UNIVERSITY OF TWENTE.

Faculty of Science and Technology

Part 1
Design of a Diameter Dashboard displaying personalized blood glucose levels, physical activity, and nutritional data for type 2 diabetes patients

Part 2
Development of an algorithm to predict blood glucose values integrating glucose parameters, activity, and nutritional data using machine learning techniques.

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Master Thesis Biomedical Engineering

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Abstract

Part 1

Introduction: Management of chronic diseases such as Diabetes Mellitus Type 2 (T2D) requires the assimilation and interpretation of multiple data. In a collaborative T2D study Ziekenhuisgroep Twente (ZGT), the University of Twente (UT) and the Roessingh Research and Development (RRD) collected data from participating patients with T2D from three different sources; Blood Glucose (BG) sensors, nutritional diaries and physical activity tracking. The individual data sources were then merged into one application, the Diameter Application (DA). The usability and interpretation of the data turned out to be challenging and time-consuming for patients and healthcare workers alike. To make the raw data readily accessible for use during patient consults, a dashboard needed to be designed to visualize and provide convenient access to all the collected lifestyle data in the DA.
Method: Taking inventory of what must, should, could, and won't be part of the dashboard in a Must have, Should have, Could have, Won't have (MoSCoW) prioritization model through interviews with the stakeholders at ZGT and participating T2D patients. During the design process feedback was requested to improve on each design. MATLAB was used to effectively consolidate the raw data.
Results: The Diameter Dashboard (DD) is in use, creating reports and freeing up valuable time for healthcare workers to coach T2D patients during consults. Furthermore through visualization of the collected data in one dashboard, patients are instantly informed of their blood glucose status, nutrition intake and physical activity parameters which can work as an encouragement to make necessary changes in nutrition intake and/or physical activity.
Conclusion: The Diameter Dashboard (DD) is an important first step towards encouraging patients' to self-manage their lifestyle and for healthcare workers to be able to coach and to care for T2D patients.

Part 2

Introduction: Upon completion of the DD the question presented itself whether there is a way to predict glucose values based on nutritional intake and physical activity by employing machine learning techniques. Diet and physical activity are key modifiable factors in the treatment of T2D, and with current technological advances in monitoring and evaluating lifestyle data via applications and smart-wearables, an algorithm that predicts glucose values based on diet and physical activity would be a step forward in the treatment in T2D.
Method: A Machine Learning (ML) algorithm approach will be tested to determine whether glucose prediction can be done accurately when using features extracted from data provided by patients participating in the DIAbetes and LifEstyle Cohort Twente (DIALECT) study. A six-layer deep learning model with two different Long short-term memory (LSTM) layers was designed. To predict the blood glucose values two different methods were studied. Method 1; Direct multi-step forecasting (DMSF) and method 2; Recursive multi-step forecasting (RMSF).
Results: When utilizing the Root-Mean-Square Error (RMSE) and Mean Absolute Error (MAE) validation measures, the prediction seems reasonable, considering the standard deviation allowed. Comparing the performance of the algorithm designed, to current research in the field of personalized LSTM models for glucose prediction, one may come to the conclusion that the algorithm can predict BG values based on physical activity and nutritional data utilizing deep learning. Yet, upon closer inspection the outcomes are insufficient and not ready to be used in a clinical setting.
Conclusion: The designed model is not ready and not yet clinically relevant.
The designed model is not yet clinically relevant however it provides a basis for further development. Future research is needed to improve the accuracy. However the field of deep learning shows promise for real-time glucose prediction using physical activity data and nutritional data.

Glossary

BG Blood Glucose. 2, 6, 7, 8, 22, 23, 31, 32, 33, 34, 37, 40, 44

CGM Continuous Glucose Monitoring. 32

DA Diameter Application. 2, 6, 8, 11, 12, 16, 20, 27, 28

DD Diameter Dashboard. 2, 7, 11, 13, 14, 15, 16, 19, 20, 21, 22, 24, 25, 26, 27, 28, 29, 31

DIALECT DIAbetes and LifEstyle Cohort Twente. 2, 6, 8, 31, 34

DMSF Direct multi-step forecasting. 2, 5, 37, 38, 42

DNN Deep Neural Network. 33

LSTM Long short-term memory. 2, 33, 34, 36, 44, 45

MAE Mean Absolute Error. 2, 5, 37, 38, 44

ML Machine Learning. 2, 31, 34, 35, 45

MoSCoW Must have, Should have, Could have, Won't have. 2, 15

NEVO Nederlands Voedingsstoffenbestand. 9, 17, 27

PH Prediction Horizon. 33, 42, 44

RMSE Root-Mean-Square Error. 2, 5, 37, 38, 44

RMSF Recursive multi-step forecasting. 2, 5, 37, 38, 42, 43, 44

RNN Recurrent Neural Network. 36

RRD Roessingh Research and Development. 2, 6, 8, 16, 20

T2D Diabetes Mellitus Type 2. 2, 6, 8, 11, 12, 13, 14, 15, 16, 20, 22, 27, 28, 29, 31, 33, 34, 45

TAR Time above range ($> 10mmol/L$). 22, 23, 34

TBR Time below range ($< 3.9mmol/L$). 22, 34

TIR Time in range (percent and minutes); The amount of time spend in the target blood glucose range ($3.9 - 10mmol/L$). 22, 23, 34

UT University of Twente. 2, 6, 8

ZGT Ziekenhuisgroep Twente. 2, 6, 8, 12, 15, 25, 29

Contents

1 Introduction

More than 1.2 million people suffer from diabetes in the Netherlands, and approximately 90% of them have T2D. T2D most often develops in people over age 45, but more and more children, and young adults are also developing it. Nine out of ten people with diabetes have type 2 diabetes, moreover it is expected that 1 in 3 of the current adult Dutch population aged 45 and older will develop type 2 diabetes in the future, with predictions estimating that 1.5 million people will have diabetes in 2040. Worldwide, the number of people with diabetes mellitus has more than doubled over the past three decades, making it one of the most important public health challenges to all nations.[1], [2]

In 2018 ZGT [3], the UT [4] and the RRD [5] collaborated in a study with the title Diameter Study [6]. In the Diameter Study, data from participating patients with T2D were collected from three different sources; BG sensors, nutritional diaries and physical activity tracking. The individual data sources were then merged into one application, the DA. For background information on the Diameter Study and the DA please see appendix A.

Currently the patient data in the DA is only available as raw data making the usability and interpretation of the data challenging for patients and healthcare workers. Furthermore the collected data is not readily accessible for use during patient consults. Before a patient consult, healthcare workers need to import the collected lifestyle data from different sources, which is time consuming. Add to that, the fact that nutritional intake data, physical activity data and glucose levels are measured at different time intervals, which makes the data even more difficult to interpret.

A proposed solution to this problem would be to design a dashboard that visualizes and provides convenient access to all the collected lifestyle data in the DA; glucose levels, nutrition intake, and physical activity. With access to a 'Diameter Dashboard' (DD) healthcare workers have to spend less time on manually creating reports, freeing up time for healthcare workers to coach T2D patients during consults. Furthermore by visualization of the collected data in one dashboard, patients are instantly informed on their glucose status, nutrition intake and physical activity parameters which can work as an encouragement to make necessary changes in nutrition intake and/or physical activity.

1.1 Research Project Question 1

"What are the requirements for a Diameter dashboard that will assist type two diabetes patients in managing their condition, as well as provide easy access to patients' glucose values, physical activity and nutritional data, so healthcare workers can monitor and coach their patients efficiently?"

Sub-questions

1. How to combine relevant data from multiple sources, selecting the correct metrics?
2. What do patients and healthcare workers prefer as far as optimal content and lay-out for a dashboard?

To visualize aforementioned Diameter Application (DA) data in one dashboard, the timing of the glucose level data has to be leading since it is the most important data in monitoring and treating patients with T2D. Since glucose data is so important the question arises if there is a way to predict glucose values based on nutritional intake and physical activity using lifestyle data collected through applications and smart wearables?
The DIALECT study is a prospective cohort study in patients with T2D, which includes lifestyle data form a large group of outpatient population of T2D patients. This data may be used to present a new approach to the problem of glucose prediction by employing machine learning techniques using free-living data.
To date, an algorithm that predicts glucose values based on diet and activity data, has not yet been published.

1.2 Research Project Question 2

Is it possible to predict blood glucose values based on physical activity and nutritional data, using a deep learning algorithm?

Sub-questions

1. What should the algorithm predict and what data is needed?
2. How to prepare data for machine learning and predict future blood glucose levels?

1.3 Thesis outline

The design of a Diameter Dashboard (DD) will be discussed in part 1 of the thesis. The development of an algorithm to predict Blood Glucose (BG) levels in type 2 diabetes patients will be discussed in part 2 of the thesis. Both in part 1 and in part 2 the research is organized as follows: introduction, literature research, methodology and the answers to the sub-questions. In the conclusion the main research questions will be answered.

Both studies are interconnected yet are presented separately to maintain the integrity of said research questions. It must be noted that the researcher aims to include, if possible, the glucose blood levels prediction algorithm in the Diameter Dashboard.

2 Background

2.1 The pathophysiology of Type 2 Diabetes (T2D)

There are three main processes contributing to elevated glucose levels. Insulin resistance results in reduced peripheral glucose utilization in skeletal muscle, adipose tissue and the liver. Excess hepatic glucose release as a result of pancreatic islet dysfunction associated with impaired beta-cell insulin release and excess glucagon release from the alpha-cells contribute to hyperglycemia. Along with this, less insulin release is associated with reduced glucose uptake in the periphery. The situation worsens with time as glucotoxicity and associated inflammation and oxidative stress result in further beta-cell dysfunction and insulin resistance.[7] The management of T2D should be personalized and tailored to the stage that the individual exists within the diabetes continuum.

2.2 Personalized approach to Type 2 Diabetes management

Currently, the management of T2D is driven by established international guidelines, and until recent years these did not take account of individual characteristics and the presence of comorbidities for individual patients. Individuals differ in their presentation of T2D, some have a short duration, others a long duration and other complications at the time of presentation. Therefore, with respect to treatment, "one size does not fit all". Personalized diabetes management is based on developing a clinical plan that is tailored to the individual. Therefore, the concept of personalized management is complex and broad. The therapeutic options for managing T2D have increased considerably in the past 10 years, so perhaps the time has come to focus and tailor therapy to the phenotype , and personal characteristics of the patient. Personalized care may provide the opportunity to address two potential reasons for the continued morbidity and mortality associated with T2D. The use of a personalized approach in the management of people with T2D can reduce the cost and failure associated with the algorithmic "one-size-fits-all" approach.[7]

Current treatment of T2D patients does not reach the full potential for improvement of a sufficient lifestyle management. With innovations in technology the ease and availability for monitoring and evaluating lifestyle choices via applications and smart-wearables have greatly improved. The technology for acquiring objective data from BG sensors, nutritional diaries, activity tracking and tailored coaching does exist. To improve upon the current treatment of patients with T2D, ZGT first started the DIALECT study in several phases around 2009 [8] with the inclusion of patients in subcohort DIALECT-1. The focus of this study was pharmacological and nutritional management in T2D patients.[8]
Subcohort DIALECT-2 started inclusion in 2017 and includes continuous glucose monitoring.[9] In 2018 ZGT joined forces with the UT and the RRD to work together on the Diameter study, while designing a Diameter Application (DA).[10]

In part 1 of this thesis data from the Diameter study is used. In part 2, the data from the DIALECT-2 study is used. To clarify the difference between these studies a short explanation will follow. For a more detailed background on the Diameter study please see appendix A.

DIALECT Study: The DIAbetes and LifEstyle Cohort Twente (DIALECT) cohort study was designed to study pharmacological and non-pharmacological management of T2D in a secondary health care center.[8], [9]
Diameter Study: The aim of the Diameter Study was to develop the Diameter Application as blended-care and stand-alone intervention in primary and secondary care.

2.3 Data collection methods

The study populations in both the DIALECT and DIAMETER study are derived from the population of T2D patients attending the outpatient clinic at ZGT. The Dialect is an observational cohort study, the DIAMETER is an intervention study.

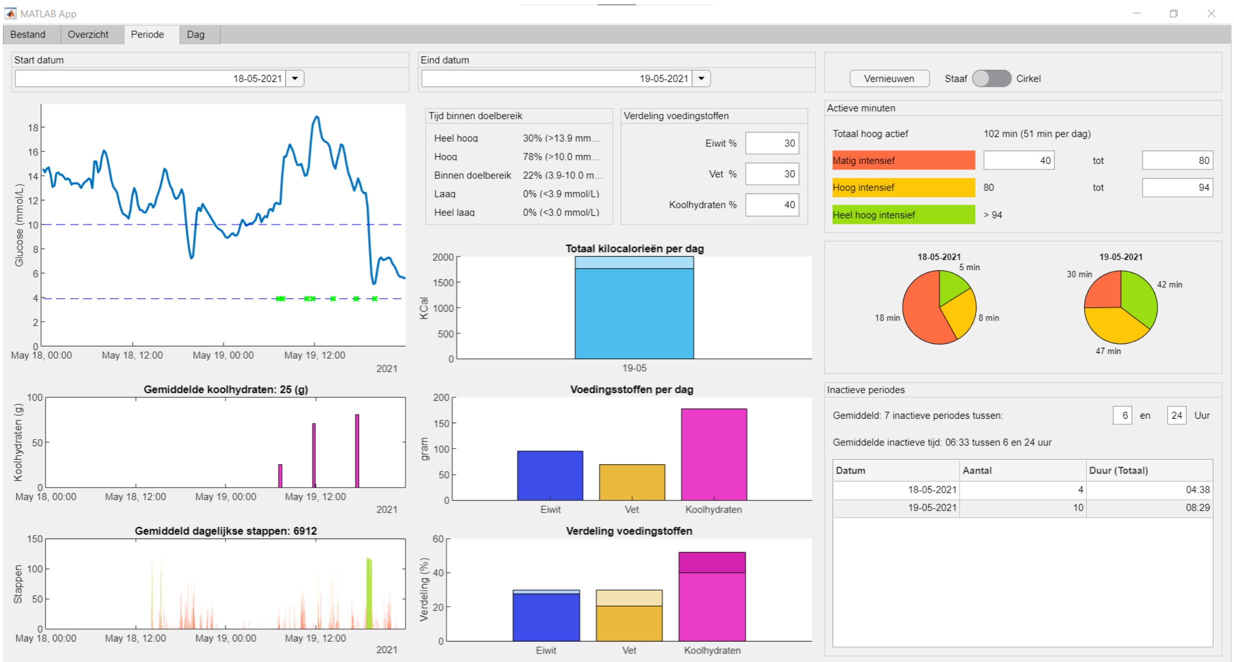
It is important to note that the DIALECT-2 and Diameter studies used different study populations, however in both studies the data collection was done through the use of the same three systems. First, to monitor glucose levels participants used a FreeStyle Libre®(Abbott Diabetes Care, Witney, UK). A FreeStyle Libre sensor is a factory-calibrated interstitial glucose monitoring system in which a sensor is applied to, for example, the upper arm and collects glucose readings over a 14-day wear period. The sensor automatically measures glucose in 15-minute intervals and the readings are stored on the sensor.

Second, for the collection of physical activity data participants used a Fitbit®(Fitbit Inc., San Francisco, CA, USA). A Fitbit is an activity tracker worn on the wrist just like a watch. It tracked day-to-day activity of participants in the number of steps taken during daily activities like walking, cycling, or daily household choirs. The amount of steps taken are stored and accessible through an app on a smartphone.

Third, nutritional intake data was also collected through an app on participants' smartphones using mostly the Nederlands Voedingsstoffenbestand (NEVO).[11] NEVO is a database containing the nutritional values of over 2500 products broken down in 136 nutrients. To clarify, most of the patients used the NEVO database to enter nutrition data. However some of the patients participating in the DIALECT-2 study used 'Mijn Eetmeter", which is the only app that retrieves product information directly from the NEVO database.[12]

PART 1

Design of a Diameter Dashboard displaying personalized blood glucose levels, physical activity, and nutritional data for type 2 diabetes patients.



1 Introduction

The goal is to design a dashboard that visualizes the collected lifestyle data in the Diameter Application (DA). This, to provide convenient access during a patient consult to all the collected lifestyle data in the DA; glucose levels, nutrition intake, and physical activity. With access to a 'Diameter Dashboard' healthcare workers have to spend less time on manually creating reports, freeing up valuable time for healthcare workers to coach T2D patients during consults. Further, a dashboard will not only assist healthcare workers, but also patients by providing an instant and easy to interpret overview of their glucose status, nutrition intake and physical activity parameters, which can work as an encouragement to make necessary changes in nutrition intake and/or physical activity.

Ultimately, a personalized approach to the management of T2D will reduce treatment costs and increase the well-being of patients with T2D. T2D patients need to not only be monitored in a clinical setting but they need to be encouraged to partake in lifestyle interventions by paying careful attention to their nutritional intake combined with physical activity and the impact on their glucose levels.

