POWER2DM

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

Research and Innovation Project
PHC 28 – 2015: Self-management of health and disease and decision support systems based on predictive computer modelling used by the patient him or herself

POWER2DM D2.1

D2.2.1. Short-term Predictive Component

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PP	Restricted to other programme participants (including the Commission Services)	
RE	Restricted to a group specified by the consortium (including the Commission Services)	
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POWER2DM Consortium Partners

Abbv	Participant Organization Name	Country
TNO	Nederlandse Organisatie voor Toegepast Natuurwetenschappelijk Onderzoek	Netherlands
IDK	Institute of Diabetes “Gerhardt Katsch” Karlsburg	Germany
SRDC	SRDC Yazilim Arastirma ve Gelistirme ve Danismanlik Ticaret Limited Sirketi	Turkey
LUMC	Leiden University Medical Center	Netherlands
SAS	SAS Servicio Andaluz de Salud	Spain
SRFG	Salzburg Research Forschungs Gesellschaft	Austria
PD	PrimeData	Netherlands
iHealth	iHealth EU	France

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1 Introduction

The primary goal of work packed WP2 is to develop innovative programs, modules, and tools for short-term (Task 2.1) and long-term (Task 2.2) risk detection and risk prevention (Task 2.3) in personalized diabetes care and management by supporting patients efficiently in diabetes home monitoring and diabetes home care with patient-centered, real time decision support systems (DSS) which can finally be implemented into mobile-phone-based self-management equipments (Task 2.4). To meet these goals WP2 comprises the following objectives, tasks, and deliverables:

Objectives

- Development of innovative programs, modules, and tools for short-term risk detection and risk prevention
- Development of innovative programs, modules, and tools for mid- and long-term risk detection and risk prevention
- Designing patient-centered, real time decision support systems for assisted diabetes home monitoring and diabetes home care
- Implementation into mobile-phone-based self-management equipments for visualization of predictions/simulations

Tasks

- T2.1 Calibration of short-term predictive model KADIS® – IDK, iHealth, LUMC
- T2.2 Calibration of medium-to-long-term predictive models MT2D-Marvel and Risk Scores – TNO, iHealth
- T2.3 Development of patient-centered prediction services – IDK, iHealth, TNO, PD
- T2.4 Visualization of predictions and simulations – SRDC, IDK, PD, TNO, LUMC, SAS

Deliverables

- D2.1.1 Short-term predictive component – M10
- D2.2.1 Mid-and-long-term predictive component – M10
- D2.3.1 POWER2DM integrated prediction service and API – M15, 21, 28
- D2.4.1 Mockups for GUI components – M8
- D2.4.2 Web-based GUI components for visualization of predictions/simulations – M21, 28
- D2.4.3 Mobile GUI components for visualization of prediction/simulations - M21, 28

This deliverable reports on **Task 2.1**.

1.1 Purpose and Scope

The purpose of Task 2.1 "Calibration of Short-term Predictive Model KADIS®" is to:
a· define inputs and outputs of a home monitoring tool for the model of a real time, patient-centred predictive DSS module (IDK, LUMC)
b· develop a problem related, personalized home monitoring module (IDK, iHealth)
c· define a personalized risk stratification module (IDK)
d· validate that the data quality from the pilot settings meets standards to properly drive the KADIS® model for the intended functionalities in the POWER2DM SMSS (IDK)

In the past period, R&D work of the IDK was concentrated on subtasks a and c.

1.2 Reference Documents

- POWER2DM Description of Work (Proposal)
- D1.1 User Requirements and Use Case Scenarios
- D1.2 Requirements Specification of the POWER2DM Architecture
- D1.3 Conceptual Design of the POWER2DM Architecture
- D2.2 Mid- and Long-term Predictive Component
- D2.5 Mockups for GUI Components

1.3 Definitions and Acronyms

Table 1: List of Abbreviations and Acronyms

Abbreviation/ Acronym	DEFINITION
CGM	Continuous glucose measurement
SMBG	Self-monitoring blood glucose
GUI	Graphical User Interface
API	Application programming interface
cDGP	Current daily glucose profile
tDGP	Target daily glucose profile
BG	Blood glucose
SDM	POWER2DM Shared Decision Making Application
SK-data	Self control data of glucose monitoring
SMSS	POWER2DM Self-Management Support System

2 Short-term Prediction Model

2.1 Introduction

Health care is shifting towards personalized health and patient/citizen empowerment. There is a great need for tools that provide personally relevant health awareness and motivate behavior change. Forecasting models showing anticipated changes in health parameters over time, based on the current health status and different behavior scenarios, can provide such health awareness. These models are only relevant when both individual health parameters as well as environmental variables are incorporated. Whereas the MT2D-Marvel model is such a novel multi-domain type 2 diabetes (T2D) forecasting model intended for an intermediate timescale (months-years), the KADIS® model does so for the short term (i.e., days) prediction of the metabolic outcome to be expected in a given diabetic patient.

2.2 KADIS® Model

2.2.1 Background

The KADIS® model based diabetes decision support programs and e-health diabetes care services were developed in the IDK over a period of about three decades by performing extended and innovative research and development activities. The world wide unique, patented KADIS® program supports initially primary care providers in their outpatient settings by patient-focused visualization and evaluation of the current metabolic situation of a given individual patient and by predicting the outcome of metabolic control in association with therapeutic interventions.

