Empowerment of diabetic patients through mHealth technologies and education : Development of a pilot self-management application

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ABSTRACT

Diabetes is a major, global and increasing condition that occurs when the insulin-glucagon regulatory mechanism is affected, leading to uncontrolled hyper- and hypoglycaemia events that may be life-threatening. However, it has been shown that through daily monitoring, appropriate patient-specific empowerment, lifestyle behavior of diabetics can be positively influenced and the associated and costly diabetes complications significantly reduced. As personal face-to-face coaching is costly and hard to scale, mobile applications and services have now become a key driver of mobile Health (mHealth) deployment, especially as a helpful way for self-management.

Despite the huge mHealth market, a major limitation of many diabetes apps is that they do not use inputted data to help patients determine their daily insulin doses. On the other hand, the majority of existing insulin dose calculator apps provide no protection against - or even may actively contribute to - incorrect or inappropriate dose recommendations that put users at risk. Besides, there is clear evidence that lack of education on insulinotherapy and carbohydrate counting is associated with higher blood glucose variability with type 1 diabetes. Hence, there is a need for an accurate modelling of glucose-insulin dynamics together as well as providing adequate educational support.

The aims of this paper are: a) to highlight the usefulness of mHealth technologies in chronic disease management; b) to describe and discuss the development of an insulin bolus calculator integrated into a pilot mHealth app; c) to underline the importance of diabetes self-management education.

Keywords: diabetes management, mobile health, functional insulin therapy, flexible insulin therapy, bolus calculator, self-management, patient empowerment, patient education

1. BACKGROUND

1.1 Diabetes Mellitus

Pathophysiology

Diabetes is a condition that occurs when the insulin-glucose-glucagon regulatory mechanism is affected. Normally, plasma glucose levels are maintained within a narrow range through the antagonistic and combined action of the two pancreatic hormones, i.e. the insulin and the glucagon, produced by Beta and Alpha cells of the islets of Langerhans, respectively.[1] In normal individuals, high blood glucose levels (BGLs) induce the release of insulin, which enables its target cells to take up glucose. In low-glucose conditions, glucagon induces the breakdown of glycogen into glucose.

In opposition, this synchronized mechanism is disrupted in diabetic individuals, resulting in persistent too high blood glucose levels or *hyperglycemia*. Medically, diabetes is defined by the following criteria: patient fasting plasma glucose level $\geq 126mg/dl$ or HbA1c (glycated hemoglobin) $\geq 6.5\%$ or patient plasma glucose level 2-h after OGTT (oral glucose tolerance test) $\geq 200mg/dl$.[2] Dealing with this condition is highly complex and in many cases, due to inappropriate lifestyle or medication intake, diabetic patients also strive to avoid too low BGLs, known as *hypoglycemia*.

Complications

Hyperglycaemia, left untreated, can lead to several long-term complications. Amongst others, we can enumerate neuropathy (i.e. nerve damage, that can lead to diabetic foot disorders and may require amputation), nephropathy (kidney failure), retinopathy (i.e. bloods vessels of the retina are damaged and can lead to blindness), as well as cardiovascular diseases such as heart attacks and strokes.[3] In the same manner, hypoglycemia - of which immediate symptoms are amongst others weakness, shaking, sweating, neurological disorders - can also increase significantly the risk of cardiovascular diseases, leading to coma or death in the most severe cases if not treated in time.

T1D management and empowerment

In type 1 diabetes (T1D), formerly called juvenile-onset or insulin-dependent diabetes, there is almost complete destruction of beta cells. Hence T1D - being a complex genetic and autoimmune disorder - can not be prevented or cured, but it can be effectively treated with external supplies of insulin and managed through BGLs control.[4,5]

The most common method for T1D management is taking fingerprick blood tests several times a day and adjusting insulin doses based on these readings. For a dynamic, nonlinear, and complex condition such as diabetes, this can be far from satisfactory. Factors such as insulin type and dose, diet, stress, exercise or illness all have significant influences on the BGLs. Management may be compromised through lack of data and, for some patients, an inability to interpret data adequately.[6]

However, it has been shown that through patient-specific empowerment and education, lifestyle behavior of diabetics can be positively influenced and the associated and costly diabetes complications significantly reduced.[7,8] As personal face-to-face coaching is costly and hard to scale, mobile applications and services have become a game changer in chronic disease management.

