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Contents

Original Paper

Outcomes of a Digitally Delivered Low-Carbohydrate Type 2 Diabetes Self-Management Program: 1-Year Results of a Single-Arm Longitudinal Study

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Abstract

Background: Type 2 diabetes mellitus has serious health consequences, including blindness, amputation, stroke, and dementia, and its annual global costs are more than US $800 billion. Although typically considered a progressive, nonreversible disease, some researchers and clinicians now argue that type 2 diabetes may be effectively treated with a carbohydrate-reduced diet.

Objective: Our objective was to evaluate the 1-year outcomes of the digitally delivered Low-Carb Program, a nutritionally focused, 10-session educational intervention for glycemic control and weight loss for adults with type 2 diabetes. The program reinforces carbohydrate restriction using behavioral techniques including goal setting, peer support, and behavioral self-monitoring.

Methods: The study used a quasi-experimental research design comprised of an open-label, single-arm, pre-post intervention using a sample of convenience. From adults with type 2 diabetes who had joined the program and had a complete baseline dataset, we randomly selected participants to be followed for 1 year (N=1000; mean age 56.1, SD 15.7 years; 59.30% (593/1000) women; mean glycated hemoglobin A_{1c} (HbA_{1c}) 7.8%, SD 2.1%; mean body weight 89.6 kg, SD 23.1 kg; taking mean 1.2, SD 1.01 diabetes medications).

Results: Of the 1000 study participants, 708 (70.80%) individuals reported outcomes at 12 months, 672 (67.20%) completed at least 40% of the lessons, and 528 (52.80%) completed all lessons of the program. Of the 743 participants with a starting HbA_{1c} at or above the type 2 diabetes threshold of 6.5%, 195 (26.2%) reduced their HbA_{1c} to below the threshold while taking no glucose-lowering medications or just metformin. Of the participants who were taking at least one hypoglycemic medication at baseline, 40.4% (289/714) reduced one or more of these medications. Almost half (46.40%, 464/1000) of all participants lost at least 5% of their body weight. Overall, glycemic control and weight loss improved, especially for participants who completed all 10 modules of the program. For example, participants with elevated baseline HbA_{1c} ($\geq$7.5%) who engaged with all 10 weekly modules reduced their HbA_{1c} from 9.2% to 7.1% (P<.001) and lost an average of 6.9% of their body weight (P<.001).

Conclusions: Especially for participants who fully engage, an online program that teaches a carbohydrate-reduced diet to adults with type 2 diabetes can be effective for glycemic control, weight loss, and reducing hypoglycemic medications.

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Introduction

Type 2 diabetes mellitus is prevalent, costly, and a potentially progressive disease with serious health consequences including blindness, amputation, stroke, dementia, and premature death [1]. Globally, one in 11 people, or 422 million adults, have diabetes (with most of those cases being type 2 diabetes) [2]. It is the most expensive disease in the United States [3], and its annual global costs are more than US $800 billion [4]. In community settings, type 2 diabetes is rarely reversed. For example, a study that followed more than 100,000 patients with type 2 diabetes over 7 years found that less than 1% of patients experienced complete remission [5].

Although typically considered a progressive, nonreversible disease, some researchers and clinicians now argue that type 2 diabetes may be effectively treated with a carbohydrate-reduced diet, which could improve type 2 diabetes management and potentially even lead to remission [6]. Indeed, previous research with carbohydrate-reduced diets for type 2 diabetes do show improved outcomes (eg, glycemic control, weight loss, and reductions in the use of hypoglycemic medications) for both very low-carbohydrate diets (approximately 20% or fewer of total dietary calories derived from carbohydrates) [7-9] or lower carbohydrate diets (approximately 40% or fewer of total dietary calories derived from carbohydrates) [10,11].

Although dietary interventions have historically been in-person, online programs can be just as effective for some participants, as suggested by research that has examined diet and lifestyle interventions in adults with prediabetes [12]. Therefore, it is perhaps not surprising that the beneficial results of carbohydrate-reduced diets for people with type 2 diabetes (glycemic control, weight loss, and reductions in the use of hypoglycemic medications) have been replicated using online programs [13,14]. Notably, both previous trials of a very low-carbohydrate diet online for adults with type 2 diabetes included the use of a coach. However, previous research on weight loss (including some people with type 2 diabetes), have shown some success with a completely automated online weight loss program, with approximately 50% of participants losing at least 5% of their body weight by 6 months [15,16].

In this naturalistic pilot study, our objective was to evaluate the 1-year outcomes of the Low-Carb Program, a digitally delivered, nutrition-focused, structured lifestyle intervention with 10 weekly sessions for glycemic control, hypoglycemic medication use, and weight loss for adults with type 2 diabetes. We hypothesized that this program would lead to improvements compared to baseline: better glycemic control (as measured by glycated hemoglobin A_{1c} or HbA_{1c}), weight loss, and reductions in hypoglycemic medication use. Our goal was to explore whether the program might be an effective option for increasing access to diabetes management solutions and help halt the prevalent, costly, and dangerous type 2 diabetes epidemic.

Methods

Research Design

We used a quasi-experimental research design comprised of a single-arm pre-post intervention. Participants were not paid for their participation, but because the program was free, they took part in the program at no cost. The University of Michigan Institutional Review Board (IRB) ruled that analyses of these previously collected and de-identified data were not subject to IRB regulation.

Participants

We recruited participants to this trial in three phases. The first phase recruited a sample of convenience following the launch of the Low-Carb Program (November 14, 2015-November 14, 2016), whereby 105,950 adults with type 2 diabetes between the ages of 18 and 99 years signed up to participate in the program. Participants could live anywhere in the world. To have a broad applicability to a nonclinical trial setting, the only de facto exclusion criterion was the inability to understand English. Second, upon sign-up, the program prompted individuals to complete an initial baseline survey; 19,646 of 105,950 (18.54%) did so. Of those, 7809 people had complete baseline datasets including weight, a recent HbA_{1c} result (taken within 4 months), and medication use. Third, we used GraphPad Random Generator Software to randomly select a subset of 1000 participants to be followed for 12 months, thus enabling us to select participants for no other reason than that they were randomly selected by the software. Therefore, we did not include all the 7809 patients to follow over a year, but instead followed a random subsample of 1000 (see Figure 1).

The Low-Carb Program

The Low-Carb Program is a completely automated, structured 10-week health intervention for adults with type 2 diabetes. Participants are given access to nutrition-focused modules, with a new module available each week over the course of 10 weeks. The modules are designed to help participants gradually reduce their total carbohydrate intake to less than 130 grams per day to meet their self-selected goals. The program encourages participants to make behavior changes based on "action points" or behavior change goals at the end of each module. These goals are supported with resources that are available to download, including information sheets, recipes, and suggested food substitution ideas. The Low-Carb Program online platform also includes digital tools for submitting self-monitoring data on a number of different variables including blood glucose levels, blood pressure, mood, sleep, food intake, and body weight. Weekly automated feedback is provided to users based on their use of the program through email notifications, and participants are notified when the next week's module has been opened. Lessons are taught through videos, written content, or podcasts of varying lengths (approximately 3 to 12 minutes long).

Figure 1. Study participant flowchart for the study.
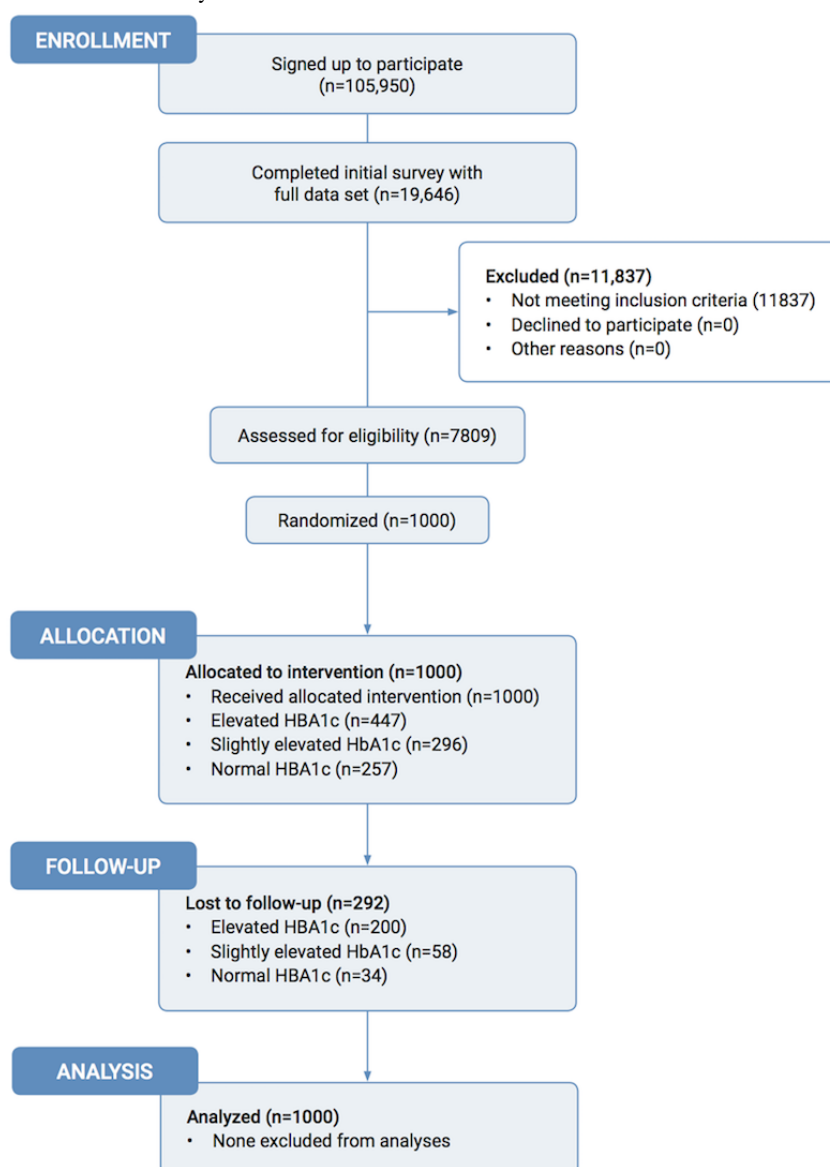
The first 2 weeks of the program contain an explanation of the physiology of type 2 diabetes and the role of diet, including a description of how a low-carbohydrate diet can help manage postprandial blood glucose levels and weight. The subsequent week's modules explore strategies to reduce dietary sources of sugar, in particular, high-starch foods, such as bread, pasta, and rice. Participants are encouraged to make portion control and carbohydrate restriction decisions based on visual plate representations. In place of carbohydrate-rich foods, an increased intake of green vegetables, low-glycemic index fruits (eg, blueberries, strawberries, and raspberries) and fats (eg, from olive oil, butter, eggs, nuts, and full-fat dairy) are advocated. The program stresses the importance of regular contact with the participants' health care providers for adjustments in medications in weeks 1, 2, and 10. After the 10 weeks of modules have been opened, participants continue to have access to the education content as well as the ability to continue to track their health (glycemic control, weight) and access support