Assessment of each patients´s individual metabolic situation requires only an input of baseline characteristics, such as insulin dosage, caloric intake, and physical activity and a patient-related, individually characteristic daily glucose profile. As a therapy simulator, the KADIS®-based personalized decision support program assists physicians in choosing quick and save individually related diabetes management regimes that are most appropriate for achieving patient-focused glycaemic targets.

Several national and international pilot studies, including in the United Arab Emirates, have convincingly demonstrated, that in patients with insufficient glycaemic control, HbA1c can be significantly reduced by up to 1.5% if KADIS®-based decision support is implemented in diabetes care and management.

Since 2007 KADIS®-based decision support has been permanently and successfully used in Germany by about 300 physicians within routine diabetes health care for about 1.000 diabetic patients. The convincing results from running the KADIS®-based decision support program revealed a mean benefit in HbA1c of about 0.9% and an annual cost reduction of up to 900 Euro per patient.

Progress in the development of KADIS® model based versions applicable for patient empowerment as planned in the POWER2DM project within the subtasks a and c, including examples of screenshots of implementation of the KADIS® based prediction services, is described below.

3 WP2 Progress – Task 2.1

- What was planned?
  - **Objective:** Provide a personalized home supporting tool for KADIS®-based short-term risk detection and risk prevention
  - **Task:** T2.1 - Definition of Inputs and Outputs of a Home Monitoring Module (IDK, LUMC)
    - Development of a Home Monitoring Module (IDK, iHealth)
    - Definition of a personalized Risk Stratification Modul (IDK)
    - Validation of data quality to properly drive the KADIS® model
  - **Deliverable:** T2.1 Short-term Predictive Components

- What is done?
  - **Inputs and Outputs of the KADIS® Home Monitoring Modul are defined**
  - **First Draft of the KADIS® Home Monitoring Module are developed and programmed –** continuation of discussion for implementation in daily blood glucose management
  - **Risk Stratification Modul is defined**
  - **Concept of a Validation Strategy was generated-** continuation of discussion for implementation in daily blood glucose management

3.1 Definition of Inputs and Outputs of a Home Monitoring Module

3.1.1 Inputs of the KADIS® Home Monitoring Module

Inputs of the KADIS® Home Monitoring Module:

Measured Glucose Data: structured finger stick measurements or FreeStyle Libre (FSL), Fig. 1

Basic Data (Age, Gender, Type of Diabetes, Onset of Diabetes, BMI), Fig. 2

Self Control Data (SK-Data):

Medications: - Insulin (type, time, dosage)
- OAD (type, time, dosage)
Meals (time, quantity)
Regular Exercise (time, duration, quantity)