1.2 The rise of mHealth

The expansion of mHealth technology

MHealth is defined as a use of mobile communication devices, which include mobile phones, patient monitoring devices, tablets, personal digital assistants, and other wireless devices for health services, and information.[9] Currently, growing use of those devices can be seen in practically every part of the world. As highlighted by Silva et al. (2015) in their review,[10] mHealth is the new edge on healthcare innovation. With the advent of mobile communications using smart mobile devices that support 4G mobile networks for data transport, mobile computing has been the main attraction of research and business communities. It offers numerous opportunities to create efficient mHealth solutions, proposes to deliver healthcare anytime and anywhere, surpassing geographical, temporal, and even organizational barriers.

Typical mHealth services architectures - illustrated in Figure 1 - use the Internet and Web services to provide an authentic pervasive interaction among doctors and patients. A physician or a patient can easily access the same medical record anytime and anywhere through his/her personal computer, tablet, or smartphone. The patient can contact the physician in case of an emergency, or even, have access to medical registers or appointments regardless of time and place.

Besides, because they greatly facilitate data gathering (e.g. amongst others, through interoperability with wearable sensors and IoT devices) and mining, mHealth systems have a strong impact on typical healthcare monitoring, prediction and decision support systems.

The growth of the diabetes app market

Of all the medical conditions, diabetes is the most common condition targeted by current commercial apps, followed by depression and asthma.[11] Review of accessible diabetes applications has shown that they mostly focus on blood glucose monitoring, medications, physical exercise, and diet management, while they also may include other features such as education, communication, weight and blood pressure tracking, integration with public health records, decision support systems, and social networking.[12]

According to Research2Guidance's annual survey, 76 % of mobile health app publishers see diabetes as the therapeutic area with the highest business potential for mHealth. In 2013 only 1.2 % of people with diabetes

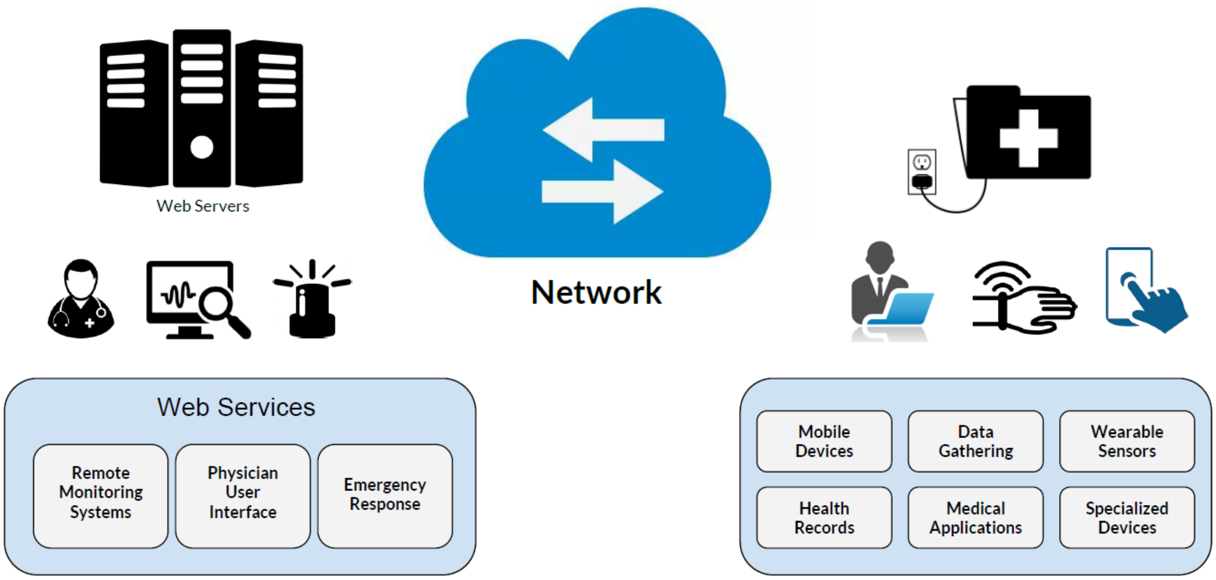

Figure 1: Illustration of a typical architecture of mHealth services.
Adapted from Silva et al. (2015)[10]

who owned a smartphone or tablet used apps to manage their condition. Research2Guidance is predicting that this number will increase to 7.8 % in 2018.[13] In the iTunes App Store for iOS and Google Play for Android, diabetes is one of the top-ranked categories, with more than 1100 different apps available for download.[14]