In the Diameter study an important step towards personalized monitoring was taken. The next step is to utilize the raw data from the DA to be consolidated in one dashboard which is populated upon patient selection by the treating healthcare worker or the patient himself.

2 Literature research

Even though extensive research on dashboard design methods, utilizing data from different sources exists, every healthcare worker and patient will have certain personal preferences as to what the dashboard should show. Add to that, that evidence shows that monitoring of the diabetes-related markers is not performed optimally in routine clinical settings, making the need for an innovative dashboard to interface with the Diameter Application used by Ziekenhuisgroep Twente a necessity to be able to optimally care for T2D patients.

2.1 Dashboard design literature

Effective design is crucial for dashboards. A good information design will clearly communicate key information to users. Dashboards and visualization are cognitive tools that improve and help people visually identify trends, patterns and anomalies. With the prevalence of scorecards, dashboards and other visualization tools now widely available for users to review their data, the issue of visual information design is now more important than ever.

Rabiei and Almasi [13], researched the requirements and challenges of hospital dashboards in a systematic literature review. For this study fifty-four out of 1254 retrieved articles were selected resulting in specific functional requirements for dashboards including reporting, reminders, customization, tracking, alert creation, and assessment of performance indicators including visualization elements based on the user's needs. The identified challenges were categorized into four groups: data sources, dashboard content, dashboard design, and integration in other systems at the hospital level.[13]

Data sources: A service-oriented architecture is necessary for encapsulating data from different systems in a middleware layer for data integration in dashboards, and understanding various data hosting structures, different methods of data proliferation and transfer, and the best query language necessary for this data structure.[14]
Dashboard content: Evidence suggests the necessity of engaging users in dashboard development and adaptation processes to reduce resistance to the implementation of these systems.[15]
Dashboard design: Customization is an essential feature for organizing the dashboard content according to the users' needs and promoting its application by the users. Besides, a color-coding system can be useful for a better understanding and interpretation of displayed information. A variety of interactive and visualization techniques are employed in dashboard design.[16]

Ratwani and Fong [17] worked on a system-level dashboard, summarizing data from multiple hospitals, and a set of hospital-level dashboards were developed. In the resulting paper, a novel informatics approach was presented to address the challenge of medication adherence in patients with chronic and complex diseases such as T2D. The goal: facilitating meaningful discussion between patient and provider using an integrated informatics strategy combining objective and subjective data. This approach increased patient engagement and meaningful clinical discussion that may improve health outcomes. The dashboards allowed users to navigate and monitor the data through coordinated displays in different formats, and to quickly zoom in to specific variables of interest.[17]

The dashboard designed by Ratwani and Fong [17] integrated existing clinical workflows used in the pilot's primary care clinics. Clinicians in these clinics are accustomed to opening patient charts before entering the exam room. Since the dashboard is populated upon patient selection, the data are available for review before the clinical encounter. Furthermore, a reminder prompts clinicians that the dashboard is available when they select a diabetic patient whose data can be viewed.

2.2 Gaps or limitations in existing research

Management of chronic diseases such as T2D requires the assimilation and interpretation of multiple data. This makes the assembly and interpretation of results related to diabetes care challenging. Even though extensive research on dashboard design methods, utilizing data from different sources exists, evidence shows that monitoring of the diabetes-related markers is not performed optimally in routine clinical settings. A possible contributing factor to this sub-optimal monitoring could be the conventional way of presenting lifestyle data, which are often piecemeal and segregated. A clinical data interface that effectively consolidates data or provides recommendations and reminders to clinicians and patients will improve the monitoring process in patients with T2D.

Existing research shows that patient participation in collecting lifestyle data is low, even though those patients that do collect all the necessary data report an overall improvement in care. It turns out that even with smart wearables that monitor physical activity and applications on smartphones to scan nutritional intake, over time, T2D patients lack the motivation to keep up with data collection.

Automation of lifestyle data collection is taking steps forward through for example placing sensors in a patients' home that record when a patient opens a bottle or puts a pan on the stove. But no matter what new ideas are developed, the patient is leading as far as successful coaching and monitoring goes. Healthcare workers must accept discrepancies in interpreting the collected data. Currently there is not one application that does it all.

2.3 Conclusion literature research

To answer the research project main question; Designing a dashboard that will assist T2D patients in managing their condition and help healthcare workers to monitor and coach T2D patients, desk research shows that the greatest challenge will be to convince and encourage patients to be vigilant in collecting lifestyle data.

The design of the dashboard needs to focus on easy access for patients to convince them that collecting lifestyle data, even though tedious, is worth the time and effort it takes to improve their health. Next to that the dashboard needs to have the option for healthcare workers to set parameters before a patient consult, which translates into making sure that the design includes the options to select a specific period of time to present an overview of glucose data, physical activity and nutritional intake, the three most important markers to coach a T2D patient. Special attention needs to be given to the colors and design of the visuals.

2.4 Recommendations

The theory behind designing a dashboard complementing the da is to assist in improving the care of T2D patients with the benefit for all users to enhance intervention. While lifestyle interventions are seen as possible solutions to stop the increasing trend in T2D, or reverse T2D, studies backing this up are rare. Lifelong changes in nutrition and physical activity, a Guided Lifestyle Intervention (GLI) is needed and scarcely implemented in the treatment of T2D.

Designing a 'Diameter Dashboard' is an important first step towards encouraging patients' to self-manage their lifestyle and for healthcare workers to be able to identify important signals concerning caring for T2D patients.

3 Methodology

In the following chapter the data collection and design methodology are presented. The dashboard design method used can be characterized as a qualitative goal-driven design. Whereas quantitative data is used to populate the dashboard.
The process of developing the dashboard is referred to in literature as an iterative process. In this case, the iterative process consists of the practice of building, refining, and improving the design, based on input from healthcare workers, T2D patients and a design team, until everyone is satisfied with the end result. The process of designing a dashboard is a process of co-creation with many partners, most importantly the patients whose data is used to populate the dashboard.
The Diameter Dashboard will be written in MATLAB®(2021b, The MathWorks, Inc., Natick, MA, USA).

3.1 Iterative process

Dashboarding, as mentioned prior, follows certain steps.

1. Define goals.
2. Choose the right metrics.
3. Present data correctly.
4. Eliminate clutter and noise.
5. Use layout to focus attention.
6. Tell a story with data.

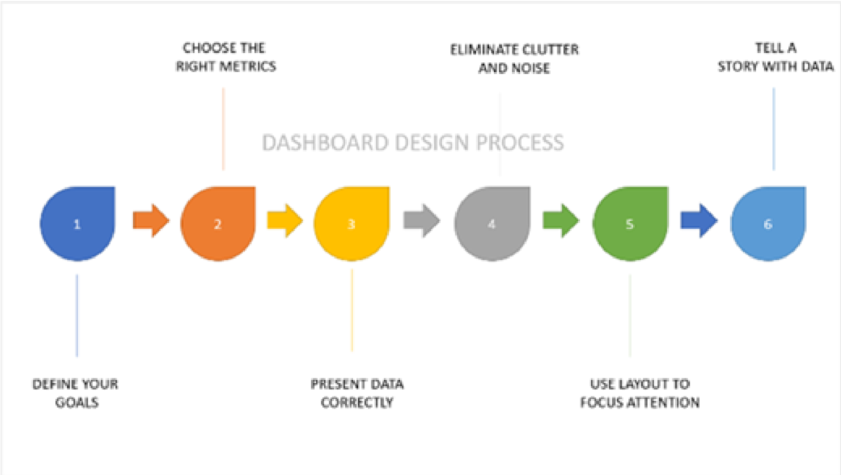


Figure 1: Dashboard design process [18]

4 Results

Following a summary of the iterative process with the aforementioned dashboard design steps as the basis. Images of the dashboard design in process are included, including feedback from patients during the design process. Further specific areas of concern for users, a discussion pertaining to additional features and further recommendations can be found in the chapter discussion.

4.1 Define goals

Research on the topic of dashboards for medical purposes, and interviews with the stakeholders at ZGT, leads to the following MoSCoW prioritization model [19], used for a thorough inventory of what must, should, could, and won't be part of the dashboard.

Must
Option for healthcare workers to set parameters before a patient consult.
Visually identify trends, patterns and anomalies over a period of time.
Track meals and exercise.
Blood glucose monitoring before and after each meal.
Blood glucose monitoring relative to activity.
Highlight hyper and hypo episodes.
Easy access for patients.
Track the intake of carbohydrates.
Should
Visualize of macronutrient distribution.
Print out reports for the medical provider.
Encourage patients to make lifestyle changes.
Encourage discussion between healthcare worker and T2D patient.
Could
Offer personalized health and diet tips.
Include motivational messages.
Predict future glucose levels.
Won't
Offer food tips based on glucose levels.
Scan barcodes on food and beverage.
Weight loss support based on food intake.

Table 1: MoSCoW method for Diameter Dashboard

4.2 Choose the right metrics

Before starting the design of the dashboard, an assessment needed to take place of the available data.

4.2.1 Study population

The data used was made available, with consent of patients, participating in the 'Diameter Pilot Study'. To be included in the Diameter Pilot Study the patients had to meet the following criteria:

- Diabetes Mellitus Type 2 being treated at ZGT;
- Familiar with a smartphone;
- Minimum age of 18 years;
- Competent: person can understand information provided by researcher and can understand what the consequences of participation are.

With the following exclusion criteria:

- Dependence on renal replacement therapy;
- Severe general diseases or mental disorders;
- Drug abuse;
- Insufficient mastery of the Dutch language.

For the development of the Diameter Dashboard 10 patients with T2D were selected from the Diameter Pilot Study population, resulting in a homogenic group T2D patients, 60+ with obesity. To protect the privacy of participating patients further details will not be shared and all patient feedback is anonymized.

4.2.2 Patient data collection

Patients participating in the Diameter study install the Diameter Application on their smartphones. Data acquisition from the Diameter Application follows three distinct paths.

- Raw blood glucose data is gathered from either the FreeStyle Libre Reader or the accompanying online tool LibreView source.
- Physical activity is uploaded from the Fitbit.
- Nutritional data is collected from the nutritional diary that the patients keep.

The data collected by patients in the Diameter Application needed to be manually processed in Microsoft Excel [20] and discussed with the patients during a consult. See the following examples of the visuals created.
Figure 2 shows that a Diameter Dashboard can definitely assist in making the raw data more accessible and easier to interpret.

tu	kcalu	protu	fatu	carbsu	sugaru	starchu			prot%	Fat%	carbs%
17-12-20 08:35	269.5	9	4.3	48.125	37.575	10.55					
17-12-20 12:30	208.8	11.72	10.12	16.21	1.77	14.44					
17-12-20 15:25	62	0.2	0.2	14.8	14.8	0					
17-12-20 16:25	188.8	1.52	7.72	28.08	14.68	13.4					
17-12-20 17:45	36	0.45	0.05	8.05	8.05	0					
17-12-20 19:15	640.95	12.535	32.84	71.165	2.44	68.725					
17-12-20 19:20	**40.56**	**0.912**	**0.048**	**9.072**	**6.12**	**2.952**		**10.032**	9.090909	0.478469	90.43062
17-12-20 22:20	36	0.45	0.05	8.05	8.05	0					
18-12-20 10:15	391.3	16.5	13.61	48.96	29.36	19.6					
18-12-20 11:30	188.8	1.52	7.72	28.08	14.68	13.4					
18-12-20 14:00	176.75	6.095	4.095	28.04	1.875	26.165					
18-12-20 14:20	**4**	**0.2**	**0.2**	**0.4**	**0.4**	**0**		**0.8**	25	25	50
18-12-20 16:30	48	0.795	0.03	11.1	7.38	3.75					

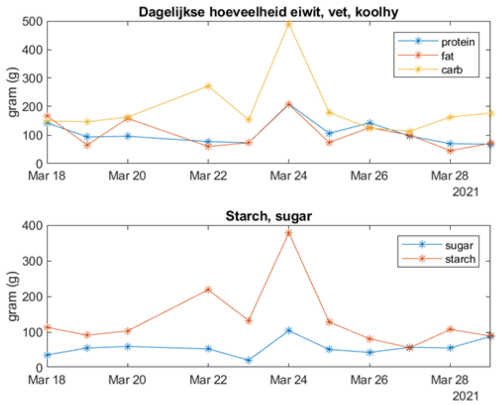


Figure 2: Manual calculation of nutritional values versus visualization in graphs

Feedback from patients:
Importing the raw data is too time consuming.
Difficult to understand.
Colors are hard to distinguish.
I miss the added value of this information.

4.3 Present data correctly

While designing the Diameter Dashboard several options were presented to patients and healthcare workers to visualize nutritional data, physical activity data and glucose data. Even though the raw data was available through the Diameter Application, to import the raw data into a dashboard, the data needed to be processed in various analysis scripts in MATLAB. Through this process various images, with parameters, were created to be used to obtain feedback from patients as well as healthcare workers.

4.3.1 Visualizing nutrition data for use during a patient consult

Participating patients keep track of their nutritional intake through a food diary on the Diameter Application. To import the nutritional data, one of the partners in the Diameter Study RRD developed a tool to read nutritional data from the Diameter Application.

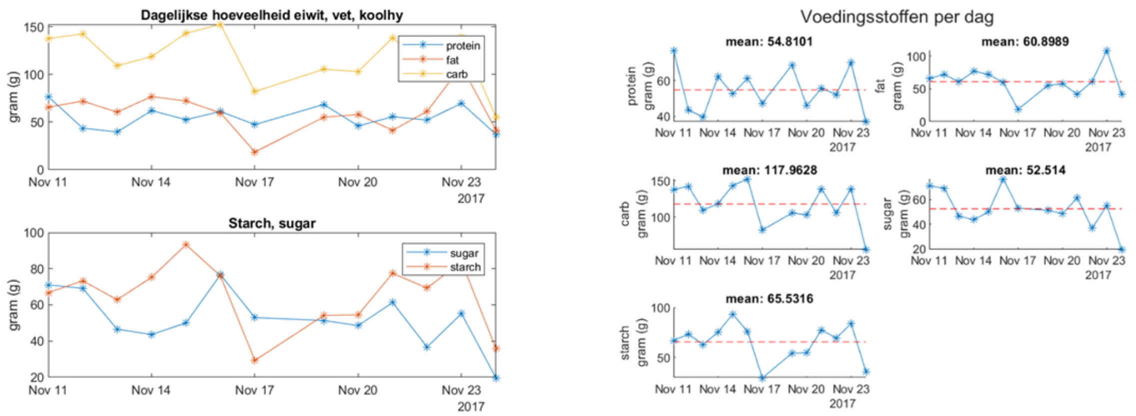
The NEVO is a database containing the nutritional values of over 2500 products broken down in 136 nutrients. To clarify how the nutritional values are collected see figure 3 depicting the raw data from the NEVO database.

isotime	datetime	ms	mealType	order	productCo	productNa	measureC	measureN	measureC	measureU	measureU	kilocalorie	carbohydr	proteins	sugar	starch	fat	foodDbVe	createdTin	createdTin	extra
2021-05-0	########	0	BREAKFAS	1	2519	Halfvolle v	52	schaaltje	1	GRAM	150	130.5	24.45	2	12	4.3	1.5	1	1.62E+12	Europe/An	{"foodDbId":"nl_nevo"}
2021-05-0	########	0	BREAKFAS	2	213	Havermou	36	eetlepel	1	GRAM	5	18.65	3.035	12.8	2	58.3	7.3	1	1.62E+12	Europe/An	{"foodDbId":"nl_nevo"}
2021-05-0	########	0	OTHER_M	1	2795	Wit broodj	63	stuk	3	GRAM	150	415.5	81.6	10	3	51.4	1.5	1	1.62E+12	Europe/An	{"foodDbId":"nl_nevo"}
2021-05-0	########	0	OTHER_M	2	2756	Kaas 48+ j	60	voor 1 sne	1	GRAM	20	72.8	0	22.8	0	0	29.6	1	1.62E+12	Europe/An	{"foodDbId":"nl_nevo"}
2021-05-0	########	0	OTHER_M	3	810	Filet ameri	60	voor 1 sne	2	GRAM	40	96	1.2	14.2	1.3	1.7	18.8	1	1.62E+12	Europe/An	{"foodDbId":"nl_nevo"}
2021-05-0	########	0	MAIN_ME	1	1326	Gehakt hal	312	portie	1	GRAM	80	253.6	0.32	30.1	0.4	0	21.6	1	1.62E+12	Europe/An	{"foodDbId":"nl_nevo"}
2021-05-0	########	0	MAIN_ME	2	982	Aardappel	61	middel	1	GRAM	88	73.04	15.224	1.9	0.2	17.1	0.3	1	1.62E+12	Europe/An	{"foodDbId":"nl_nevo"}

Figure 3: Example of raw data of nutritional diary

Visualization of nutritional intake shows the consumption of proteins, fats and carbohydrates. When eaten in the right ratios, these three macronutrients can improve weight, health and overall physical well-being. In general, most adults should target their diets to comprise of $45-65\%$ carbohydrates, $10-35\%$ protein and $20-35\%$ fat. In patients with T2D, the recommended ratios are 40% carbohydrates, 30% protein and 30% fat.[16]

Initially the nutritional intake was visualized as follows, see figure 4. Graphs were created, to not only show the daily intake of macronutrients, but also the average daily intake. Furthermore, a graph was created to show the amount of sugar and starch intake over a period of time. Participating patients indicated that they liked the fact that starch and sugar were also visualized. Patients did not see any value added by showing the average daily intake per ingredient.[21]



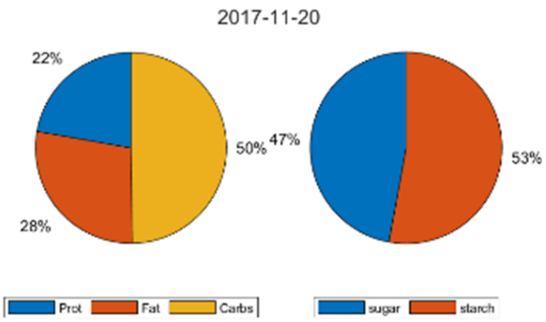
(a) (b)

Figure 4: Early example of graphs portraying nutritional data. (a) Daily amount of macronutrients visualized in one graph and a separate graph for starch and sugar. (b) A graph for each macronutrient with the average values visible through a dashed-red line as well as a number.