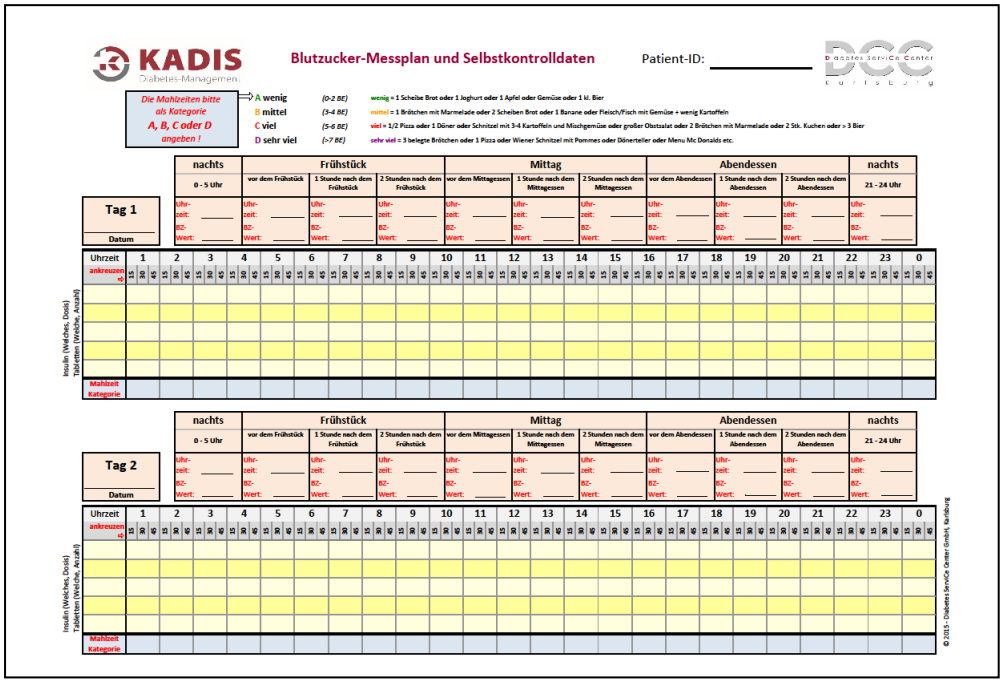

Fig. 1: Input data sheet for measured glucose data and SK-data

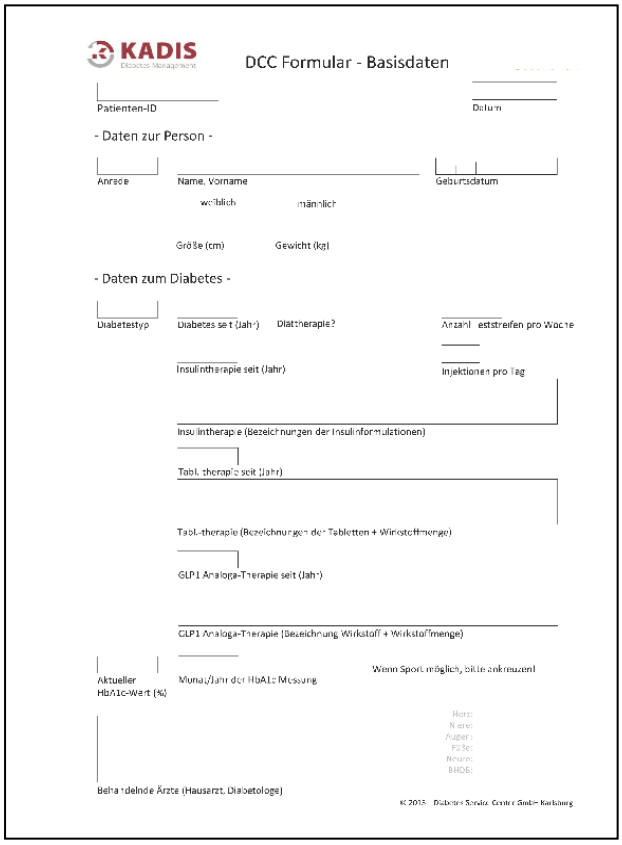

Fig.2: Input data sheet for basis data

3.1.2 Outputs of the KADIS® Home Monitoring Module

Outputs of the KADIS® Home Monitoring Module:

KADIS®-based calculated individual current Daily Glucose Profile (cDGP)
(from structured finger stick measurements or FSL), Fig. 3 and Fig. 4

Short-Time Risk Evaluation of the cDGP (Q-Score), see (sub)task 3.3

KADIS®-based prediction of the individual Target Daily Glucose Profile (tDGP) including Personalized Supporting Tools for the Glucose Self Management in order to meet the tDGP (Fig.5):

- Insulin Bolus Calculator
- Meal Adaptation Calculator
- Calculation of Insulin Dose Equivalents of Exercise

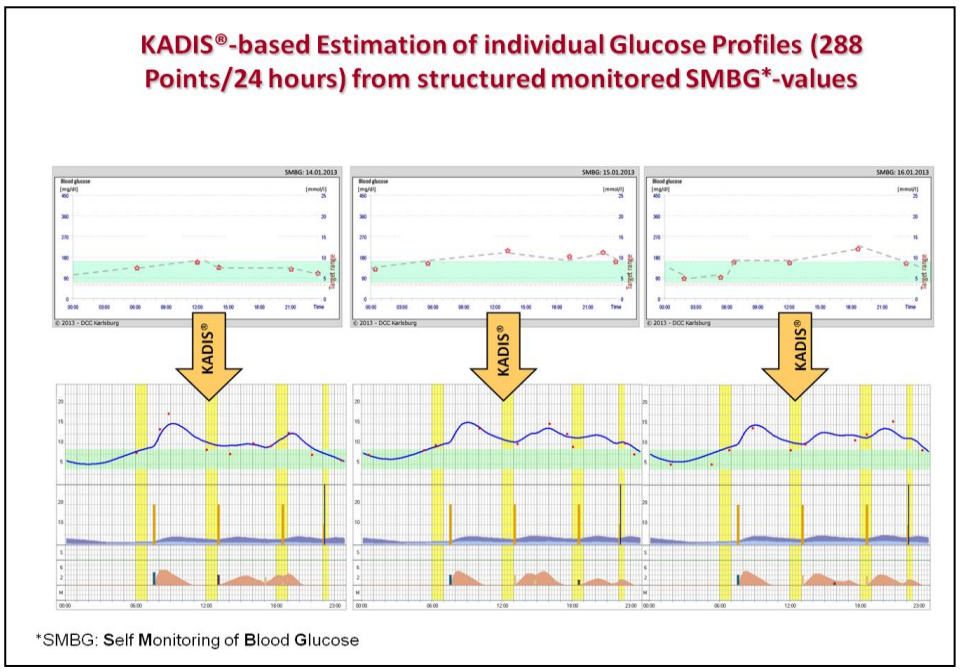

Fig. 3: KADIS®-based calculation of the current Daily Glucose Profiles (cDGP) from structured measured SMBG values on three subsequent days