2. DEVELOPMENT OF AN INSULIN BOLUS ASSISTANT

Despite the huge market, a major limitation of many diabetes apps is that they do not use inputted data to help patients determine their daily insulin doses. Most often the patient has to rely on hand calculations based on insulin-to-carbohydrate ratios provided by health care professionals.[15] Such calculations are not straightforward and have to integrate expected carbohydrate intake, measured blood glucose levels, past insulin doses for post-prandial ("mealtime", "short-action") doses, and ideally take into account individual lifestyle behaviour such as exercise. In addition, the use of a smartphone - an object not typically associated with medical care - may offer a discrete way to determine dosage in social situations like mealtimes. Automated insulin dose calculations are thus a desirable feature in diabetes mobile apps.

On the other hand, the majority of existing insulin dose calculator apps provide no protection against, and may actively contribute to, incorrect or inappropriate dose recommendations that put users at risk of both catastrophic overdose and more subtle harms resulting from suboptimal glucose control.

In their research, Huckvale, Kit, et al. (2015) found that considering input, only 59% calculators included clinical disclaimer and only 30% documented the calculation formula. 91% lacked numeric input validation, problems were also with calculation with missing values, ambiguous terminology, even with numeric precision. Considering output, 67% of calculators carries a risk of inappropriate output dose recommendation that either violated basic clinical assumptions or did not match a stated formula or correctly update in response to changing user input.[16] Hence, there is a need for an accurate modelling of glucose-insulin dynamics and effective implementation.

2.1 Functional insulin therapy

Basic principles

Flexible or *Functional insulin therapy*(FIT) - represented by basal-prandial insulin regimens - is a well-established way to achieve strict glycaemic control of type 1 diabetes.[17–19] Such regimens use a long-acting insulin analogue to control fasting blood glucose levels and a short-acting insulin analogue for post-meal glucose excursions to replace insulin in a way that closely approximates normal physiological patterns.

This more recent approach contrasts with conventional insulin therapy. Instead of minimizing the number of insulin injections per day - a technique which demands a rigid schedule for food and activities - the functional approach allows flexible meal times with variable carbohydrate as well as flexible physical activities.

Positive results

Regarding the clinical and metabolic risks, all experiments on FIT have shown reassuring results. Decrease of severe hypoglycaemia episodes, stability or even improvement of HbA1c have been observed.[20–22]

In regards to psychological repercussions stemming from increased autonomy and self-reliance, results were once again positive. According to studies, it seems that patients really appreciate the greater control of their disease and the deeper understanding of the condition.[20] The FIT turned out to improve life quality and significantly decrease anxiety and depression symptoms.[22]

2.2 Parameters

Based on meetings with physicians and relying on literature,[23–25] we were able to identify all the parameters required to properly calculate insulin boluses, as well as the amount of carbohydrate needed to cover exercise or correct hypoglycaemia.

1. *The Basal dose* : Although basal doses are not typically entered in bolus calculators (BC), determining an appropriate basal dose is a prerequisite for optimal BC performance. This long-acting insulin dose should be determined in agreement with the diabetologist. However, according to Walsh, Roberts, & Bailey's (2011) guidelines,[25] it can be estimated by :

$$\widehat{Basal}(U/day) = TDD \times 0.48 \tag{1}$$

   where TDD corresponds to the patient total daily insulin dose.