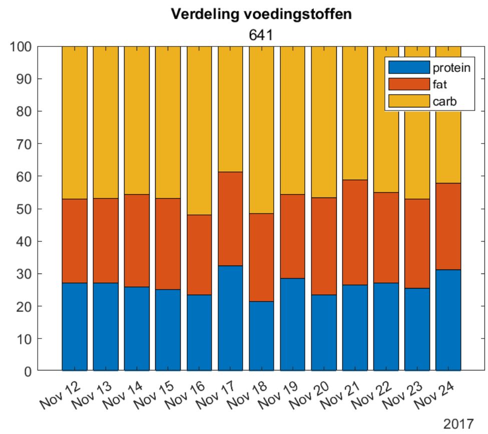
Feedback from patients:
At first glance the information is difficult to understand.
Patients prefer that targets are shown in the dashboard as well.
Furthermore the graphics are not easy to interpret.

Based on the feedback, new visuals were created including pie and bar charts.

During the second round of patient interviews the group was shown the following two distinct graphs depicting the same information but presented differently, see figure 5.

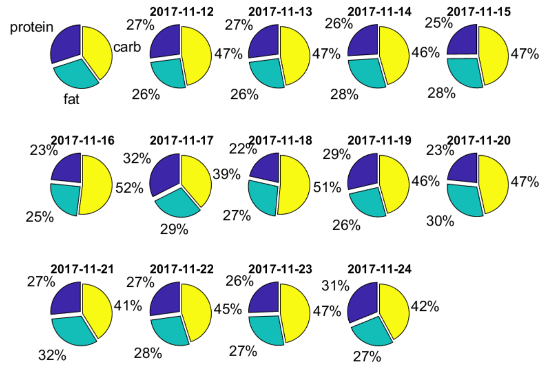


(a)



(b)

Feedback from patients:
Patients like bar charts over pie charts, however the group does not care for all the different color schemes. Sugars vs slow carbohydrates intake is fine to present in a bar chart.
Patients find it useful that the visual shows how the total food intake is divided up.
Patients suggest to add a 'goal' in the nutritional chart.



(c)

Figure 5: In (a) a pie chart of distribution of macronutrients of one day; in (b) a bar chart of distribution of macronutrients for multiple days; and in (c) the same but in pie charts.

Adding nutritional goals also became a priority as a result of the patients' feedback.

Feedback from patients:
Patients are enthusiastic about the new visuals but do not understand the use of the color red. Red means bad, according to the group, so red needed to be replaced by a different color.

During the visualization process it became clear that patients and healthcare workers preferred different color schemes than the colors automatically selected by the software. Figure 5 shows the colors used by MATLAB. The first combination, figure 5b, shows the bar charts in red, blue and orange and the pie charts in yellow, blue and cyan, see figure 5c. According to a 2021 experimental study on the relationship between the harmony and cognitive load of business intelligence dashboard color combinations by Wu *et al.* [22], color combination is an important factor affecting dashboard visual design and is key to triggering the operator's visual harmony and emotion.[22]

To find the perfect color combination, colors from the Fitbit application were used, which turned out to be the most recognizable because patients already use the Fitbit app.

Using the Fitbit color scheme, the colors in figure 7 were selected to use in the next version of the Diameter Dashboard.

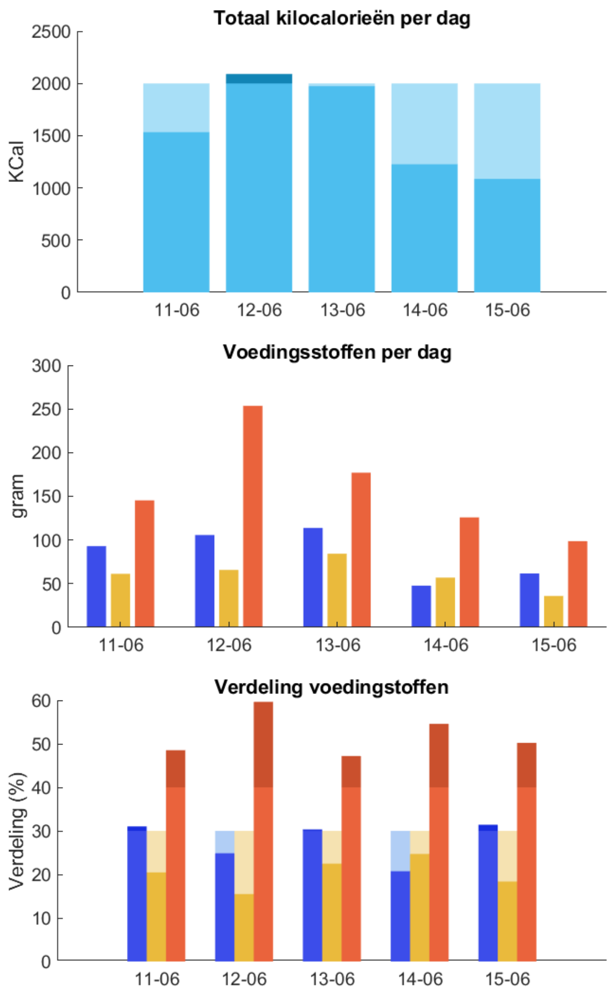
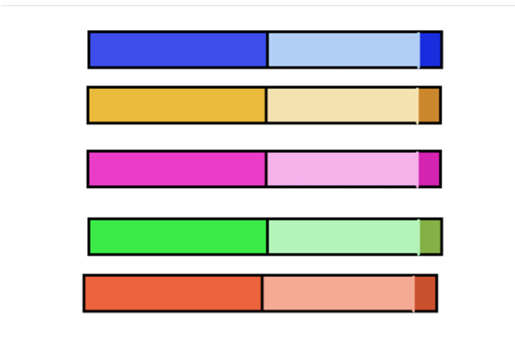


Figure 6: In (a) the total amount of calories with goals added; in (b) the amount in grams of macronutrients; in (c) the distribution of macronutrients with goals.



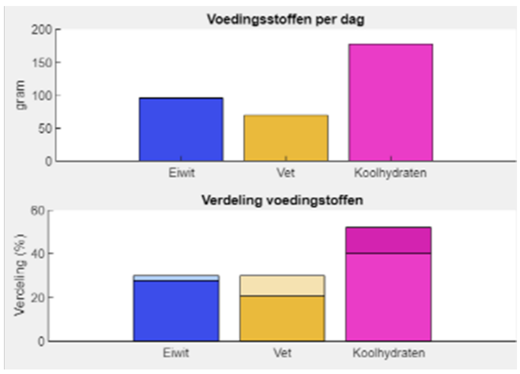


Figure 7: Custom colors on the left and example for nutrition on the right.

The color blue represents the intake of protein. When a goal is not yet reached, a lighter blue shows the remaining amount of protein that still needs to be consumed. When a patient eats too much protein the bar changes gradually to a darker shade of blue. In short, patients do not like confrontational colors but do like contrasting colors to enhance interpretation.

The final version of the visualization of nutrition in the Diameter Dashboard was approved by all. Patients especially like the goal section and the distribution of nutrients, see figure 8.

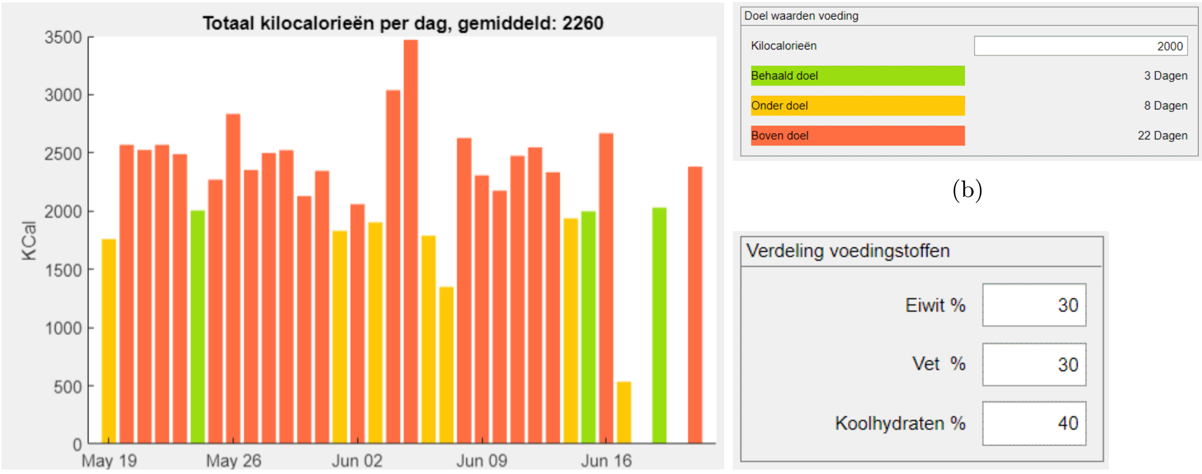


Figure 8: (a) Total amount of kilocalories per day with mean and color coded according to the goal in (b), with additional goals for distribution of macronutrients (c).

4.3.2 Visualizing activity data for use during a patient consult

During the process of designing the visuals for the nutrition intake, a lot was learned already which made the design process of visualizing physical activity easier. Physical activity is extremely important at any age to improve glycemic control, to reduce the risk of cardiovascular disease (CVD) and mortality in patients with T2D. Moderate to vigorous physical activity is recommended to manage T2D; however, patients with T2D can be physically weak, making it difficult to engage in the recommended levels of physical activity. Daily physical activity includes various activities performed during both occupational and leisure time such as walking, gardening, and housework that type 2 diabetes patients should be able to perform without considerable physical burden.[23]

Participating patients keep track of their physical activity by wearing a Fitbit that syncs to the Diameter Application. To import the physical activity data, one of the partners in the Diameter Study the RRD developed a tool to read the activity data from the Diameter Application.

In the Diameter Study physical activity is measured in steps, at one-minute intervals. This data is then imported in MATLAB and analyzed.

The first visual was presented as figure 9 focusing on daily activity measured in steps.

Feedback from patients:
The patients in the focus group did find this graphic useful.
Patients want to know how many steps they have to take and what the intensity of the physical activity should be.

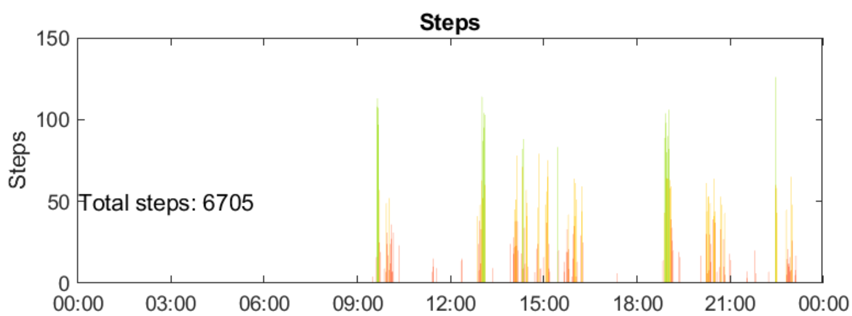
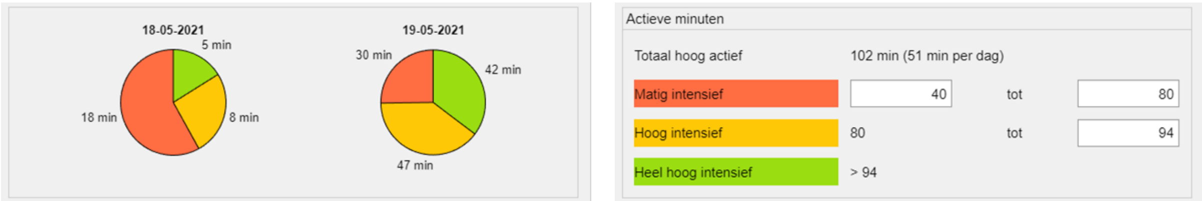


Figure 9: Steps shown per minute with total amount of steps.

During the second showing of the visuals the physical activity was shown in a pie chart and included three levels of intensity. Figure 10 now also shows individual fitness levels. Patients as well as healthcare workers can set personalized goals.



(a) (b)

Figure 10: Distribution of active minutes (a) based on goals set (b).

This received positive feedback from patients.

During the third and final round of the iterative process another feature was added to the Diameter Dashboard indicating inactive periods, see figure 11. This allows for regular inactivity such as sleep to not be included into the overall assessment of physical activity.

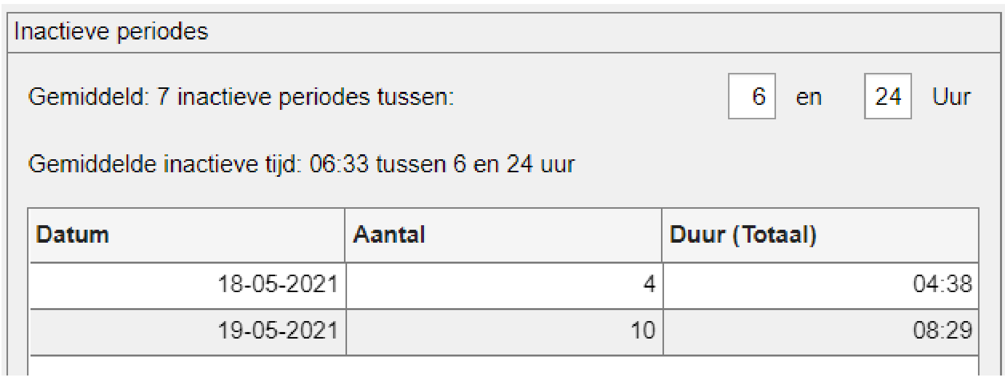
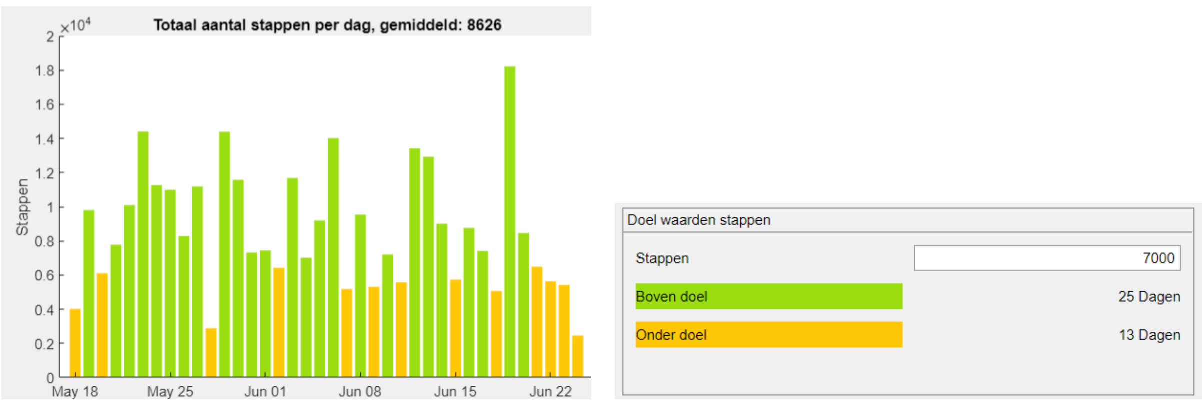


Figure 11: List of inactive periods where $< 10 steps/min$ were recorded. Regular sleep patterns can be entered to assure that the dashboard does not record them as inactive or sedentary.

A feature which allows for setting a specific physical activity goal was added, paying special attention to the colors. If a patient does not meet the target, the color is yellow versus red. Green means that the goals have been met. Again the colors make all the difference, see figure 12.