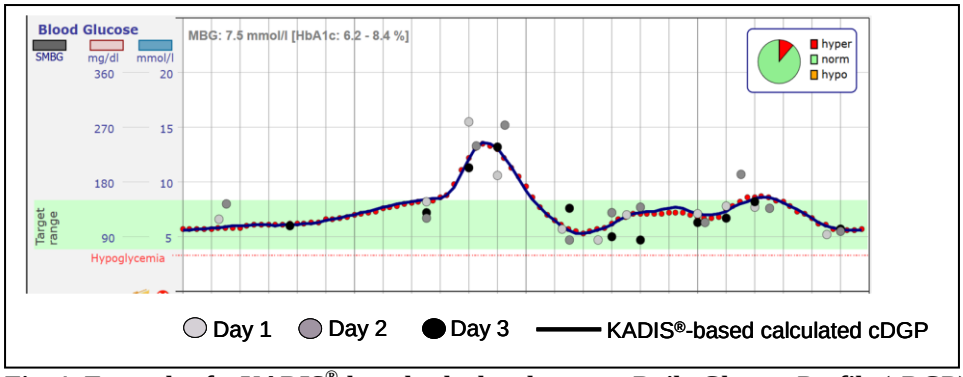

Fig. 4: Example of a KADIS®-based calculated current Daily Glucose Profile (cDGP)

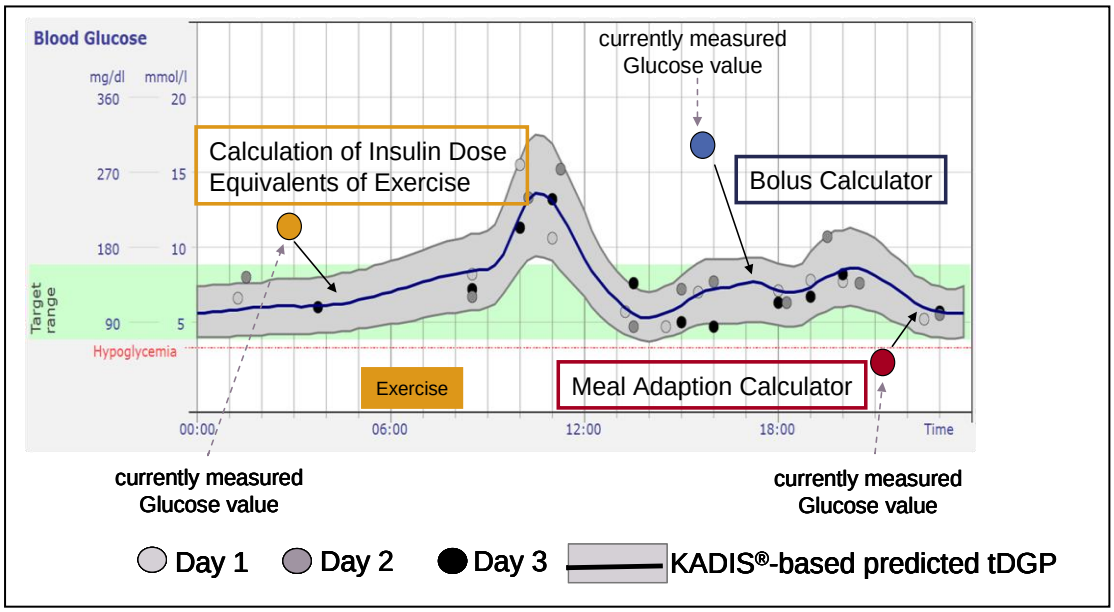

Fig. 5: Concept for the development of KADIS®-based short-term prediction tools, which support personalized daily glucose management

3.2 Development of a Home Monitoring Module

In (sub)task 3.2 the development, programming, and implementation of the input data sheets into patient-centred e-health devices were started by definition of the KADIS® data upload protocol (Appendix 1) and designing and testing a first prototype draft versions of a Home Monitoring Module, which will be implemented in mobile-phone-based self-management Home Monitoring Devices (Fig. 6).

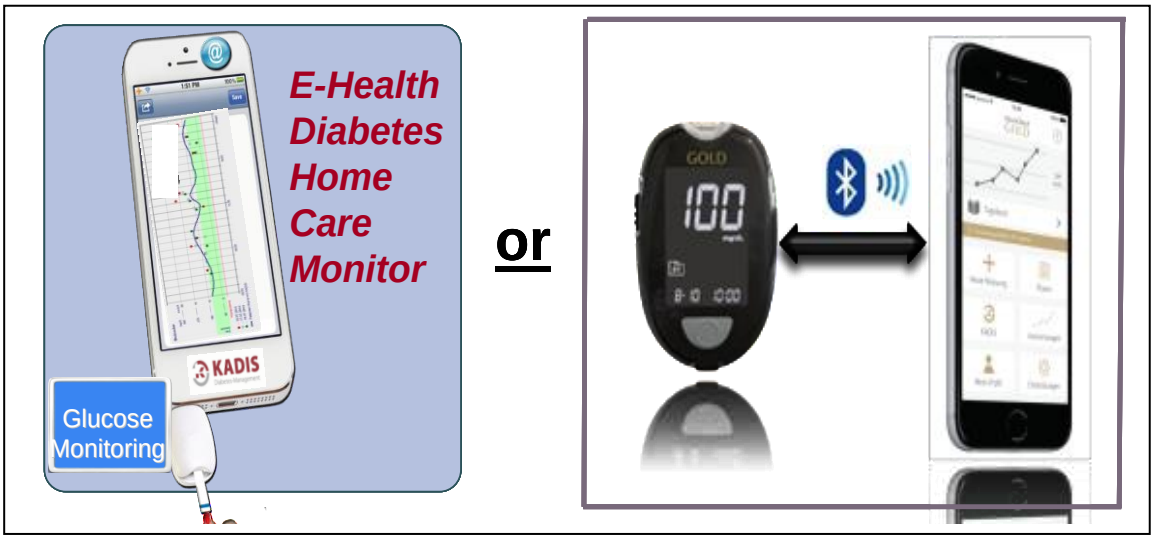

Fig. 6: E-Health Diabetes Home Monitoring Devices (conceptual phase)