2. The *Insulin to carbohydrate ratio* (ICR) corresponds to the number of grams of carbohydrate covered by each unit of rapid- or short-acting insulin. This ratio - the inverse of the *carb factor* - serves as the foundation for adjusting pre-meal bolus insulin doses. A fairly typical ICR is 1 unit of insulin for every 15 grams of carbohydrate. However, the ratio varies considerably from one person to another, and a persons own ratio may change over time or even from meal to meal. This parameter is commonly calculated with help of a dietitian, but can be basically estimated[25] by :

$$\widehat{ICR} = \frac{TDD}{5.7 \times Weight(kg)} \tag{2}$$

   In other words, the insulin bolus (B_{meal}) needed to cover an uptake of carbohydrate (CHO_{meal}) can be written as :

$$B_{meal} = CHO_{meal} * ICR(t) \tag{3}$$

3. *The Glycaemic Target* (BG_{opt}) : The typical *glycaemic targets* recommended by the American Diabetes Association[26] can be found in Table 1. Note that BG target range may need to be individualized with help of the diabetologist. In addition, postprandial measurements should be made 1-2 hours after the beginning of the meal.

   In our algorithm, BG_{opt} is defined as the mean of the - non-constant - BG target range.

Table 1: *Typical Blood Glucose Targets for Nonpregnant Adults With Diabetes*[26]

HbA1C	<7.0%
Preprandial capillary plasma glucose	80-130 mg/dL
Peak postprandial capillary plasma glucose	<180 mg/dL

4. *The Insulin On Board (IOB)* : If insulin from previously administered boluses is still active, IOB should be subtracted. In pump patients, 65% of all insulin boluses are given within 4.5 hours of a prior bolus, that is, within the duration of insulin action (DIA), and thus inclusion of IOB in the BC is important to avoid insulin stacking.[24]

   Some bolus calculators approximate residual insulin activity linearly (i.e. 20% per hour for a 5-hour DIA), while others use a curvilinear formula that more closely approximates insulins delayed onset of action and its gradual tailing off in activity. DIA times between 4.0 to 5.5 hours work well for calculators that use a linear approach, while DIA times of 4.5 to 6.0 hours are more appropriate for curvilinear systems.[24]

   Note that, ideally, IOB should be determined based on patient-specific DIA and assumptions of insulin kinetics.[27] In their paper, Walsh, J., Roberts, R., & Heinemann, L. (2014) provide recommendations that can guide the clinician in adjusting DIA settings.[28]

5. *The Correction Factor (CF)* : This factor, sometimes referred to as the insulin sensitivity factor, is inversely related to the TDD and measures how far an individuals elevated glucose concentration will fall per unit of insulin. This parameter should be determined by the diabetologist but can however be approximated[24] by :

$$\widehat{CF} = \frac{1960 \text{ mg/dL}}{TDD} \tag{4}$$

   Hence, in case of hyperglycaemia with blood glucose level BG_k, the correction bolus (B_{corr}) can be written as :

$$B_{corr} = \frac{BG_k - BG_{opt}(t)}{CF} \tag{5}$$

6. *The Physiological State (PS)* : Often, the sum of the meal and correction insulin part should be multiplied by a proportion reflecting the current *physiologic state* of the patient. When insulin sensitivity is increased, for example due to physical activity, the PS is < 1 and when insulin sensitivity is decreased, for example, during illness, the PS is > 1.[24] In our algorithm, we provide an estimation of PS in case of planned physical activity (PA) with intensity I and duration D, adapted from a diaTribe online publication.[29]

$$PS_{PA}(I,D) = \begin{pmatrix} 0.90 & 0.86 & 0.82 & 0.78 & 0.74 & 0.70 \\ 0.75 & 0.70 & 0.65 & 0.60 & 0.55 & 0.50 \\ 0.67 & 0.60 & 0.53 & 0.44 & 0.37 & 0.30 \end{pmatrix}$$

   The D indexes ($d = 1,2,3,4,5,6$) correspond respectively to durations of $15, 30, 45, 60, 75$ and 90 (or more) minutes. The I indexes ($i = 1,2,3$) correspond respectively to light (i.e. < 3 METS*), moderate (between 3 and 6 METS) and vigorous (> 6 METS) physical activities. Tables summarizing and presenting energy expenditure values for numerous household and recreational activities can be found in literature.[31] Moreover, many of today's wrist-worn activity trackers allow to efficiently recognize and quantify physical activities.