(a) (b)

Figure 12: (a) Total amount of steps per day with mean and color coded according to the goal in (b).

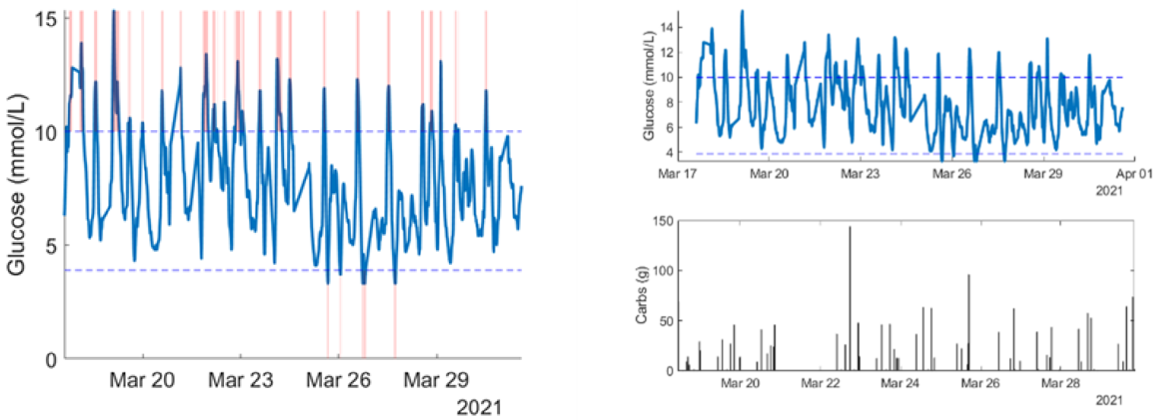
4.3.3 Visualizing glucose data for use during a patient consult

Health experts advise that a person living with T2D should aim to keep their BG range between 4.0 and 8 $mmol/L$ before a meal and less than 10 $mmol/L$ 2 hours after. However, these ranges can differ between patients.

Prior to the design of the Diameter Dashboard visualizing glucose data for use during a patient consult was done through a summary of the parameters acquired from the raw data.[9]

- TIR = Percentage showing time in healthy BG range ($3.9 - 10\ mmol/L$).
- TAR = Percentage showing time above healthy BG range ($\geq 10\ mmol/L$).
- TBR = Percentage showing time below healthy BG range ($\leq 3.9\ mmol/L$).
- $\text{TBR}_1 = 3.0 - 3.9\ mmol/L$, $\text{TBR}_2 = < 3.0\ mmol/L$, $\text{TAR}_1 = 10.0 - 13.9\ mmol/L$, $\text{TAR}_2 = > 13.9\ mmol/L$.
- SD = standard deviation in $mmol/L$, spread around average glucose.
- CV = coefficient of variation is the SD divided by the mean.[9]

Figure 13 shows the first versions of visualizing glucose levels shows the patients' blood glucose levels over a period of time. Before sharing this visual with the patient group for feedback, a feature was added to visualize nutrition.



(a) (b)

Figure 13: (a) The horizontal blue dotted line represent the target values of 10 $mmol/L$ and 3.9 $mmol/L$. The blue lines are the actual BG values measured by the sensor, and the pink lines represent periods of hyper- and hypoglycemia. (b) also shows the amount of carbohydrates set at the correct time corresponding to a nutritional entry.

Feedback from patients:

The group found the glucose graph on the left easy to understand although the hyperglycemia and hypoglycemia colors were difficult to see.

The question arose whether there was a way to incorporate the intake of nutrition in the glucose graph.

Incorporating nutrition into the glucose graph as followed by feedback from the patients resulted in figure 14.

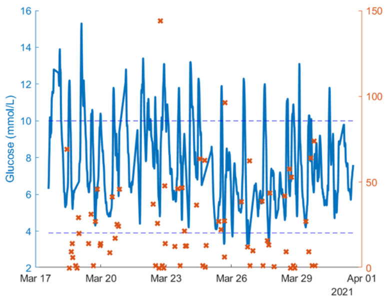
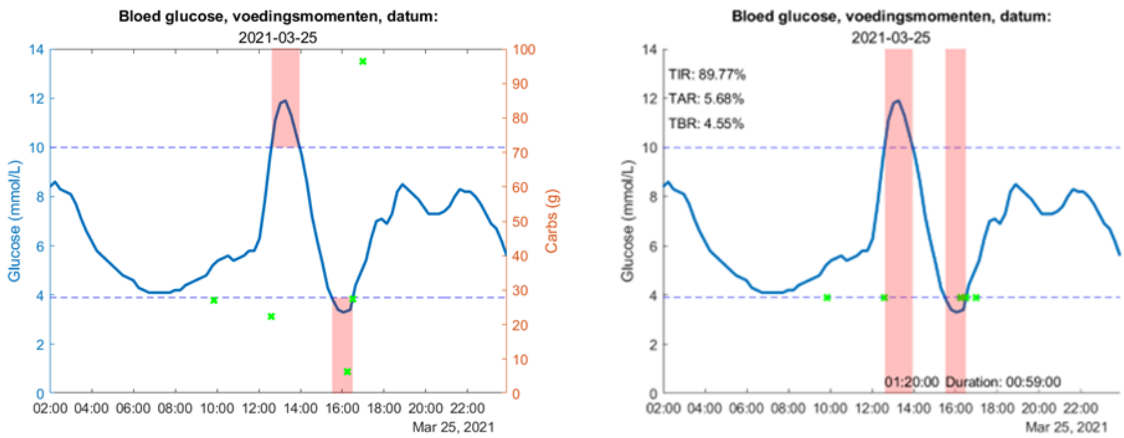


Figure 14: The horizontal blue dotted line represent the target values of 10 $mmol/L$ and 3.9 $mmol/L$. The blue lines are the actual blood glucose values measured by the sensor. Red crosses show nutrition entries with carbohydrates as second y-axis.

Feedback from patients:
The patient group found this visual unclear and not at all easy to understand.

During the second showing of the blood glucose visuals in the iterative process, patients were asked to give feedback on the following two graphics, figure 15.

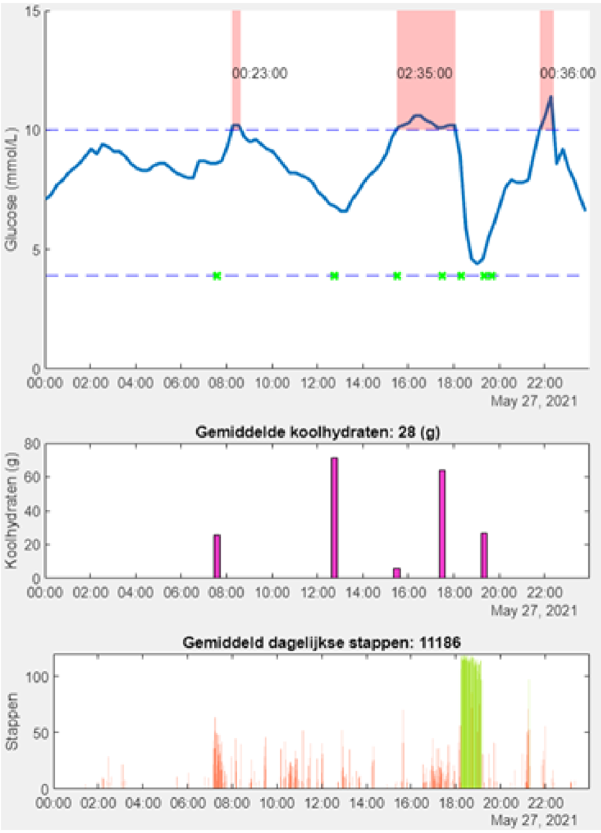


(a) (b)

Figure 15: (a) The horizontal blue dotted line represent the target values of 10 $mmol/L$ and 3.9 $mmol/L$. The blue lines are the actual BG values measured by the sensor, and the pink lines represent periods of hyper- and hypoglycemia. Green crosses show nutrition entries with carbohydrates as second y-axis. (b) shows the same but with green crosses fixed to the blue line, therefore losing the information about the amount of carbohydrates. Also added in are TIR, TAR and tbr percentages and duration of hypo- and hyperglycemia periods.

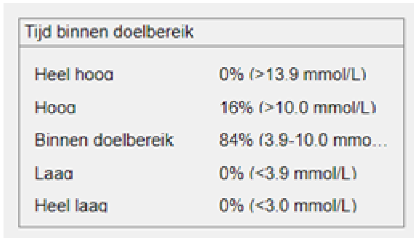
Feedback from patients:
Even though this graphic was easier to understand, the question arose why carbohydrates were represented in red and what the little green crosses meant?
Combining too much information in one graph leads to confusion.
Patients are already much more satisfied with the suggested visuals.
The group preferred to have nutrition intake in relation to their blood sugar levels in a separate visual.
The graphics need to include text to explain what the data represents.

During the third round of interviews patients were shown the following visuals, figure 16. Nutrition moments are still in green, with the added feature that the duration of hypo and hyper episodes are clearly indicated. Carbohydrate intake is now shown in a separate visual using purple instead of red.



(a)

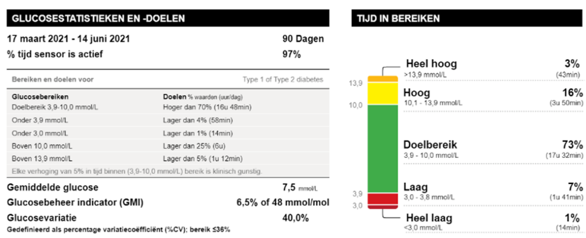
Feedback from patients:
The patient group is now unanimous in their approval and satisfied with the visualization of blood glucose levels.



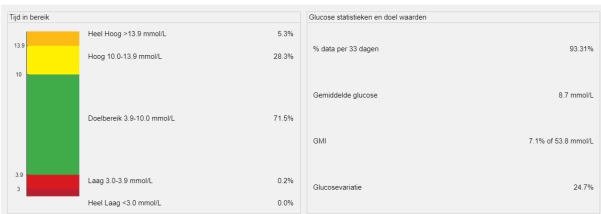
Tijd binnen doelbereik	
Heel hoog	0% (>13.9 mmol/L)
Hoog	16% (>10.0 mmol/L)
Binnen doelbereik	84% (3.9-10.0 mmo...
Laag	0% (<3.9 mmol/L)
Heel laag	0% (<3.0 mmol/L)

(b)

Figure 16: In (a) the pie chart of distribution of macronutrients of one day; in (b) the bar chart of distribution of macronutrients for multiple days; and in (c) the same but in pie charts.



(a)



(b)

Figure 17: (a) Glucose parameters as seen in LibreView® (Abbott Diabetes Care, Alameda, CA, USA) and (b) in Diameter Dashboard.

Feedback from patients:
Patient likes the use of the color red to indicate very low glucose levels.
Multiple patients do not understand the glucose values in the right lower quadrant.
The information in the right lower quadrant and top left quadrant are useful for the healthcare workers.
Can I choose what information I want to see?

4.4 Eliminate clutter and noise

During the process the feedback from 10 participating patients and healthcare workers at ZGT on the content, presentation, general remarks and suggestions for improvements were implemented leading to the final version. What became clear is that all patients want specific targets/goals in the Diameter Dashboard. The patient group also finds bar charts easier to interpret versus pie charts but when presented as a whole they prefer a combination of both. Most noticeable in all the feedback was the way the group felt about the colors used. When carbohydrates were shown in the color red patients immediately wondered if they had done something wrong. Further, patients wanted consistency in colors to make the dashboard easier on the eyes and help with interpretation.

4.5 Final design

The final design includes a 'file tab' which needs to be opened to upload data from a patient folder, see figure 18. The program checks for available data files from that patient pertaining to measured glucose levels, nutritional intake and patient activity data. If any of these data types are not found in the selected folder, the checkbox will not be selected. After pushing the analysis button, only the selected scripts are executed. Note: boxes can be manually checked and unchecked, depending on which data needs to be visualized.

Under the 'overview tab' users can upload data from a set period of time, see figure 19. Through plotting, the data is visualized showing hyper- and hypoglycemia variables. Collected nutritional data is visualized through a bar chart but can also be shown in a pie chart. Activity data is shown through a pie chart but the option is available to visualize physical activity as a bar chart depending on the preference of the user. Near the top of the page users can select whether the report shows daily data or multiple days setting a specific time-period to visualize the collected data, see figures 20 and 21.

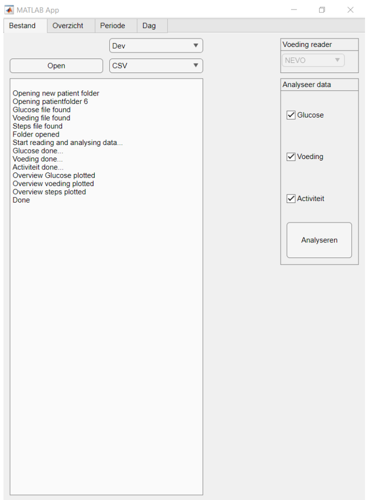


Figure 18: File tab of Diameter Dashboard

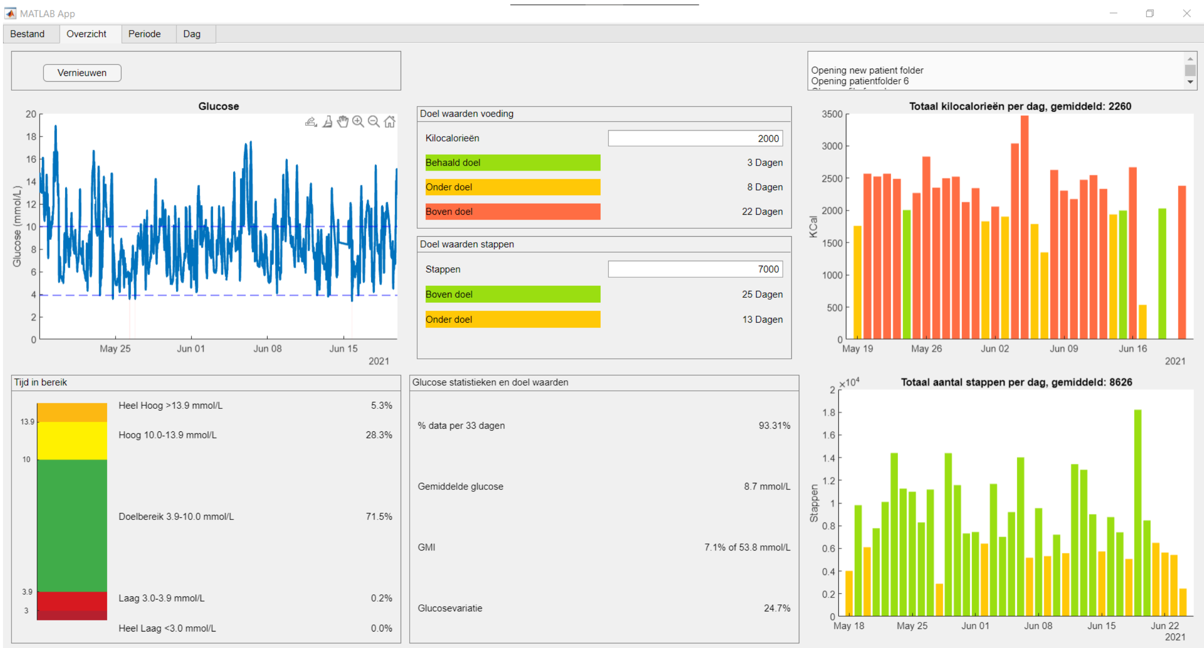


Figure 19: Overview tab of Diameter Dashboard

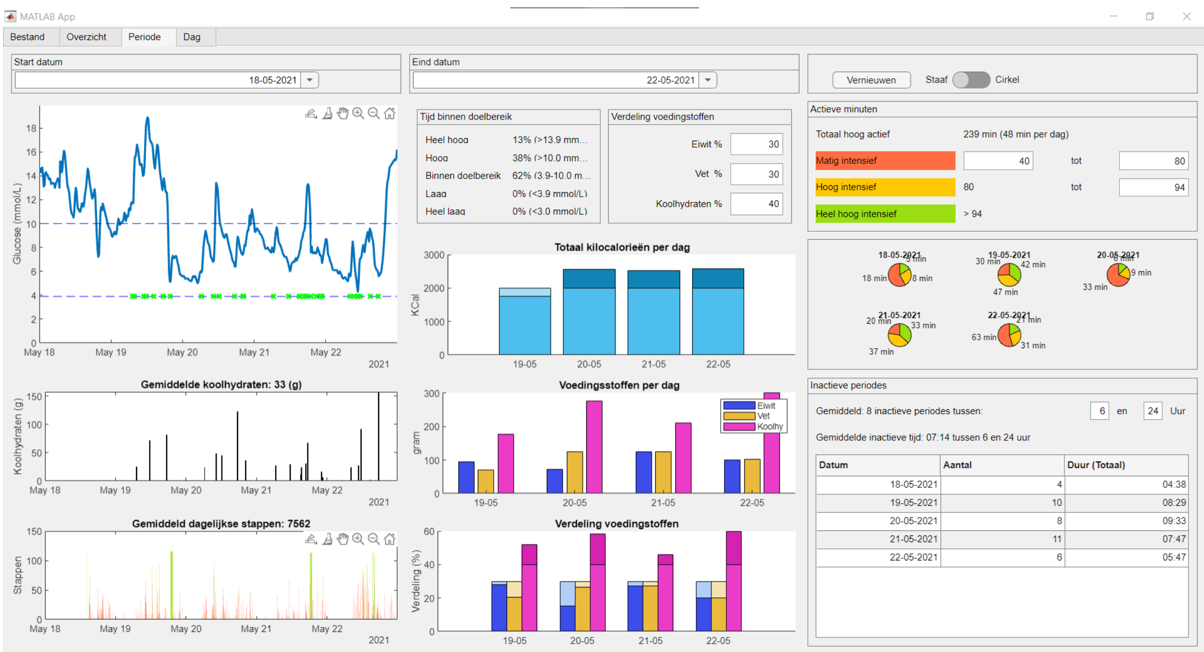


Figure 20: Period tab of Diameter Dashboard showing multiple days of patient data.