3.3 Definition of a personalized Risk Stratification Module

In (sub)task 3.3 a metric for automated, objective evaluations of glucose profiles was developed, called the Q-Score. The Q-Score comprises the 5 most important factors describing a glucose profile: central tendency(MBG); time in hyperglycaemia (t_{hyper}), time in hypoglycaemia (t_{hypo}) intra-daily variation (RANGE), and inter-daily variation (MODD). Therefore, the Q-Score provides global information on glucose profiles, summarised in one value (Fig. 7, Fig. 8, and Fig. 9). The Q-Score can be categorised, and is suitable for screening profiles of individuals with insufficient metabolic control. In addition, it allows identification of factor(s) underlying the profiles that are mainly responsible for the quality of metabolic control in a given patient. Those parameters with improvement potential can be identified and addressed by therapeutic actions. Therefore, the Q-Score may efficiently contribute to designing a personalized Risk Stratification Module to support patient-tailored diabetes care and management (Fig. 10).

The Q-Score is an efficient short-term indicator for evaluating glycaemic control by automated evaluation of the potential risk inherent in KADIS®-based calculated or FSL-based measured cDGPs. The Q-Score is the first available unified metric for automated, objective evaluations of glucose profiles that considers all essential aspects of measured glucose concentrations. The Q-Score is a promising development, because it is a simple way to combine many different types of information acquired by reading and analysing glucose profiles. The Q-Score automatically categorize cDGPs in no risk, low risk, moderate risk, high risk, and dangerous risk (Fig. 9), and therefore, it is the first objective short-term metric that can automatically describe and evaluate cDGPs. The Q-Score can be calculated readily, and is independent of subjectively influenced evaluation procedures. In addition, the Q-Score allows identification of risk factors and potential of improvements underlying the glucose profiles that are mainly responsible for the quality of short-term metabolic control in a given patient. Therefore, the Q-Score can after implementation in a mobile-phone-based self-management Home Monitoring Device (Fig. 11) efficiently contribute to designing strategies for patient-tailored short-term diabetes care and management.

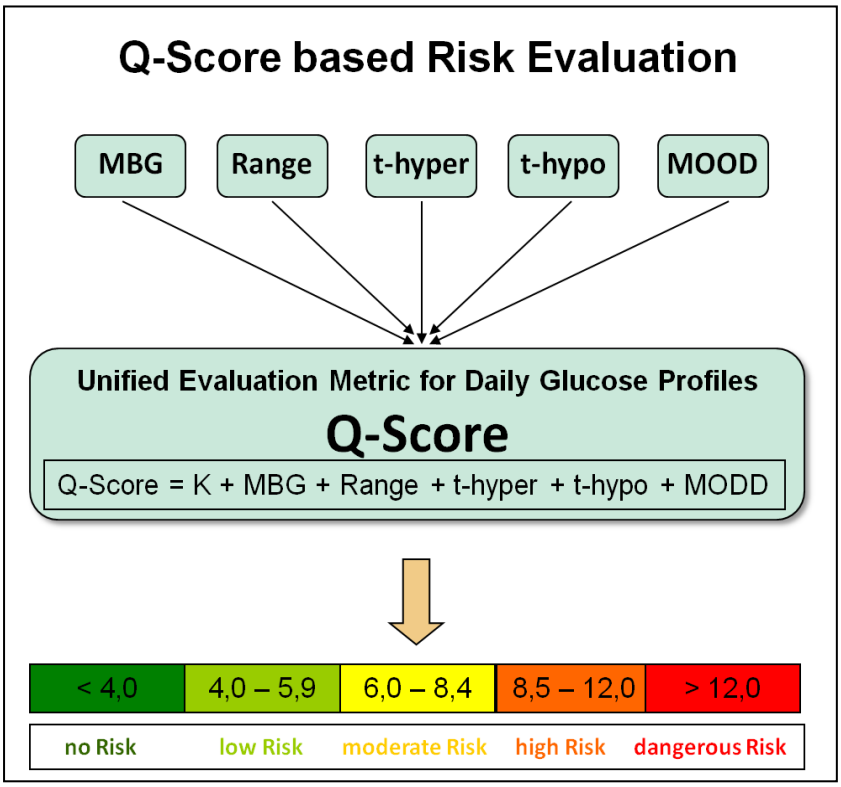

Fig. 7: The Q-Score, unified evaluation and risk stratification metric for glucose profiles