   Besides, for the reason that diabetic patients are recommended to take an appropriate amount of carbohydrate to balance an expected drop in sugar levels before starting an exercise, we also derived[29]

*MET refers to *Metabolic Equivalent of Task*, i.e. the ratio of exercise metabolic rate to resting metabolic rate. One MET is defined as the energy expenditure for sitting quietly, which, for the average adult, approximates 3.5 ml of oxygen uptake per kilogram of body weight per minute.[30]

CHO_{PA} - the amount of carbohydrate needed to cover physical activity of duration d and intensity i - as follows :

$$CHO_{PA}(w, i, d) = w \times (1 - PS_{PA}(i, d)) \times 1,3 \tag{6}$$

where w corresponds to the patient's weight.

2.3 The algorithm

From the parameters we identified, we were finally able to derive our BC's algorithm. This latter is divided in three parts, corresponding to three typical use cases (i.e. before meal, before sport and between meals) and gives recommendations on bolus insulin doses B_k or preventive carbohydrate intake CHO_k.

1. Before meal - Prandial bolus
   (a) *No physical activity is planned* :

$$B_k = B_{meal} + B_{corr} - IOB \tag{7}$$

$$= CHO_{meal} \times ICR(t) + \frac{BG_k - BG_{opt}(t)}{CF} - \frac{\Delta k}{DIA} \times B_{k-1} \tag{8}$$

   (b) *A physical activity is planned within 120 minutes after meal ingestion :*

$$B_k = (B_{meal} + B_{corr} - IOB) \times PS_{PA}(i, d) \tag{9}$$

2. Before Physical Activity

$$CHO_k = CHO_{PA}(w, i, d) - \left(\frac{B_{corr} - IOB}{ICR(t)}\right) \tag{10}$$

3. Between Meals

   If $B_{corr} > IOB$ then :

$$B_k = B_{corr} - IOB \tag{11}$$

   else :

$$CHO_k = \frac{B_{corr} - IOB}{ICR(t)} \tag{12}$$

2.4 Integration into a Mobile Web App

As highlighted in the background section, smartphones have become a key driver of mHealth deployment, especially as a helpful way for self-monitoring and empowerment of chronic diseases. It appears thus convenient to integrate our BC into a mobile web application that we briefly describe in this section.

Software development life cycle

To develop our BC, we decided to adopt the software development life cycle (SDLC) described by Kieffer, Ghouti, & Macq (2017). In their paper,[32] they present the *agile user experience development lifecycle*, a tool intended for development settings in which cross-functional teams with both user expererience (UX) and agile expertise wish to integrate user-centred design (UCD) and agile software development (ASD) methods. The paper also describes how this tool was used to develop *Egle*, the diabetes self-management application into which we decided to integrate our BC.

Egle

The development environment of *Egle* uses the MEAN stack[33] (i.e. MongoDB, ExpressJS, AngularJS, Node.js) as well as Bootstrap[34] components, supporting fast prototyping and multi-platform deployment.

Egle provides a lot of tools aiming at empower diabetic patients. Amongst others, user-friendly widgets have been UX-validated[32] and allow to efficiently monitor BG, diet, medication, physical activities. It also provides educational "Tips and Tricks", reminders, HbA1c estimation and is interoperable with wearable fitness trackers and Wi-fi connected scales.

Figure 2 and Figure 3 illustrate the BC user interface in Egle. In Figure 2, based on estimated carbs, current BGL and planned physical activity entered by the user, the BC gives a recommendation for an appropriate prandial bolus. A tooltip helps the user to select the appropriate physical intensity level. In Figure 3, details on the recommendation and algorithm parameters are provided to the user and allow him to easily access and modify BC settings.