from the discussion board. See Table 1 for a list of the weekly topics.

Much of the content of the Low-Carb Program is based on an in-person, nurse- and physician-led, low-carbohydrate training program conducted in a primary health care setting [17]. For example, the dietary recommendations reflect an understanding of the glycemic index, a relative ranking of carbohydrates in foods according to how they affect blood glucose levels. A meal of pure glucose (the index food) has a score of 100, boiled potatoes are scored at 96, cornflakes at 93, and brown bread at 74, all of which are higher than table sugar at 63 [18]. This kind of information helps participants understand that both sugary and starchy foods increase blood glucose, and it also explains why the UK's National Institute for Health and Care Excellence advises physicians to "encourage high-fiber, low-glycemic index sources of carbohydrate in the diet" for type 2 diabetes [19]. Based on this, the program suggests a reduction in all sugary foods and replacing starchy foods, such as potato or rice, with green leafy vegetables, healthy fats, and some protein.

Table 1. Weekly topics of the Low-Carb Program.

Week	Title	Objective
1	Welcome to the Low-Carb Program	Safety notes and alerts to medications that require health team's assistance; initiate conversation with health care providers prior to making any dietary adaptations; benefits of a reduced carbohydrate diet for people with type 2 diabetes
2	Type 2 diabetes and diet	Factors that affect blood glucose levels; encouragement to engage with their health care providers
3	Controlling portion sizes	Visual methods of interpreting portion size
4	Processed versus unprocessed foods	Identifying and eliminating refined and processed food
5	Healthy and unhealthy fats	Discussion of fat types and making appropriate choices depending on goals
6	Vegetables	The carbohydrate content of vegetables; cooking methods
7	Sugar and starch	Reviewing the amount of sugar and starch in fruit and vegetables
8	Snacks, desserts, and drinks	Examining low-carb snack, dessert, and drink options
9	Alcohol, eating away from home	Alcohol; options for eating away from home
10	Practical ways of reducing carbohydrate intake further	Practical tips for reducing carbohydrate intake further; safety information—highlighting medications that require assistance from their physicians and how to involve their physician and wider health care team

The content and strategies used in the program build off prior research and theory. For example, evidence suggests that goal setting can act as an effective behavior change strategy used to improve adherence to lifestyle intervention programs in obesity management programs [20]. Therefore, the program encourages participants to select a goal at the beginning of the program (eg, to lose weight, reduce medication dependency, or make healthier choices for their whole family). Participants are also prompted to consider how their health would benefit from attaining their goal. Throughout the program, participants are periodically prompted to consider how close they are to attaining their goal.

The program further reinforces behavior change through integrated tracking whereby program users are encouraged to track their health data including mood, food intake, blood glucose levels, weight, sleep, and HbA_{1c}. According to the Control Theory of behavior change, monitoring goal progress—that is, evaluating one's ongoing performance relative to the standard—and responding accordingly is critical to goal attainment [21]. Recent findings suggest that program interventions that elevate the frequency of progress monitoring are likely to induce behavior change [22].

In addition, prior studies demonstrate that peer support may improve blood glucose control [23,24], peer-based support may be as effective for weight loss as coach-based support [25], and that online discussion boards can be supportive for weight loss [26]. Therefore, the program encourages social support by matching new participants of the program to a "buddy," a previous graduate of the program, based on similar demographics including age, gender, and their self-selected goal. Participants are encouraged to interact with that buddy and peers on the program's moderated online discussion board.

Measures

At baseline, an online survey asked participants to report on their type of diabetes, year of diagnosis, their most recent HbA_{1c} test result and date, current medications (medication name, dose, and regimen), age, gender, socioeconomic status (based on

household income), and presence of comorbid chronic illnesses. At 12 months, participants were again asked to report on their current HbA_{1c}, weight, and medications.

Statistical Analyses

Analyses were performed using the SPSS version 21.0 (SPSS Inc, Chicago, IL, USA). We examined the difference in characteristics from baseline to 12-month follow-up using paired t tests. The primary outcome was change in HbA_{1c} and body weight (kg, percent of initial body weight). The secondary outcome was change in need for diabetes medication. We stratified our cohort into three groups according to baseline glycemic control as defined by baseline HbA_{1c}: (1) elevated baseline HbA_{1c} greater than or equal to 7.5%, (2) slightly elevated baseline HbA_{1c} 6.5% to 7.4%, or (3) normal baseline HbA_{1c} less than 6.5%. Outcomes were also analyzed within strata based on participant's Low-Carb Program completion (ie, completers: engaged with all 10 of the Low-Carb Program weekly modules; n=528), partial completers (engaged with 4-9 modules; n=144), or noncompleters (engaged with ≤3 modules; n=328).

Some of our results took into account the entire sample, regardless of follow-up information or lesson completion. For participants who did not report their outcomes at 12 months, we followed the highly conservative approach of assuming that they did not improve at all (last observation carried forward), by imputing their baseline values as their outcome values. For example, participants who did not comply with reporting a 12-month outcome were treated as having no change in the outcome variable, and thus were not counted as having any HbA_{1c} or weight improvement.

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Results

Participant Characteristics at Baseline

At baseline, mean HbA_{1c} was 7.8% (SD 2.1%), mean weight was 89.6 kg (SD 23.1), and mean age was 56.1 years (SD 15.7) years. More than half of participants were female (59.3%, 593/1000), 90.4% (904/1000) were white, all were from the United Kingdom, and more than one-third had comorbid hypertension (39.7%, 397/1000) or hypercholesterolemia (35.0%, 350/1000). At baseline, participants were taking a mean of 1.21 (SD 1.01) hypoglycemic medications. See Table 2 for details.

Retention

Of the 1000 baseline participants, 708 (70.80%) reported outcomes at 12 months, 528 (52.80%) completed all lessons, and 672 (67.20%) completed at least 40% of the lessons. For the remaining 292 people lost to follow-up, the last recorded data point was carried forward. Of 447 people with elevated HbA_{1c} (≥7.5%) at baseline, 247 (55.3%) reported outcomes at 12 months and 191 (42.7%) completed all lessons. Of 296 people with slightly elevated HbA_{1c} (6.5%-7.5%) at baseline, 238 (80.4%) had outcomes at 12 months and 182 (61.4%) completed all lessons. Of 257 people with a normal baseline HbA_{1c} level (HbA_{1c} <6.5%) who began the study, 223 (86.8%) had outcomes at 12 months and 155 (60.3%) completed all lessons (see Figure 1 for the participant flowchart of the study).

Table 2. Participant characteristics at baseline.