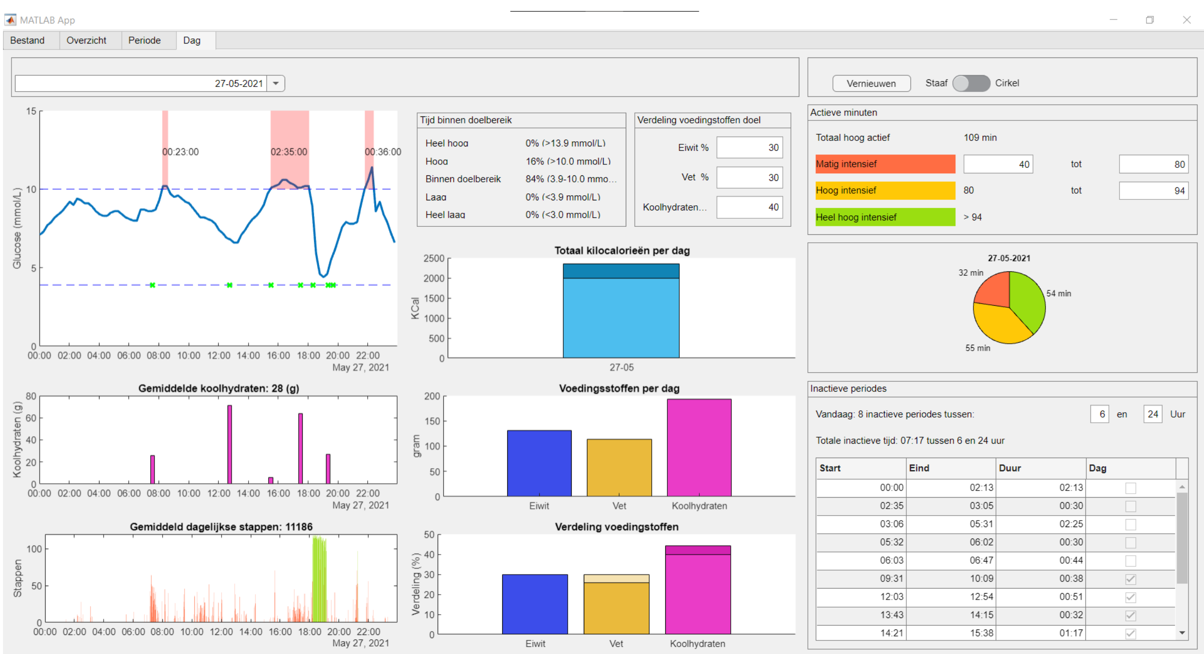


Figure 21: Diameter Dashboard populated with patient data per day.

5 Discussion

The end result, the Diameter Dashboard, was well received by patients as well as the healthcare workers, and even better, the dashboard is currently in use.

Having said that, the Diameter Dashboard is a solid first step towards monitoring and coaching T2D patients and even more important, encouraging dialogue between healthcare workers and patients. For example, patients indicated that they appreciated the fact that their treating physician could now see that they adhered to the physical activity goals.

For a person who thinks in numbers, it was challenging to let go of presenting all kinds of data and keep the dashboard easy to interpret for the patients that use it, a homogeneous group consisting of senior citizens. It would be great to actually input data from younger patients with T2D. For example the physical activity parameters can be expanded when dealing with younger patients who might be able to walk 5 kilometers per day. One could observe interesting results in the Diameter Dashboard when working with a heterogeneous group. An interesting twist was the importance of the colors used in the dashboard. At first the impact of the color scheme was overlooked. However, after careful research and feedback from patients a color scheme that worked was found. It is important to have a consistent color scheme that enhances understanding of what patients see.

5.1 Obstacles

During the process of designing the Diameter Dashboard multiple obstacles, or rather challenges, needed to be resolved.

First, nutrition data is collected in different formats depending on which application a patient uses; NEVO 2017, New-NEVO or Eetmeter. This was resolved by writing different scripts. Further, when uploading nutrition data very small details that causes a problem can occur. For example whether the data uses a : with a colon or a ; with a semi-colon.

Nutrition diaries are not always correctly populated, which meant that sometimes errors from some patients' food diaries had to be removed.

While uploading the glucose data a problem came up in the recording of date and time. It was either 2021 but also 0021. By writing a script this was able to be fixed. Additionally, the FreeStyle Libre sensor produces a text file, yet the online LibreView data is presented in a 'csv' file. Different scripts for this had to be written as well.

Processing the physical activity data was relatively easy with the exception of interpreting sedentary bouts. The question arose whether the time between sedentary bouts should be taken into account. For example, if there is a one minute gap in the data collection between physical activity, and the amount of steps exceeds the threshold of for example ten steps per minute, is it represented as one sedentary bout or should they be counted as separate bouts of activity?

5.2 Limitations

The Diameter Dashboard presents an overview of the data available, but it does not include patient recommendations, specifically concerning physical activity and nutrition. It would be fantastic if a future dashboard will encourage a patient as to what they can do better.

A limitation of the Diameter Study and Application is that the patient group does not always have an up-to-date smartphone that they know how to use. One solution could be to lend those patients a smartphone with the Diameter Application installed.

Having said that, the biggest limitation that was observed is that the interpretation of the data and the resulting coaching still needs to be done by a medical professional. However, with the Diameter Dashboard the first step was taken to reduce the amount of difficult parameters and keeping the explanations simple for patients, while still showing the important variables.

5.3 Recommendations & Future research

Future development should include a personalized coaching feature, preferably with a spoken message feature. Also, a smart next step would be to integrate the DD in the Diameter Application or to design a dedicated website for the Diameter Dashboard.

Finally, it would not hurt the outcome of the study if a fund would be made available to start a smartphone lending program. The smartphones can be preloaded with the necessary applications and solely used for the collection of lifestyle data to make sure that patients have the equipment they need. After all most diabetes care occurs in outpatient settings and involves ongoing patient self-management.

Future development of the Diameter Dashboard should include monitoring nutrition data in real time, preferably two hours after a patient has a meal. Furthermore, a useful addition would be to include monitoring of medication intake. T2D patients benefit from a personalized approach, therefore the DD was predominantly designed based on the preferences of participating patients consisting of a homogenous group of senior citizens.

It would be interesting to work with data from a heterogeneous group of T2D patients. This would include expanding physical activity parameters but also whether younger T2D patients prefer different colors and/or graphics. A heterogeneous group of T2D patients would allow for evaluating whether familiarity with wearable devices used in the data collection leads to more accurate input.

6 Conclusion

The Diameter Dashboard (DD) is currently in use at ZGT and is well-received by patients and healthcare workers. The requirements of a functional clinical dashboard are met, making this first version of the DD a solid first step towards monitoring and coaching T2D patients, encouraging dialogue between healthcare workers and patients, while improving treatment.

PART 2

Development of an algorithm to predict blood glucose values integrating glucose parameters, activity, and nutritional data using machine learning techniques.

1 Introduction

Glucose levels are of the utmost importance in managing T2D. In the Diameter Application (DA) glucose levels are measured through the FreeStyle Libre sensor. However this real time data has no predictive capabilities.

Upon completion of the Diameter Dashboard the question arises whether there is a way to predict glucose values based on nutritional intake and physical activity by employing machine learning techniques using free–living data. The reason to focus on physical activity and nutritional data is due to the fact that in the Diameter Study these values where selected to monitor in patients participating in the study. More importantly, diet and physical activity are key modifiable factors in the treatment of T2D. Regular Blood Glucose testing can uncover patterns, and with current technological advances in monitoring and evaluating lifestyle data via applications and smart-wearables, an algorithm that predicts glucose values based on diet and physical activity would be a step forward in the treatment in T2D. Currently no algorithms exist that use BG, nutritional and physical activity data to predict BG levels. A Machine Learning algorithm approach will be tested to determine whether glucose prediction can be done accurately when using features extracted from data provided by patients participating in the DIALECT study.

The main research question of part 2 is: Is it possible to predict BG values based on physical activity and nutritional data, using a deep learning algorithm?

Part 2 is organized as follows. In the literature research related work in the field of predicting glucose levels in diabetic patients is presented. In the section methodology, the study population is presented together with two proposed glucose prediction methods followed by the derived results. In closing a discussion section will follow with an interpretation and analysis of the results and limitations.

2 Literature research

2.1 Glucose prediction

It is evident that the prediction of glucose concentrations could facilitate the appropriate patient reaction in crucial situations such as hypoglycemia.

Several recent studies have considered advanced data-driven techniques for developing accurate predictive models of glucose metabolism. Data-driven techniques exploit the information hidden in the data (e.g. medication, diet, physical activity, glucose measurements) in order to learn the glucose response to various stimuli. In this direction, the appearance of advanced Continuous Glucose Monitoring (CGM) technologies as well as of activity monitoring devices could significantly enhance the prediction of glucose.

Scientists around the world are continuously researching how to predict whether a person is vulnerable to developing diabetes but also how to efficiently predict glucose values. Deng *et al.* [24] systematically examined three neural network architectures, different loss functions, four transfer-learning strategies, and four data augmentation techniques, including mix-up and generative models. Taken together, utilizing these methodologies they achieved over 95% prediction accuracy and 90% sensitivity for a time period within the clinically useful 1 h prediction horizon that would allow a patient to react and correct either hypoglycemia and/or hyperglycemia. "Owing to the complexity of the BG dynamics, it is difficult to design accurate predictive models in every circumstance, i.e., hypo/normo/hyperglycemic events." Deng *et al.* [24] developed deep-learning methods to predict patient-specific BG during various time horizons in the immediate future using patient-specific every 30-min long glucose measurements by the CGM to predict future glucose levels in 5 min to 1 h.

A new approach to the problem is by employing machine learning techniques using free–living data. Several studies have been presented in the literature aiming at the prediction of glucose in diabetic patients. The reported methods can be divided into two major groups. The first one includes mathematical models that simulate the underlying physiology of the glucose – insulin regulatory system. Compartmental models, which are a class of linear dynamic models, have been widely used for studying various aspects of normal physiology and the pathophysiology of diabetes. [25], [26]

Recently, new important quantitative knowledge has been gained on glucose metabolism and control by insulin (e.g., the EGP profile during a meal, the hepatic glucose production, the muscle glucose utilization, the kinetics of regular and slowly acting insulin after a s.c. injection), which has allowed the development of new and more accurate simulation models [27]. Nevertheless, they are still limited because of the inherent complexity of the glucose–insulin system.

On the other hand, the second group of methods provides data-driven models which are able to predict the glucose concentration based only on existing input-output data. Several specific methods are available for formulating such data models, including methods of machine learning and time series analysis.

2.2 Time series analysis and machine learning methods

Time series analysis provides methods that can be used to identify systematic patterns in time series data as well as methods for time series modelling and prediction. Auto-correlation analysis of CGM time series made clear that glucose dynamics have a detectable structure and, thus, the glucose can be predicted by exploiting its recent history. [28] In time series analysis, analysts record data points at consistent intervals over a set period of time, rather than just recording the data points intermittently or randomly. Time series analysis is a specific way of analyzing a sequence of data points collected over an interval of time. However, this type of analysis is not merely the act of collecting data over time.

What sets time series data apart from other data is that the analysis can show how variables change over time. In other words, time is a crucial variable because it shows how the data adjusts over the course of the data points as well as the final results. It provides an additional source of information and a set order of dependencies between the data.

Time series analysis typically requires a large number of data points to ensure consistency and reliability. An extensive data set ensures you have a representative sample size and that analysis can cut through noisy data. It also ensures that any trends or patterns discovered are not outliers and can account for seasonal variance. Additionally, time series data can be used for forecasting—predicting future data based on historical data.

A 2021 study by Prendin *et al.* [29] explores an efficient medical decision system for diabetes prediction based on a Deep Neural Network (DNN). When these algorithms are applied in healthcare for prediction and diagnosis purposes, they can produce highly accurate results. Moreover, they can be combined with medical knowledge to improve decision-making effectiveness, adaptability, and transparency. A performance comparison between the DNN algorithm and some well-known machine learning techniques as well as the state-of-the-art methods is presented in this study showing that the proposed method based on the DNN technique provides promising performances with an accuracy of 99.75% and an F1-score of 99.66. [29]

Digital health is improving the treatment of people with diabetes, and has been widely adopted in recent years. Zhu *et al.* [30] presented a research paper in 2020 on Deep Learning for Diabetes with promising results of deep learning within the field of diabetes. In a 2021 study a deep learning network was also used to predict future BG levels. A sequential model with one LSTM layer, one bidirectional LSTM layer and several fully connected layers was used to predict BG levels for different Prediction Horizon (PH). The method was trained and tested on 26 datasets from 20 real patients concluding that the proposed network outperforms the baseline methods in terms of all evaluation criteria. [30], [31]

The prediction of the glucose as a function of the input variables can be considered as a regression problem with a time component. The fact that the relationship among input variables (i.e. medication, diet, physical activity, stress etc.) and glucose levels is nonlinear, dynamic, interactive and patient-specific, demands the application of non-linear regression models such as support vector regression, Gaussian processes and artificial neural networks.[28]

2.3 Findings on Time Series Analysis and machine learning methods

It is evident from recent studies that progress is being made utilizing time series analysis and deep learning networks to predict glucose values while taking into account other lifestyle data. In an ideal world the combination of nutritional intake and physical activity should lead to glycemic control. However in T2D patients, glucose remains in the bloodstream and will not reach all body cells, which remains a challenge to predict as it involves different parameters.

Notwithstanding the urgent need to put a stop to the increase of T2D patients worldwide, as mentioned prior, an intervention in lifestyle change is essential. To convince T2D patients in making lifestyle changes and for healthcare workers to understand the barriers patients face to do so, predictive glucose models that take nutrition and exercise into account will help tremendously when it comes to making lifestyle choices that lead to glycemic control.

2.4 Research objective

The goal is how to efficiently predict Blood Glucose values incorporating nutritional and activity data with the use of a deep-learning model.

3 Method

An algorithm predicting BG levels, including nutrition and activity data, has not yet been published. Therefore, an algorithm to predict BG values should be developed integrating glucose parameters, activity and nutritional data using machine learning techniques.
The following process is followed to develop an algorithm:

1. Clear definition of what the algorithm should predict to decide which data is needed and where the data can be found.
2. Data exploration
3. Select usable data from the study population
4. Dataset preprocessing
5. Prepare the selected data for Machine Learning
6. Use a deep learning algorithm to predict future values.
7. Prediction of future BG levels

Sub- question 2a) "What should the algorithm predict and what data is needed?", will be answered during step one, two and three of the aforementioned strategy. Sub-question 2b) "How to prepare data for machine learning and predict future blood glucose levels?" will be answered during step four, five, and six.

3.1 Clear definition of what the algorithm should predict to decide which data is needed and where the data can be found

The algorithm should predict BG levels as accurately as possible and ideally as far in the future as possible, which requires historical glucose, physical activity, and nutrition data.
Glucose data is considered a time series, therefore a LSTM for regression to predict future values of BG levels is the logical choice.

3.2 Data exploration

Historical data from the DIALECT study is used to create a dataset for machine learning.

The study population consisted of 256 patients with T2D aged $\geq$ 18 years, treated in an outpatient clinic as part of routine secondary care. Participating patients used smart wearables (Fitbit and smartphone) to collect nutritional- and activity data, as well as the FreeStyle Libre sensor to upload glucose values.

3.3 Select usable data from the study population

From the raw DIALECT data 43 T2D patients met the requirements to create a dataset used for machine learning. The requirements: glucose data recorded every 15 minutes for fourteen consecutive days, as well as uploaded activity- and nutrition data.