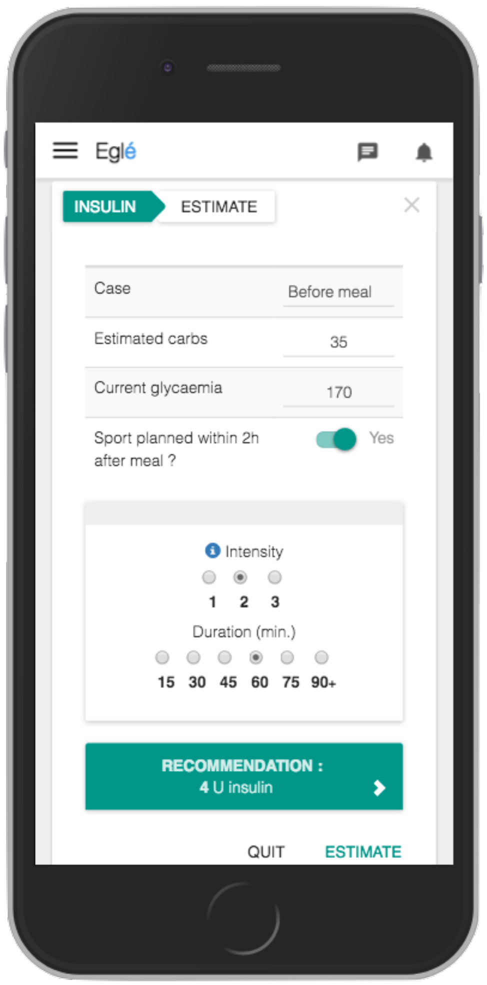

Figure 2: BC - Prandial bolus (Egle)

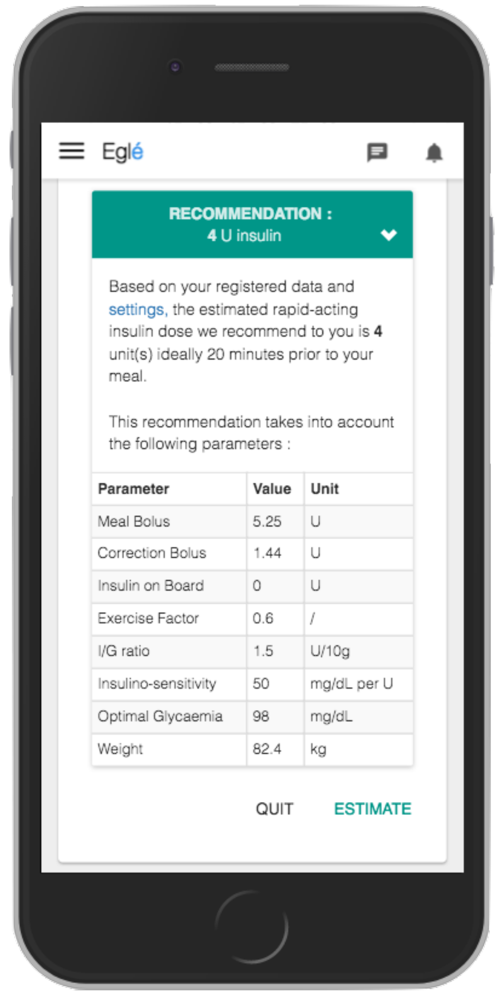

Figure 3: BC - Recommendation details

2.5 The need for education

As highlighted by A.Mohn et al. (2012), the FIT should not be perceived as an arithmetic model, but more as model of educational approach. Although FIT can theoretically be applied to any patient with T1D condition, training must be adapted to patients needs, and not the other way around.[35]

In a recent study,[36] it has been shown than around 64% of patients estimated their prandial insulin need inappropriately, suggesting that estimation of the optimal prandial insulin dose is not easy, even after a long duration of diabetes. Main causes are inadequate FIT parameters and inaccurate carbohydrate counting (CC). Inability to properly estimate carbohydrate is frequent and associated with higher daily blood glucose variability in adults with type 1 diabetes.[37] Several studies suggest that more intensive intervention might be required to improve adolescents' CC accuracy and nutrition management of type 1 diabetes.[38,39] Moreover, in their review,[12] Hood, Megan, et al. (2016) surprisingly noticed that diabetes education has not seemed to be well-integrated in most of current apps, despite this being stressed in clinical standards.