Characteristic	Pooled (N=1000)	Baseline HbA_{1c} level[a]		
		Elevated (n=447)	Slightly elevated (n=296)	Normal (n=257)
Age (years), mean (SD)	56.1 (15.7)	54.8 (14.6)	56.7 (16.9)	57.9 (15.8)
HbA_{1c} (%), mean (SD)	7.8 (2.1)	9.6 (1.8)	6.90 (0.3)	5.68 (0.7)
Weight (kg), mean (SD)	89.6 (23.1)	92.9 (24.0)	88.2 (22.4)	85.7 (21.8)
Gender, n (%)				
Male	401 (40.1)	175 (39.1)	124 (41.9)	102 (39.7)
Female	593 (59.3)	271 (60.6)	171 (57.8)	151 (58.8)
Intersex	6 (0.6)	1 (0.2)	1 (0.3)	4 (1.6)
Ethnicity, n (%)				
White	904 (90.4)	409 (91.5)	259 (87.5)	236 (91.8)
Indian/Pakistani	36 (3.6)	12 (2.7)	16 (5.4)	8 (3.1)
Mixed/Multiple ethnic groups	16 (1.6)	6 (1.3)	8 (2.7)	2 (0.8)
Chinese/Japanese/Other East Asian	8 (0.8)	3 (0.7)	4 (1.4)	1 (0.4)
Black/African/Caribbean	21 (2.1)	10 (2.2)	5 (1.7)	6 (2.3)
Unknown	15 (1.5)	7 (1.6)	4 (1.4)	4 (1.6)
Employment, n (%)				
Full-time employment	315 (31.5)	171 (38.3)	88 (29.7)	56 (21.8)
Part-time employment	135 (13.5)	61 (13.6)	37 (12.5)	37 (14.4)
Retired	480 (48.0)	179 (40.0)	154 (52.0)	147 (57.2)
Student	7 (0.7)	3 (7.4)	2 (0.7)	2 (0.8)
Unemployment	63 (6.3)	33 (0.7)	15 (5.1)	15 (5.8)
Comorbidities, n (%)				
Hypertension	397 (39.7)	184 (41.2)	109 (36.8)	104 (40.5)
High cholesterol	350 (35.0)	149 (33.3)	105 (35.5)	96 (37.4)
Medications in current use, n (%)				
Insulin	157 (15.7)	102 (22.8)	35 (11.8)	20 (7.8)
Metformin	596 (59.6)	301 (67.3)	165 (55.7)	130 (50.6)
Other	452 (45.2)	305 (68.2)	90 (30.4)	57 (22.2)

[a]Elevated: baseline HbA_{1c} ≥7.5%; slightly elevated: baseline HbA_{1c} 6.5%-7.4%; normal: baseline HbA_{1c} <6.5%.

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Changes in Glycemic Control

Considering all participants pooled across baseline HbA_{1c}, those who completed the Low-Carb Program showed a statistically significant change in HbA_{1c} of –1.17% (SD 1.43; t_{527}=18.724, P<.001). Partial completers showed a statistically significant change in HbA_{1c} of –0.6% (SD 1.69; t_{143}=4.276, P<.001) and noncompleters showed a nonsignificant HbA_{1c} change of only –0.16% (SD 1.13; t_{328}=2.54, P=.01). Results stratified by baseline HbA_{1c} are presented in Table 3, and results for just Low-Carb Program completers are presented in Figure 2.

Body Weight

Considering all baseline HbA_{1c} groups combined, Low-Carb Program completers (n=528) showed a significant reduction in weight, with a mean body weight change of –7.45 kg (SD 12.63) or –7.0% (SD 12.81%; t_{527}=13.551, P<.001). Partial completers (n=144) showed a reduction in weight, with a mean body weight change of –2.13 kg (SD 16.40) or –1.1% (SD 25.42%); however, this weight change was not statistically significant (t_{143}=1.563, P=.12). Noncompleters (n=328) did not have a statistically significant change in weight, with mean change of –0.35 kg (SD 10.13) or 0.7% (SD 13.41%; t_{327}=0.625, P=.53). Results, stratified by baseline HbA_{1c}, are presented in Table 4, and results for just Low-Carb Program completers are presented in Figure 3.

Hypoglycemic Medications

The majority of participants (714/1000, 71.40%) were prescribed at least one hypoglycemic medication at baseline. At 1 year, of those originally prescribed medications, 289/714 (40.4%) individuals were able to stop one or more hypoglycemic medications. Of the 743 participants who started with an HbA_{1c}, equal to or above the type 2 diabetes threshold of 6.5%, 195 (26.2%) reduced their HbA_{1c} to below the threshold while taking no glucose-lowering medications or just metformin.

For participants who completed the program, the proportion prescribed hypoglycemic medications changed significantly between baseline and follow-up for metformin (χ^2_{24}=146.5, P<.05) and other hypoglycemic medications (all hypoglycemic medications other than metformin and insulin: χ^2_{24}=73.8, P<.05). However, there was no significant change in being prescribed insulin (χ^2_{24}=34.1, P=.08; see Figure 4).

Table 3. Change in HbA_{1c} from baseline to 1-year follow-up by intervention completion.

Baseline HbA_{1c} group	Baseline HbA_{1c} (%), mean (SD)	1-year HbA_{1c} (%) mean (SD)	HbA_{1c} change (%), mean (SD)	P value
Pooled (all participants)				
All participants (N=1000)	7.78 (2.10)	7.03 (2.04)	–0.76 (1.46)	<.001
Completers (N=528)	7.40 (1.81)	6.23 (1.19)	–1.17 (1.43)	<.001
Partial completers (N=144)	7.00 (1.72)	6.40 (1.44)	–0.60 (1.69)	<.001
Noncompleters (N=328)	8.75 (2.33)	8.59 (2.43)	–0.16 (1.13)	.01
Elevated ($HbA_{1c} \geq 7.5\%$)				
All participants (n=447)	9.58 (1.80)	8.36 (2.22)	–1.22 (1.75)	<.001
Completers (N=191)	9.23 (1.71)	7.06 (1.35)	–2.16 (1.76)	<.001
Partial completers (N=47)	8.88 (1.37)	7.26 (1.67)	–1.62 (1.97)	<.001
Noncompleters (N=209)	10.06 (1.84)	9.79 (2.12)	–0.28 (1.06)	<.001
Slightly elevated (HbA_{1c} 6.5-7.4%)				
All participants (N=296)	6.90 (0.28)	6.22 (0.90)	–0.68 (0.89)	<.001
Completers (N=182)	6.88 (0.27)	6.01 (0.69)	–0.87 (0.68)	<.001
Partial completers (N=42)	6.92 (0.31)	6.23 (0.86)	–0.69 (0.87)	<.001
Noncompleters (N=72)	6.93 (0.27)	6.74 (1.18)	–0.19 (1.16)	.16
Normal ($HbA_{1c} < 6.5\%$)				
All participants (N=257)	5.68 (0.68)	5.65 (0.95)	–0.03 (1.06)	.64
Completers (N=155)	5.77 (0.61)	5.47 (0.75)	–0.30 (0.75)	<.001
Partial completers (N=55)	5.45 (0.80)	5.79 (1.22)	0.33 (1.36)	.07
Noncompleters (N=47)	5.66 (0.69)	6.08 (1.07)	0.42 (1.24)	.02

Figure 2. Mean glycated hemoglobin A_{1c} (HbA_{1c}) levels at baseline and 1-year follow-up for participants who completed the program (engaged with all 10 weekly Low Carb Program modules). Error bars represent the SD; * represents significant difference from baseline.
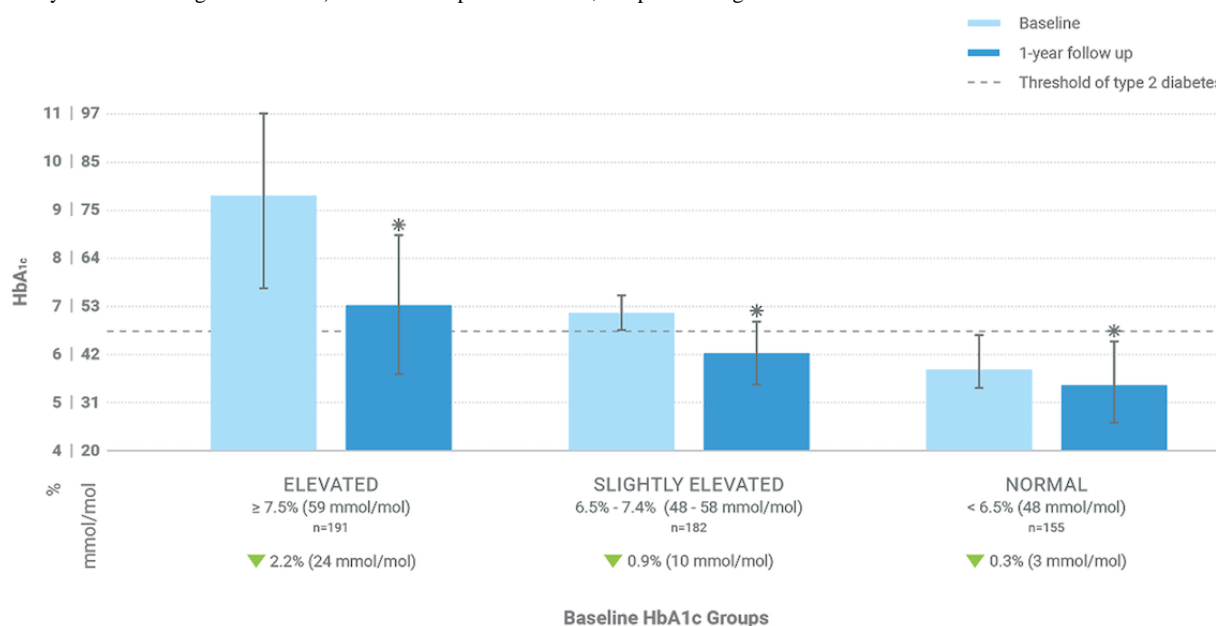

Table 4. Change in participant body weight from baseline to 1-year follow-up for people with elevated or slightly elevated baseline HbA_{1c} by intervention completion amount.