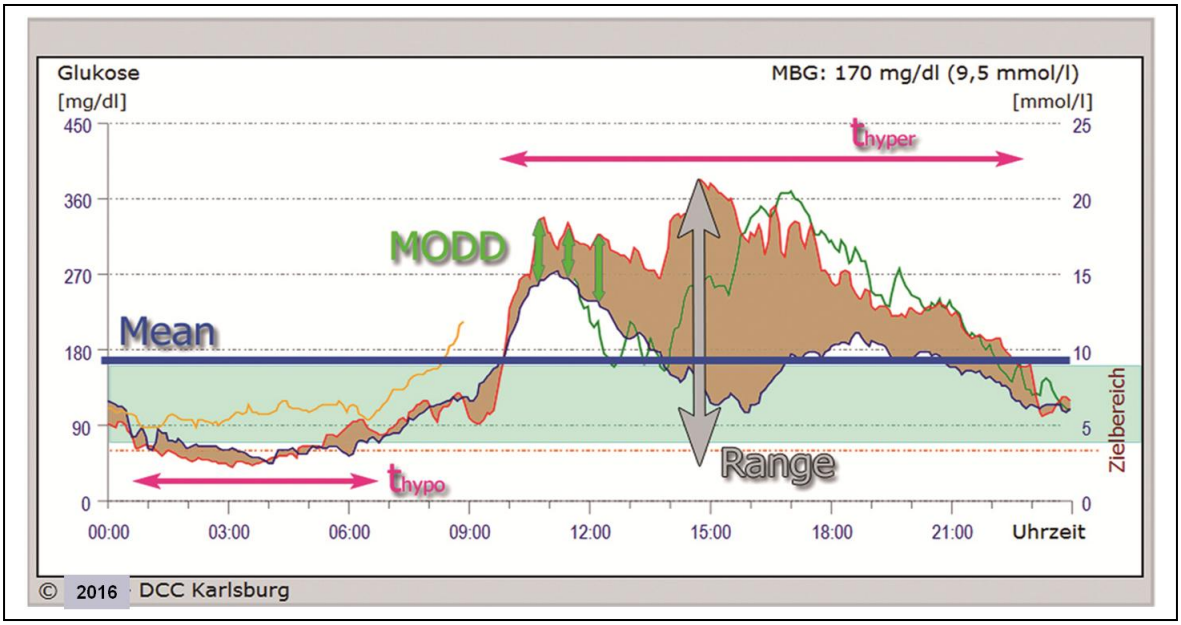

Fig. 8: Components of the Q-Score

Q-Score	Category	Criteria
< 4	**no risk**	Glycaemia completely within the target range, negligible glycaemic variability, no hypoglycaemic events
4.0 – 5.9	**low risk**	Glycaemia mostly within the target range (80–100%), low variability, no hypoglycaemic episodes
6.0 – 8.4	**moderate risk**	Glycaemia partially outside the target range (20-50%), reasonable variability
8.5 –11.9	**high risk**	Glycaemia often outside the target range (5-80%), high variability, hypoglycaemic episodes can occur
> 12.0	**dangerous risk**	Glycaemia mostly outside the target range (>80%), very high variability, hypoglycaemic episodes occur

Fig. 9: Q-Score based Risk Evaluation Criteria

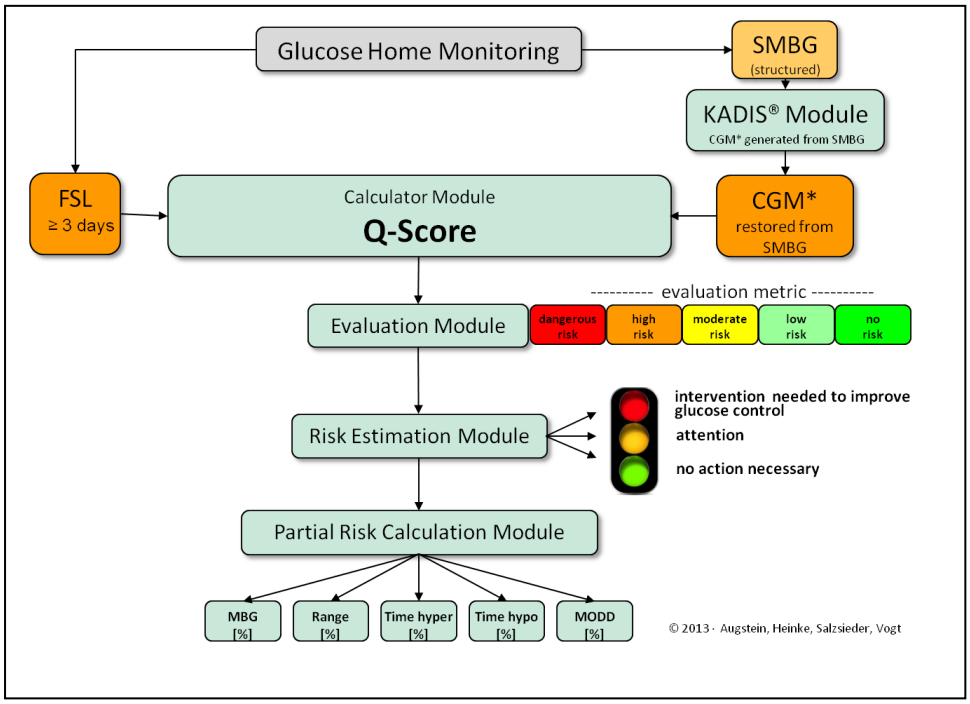

Fig. 10: Definition of a personalized Risk Stratification Module

Fig. 11: Conceptual Design for Implementing the Q-Score based Risk Evaluation Tool into a Mobile Device for Daily Glucos Management

3.4 Validation of Data Quality to Properly Drive the KADIS® Model

In (sub)task 3.4 was a first version of the basic strategy for validation of the KADIS®-based short-term decision support services defined (Fig. 12). The basic structure of the validation strategy comprises the following main components:

- a structured home glucose monitoring which is to perform first,
- KADIS®-based analysis and evaluation of the monitored data to generate the cDGP and the Q-Score based risk metric for the patient and the KADIS® Report for the responsible physician of the patient with recommendation for optimizing personalized metabolic control,
- KADIS®-based short term home care support for the patient after physicians visit by applying the supporting tools to be developed in POWER2DM.