Various features or parameters were extracted from the time series and subsequently utilized as input into a deep learning model. After, analysis was performed and features extracted from the data to use in the LSTM model. The analysis of the data was done in MATLAB 2021B.

3.3.1 Glucose parameters

There were several glucose parameters in addition to the raw glucose values.

- Mean = Average of the glucose values.
- Time in range (percent and minutes); The amount of time spend in the target blood glucose range ($3.9 - 10 mmol/L$) (TIR)
- Time above range ($> 10 mmol/L$) (TAR)
- Time below range ($< 3.9 mmol/L$) (TBR)
- $\text{TBR}_1 = 3.0 - 3.9\ mmol/L$, $\text{TBR}_2 = < 3.0\ mmol/L$, $\text{TAR}_1 = 10.0 - 13.9\ mmol/L$, $\text{TAR}_2 = > 13.9\ mmol/L$.
- SD = standard deviation in mmol/L, spread around average glucose.
- CV = coefficient of variation is the SD divided by the mean. [9]

3.3.2 Physical activity parameters

Step data are measured at 1 minute intervals. Due to the fact that glucose data has to be leading in the calculations, the step data was condensed to 15 minute intervals matching the glucose measurement points with the input from the step data.

When creating datasets for the steps taken, the activity/steps data was taken from the 15 minutes prior to the moment that the glucose value is measured. For example, steps taken from 17:46 - 18:00 are summed up to match the glucose value of 18:00. In short, steps are re-sampled to 15 minutes. Also note that due to these selections, the last 15 minutes of each day are not taken into account.

The following physical activity parameters were chosen [32]:
- Total amount of steps.
- Mean amount of steps.
- Total Active minutes (≥ 20 $steps/min$).
- Sedentary activity (< 20 $steps/min$).
- Sporadic movement (min/day with $20 - 39$ $steps/min$).
- Purposeful steps (min/day with $40 - 59$ $steps/min$).
- Slow walking (min/day with $60 - 79$ $steps/min$).
- Medium walking (min/day with $80 - 99$ $steps/min$).
- Brisk walking (min/day with > 100 $steps/min$).

3.3.3 Nutritional parameters

The raw nutrition data is re-sampled to the aforementioned fifteen minute intervals, setting all entries to start at a full quarter. This creates overlapping entries as nutrition was entered at for example 7:20 am and 7:25 am, which was rounded up to 7:30 am using a script made in MATLAB.

Nutritional data is entered right before or or after a patient eats, resulting in raw data consisting of kilocalories, proteins, fats and carbohydrates, which were chosen as the nutritional parameters.

3.4 Dataset preprocessing

In total 22 parameters were extracted from glucose values, physical activity, and nutritional data.

Data with up to two missing data-points were interpolated using MATLAB's fill missing function which uses piecewise cubic spline interpolation. Data with more missing points were discarded.

3.5 Prepare the selected data for machine learning

The data was normalized using a min-max normalization with a minimum of 0 and a maximum of 1.

All 43 patients are analyzed and the input dataset is ready for a ML model.
Of the 43 patients 5 random patients were selected as test patients. The model was not trained on these patients, but they were used to validate the model.

3.6 Use a deep learning algorithm to predict future values

The Long short-term memory model chosen to start testing is a type of Recurrent Neural Network (RNN).

Because of their internal memory, LSTMs can remember important things about the input they received, which allows them to be very precise in predicting what is coming next. This is why they are the preferred algorithm for sequential data like time series. Long short-term memorys can form a much deeper understanding of a sequence and its context compared to other algorithms.

The prediction model used was designed as follows, see figure 22.

A six-layer deep learning model with two different LSTM layers.

- The first layer is the sequence input layer, which inputs a sequence (the dataset) into the neural network. This layer has 22 nodes corresponding to the 22 features of the dataset.
- The second layer is a LSTM layer with 128 hidden units. The number of hidden units corresponds to the amount of information that the layer remembers between time steps.
- The next layer is a dropout layer which randomly sets input elements to zero with a given probability of 20%.
- Following the dropout layer another LSTM layer is added with 64 hidden units.
- After this layer a fully connected layer follows which multiplies the input by a weight matrix and adds a bias vector. The output size of this layer matches the number of channels of the input data.
- The final layer is a regression layer to calculate the mean-squared-error loss.

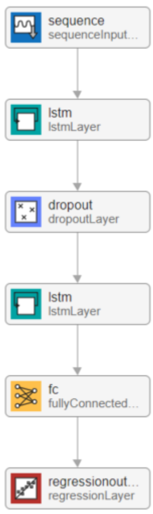


Figure 22: Proposed LSTM Model by the researcher (S.F. Peters)

3.7 Prediction of future blood glucose values

To predict the BG values two different methods were studied.

3.7.1 Direct multi-step forecasting

The first method used to predict future BG values is based on developing a separate model for each forecast time step. Each model uses the prediction of the last step to predict the next future BG step. This is called Direct multi-step forecasting (DMSF).

Input	Output
x(t=0), y(0)	$\hat{y}(t=1)$
x(0), $\hat{y}(1)$	$\hat{y}(2)$
x(0), $\hat{y}(2)$	$\hat{y}(3)$
...	...

3.7.2 Recursive multi-step forecasting

In the second method, the predicted value is added to the data set for the next prediction. This increases the number of input nodes with each subsequent model.This is called Recursive multi-step forecasting (RMSF).

Input	Output
x(t=0), y(0)	$\hat{y}(t=1)$
x(0),y(0),$\hat{y}(1)$	$\hat{y}(2)$
x(0),y(0),$\hat{y}(1)$,$\hat{y}(2)$	$\hat{y}(3)$
...	...

3.8 Validation measures

This research uses three main outcome measures, the Root-Mean-Square Error (RMSE), the Mean Absolute Error (MAE) and the standard deviation of the error.

3.8.1 RMSE

The Root-Mean-Square Error (RMSE) is a measure of the difference between the predicted and the measured values.

$$RMSE = \sqrt{\sum_{i=1}^{n} \left(\frac{\hat{y}_i - y_i}{n}\right)^2}$$

The RMSE is scale-independent and gives a relatively high weight to large errors. Therefore, it is useful to compare forecasting errors in different models.

3.8.2 MAE

The Mean Absolute Error (MAE) is another measure of errors and calculates the average of the absolute error. Since each error influences the MAE in direct proportion to the absolute value of the error it is a good addition to the validation measures.

$$MAE = \frac{1}{n} \sum_{i=1}^{n} \hat{y}_i - y_i$$

3.8.3 Standard deviation of the error

The standard deviation of prediction errors provides insights into the spread and variability of errors around the mean.

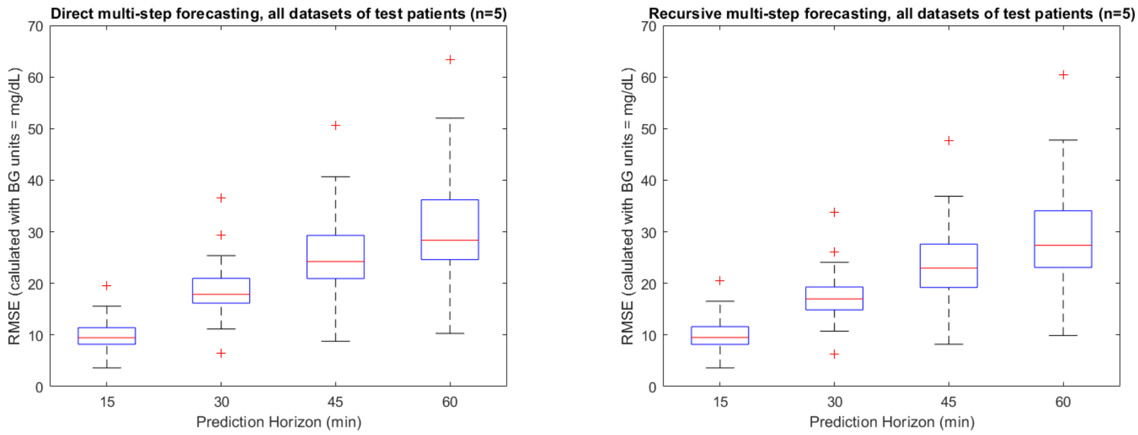
$$\sigma^2 = \frac{1}{n} \sum_{i=1}^{n} ((\hat{y}_i - y_i) - \mu)^2$$

4 Results

The two models were tested on a one-hour prediction horizon corresponding to predicting 4 samples in the future.
Below are the two outcome measures, the RMSE, the MAE and the standard deviation of the error shown.
Due to a difference between the units used for the blood glucose in the Netherlands and the international literature, here the unit mg/dL corresponding to the literature is shown. For the results with the unit $mmol/L$, used in the dutch hospitals, see appendix B.

4.1 RMSE

Below are the RMSE of the two proposed methods shown. As can be seen the error of the prediction increases with each predicted time step in the future. Several outliers can be seen and upon inspection these are from datasets with a very small amount of samples.

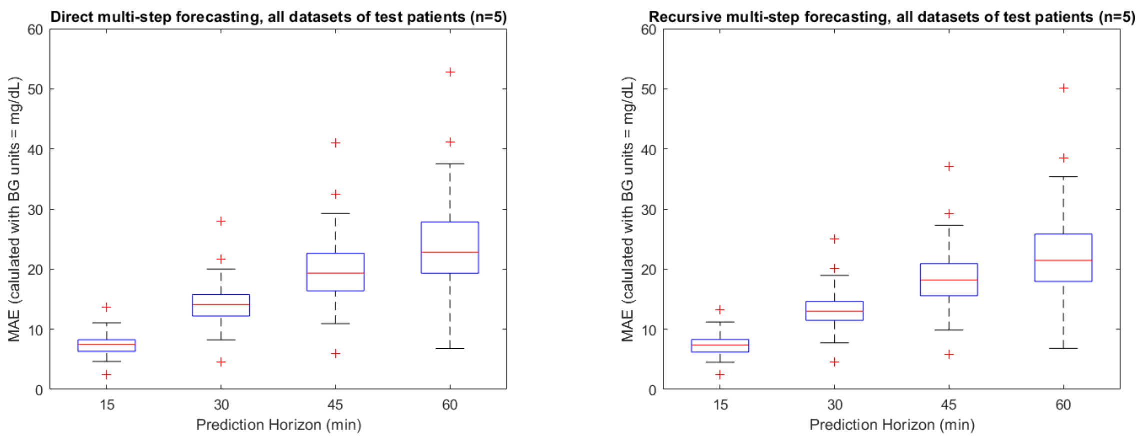


(a) (b)

Figure 23: RMSE of all datasets of all patients of the DMSF method (a), and the RMSF method (b).

4.2 MAE

Below are the MAE of the two proposed methods shown. As with the RMSE here the error of the prediction increases also with each predicted time step in the future. Several outliers can be seen and upon inspection these are again from datasets with a very small amount of samples.



(a) (b)

Figure 24: MAE of all datasets of all patients of the DMSF method (a), and the RMSF method (b).

4.3 Standard Deviation of the Error

Next to RMSE and MAE the standard deviation of the error provides extra insight into the prediction accuracy of the presented model.
For example one test patient shows:
Prediction horizon of 15 minutes std. of the error 0.5 while a prediction horizon of 60 minutes std. of the error 1.45.

Figure 25 shows the error of one test patient for prediction horizon = 60 minutes. This represents the other datasets. One can observe the small difference in over- and underestimation which is proven as well in the calculations: overestimation 47% and underestimation 53%.

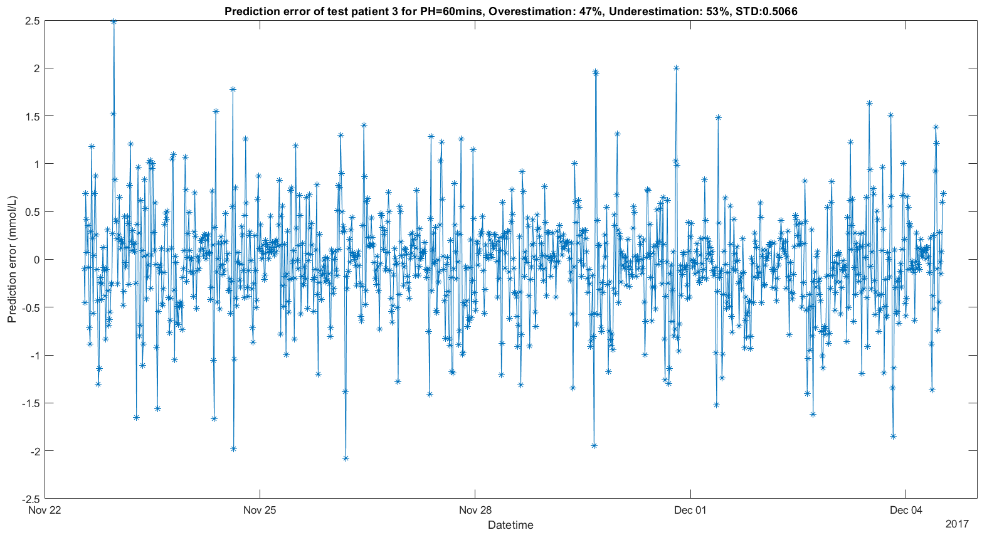


Figure 25: Prediction error of one dataset of one test patient for PH = 15 mins.

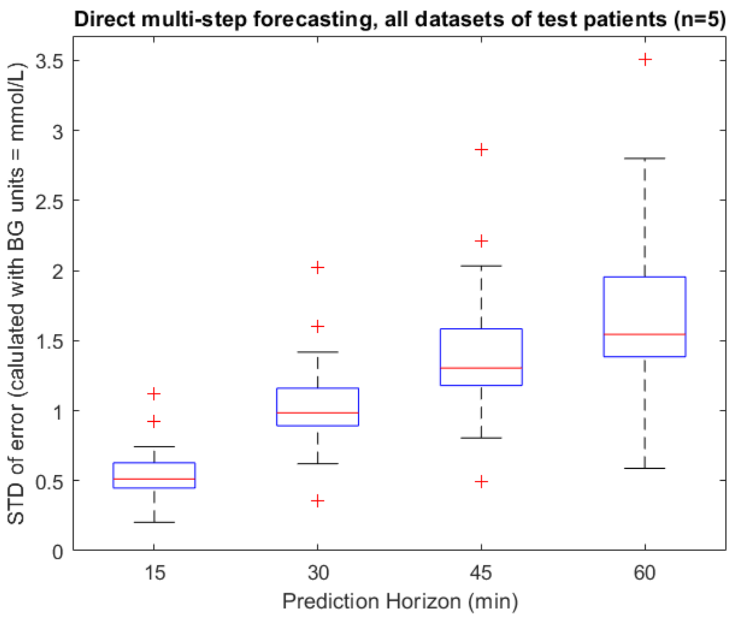
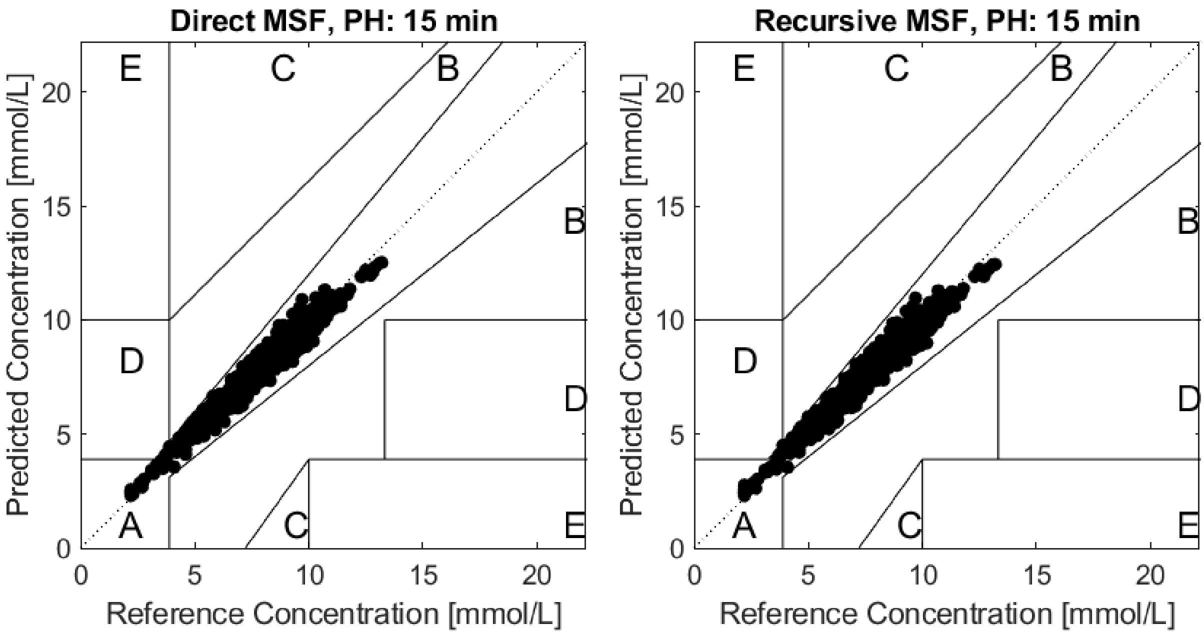


Figure 26: STD of error of all datasets of all patients of the DMSF method.