Baseline HbA_{1c} group	Baseline weight (kg), mean (SD)	1-year weight (kg), mean (SD)	1-year percent weight change, mean (SD)	1-year weight change (kg), mean (SD)	P value
Pooled (all participants)					
All participants (N=1000)	89.63 (23.13)	85.28 (20.73)	−3.31 (15.93)	−4.35 (12.93)	<.001
Completers (n=528)	88.88 (22.16)	81.43 (17.98)	−6.97 (12.83)	−7.45 (12.63)	<.001
Partial completers (n=144)	87.77 (22.91)	85.64 (19.02)	1.09 (25.51)	−2.13 (16.39)	.12
Noncompleters (n=328)	91.66 (24.63)	91.31 (23.93)	0.65 (13.41)	−0.35 (10.13)	.53
Elevated ($HbA_{1c} \geq 7.5\%$)					
All participants (N=447)	92.88 (23.96)	89.46 (22.24)	−2.39 (14.70)	−3.42 (12.32)	<.001
Completers (n=191)	92.98 (23.62)	84.96 (18.85)	−6.94 (13.90)	−8.01 (13.83)	<.001
Partial completers (n=47)	90.49 (20.17)	89.76 (19.60)	0.98 (19.88)	−0.72 (13.77)	.72
Noncompleters (n=209)	93.33 (25.09)	93.49 (24.83)	1.00 (12.89)	0.16 (8.64)	.79
Slightly elevated ($6.5 < HbA_{1c} < 7.4\%$)					
All participants (N=296)	88.16 (22.36)	82.44 (19.37)	−5.14 (13.83)	−5.72 (12.61)	<.001
Completers (n=182)	87.94 (20.60)	80.64 (16.87)	−7.27 (10.78)	−7.30 (11.34)	<.001
Partial completers (n=42)	87.37 (24.09)	80.83 (18.78)	−4.66 (20.47)	−6.54 (15.17)	.008
Noncompleters (n=72)	89.17 (25.67)	87.94 (24.27)	0.02 (14.79)	−1.23 (13.15)	.43
Normal ($HbA_{1c} < 6.5\%$)					
All participants (N=257)	85.67 (21.79)	81.27 (18.06)	−2.79 (19.70)	−4.41 (14.19)	<.001
Completers (n=155)	84.93 (21.34)	78.00 (17.46)	−6.65 (13.70)	−6.93 (12.56)	<.001
Partial completers (n=55)	85.76 (24.33)	85.79 (18.19)	5.58 (31.97)	0.03 (18.80)	.99
Noncompleters (n=47)	88.04 (20.38)	86.77 (17.74)	0.14 (13.74)	−1.27 (11.02)	.43

Figure 3. Mean weight at baseline and 1-year follow-up for participants who completed the program (engaged with all 10 weekly Low Carb Program modules). Error bars represent the SD; * represents significant difference from baseline.
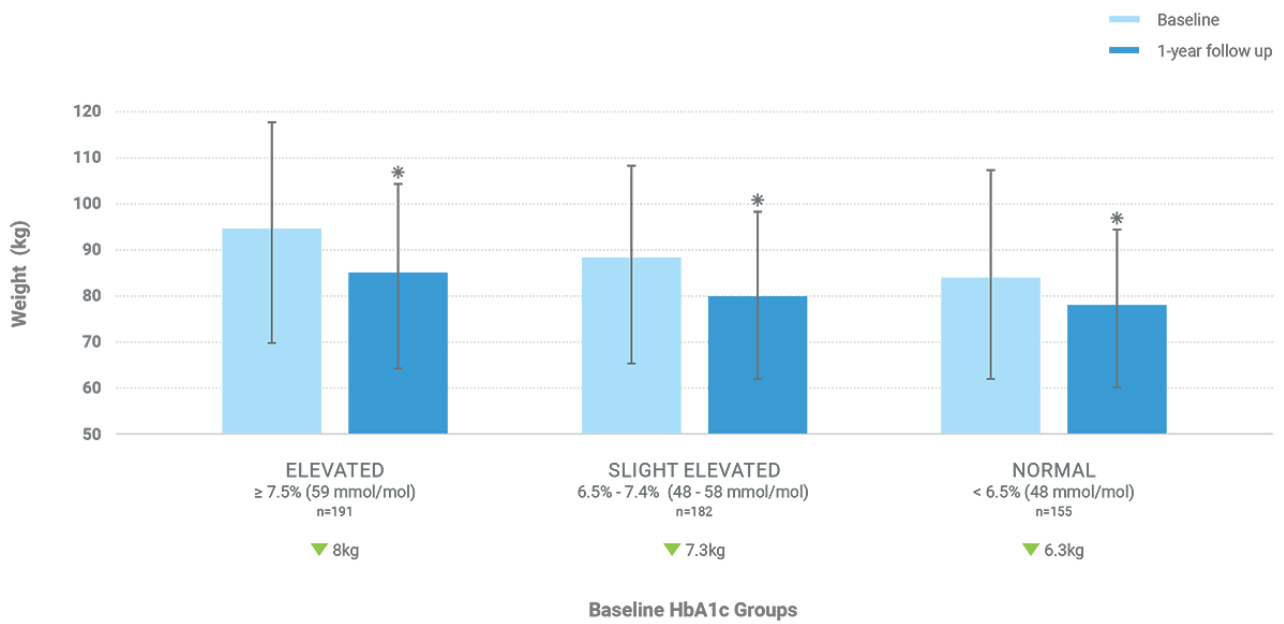
Figure 4. Frequency of change in the number of medications taken for all completers. Bars represent total users of each drug type with the type of change (increase, no change, or elimination) stacked within the bar and the relative frequency noted next to each section. The total number of users of each medication type is noted at the top of each bar.
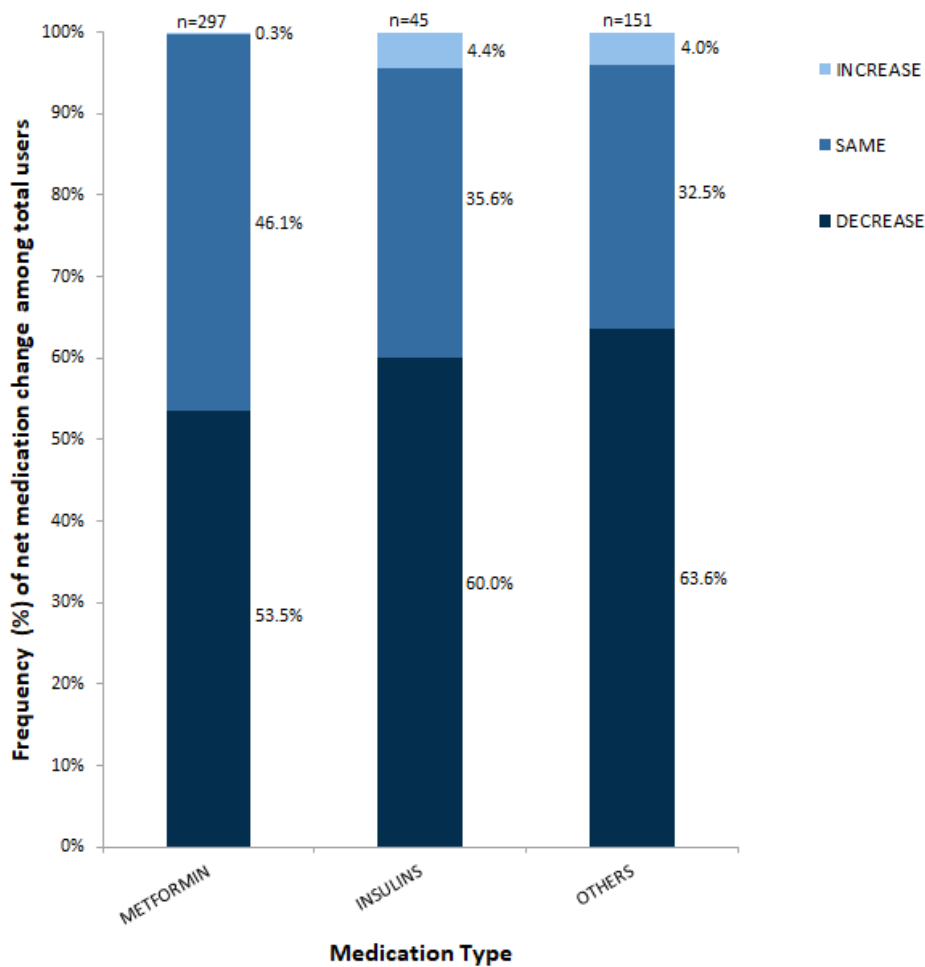
Discussion

The Low-Carb Program is a digitally delivered, peer-supported, nutrition-focused, structured 10-week health intervention aimed at improving glycemic control, reducing hypoglycemic medication use, and promoting weight loss among adults with type 2 diabetes. This was not a randomized controlled trial, so we cannot compare the 12-month results to a control or standard-of-care group; therefore, the results of our trial should be interpreted cautiously because the study used convenience sampling, open-label, single-arm design, pre-post self-reported outcomes, and 71% of participants reported outcomes at 12 months. Even so, when adults with type 2 diabetes participate in the Low-Carb Program, and especially when they finish all 10 modules of the program, they report significantly reduced HbA_{1c}, weight loss, and reduced medications. The percentage of individuals with an HbA_{1c} level less than 6.5% (indicating good diabetes control) increased from 25.70% (257/1000) to 50.30% (503/1000). Furthermore, 46.00% (464/1000) of participants lost at least 5% of their body weight. Also, of participants who were taking at least one hypoglycemic diabetes medication at baseline, 289/714 (40.5%) reduced one or more of these medications.

