blood glucose levels with medication usage and carbs intake, heart rate, number of steps and respiratory rate

```
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   "identifier": "99993001",
   "diabtyp": "Typ2",
   "diabseit": "2002",
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   "glp1": "0",
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          "form": "kurz",
          "mix": "",
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      },
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Figure 6. Example of JSON output generated by STATA syntax for the KADIS model

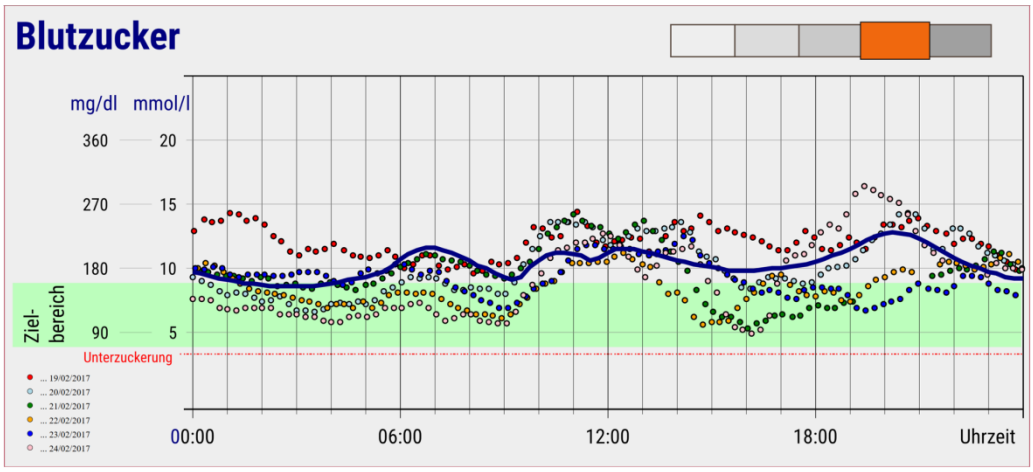

Figure 7. Example KADIS graph based on 6 days FSL data from the QC

7. DATA ANALYSIS PLAN

Currently, the KADIS model is based on data from an initial 72 hour period which is used to create a metabolic fingerprint. Data from the total QC period will be used to see to what extent additional parameters such as day of week and physical activity based on Fitbit heart rate and number of steps, stress levels or a 1-week basis of the model improve the accuracy of the KADIS model. The purpose of the 2 week monitoring in phase 2 of follow-up is to check the long-term stability of the KADIS model predictions based on data gathered in phase 1. To that end, KADIS blood glucose model predictions will be compared with actual measured blood glucose levels measured by FSL.

8. CONCLUSIONS

The lessons learned from the data collection by patients via mHealth devices and online questionnaires QC were that the FSL and Fitbit devices were appreciated by the patients and data collection worked quite well. In contrast, the Spire device garnered little positive feedback and its worse usability frustrated the data collection. In addition, the mobile diary used in the QC was not optimal and the patient feedback, including offline data entry and data review functionality should be considered with the design of the Power2DM app. Since the resulting dataset shows high variations in data quality and frequency of missing values within and between patients we produced smoothed values of sensor signals that will be used in further analyses and visual examination of trends in the individual patient data. The QC has been successfully in the sense that we produced a valuable dataset for further analyses and that it has provided valuable insights into monitoring issues and the user experience of mHealth devices by patients with type 1 and type 2 diabetes. This helps making choices for devices and the design of the Power2DM system.