4.4 Clarke Error grid

The Clarke Error grid is one of the most widely used tools to assess the clinical accuracy of BG estimation. The Clarke Error grid is a plot with five major zone of attention (zone A, B, C, D, and E) for interpretation of the predicted glucose levels.

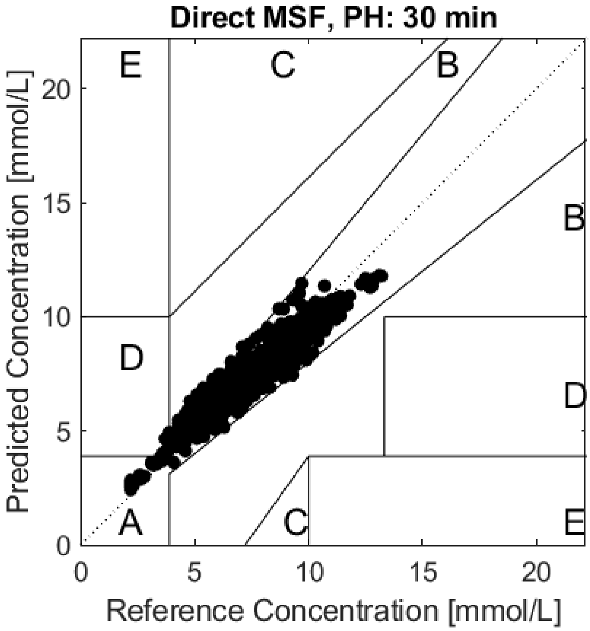


(a) (b)

Figure 27: Clarke Error grid of one patient with a 15 minute prediction horizon of the DMSF method in (a), and the RMSF method (b).

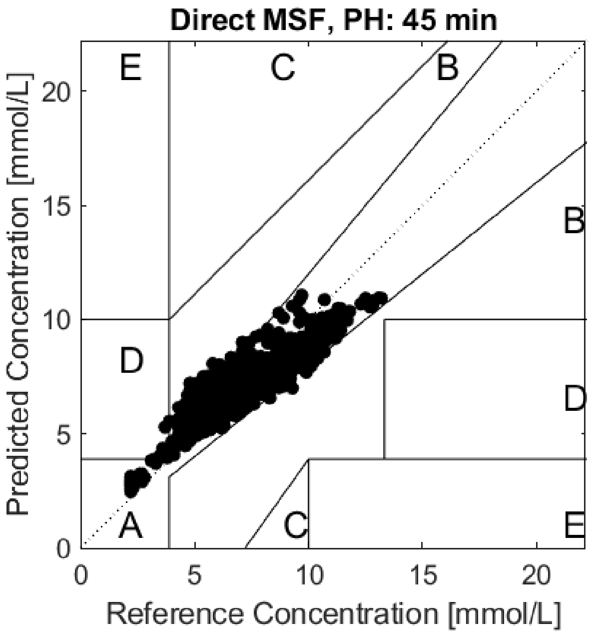
For a prediction horizon of 15 minutes, 100% of the predictions are within region A of the grid, for the direct as well as the recursive method, see figure 27.

For both methods the increase of the prediction horizon to 30 minutes, see figure 28, leads to a small change in the grid, with movement towards region B. This prediction zone still falls within an acceptable value as it will not lead to inappropriate treatment.



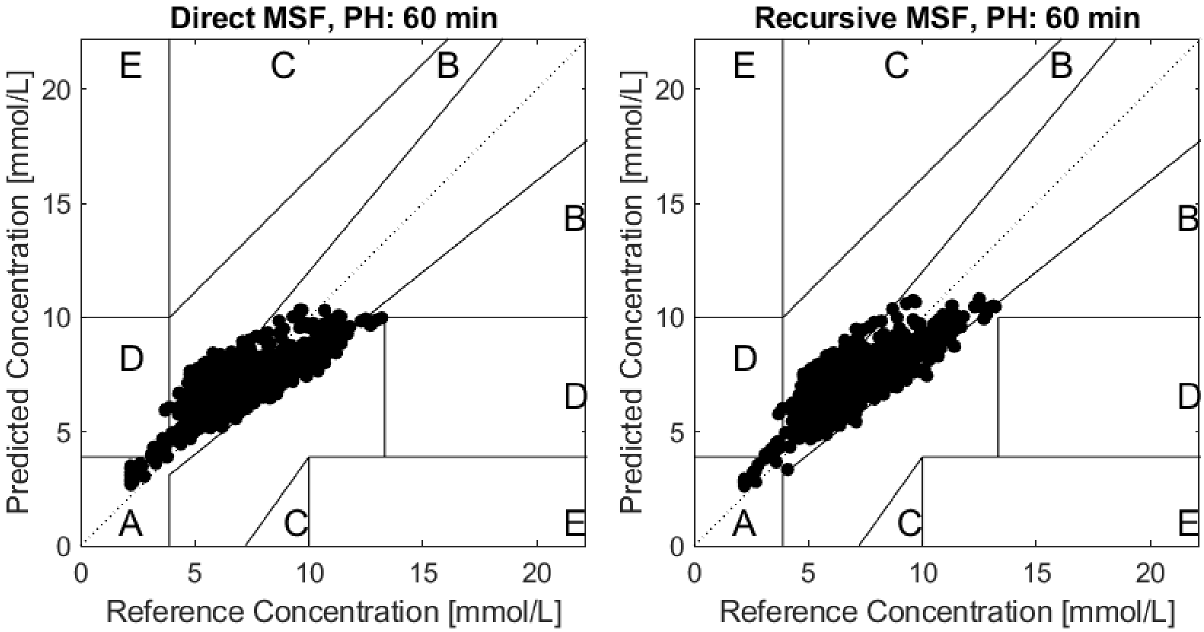
(a) (b)

Figure 28: Clarke Error grid of one patient with a 30 minute prediction horizon of the DMSF method in (a), and the RMSF method (b).



(a) (b)

Figure 29: Clarke Error grid of one patient with a 45 minute prediction horizon of the DMSF method in (a), and the RMSF method (b).



(a) (b)

Figure 30: Clarke Error grid of one patient with a 1 hour prediction horizon of the DMSF method in (a), and the RMSF method (b).

When the prediction horizon increases to 45 (figure 29) and 60 minutes (figure 30), one can observe that a limited amount of predictions will enter region D. Region D is the region in the Clarke Error grid that fails to detect hypoglycemia which can lead to potentially dangerous situations and decisions for diabetes patients.

An example of the predictions for one of the datasets of one test patient with the RMSF method. For the DMSF method see figure 36. Each Prediction Horizon has a different marker:

PH (min)	Marker
15	o
30	x
45	⋄
60	△

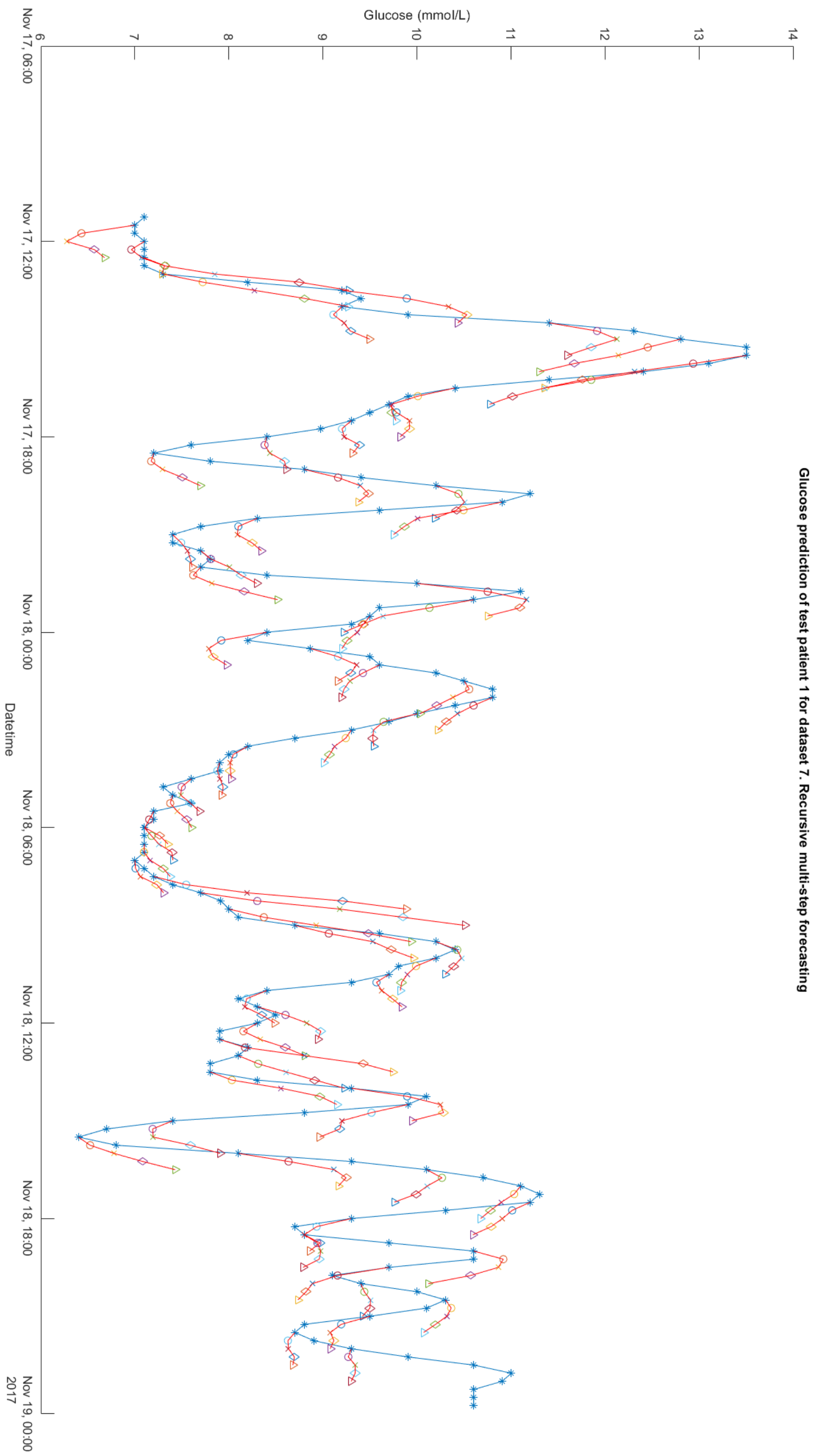


Figure 31: RMSF method.

5 Discussion

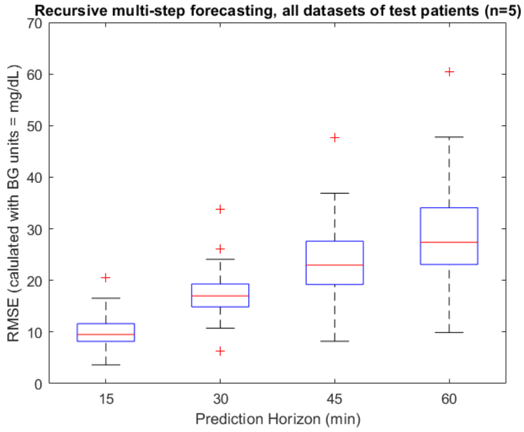
5.1 Interpretation of results

Two models were tested to predict future Blood Glucose values; direct multi-step forecasting and recursive multi-step forecasting. The second method, the RMSF provided a more accurate prediction. The errors were smaller compared to utilizing the first method, which is most likely the result of adding the predicted value as input to the data set for the next prediction.

The main research question whether it is possible to predict blood glucose values based on physical activity and nutritional data, using a deep learning algorithm can be answered as follows. At first glance the results seem impressive. When utilizing the RMSE and MAE validation measures, the prediction seems reasonable, considering the standard deviation allowed. Comparing the performance of the algorithm designed, to current research in the field of personalized LSTM models for glucose prediction [33], one may come to the conclusion that the algorithm can predict BG values based on physical activity and nutritional data utilizing deep learning. Yet, upon closer inspection the outcomes are insufficient and not ready to be used in a clinical setting. The following comparison clarifies the discrepancies.

Model	RMSE	FIT	UD	DD	PH	# subj	Data	LSTM Architecture	Input
P-LSTM	7.67	75.86	9	9	40	100	Silico	Single Layer LSTM	CGM, M, I
Sun et al. [13]	30.21	42.56	33		45	20	Silico/Vivo	LSTM + Bi-directional LSTM	CGM
Aiello et al. [14]	11.68 31.01	58.84 41.41	- -	- -	[5, ..., 60]	100 1	Silico Vivo	2 branches of stacked LSTMs	CGM, M, I
Carrillo et al. [15]	20.76	-	25	15	45	8	Vivo	Stacked LSTMs	CGM, M, I
Mirshekarian et al. [16]	2.93 18.07	- -	- -	- -	30	30 6	Silico Vivo	Memory-Augmented LSTM	CGM, M, I
Aliberti et al. [17]	7.18	88.79	0 [samples]		45	451	Vivo	Single Layer LSTM	CGM
Rabby et al. [18]	5.89 18.96	- -	- -	- -	30	6	Vivo	Stacked LSTMs w/ filtered CGM Single Layer LSTM	CGM, M, I, steps

(a) Table 2 of Iacono *et al.* [33]



(b) RMSE of the Recursive multi-step forecasting method

Figure 32

Figure 32a shows the results from several studies in the field of glucose prediction [33]. Figure 32b shows the results of the algorithm developed in this study. When comparing the column Prediction Horizon (PH) and the RMSE column, to the research results one may conclude that the results are within range. Yet the resulting glucose prediction graph, figure 31, illustrates that the algorithm is not yet accurate enough.

RMSE validation indicates that the outcome generated by the prediction model designed in this study should work. But when it comes to the actual outcome the RMSE values are misleading. Meaning that the model is not ready for use in a clinical setting because the actual predictions are off.

With a prediction horizon of 15 minutes the model produces an accurate prediction, while with each step in the prediction horizon the standard deviation of the error increases, suggesting that the data values are further apart and that the prediction is less precise. With each step into the future the BG prediction becomes less accurate, see figure 26. Looking at the over- and underestimation the model does not favor one over the other.

The Clarke Error grid was used to determine the clinical accuracy of the predictions. The strength of these findings is that no results are plotted in the E region. To clarify, the data points in the E region could lead clinically to inappropriate treatment. Furthermore the prediction results are relatively constant. For a prediction horizon of 60 minutes, see figure 28, 90% of the predictions remain clustered in regions A and B.

The clinical implications are that according to the Clarke Error grid, the model produces mostly accurate predictions, which could translate and underscore the practical application of the prediction model in the future. However, clinically this model cannot be used because even though the amount of predictions that are centered in region D is limited, it is still clinically irresponsible to have patients use these predictions in real life.

5.2 Obstacles

Examples of the challenges that needed to be resolved to create a consistent dataset that can be used for ML were:

- The sample frequency of the Freestyle Libre varies between 14-18 minutes. Only the measurements with 15 minute intervals were utilized.
- The food diary, even though in the same format presents data differently: yyyy-MM-dd and dd-MM-yy.
- Missing data.
- LSTM versus regression models. Even though LSTM would be the best approach, the concern is that the dataset is too small for LSTM. Therefore other methods were explored such as regression models.

5.3 Future research

The model is a starting point for the future development of a prediction algorithm to be used in a clinical setting. The errors and clinical accuracy illustrate that a deep learning algorithm can be used in the prediction of blood glucose levels including nutritional and physical activity data. But, first the suggested model needs to be tested with a larger and improved dataset. For example, a study including all ages and health situations (people with and without T2D).

With new digital health technologies developed every day the measurement of health variables should be more robust and increasingly more automated. When patients and/or participants in a future study do not have to input data themselves, the dataset will become more accurate.

6 Conclusion

The conclusion drawn from the main research question as stated in part 2 of this thesis: "Is it possible to predict blood glucose values based on physical activity and nutritional data, using a deep learning algorithm?" is that the designed model is not ready and not yet clinically relevant. Future research is needed to improve the accuracy. However the field of deep learning shows promise for real-time glucose prediction using physical activity data and nutritional data.

References

[1] "Diabetes mellitus." (Nov. 15, 2021), [Online]. Available: https://www.volksgezondheidenzorg.info/onderwerp/diabetes-mellitus.

[2] L. Chen, D. J. Magliano, and P. Z. Zimmet, "The worldwide epidemiology of type 2 diabetes mellitus—present and future perspectives," *Nature reviews endocrinology*, vol. 8, no. 4, pp. 228–236, 2012.

[3] "Ziekenhuisgroep twente." (Mar. 10, 2023), [Online]. Available: https://www.zgt.nl/.