The percentage of individuals with an HbA_{1c} level of less than 6.5% increased from 25.70% (257/1000) to 50.30% (503/1000). This degree of control, when achieved through pharmacotherapy, is often accompanied by weight gain and risk for hypoglycemic events [27]. Indeed, as the now famous Action to Control Cardiovascular Risk in Diabetes (ACCORD) study reported, intensive hypoglycemic medical therapy "increased mortality and did not significantly reduce major cardiovascular events" [28].

As in other studies using a carbohydrate-restricted dietary approach, including Dr Unwin's in-person program on which the Low-Carb Program was partially modeled [14,17,29], we achieved HbA_{1c} reduction with weight loss and decreased hypoglycemic medication use. This approach is given further credence by a recent meta-analysis, which concluded that carbohydrate-reduced interventions improve glucose control, in addition to other positive health effects such as improved triglyceride and high-density lipoprotein cholesterol [30].

Our study has several limitations. Although we encouraged participants to eat a carbohydrate-restricted diet, we did not measure their dietary intake. We also measured health outcomes (weight, glycemic control, and medication changes) using self-report, rather than measuring them directly or through medical records. However, previous research has found that these self-reported health outcomes can be quite close to actual values [31,32]. Another limitation was our rate of delivering the entire intervention, as only 528 (52.8%) completed all modules. However, a high rate (70.8%) reported 12-month outcomes. On the other hand, given that this program was entirely automated and had a wide reach, a large number of individuals were able to complete the program.

For participants who fully engage, an automated online program teaching a carbohydrate-reduced diet to adults with type 2 diabetes may facilitate glycemic control, weight loss, and reduced need for hypoglycemic medication. Although our design does not support causal conclusions, the program may be a useful adjunct for lifestyle self-management for adults with type 2 diabetes.

Conflicts of Interest

CS is employed by Diabetes.co.uk, which runs the Low-Carb Program. The rest of the authors declare no conflicts of interest.

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Abbreviations

HbA$_{1c}$: glycated hemoglobin A$_{1c}$
IRB: Institutional Review Board

Original Paper

Design and Development of a Context-Aware Knowledge-Based Module for Identifying Relevant Information and Information Gaps in Patients With Type 1 Diabetes Self-Collected Health Data

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Abstract

Background: Patients with diabetes use an increasing number of self-management tools in their daily life. However, health institutions rarely use the data generated by these services mainly due to (1) the lack of data reliability, and (2) medical workers spending too much time extracting relevant information from the vast amount of data produced. This work is part of the FullFlow project, which focuses on self-collected health data sharing directly between patients' tools and EHRs.

Objective: The main objective is to design and implement a prototype for extracting relevant information and documenting information gaps from self-collected health data by patients with type 1 diabetes using a context-aware approach. The module should permit (1) clinicians to assess the reliability of the data and to identify issues to discuss with their patients, and (2) patients to understand the implication their lifestyle has on their disease.

Methods: The identification of context and the design of the system relied on (1) 2 workshops in which the main author participated, 1 patient with type 1 diabetes, and 1 clinician, and (2) a co-design session involving 5 patients with type 1 diabetes and 4 clinicians including 2 endocrinologists and 2 diabetes nurses. The software implementation followed a hybrid agile and waterfall approach. The testing relied on load, and black and white box methods.

Results: We created a context-aware knowledge-based module able to (1) detect potential errors, and information gaps from the self-collected health data, (2) pinpoint relevant data and potential causes of noticeable medical events, and (3) recommend actions to follow to improve the reliability of the data issues and medical issues to be discussed with clinicians. The module uses a reasoning engine following a hypothesize-and-test strategy built on a knowledge base and using contextual information. The knowledge base contains hypotheses, rules, and plans we defined with the input of medical experts. We identified a large set of contextual information: emotional state (eg, preferences, mood) of patients and medical workers, their relationship, their metadata (eg, age, medical specialty), the time and location of usage of the system, patient-collected data (eg, blood glucose, basal-bolus insulin), patients' goals and medical standards (eg, insulin sensitivity factor, in range values). Demonstrating the usage of the system revealed that (1) participants perceived the system as useful and relevant for consultation, and (2) the system uses less than 30 milliseconds to treat new cases.

Conclusions: Using a knowledge-based system to identify anomalies concerning the reliability of patients' self-collected health data to provide information on potential information gaps and to propose relevant medical subjects to discuss or actions to follow

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could ease the introduction of self-collected health data into consultation. Combining this reasoning engine and the system of the FullFlow project could improve the diagnostic process in health care.

Introduction

Background

Providing the right explanations regarding the situation of a patient at the right time is a key for improving the diagnostic process in health care [1]. Data collected by the patients, using various applications, can be a precious source of information for characterizing and explaining the situation of a patient suffering from chronic illnesses, especially diabetes [2], for both patients as well as their clinicians. Studies have shown that patients are increasingly using applications for automatically collecting, storing, and analyzing their data [3]. However, clinicians cannot effectively use self-collected health data until it is integrated into their daily workflow and clinical systems, and often ignore the data if they do not know that it is "accurate, reliable and aligned with their agenda" [4].

The "Full Flow of Health Data Between Patients and Health Care Systems," referenced as FullFlow in this article proposes to address these issues. This can be achieved by providing a platform for integrating the patient's self-collected health data from diabetes self-management applications (eg, Diabetesdagboka [5], mySugr [6]) and wearables (eg, FreeStyle Libre [7]) into Norwegian Electronic Health Records (EHRs) and Norwegian Personal Health Records (PHRs) through Norwegian public services. FullFlow aims to (1) facilitate diagnostic processes conducted by specialists, general practitioners (GPs), and nurses, by presenting patients' self-collected health data directly in their EHRs and PHRs, and (2) empower patients and help them understand their disease. We limited the focus of FullFlow to diabetes, even if it can provide a more general service.

FullFlow consists of 3 components. First, there is a data collection component, which aggregates self-collected health data from the patients' tools, by either using application programming interfaces (ie, automatic collection from patients' tools) or Web-based schemas (ie, manual collection done by the patients). Second, there is a data analysis module, which processes the data and provides statistical analyses and medical calculations (eg, deviations, insulin sensitivity factor). Third, there is a Bundles Builder, which organizes the data into Fast Health Care Interoperability Resources (FHIR). FullFlow uses FHIR for facilitating its integration with Norwegian public services starting to implement this standard, especially Helsenorge.no [8], which contains a collection of health records generated by health care institutions (PDF only in May 2018) and accessible by both patients and clinicians in Norway. In addition to the FHIR-based data, the Bundles Builder provides reports to help medical workers consulting the data and to facilitate the integration of self-collected health data for the EHRs, which are not yet ready to handle FHIR resources but

started to implement it [9]. These reports are dashboards, similar to the dashboard proposed by Dagliati et al [10] or to Carelink by Medtronic [11] but differs regarding several points: (1) FullFlow proposes the usage of self-collected health data as source of the dashboard, (2) FullFlow is aiming to integrate self-collected data into clinical systems directly without the use of external services, and (3) FullFlow is not limiting the data source to specific companies, sensors or applications. These reports are in PDF or Hypertext Markup Language and are directly sent to Norwegian EHRs and PHRs.

Figure 1 illustrates this composition and the data flow, from the patients to the medical workers.

The reports (see Figure 2) contain distinct areas, each focusing on a specific need:

1. Overview Area-provides a summary of the data period.
2. Period-displays patient-collected data as linear graphs.
3. Daily Evolution and Daily Distribution-contain graphs with all types of data available summarized per day and hour.
4. Data List-provides a list of all data collected for the period in text format.
5. Combined Data-displays all data in a unique graph.

These areas permit clinicians to obtain an overview of a patient's self-reported health condition, as well as identify problematic events or trends, and to recommend actions for managing them. However, testing the dashboard of the FullFlow revealed unaddressed challenges.

First, the presence of information gaps in the self-collected health data. Information gaps are missing problematic events (eg, unreported hypoglycemic event) and lack of information for pointing out their causes (eg, undocumented extreme physical activity before a hypoglycemic event). Multiple factors lead to these information gaps (1) sensors and wearables used by the patients are not well calibrated, imprecise or even defective [12,13], (2) sensors and wearables are incorrectly operated by the patients [14], (3) patients make errors when registering data manually, and forget to register data or do not register at all [15], and (4) patients deliberately lie and edit the data to hide their poor performance to avoid unfavorable judgment by medical workers [16] and to avoid potential penalties. For example, in Norway, patients with more than 2 severe hypoglycemic events risk losing their driving license [17]. The information gaps limit the possibility for clinicians to interpret the data correctly and constitute the main barrier to the acceptance of the FullFlow, as the clinicians are considering the self-collected health data as less reliable compared to laboratory results for example.