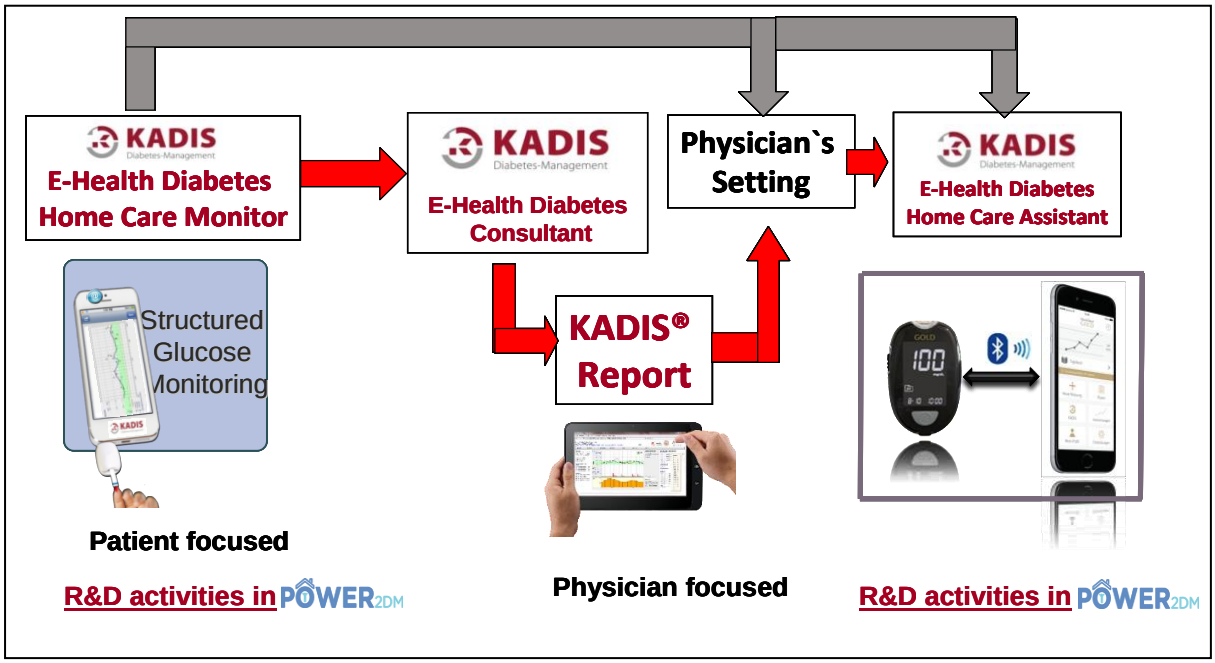

Fig. 12: Conceptual Design of the Basic Structure of the Planned Validation Strategy

3 Literature

Williams JS, Walker RJ, Smalls BL, Hill R, Egede LE. Pateint-centered care, glycemic control, diabetes self-care, and quality of life in adults with type 2 diabetes. Diabetes Technology &Terapeutics; 2016, 18: 1-6.

Williams G, Lynch, M, Glasgow R. Computer-assisted intervention improves patient-centered diabetes care by increasing autonomy support. Health Psychol 2007; 26: 728-734.

Geade P, Oellgaard J, Carstensen B, et al. Years of life gained by multifactorial interventioo in patients with type 2 diabetes mellitus and microalbuminuria: 21 years follow-up on the Steno-2 randomised trial. Diabetologia 2016; 59: 2298.

Appendix 1: KADIS® Data Upload Protocol

KADIS®/TeleDIAB® Data Protocol

Data needed for the KADIS®-based calculation of cDGP and subsequently the "Metabolic Fingerprint" (only for physicians) and to provide the ability to perform simulation on the TeleDIAB® platform should be done by using the JSON format. In the following an example and descriptions in more detailed form is presented.