[4] "University of twente." (Mar. 10, 2023), [Online]. Available: https://www.utwente.nl/.

[5] "Roessingh research development." (Mar. 10, 2023), [Online]. Available: https://www.rrd.nl/en/.

[6] "Diameter." (Mar. 10, 2023), [Online]. Available: https://www.diameterapp.nl/.

[7] D. M. Williams, H. Jones, and J. W. Stephens, "Personalized type 2 diabetes management: An update on recent advances and recommendations," *Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy*, pp. 281–295, 2022.

[8] C. M. Gant, S. H. Binnenmars, E. van den Berg, S. J. Bakker, G. Navis, and G. D. Laverman, "Integrated assessment of pharmacological and nutritional cardiovascular risk management: Blood pressure control in the diabetes and lifestyle cohort twente (dialect)," *Nutrients*, vol. 9, no. 7, p. 709, 2017.

[9] N. Den Braber, M. M. Vollenbroek-Hutten, K. M. Westerik, *et al.*, "Glucose regulation beyond hba1c in type 2 diabetes treated with insulin: Real-world evidence from the dialect-2 cohort," *Diabetes care*, vol. 44, no. 10, pp. 2238–2244, 2021.

[10] N. den Braber, M. M. Vollenbroek-Hutten, M. M. Oosterwijk, *et al.*, "Requirements of an application to monitor diet, physical activity and glucose values in patients with type 2 diabetes: The diameter," *Nutrients*, vol. 11, no. 2, p. 409, 2019.

[11] N. I. for Public Health and the Environment (RIVM). "Dutch food composition database—nevo online version 2016/5.0." (Mar. 10, 2023), [Online]. Available: https://www.rivm.nl/en/dutch-food-composition-database.

[12] S. V. Nederland. "Mijn eetmeter." (Mar. 10, 2023), [Online]. Available: https://mijn.voedingscentrum.nl/nl/eetmeter/.

[13] R. Rabiei and S. Almasi, "Requirements and challenges of hospital dashboards: A systematic literature review," *BMC Medical Informatics and Decision Making*, vol. 22, no. 1, pp. 1–11, 2022.

[14] M. P. Papazoglou and W.-J. Van Den Heuvel, "Service oriented architectures: Approaches, technologies and research issues," *The VLDB journal*, vol. 16, pp. 389–415, 2007.

[15] R. Rasmussen, "Electronic whiteboards in emergency medicine: A systematic review," in *Proceedings of the 2nd ACM SIGHIT International Health Informatics Symposium*, 2012, pp. 483–492.

[16] K. Pauwels, T. Ambler, B. H. Clark, *et al.*, "Dashboards as a service: Why, what, how, and what research is needed?" *Journal of service research*, vol. 12, no. 2, pp. 175–189, 2009.

[17] R. M. Ratwani and A. Fong, "'connecting the dots': Leveraging visual analytics to make sense of patient safety event reports," *Journal of the American Medical Informatics Association*, vol. 22, no. 2, pp. 312–317, 2015.

[18] Medium. "Dashboard design process." (Mar. 10, 2023), [Online]. Available: https://medium.com/@entango/dashboard-design-process-e31d9c4fe61e.

[19] D. Clegg and R. Barker, *Case method fast-track: a RAD approach*. Addison-Wesley Longman Publishing Co., Inc., 1994.

[20] Microsoft Corporation, *Microsoft excel*, version 365 (2208), Mar. 10, 2023. [Online]. Available: https://office.microsoft.com/excel.

[21] D. Handu and T. Piemonte, "Dietary approaches and health outcomes: An evidence analysis center scoping review," *Journal of the Academy of Nutrition and Dietetics*, vol. 122, no. 7, pp. 1375–1393, 2022.

[22] Q. Wu, Z. Tan, and J. Liu, "Experimental study on the relationship between the harmony and cognitive load of business intelligence dashboard color combinations," *Color Research & Application*, vol. 47, no. 4, pp. 920–941, 2022.

[23] H. Hamasaki, "Daily physical activity and type 2 diabetes: A review," *World journal of diabetes*, vol. 7, no. 12, p. 243, 2016.

[24] Y. Deng, L. Lu, L. Aponte, *et al.*, "Deep transfer learning and data augmentation improve glucose levels prediction in type 2 diabetes patients," *NPJ Digital Medicine*, vol. 4, no. 1, p. 109, 2021.

[25] E. Carson and C. Cobelli, *Modelling methodology for physiology and medicine*. Newnes, 2013.

[26] A. Makroglou, J. Li, and Y. Kuang, "Mathematical models and software tools for the glucose-insulin regulatory system and diabetes: An overview," *Applied numerical mathematics*, vol. 56, no. 3-4, pp. 559–573, 2006.

[27] C. Dalla Man, R. A. Rizza, and C. Cobelli, "Meal simulation model of the glucose-insulin system," *IEEE Transactions on biomedical engineering*, vol. 54, no. 10, pp. 1740–1749, 2007.

[28] K. Funatsu, *Knowledge-Oriented Applications in Data Mining*. BoD–Books on Demand, 2011.

[29] F. Prendin, S. Del Favero, M. Vettoretti, G. Sparacino, and A. Facchinetti, "Forecasting of glucose levels and hypoglycemic events: Head-to-head comparison of linear and nonlinear data-driven algorithms based on continuous glucose monitoring data only," *Sensors*, vol. 21, no. 5, p. 1647, 2021.

[30] T. Zhu, K. Li, P. Herrero, and P. Georgiou, "Deep learning for diabetes: A systematic review," *IEEE Journal of Biomedical and Health Informatics*, vol. 25, no. 7, pp. 2744–2757, 2020.

[31] Q. Sun, M. V. Jankovic, L. Bally, and S. G. Mougiakakou, "Predicting blood glucose with an lstm and bi-lstm based deep neural network," in *2018 14th symposium on neural networks and applications (NEUREL)*, IEEE, 2018, pp. 1–5.

[32] C. Tudor-Locke, H. Han, E. J. Aguiar, *et al.*, "How fast is fast enough? walking cadence (steps/min) as a practical estimate of intensity in adults: A narrative review," *British journal of sports medicine*, vol. 52, no. 12, pp. 776–788, 2018.

[33] F. Iacono, L. Magni, and C. Toffanin, "Personalized lstm models for glucose prediction in type 1 diabetes subjects," in *2022 30th Mediterranean Conference on Control and Automation (MED)*, 2022, pp. 324–329. DOI: 10.1109/MED54222.2022.9837153.

Appendix A The Diameter study

Current treatment of type 2 diabetes patients does not reach the full potential for improvement of a sufficient lifestyle management. With current innovations in technology the ease and availability for monitoring and evaluation of lifestyle via applications and smart-wearables is greatly improved. The technology for acquiring objective data from blood glucose sensors, nutritional diaries, activity tracking and tailored coaching does exist, however no application exists yet that can integrate all these aspects for clinical use.

Therefore, to improve upon the current treatment the Diameter application was developed by the ZiekenhuisGroep Twente, University of Twente and the Roessingh Research and Development institute and to test the application as a blended-care intervention the Diameter-1 study will be started. There are three phases to the Diameter-1 study:
Phase 1: A pilot study to test the research protocol and investigate the usability of the Diameter with the aim of solving user problems.
Phase 2: A feasibility study to evaluate the intervention use and acceptability of the Diameter as blended care.
Phase 3: A feasibility study to investigate the Diameter as a standalone application in primary care.

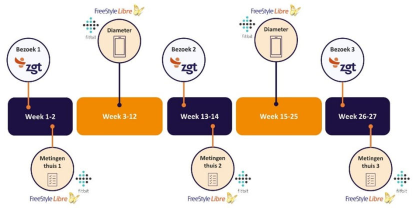


Figure 33: Timeline of the Diameter-1 study

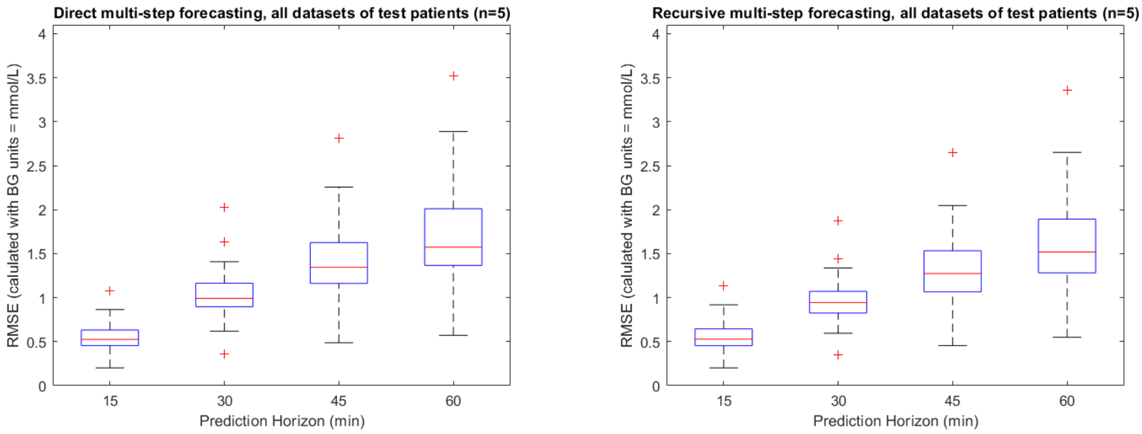
The pilot study of the Diameter-1 study will be a mixed-methods cross-sectional study with 10 T2DM patients. The duration will be 5 weeks for each participant during which they will use the Diameter application and provide feedback about the usability and comprehensibility. The use of the Diameter app consists of monitoring blood glucose levels (with a Freestyle Libre sensor), physical activities (with a Fitbit) and nutrition. Furthermore, the participants will receive 2 coaching messages per day and one weekly exercise goal. After the 5 week use of the Diameter application a follow-up meeting will take place where feedback on the collected data will be provided to the participant and an interview will be conducted with the patient about the use of the Diameter application. Also, the participant will be send a questionnaire and a think-aloud test where the participants will share their thoughts and opinions on the questionnaire and Diameter application.

During phase 2 the Diameter will be assessed using a mixed methods prospective longitudinal study with 80 T2DM patients. In this study three measure moments will be conducted. The first two weeks will consist of making baseline measurements. During these two weeks the blood glucose and nutritional data will be blinded while the physical activity will not be blinded. After two weeks the Diameter will be fully used for four weeks. During this time the participant receives 2 coaching messages per day and will use the digital personalized coach which focuses on goal setting and achievement. After this time a two week period of measurements of all clinical, physiological and behavioral outcomes will take place. The participants will also participate in an interview and fill in a number of questionnaires. Then the participants will have four more weeks where they use the Freestyle Libre sensors and during this period they will use the Diameter application without the daily coaching messages. Lastly, there is a two-week period where the participants will perform measurements of the outcomes and fill in questionnaires.

Phase 3 will be a mixed-method cross-sectional study with 10 participants recruited from primary care. Participants will use the Diameter as stand-alone application for 10 weeks in which they can monitor nutrition and physical activity. The participants will receive personalized coaching with two messages and a weekly exercise on goal-setting and achievement. After this 10-week period two questionnaires will be administered and interviews will be conducted to gain insight into their experiences with the Diameter.

Appendix B   Results in $mmol/L$

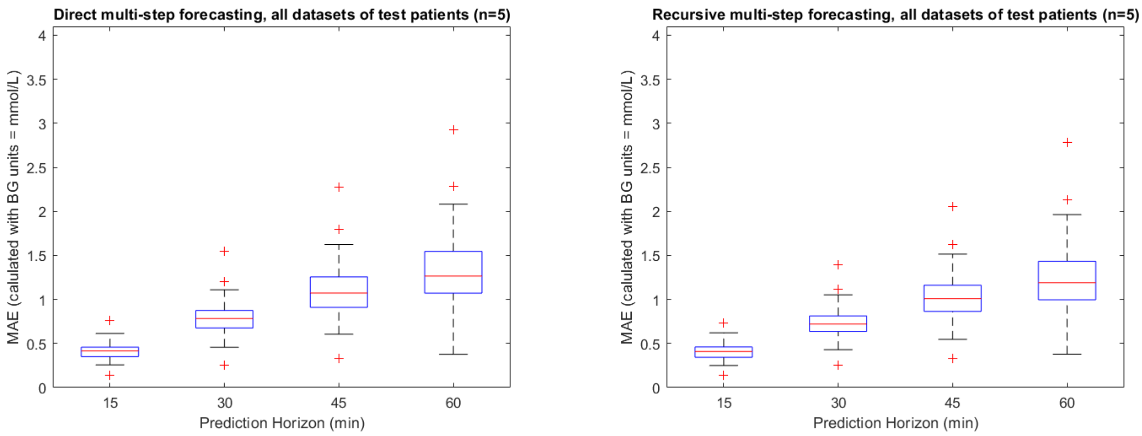
B.1   RMSE



(a) (b)

Figure 34: RMSE of all datasets of all patients of the DMSF method (a), and the RMSF method (b).

B.2   MAE



(a) (b)

Figure 35: MAE of all datasets of all patients of the DMSF method (a), and the RMSF method (b).

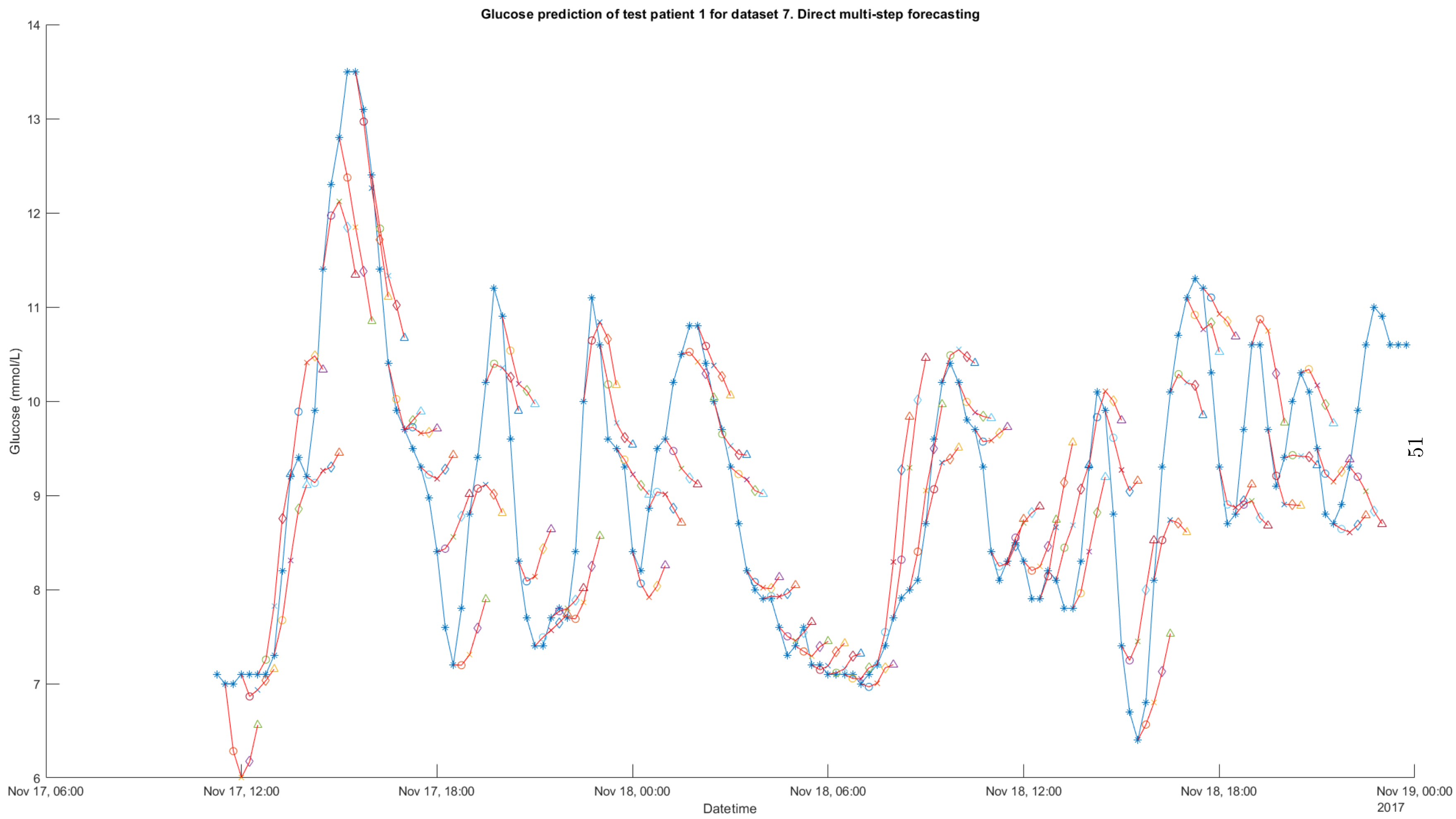


Figure 36: DMSF method.