Second, our workshops with clinicians showed that even when information gaps are not present, clinicians are unable to extract

and analyze the data in an acceptable amount of time, especially during a consultation, even with the help of graphs. According to them, self-collected health data is too time consuming because of the amount of self-collected health data (ie, the number of registrations performed by the patients), of the noise in self-collected health data (ie, irrelevant data regarding the self-reported health condition of a patient), and clinicians need to link and compare different types of health data to extract information. This constitutes the second main barrier to the acceptance of the FullFlow.

Figure 1. Simplified data flow of the FullFlow project. API: application programming interface; EHR: electronic health record; FHIR: Fast Health care Interoperability Resources; PHR: personal health record.
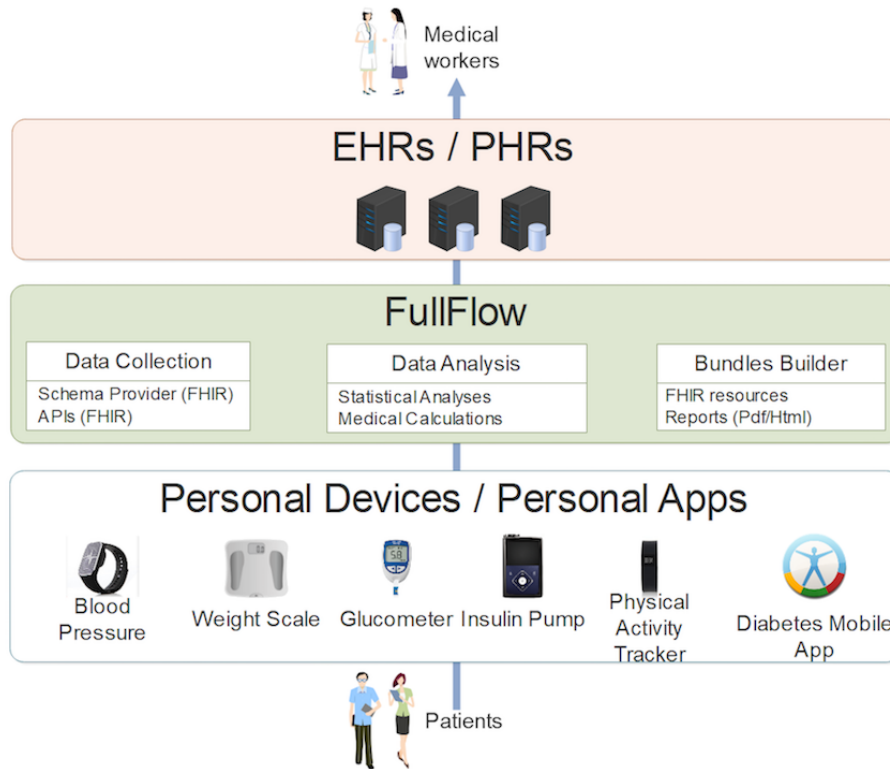

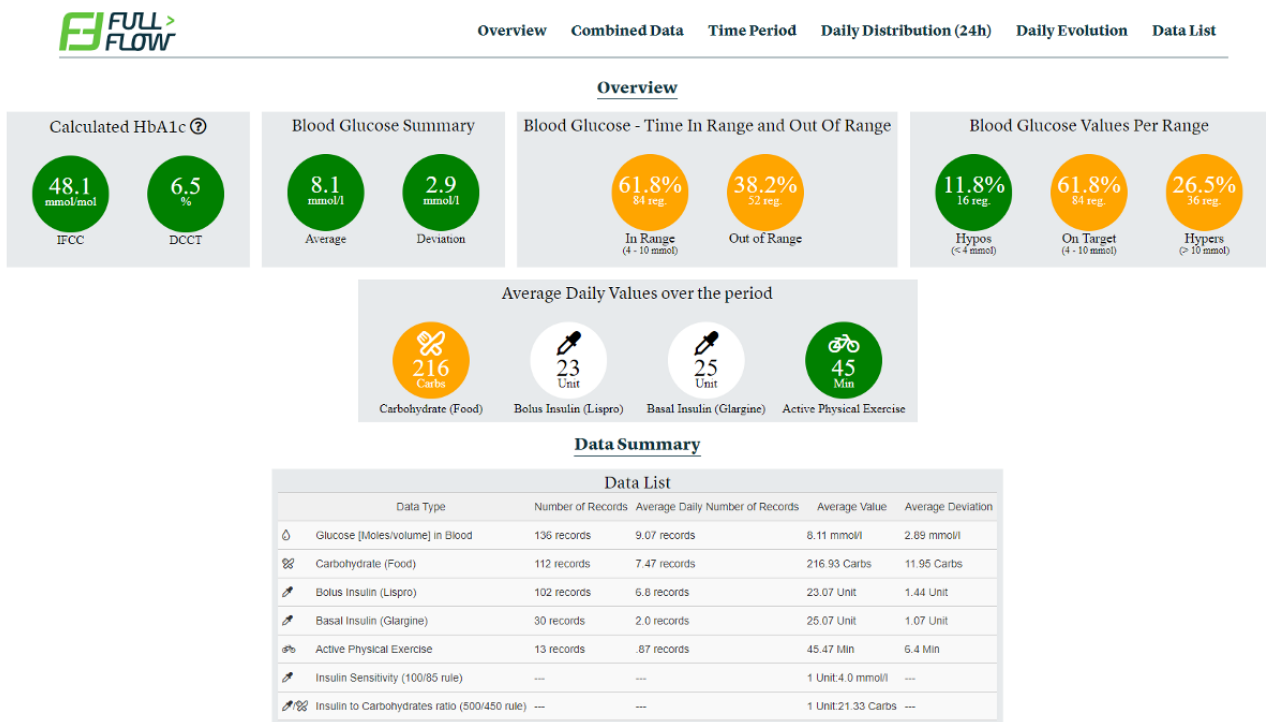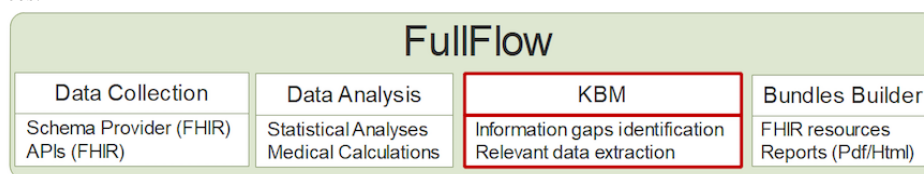**Figure 2.** Example of a FullFlow Report.

Figure 3. FullFlow components with the knowledge-based module (KBM; red). API: application programming interface; FHIR: Fast Health care Interoperability Resources.

In this paper, we address these challenges: information gaps, time-consuming processing of data and extraction of the relevance of the data by presenting the design, and implementation of a context-aware knowledge-based module (KBM). The KBM improves the FullFlow system by (1) providing information on the reliability of self-collected health data and the potential presence of information gaps, and (2) presenting relevant information about the self-reported health of a patient and the origins of problematic events.

The KBM is a complimentary module to dashboard systems such as FullFlow and could permit clinicians to focus on specific and relevant information during consultation instead of spending time consulting the self-collected health data and trying to extract information on their own. Figure 3 presents the FullFlow components with the KBM. The result section shows the impacts of the KBM on the Bundles Builder.

The knowledge base contains rules formulated by medical experts and relies on a reasoning engine (ie, component deducing information), based on contextual information, to identify and interpret relevant data. Dey and Abowd [18] define context as "any information that can be used to characterize the situation of an entity". An entity is a person, place, or object that is considered relevant to the interaction between a user and an application, including the user and applications themselves. In our setting, medical evidence, such as patients' self-collected health data, laboratory results and metadata, such as the identities of the patients and medical workers, and the rules of the knowledge base themselves compose the context. The reasoning engine combines these data using a hypothesize and test strategy for identifying data reliability problems as well as information gaps and highlighting relevant data related to problematic events.

This paper also presents the methodologies we followed from the creation to the assessment of this module, including its integration in the main system, and its future use.

Methods

This section presents an overview of the different phases and methodologies used for the design, the implementation and the testing of the KBM, as shown in Figure 4.

Design of the Module

First, a brainstorming approach to define the scope of the module for identifying functionalities and potential problems appearing at a later stage was used by the main (AG) and the second author (PO). The data flow, technology stack (ie, a combination of programming languages, tools, and functionalities) and data

model (ie, the standardization of data and relations between types of data) were also discussed.