Example of monitoring data in JSON format:


```
{
	"publicID": "P-19691250",
	"diabtype": "Typ2",
	"diabsince":1993,
	"height":162,
	"weight":114,
	"age":72,
	"gender": "f",
	"mData":[
		{
			"datetime": "24/03/2016 03:00",
			"smbg":234,
			"meal": "C",
			"insulin":[
				{
					"insname": "Apidra",
					"insform": "short",
					"insmix": "",
					"insdosis":20
				}
			],
			"oad":[
				{
					"oadsubstance": "Sitagliptin",
					"oaddosis": "100",
					"number":1.0
				}
			],
			"glp1":{
				"glp1substance": "Liraglutide",
				"glp1dosis":1.8
			},
			"exercise":{
				"intensity": "normal",
				"duration":60
			},

			"event": "Party"
		},{
			"datetime": "24/03/2016 06:00",
			"smbg":234,
			"meal": "C",
			"insulin":[
				{
					"insname": "Apidra",
					"insform": "short",
					"insmix": "",
					"insdosis":20
				}
			],
```

```
                "oad":[
                        {
                                "oadsubstance": "Sitagliptin",
                                "oaddosis": "100",
                                "number":1.0
                        }
                ],
                "glp1":{
                        "glp1substance": "Liraglutide",
                        "glp1dosis":1.8
                }
        }
    ]
}
```


Data descriptions:

Data name	Data type	Valuelist	Description
publicID	string		A unique ID (string) for patient identification
diabtype	string	Type1, Type2, LADA	Diabetes type
diabsince	integer		Year of diabetes onset
height	integer		Body height in cm
weight	integer		Body weight in kg
age	integer		
gender	string	f, m	
datetime	string		Date and time of glucose measurement, meal intake, medication (insulin, OAD, GLP1 analogues), event
SMBG	integer		Glucose value in mg/dl (test strip measurement)
meal	string	A,B,C,D	Amount of CHO in the meal (A: small, B: normal, C: high, D: very high)
insname	string	See list	Name of the insulin
insform	string	short, regular, basal, long, extralong, mix, analogamix	
insmix	string	10:90,20:80,30:70,50:50	
insdosis	float		Insulin dosage in IU
OADsubstance	string	See list	Name of the OHA action substance
OADdosis	float		
number	float		Number of pills
GLP1substance	string	See list	Name of the GLP-1 analogue
GLP1dosis	float		
exeduration	integer		Duration of exercise in minutes
exeintensity	string	low, normal, intensive	
event	string		

List of insulins

Name	**Mix**	**form**
Abasaglar		long
Actraphane H	30/70	mix
Actraphane HM	10/90	mix
Actraphane HM	20/80	mix
Actraphane HM	30/70	mix
Actraphane HM	40/60	mix
Actraphane HM	50/50	mix

Actrapid		regular
Actrapid HM		short
Actrapid Human		short
Apidra		short
B-Insulin S		basal
B-Insulin S.C.		basal
B. Braun ratioph. Rapid		regular
Berlinsulin H	20/80	mix
Berlinsulin H	30/70	mix
Berlinsulin H Basal		basal
Berlinsulin H Normal		regular
Berlinsulin H Normal		regular
Depot-Insulin		long
Humaject Basal		basal
Humaject Normal		short
Humaject Prof. III	30/70	mix
Humalog		short
Humalog Mix	25/75	analogamix
Humalog Mix	50/50	analogamix
Huminsulin		short
Huminsulin Basal		basal
Huminsulin H	30/70	mix
Huminsulin Normal		regular
Huminsulin Prof. II	20/80	mix
Huminsulin Prof. III	30/70	mix
Humulin L		long
Hypurin Bovine Lente		long
Ins. B. Braun		basal
Ins. B. Braun Comb	30/70	mix
Ins. B. Braun Rapid		regular
Insulatard		long
Insulatard Human		basal
Insulin S		regular
Insulin S.N.C.		regular
Insuman Basal		basal
Insuman Comb	25/75	mix
Insuman Comb	50/50	mix
Insuman Comb	15/85	mix
Insuman Infusat		short
Insuman Rapid		regular
Insumen		short
Lantus		long
Levemir		long
Liprolog		short
Liprolog Mix	25/75	analogamix
Liprolog Mix	50/50	analogamix
Mixtard Human	30/70	mix
Monotard HM		basal
Novo Nordisc		regular
Novo Semilente MC		basal

NovoMix	30/70 analogamix
NovoRapid	short
Protaphane	basal
Protaphane HM	basal
Toujeo	extralong
Tresiba	long
Ultratard HM	long
Velasulin	regular

List of OAD action substances

Action substance/ combination	
Acarbose	50, 100,150, 500 mg
Canagliflozin	100, 300 mg
Dapagliflozin	5, 10 mg
Empagliflozin	10, 25 mg
Glibenclamid	1, 1.75, 3.5, 5, 7 mg
Glibornurid	1 mg
Gliclazid	30, 60, 80 mg
Gliclazid MR	30, 60 mg
Glimepirid	1, 2, 3, 4, 6 mg
Glipizid	1, 5 mg
Gliquidon	30 mg
Glisoxepid	1 mg
Metformin	500, 850, 1000, 2000, 2550 mg
Nateglinid	60, 120 mg
Pioglitazon	15, 30, 45 mg
Pramlintide	30, 60, 120 mg
Repaglinid	0.5, 1, 2 mg
Saxagl./Metf.	2.5/850, 2.5/1000 mg
Saxagliptin	5 mg
Sitagl./Metf.	50/850, 50/1000 mg
Sitagliptin	25. 50 100 mg
Vildagl./Metf.	50/850, 50/1000 mg
Vildagliptin	50, 100 mg

List of GLP-1 analogues

GLP-1 analogue	
Dulaglutide	0.75, 1.5 mg
Exenatide	5, 10 µg
ExenatideMR	2 mg
Liraglutide	0.6, 1.2, 1.8 mg