In the light of all these observations, it appears important to provide an educational module related to FIT, self-monitoring and CC. For that purpose, "*Achievements*", "*Tips and Tricks*" and "*Quizs*" modules have been implemented in *Egle*, as illustrated in Figures 4, 5, 6 here below.

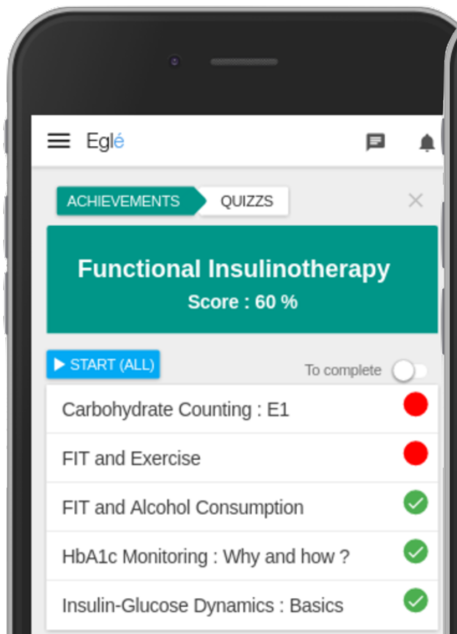

Figure 4: Scoring quiz module on FIT (EN version)

Figure 5: Tips and Tricks - HbA1c (FR version)

Figure 6: Quiz - Carbs counting (FR version)

2.6 Discussion

Algorithm validation

The BC algorithm has been informally validated by a diabetic patient and two diabetologists, Dr. Vandeleene and Dr. Orioli, from Cliniques Universitaires Saint-Luc (CUSL). However, a clinical trial should be conducted to properly assess the validity of the Bolus Advisor. For that purpose, more patients will be recruited after CUSL Ethics Committee's approval.

Fat and protein counting

CC is based on the assumption that CHO is the nutrient component with greatest impact on postprandial BG excursions and that the impact of protein and fat is minor and covered by the basal insulin. There is evidence, however, that dietary fat and protein increase BG levels by impairing insulin sensitivity and enhancing hepatic glucose production. Algorithms for insulin bolus calculation including all 3 components have been proposed but are not widely adopted in BCs and it remains to be fully clarified how the glycemic impact of fat and protein should be estimated.[40]

Parameters accuracy and customization

The parameters of the presented algorithm need to be fairly accurate and determined in agreement with health care professionals. If CF or ICR are set too low, the patient will get recurring hypos and vice versa.

Although ADA provides standard glycaemic targets,[26] more or less stringent BG_{opt} range may be appropriate for individual patients if achieved without significant hypoglycemia or adverse events. The BG_{opt} target should be set to meet patient-specific goals, with help of a diabetologist, and will be reflected in the HbA1c over time.

DIA accuracy is equally important, because a DIA set too short leads to insulin stacking and if DIA is set too long, it may lead to a compensatory increase in basal rate. Recommendations that can guide the clinician in adjusting DIA settings are available in the literature.[28]

Further work

Besides from the BC clinical trial, further work will include expert evaluation (dietitian, diabetic education nurse, diabetologist) of the educational module content as well as the development of the physician dashboard with alerts system.

With regard to patient adherence and as underlined by Hood, Megan, et al. (2016),[12] further research should also investigate the use of behavior change theories as well as motivational strategies, e.g. gamification, tailored feedback and integration of social networking features.

3. CONCLUSION

In this paper, we described and discussed the development and integration of an insulin BC - together with an educational module - into a pilot self-management diabetes app. The design and algorithms discussed here - of which parameters accuracy and customization are key requirements - have been informally validated with help of diabetologists (CUSL) and a diabetic patient. However, further work should focus on the conduct of a clinical trial in compliance with an approved protocol.

The BC and educational module we described in this paper are just tiny examples of useful features the mHealth landscape can offer to chronic diseases self-management. As highlighted by J. Wang et al. (2014) in their review,[41] mHealth interventions are more and more recognized as effective and valuable tools to assist in empowering chronic patients. More generally, the advent of mobile technologies, networks, Internet-of-Things, wearable sensors and cloud computing fosters communication between developers, healthcare professionals and patients, and opens wide perspectives on cost-effective personalized telemedicine.

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