Then, 2 facilitated workshops were organized for designing the KBM, involving the main author (AG), one patient with type 1 diabetes (in house researcher), and one clinician (AH). The workshops were used for different purposes (see Textbox 1). However, a wider range of people were invited to participate in a co-design workshop to contribute to the 3 points described above, as the 2 facilitated workshops sessions had limited participants. There were 5 patients with type 1 diabetes, 2 endocrinologists, and 2 nurses specializing in diabetes were involved in this co-design. The participants were not known to the authors and were recruited through the authors' partner institution, the University Hospital of Northern Norway and on social media. Acknowledgment from Regional Ethical Committee was applied and an exemption was received September 2017. The co-design was organized around 3 sessions: (1) patients only, (2) clinicians only, and (3) all participants together. Sessions 1 and 2 were held simultaneously at a different location and before the session 3. This approach permitted to build the patients' confidence and to ensure their thinking points were addressed during the common session. The patients' pressure and bias were lowered by the facilitators (ie, the authors) giving everyone a chance to speak and by using different methodologies, such as (1) the expense account where each participant has to use a token before speaking and cannot speak once their token pile is empty, (2) the Writing Round Robin where all participants answer a question on paper simultaneously and then present the answers in turns, and (3) the 5 whys where a participant is asked "why" 5 times to find the root of a problem. The methodologies were defined beforehand by the authors through brainstorming sessions. Time was also reserved for participants to ask their questions throughout the sessions.

The co-design was audio recorded, and the audio registrations were transcribed by the authors for further classification and analysis. All medical related decisions from these events were assessed by the third author, who is a medical doctor.

Implementation of the Module

An agile development process (ie, iterative development) was used for the software implementation when evolution, changes, and adaptability were the key points (eg, user interactions, reasoning model). Continuous input and involvement of patients and health workers were included in this process. A more classic waterfall approach (ie, sequential development) was used when stability and performance were the focus, such as the implementation of the core of the module (ie, the "engine" which does not interact directly with the users).

Figure 4. Methodologies used in three different phases: Designing, Implementing and Testing of the KBM.
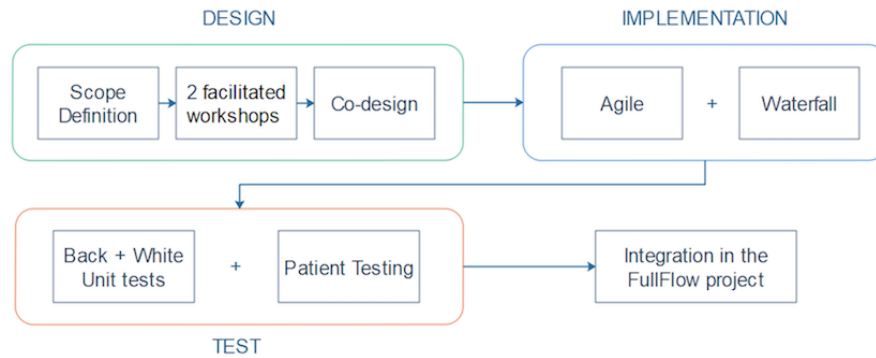
Textbox 1. The different purposes of the workshops.

1. For identifying contextual information. The context was first identified following the approach proposed by Dey and Abowd [18] with the support of brainstorming: organizing context around location, identity, time and activity and using a tiered system for further categorization per type of context, and point of view of the KBM.

2. For creating a model of context, representing the interactions between all entities involved with the KBM (eg, patients, medical workers, EHRs) and the context interacted between them. This was inspired by the model of context in computer science proposed by Bradley and Dunlop [19] and was created to provide a complete overview of the usage of the context.

3. For defining a knowledge base and a reasoning model. They were used as requirements for the implementation of the module and to describe the functionalities of the KBM and its operation.

Testing of the Module

Testing was performed in different ways: a white box (ie, testing of internal structures of code) approach was used for testing the core without involving the context and the reasoning model, while a black box (ie, testing of functionality) approach was followed for testing whether the system behaved according to what was defined by the previous creation process. Both approaches were made using unit tests. Load tests were used for determining if the performance of the modules could affect FullFlow in the event of its integration.

Results

System Architecture

This section presents a complete overview of the architecture of the KBM.

Contextual Information

The first step in the architectural design process (ie, the sequence of steps to create the KBM) was to identify the contextual information necessary for the KBM to achieve the goals for which it was designed. We adopted the context definition suggested in Dey and Abowd [18]. Their 4 main categories of context were location, identity, time, and activity. However, since the types of contextual information in health care domain is much richer than the context presented by Dey and Abowd, we introduced several types of context particularly instead of "activity" category of context.

In total, we identified 9 types of context, as shown in Figure 5. The first type is *health data*, containing *patient-collected data* and *laboratory generated data*. *Patient-collected data* represents data a patient can bring to the consultation using their sensors, mobile applications or diaries**.** The data usually collected by

patients with diabetes are mostly blood glucose, basal-bolus insulin, carbohydrates, physical activity, and to a less degree also calories, blood pressure, heart rate, medication, ketones, stress, menstruation, sickness, insulin sensitivity, polypharmacy, comorbidity, insulin-to-carbohydrate ratio (I:C), and carbohydrate absorption rate. Units of measurements can further characterize each type of the collected data. For example, physical activity could be expressed as the number of steps, a period or intensity (eg, light, moderate, extreme), while insulin intakes could be expressed in international units (UI) or mg.

Laboratory generated data represents data originated from laboratory tests (eg, blood analysis). Today, FullFlow only has automatic access to the glycated hemoglobin (HbA_{1c}) data from several EHRs and cannot obtain other types of data such as leukocytes, which are associated with diabetes complications [20], or creatinine which is useful for tracking the progression of diabetic kidney disease [21]. Therefore, they are not included in Figure 5.

Medical standards are the third type of context, which covers reference values for a specific data type. For example, the recommended range for blood ketones is less than 0.6 mmol/L or the formulae used for calculating medical values (eg, 1500/1800 rule for approximating the insulin sensitivity factor [22,23]).

Data registration regularity refers to the registration frequency for each type of data for different periods. The rationale behind this context type is to provide information on the regularity of measurements or samplings made by patients for each type of data they collect. The data registration contains the total number of registrations per self-collected data type for the whole period, as well as the distribution of the number of registrations per day, per weekday, and per hour, as well as a minimum number of registrations per data type and per period.

Figure 5. Categorization of Contextual Information Types.

Measurable personal goals are the next type of context. Patients define them according to their preferred lifestyle or based on the feedback from their clinicians. There are several types of goals: (1) keeping the values of a specific data type within a specific target range (eg, keeping blood glucose between 4-9 mmol/L), (2) reaching a specific number of measurements for a fixed period (eg, checking blood glucose values 6 times a day with a glucose meter), and (3) reaching a threshold value for a specific data type (eg, weighing 65 kilograms or under).

Goal of the consultation refers to the reason for an appointment between a patient and the clinician. Clinicians can define the goal when planning a follow-up with patients, but patients can also define it if they need help regarding their health situation. The goal of the consultation may or may not be part of the patients' diabetes situation.

System generated context refers to the context produced by the KBM itself during its execution. It includes hypotheses generated by the system that needs to be validated or refuted. The context *hypothesis result* further characterizes a hypothesis, with 3 possible states: (1) TRUE if the hypothesis is validated, (2) FALSE if the hypothesis is rejected, and (3) NOT APPLICABLE (NA) if the required context is missing (eg, the

invalidation of a hypothesis stating that "the patient has eaten too much carbohydrates a day" cannot be done if the patient did not register any carbohydrate intake).

We identified 3 main entries under the *identity* type of context, which defines who uses the KBM in an actual situation. It encompasses patients, medical workers, and their relationship. Further context characterizes patients: age, sex, diabetes type. and emotional state (eg, personality, life goals, intentions, and preferences). Further context also characterizes clinicians: their specialty (eg, GP, nurse, endocrinologist) and their emotional state.

The *time* type of context *defines* when a patient and a medical worker use the KBM. In our situation, the usage of the module corresponds to the usage of the FullFlow system: mainly during consultations. However, medical workers and patients could also use it before and after consultation. In the first case, to prepare for the consultation, and in the second case, to look up data they did not have time to view during the consultation.

Concerning the *location* type of context, the KBM can be used everywhere: at a clinician's workplace (eg, GP's office,

municipal care office, hospital department), at home or on the go for both patients and doctors, if they are willing to do so.

Instantiation of all these types of contextual information with the current situation where the KBM operates creates the "current context". The current context is dynamic and changes across patients and different situation of the same patient (eg,, a particular consultation at a certain date and time and with a particular clinician for a particular purpose). In the section "Knowledge base and reasoning engine," we describe the role of current context in the reasoning process of the reasoning engine.

Model of Context

The context taxonomy (ie, a classification scheme) in Figure 5 is the outcome of the first step of the design process. This has strong implications of the knowledge to be represented in the knowledge base as well. Context identification and modeling were performed by the designer group that consists of computer scientists and medical experts. There were 2 types of context predefined and do not change across situations: "Medical Standards" and "Data Registration Regularity".

Once we identified the categories and the taxonomy of contextual information, we needed to define the interaction between entities (ie, the actors) and the specific part of the context shared during the interactions. To address this issue, we created a model of context inspired by the approach described by Bradley and Dunlop [19], as shown in Figure 6.

The *knowledge-based module* contains 3 components: the *knowledge base*, the *reasoning engine*, and the *current context*. There are 3 sources that create different parts of the current context—in addition to the designer defined ones. The first is patients. Patients interact with the module directly or through their PHRs (not displayed in the figure for simplicity) by sending

their metadata (eg, age, sex, diabetes type) and self-collected health data. Second is medical workers and EHRs. Medical workers are not interacting directly with the KBM for sharing context, but through the EHRs they are using. EHRs provide the KBM with an authentication token for the medical workers in combination with the laboratory-generated data. Medical workers and patients interact with each other during a consultation, which could be face-to-face, remote, in real-time, or not. Third, is the reasoning engine. Outcomes of the reasoning engine of the KBM can dynamically change the current context. Here we refer to "system generated context" in Figure 5. For example, the original goal of the consultation could have been to discuss and manage nocturnal hypoglycemic events. However, the goal could shift toward discussing the insulin correction factor if the KBM finds that these events are due to wrong insulin dosage after meals, for example.

This context model allows us to have a clearer view of how the global flow of context data is in real-life situations.

Knowledge Base and Reasoning Engine

We established the reasoning engine and the knowledge base by the identified types of contextual information and the model of context presented above. The reasoning engine provides problem-identifying functions needed for determining the degree of reliability of the patients' self-collected health data and for identifying "noticeable events" and their potential causes. A noticeable event is a medical event discovered from the contextual information, where feedback from the medical worker could be useful for improving the patient's situation. To do so, the reasoning engine relies on a knowledge base and a hypothesize-and-test reasoning strategy, as shown in Figure 7.

The rectangles in the figure represent the processes of the reasoning engine, while the parallelograms show the data the processes use or produce.

Figure 6. Model of Context. The labels next to the arrow represent the different types of context. EHR: electronic health record.
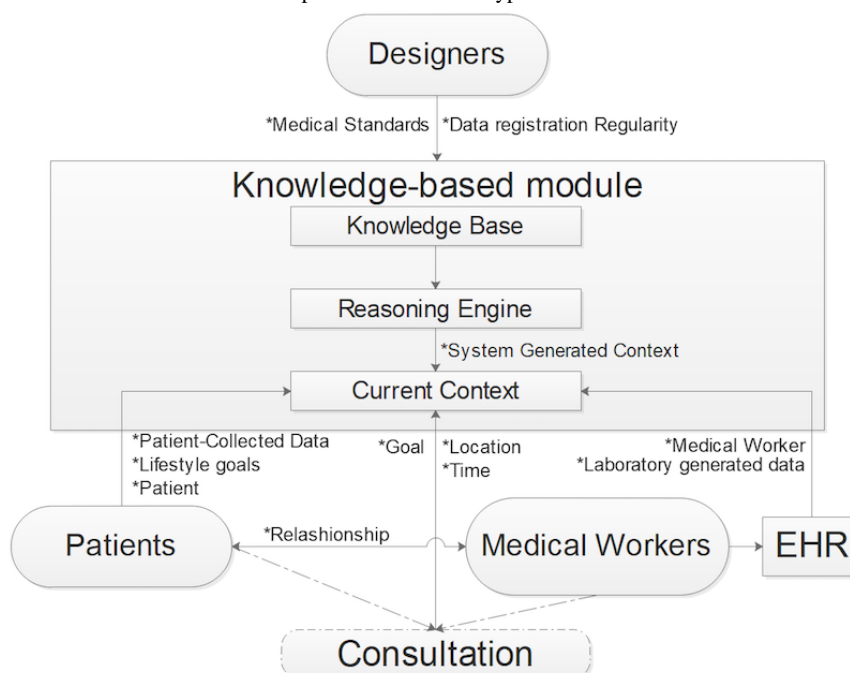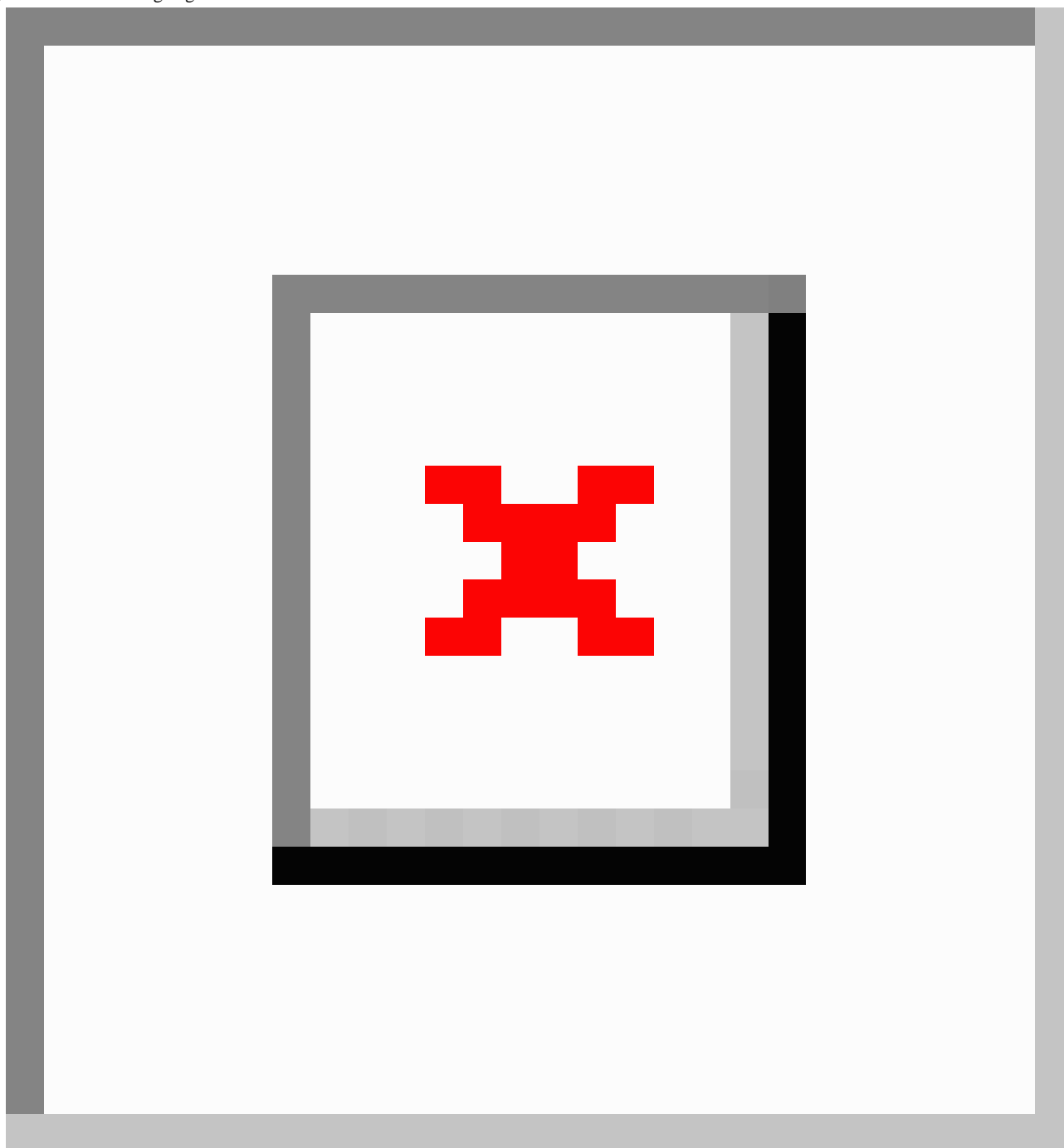
Figure 7. Our reasoning engine model.

The *knowledge base* contains the domain knowledge of medical experts that the hypothesis-and-test strategy needs in this system. Currently, knowledge base remains static. Each time a patient shares their self-collected health data with a clinician, the same knowledge base creates the problem-identifying tasks, while the Current Context is dynamic. The *Explanation Case Base* and the *Plan Case Base* compose the KB.

We now describe the structure of the *Plan Case Base,* which comprises many plans. A plan consists of sequential problem-identifying tasks to perform and can refer to or include other plans. For example, plan P1 (ie, evaluates the correctness of the amount of the last insulin dosage) uses the tasks P1T1 (ie, check the blood glucose value), and P1T2 (ie, estimate the best insulin amount in this situation) in combination with the plan P2 (ie, check the insulin sensitivity for the day), which in turn includes the tasks P2T1 (ie, define the amount of insulin intakes for a day), and P2T2 (ie, use the 1500/1800 rule for calculating the insulin sensitivity). Figure 8 illustrates this example. This hierarchical structure, however, does not indicate in what sequence the tasks and plans are executed, but this is handled by *rules*.

There are 3 types of rules. The *Plan Rules* define the sequence of the plans and the tasks composing them (eg, perform the task "check if insulin registrations are present' before the task 'check the amount of insulin intake for a day"). The *Activation Rules* define which data are necessary for performing a task (eg, insulin and carbohydrates registrations are mandatory for the task "check if the patient forgot to take insulin before or after

a meal") and potential conditions for performing the task (eg, "a carbohydrate intake is considered a meal if done between 11:00 and 13:00"). The *Evaluation Rules* define the concrete actions to be taken in order to accomplish a task (eg, for the task "check if the patient forgot to take insulin before or after a meal," the rules define 3 actions: (1) check the carbohydrates intakes, (2) check if the intakes correspond to a meal time, and (3) check if an insulin registration is present in a 30 minutes window before or after the carbohydrates intakes).

The *Explanation Case Base* defines the complementary or hierarchical relations between the problem-identifying tasks and the interpretation of identified problems based on the results of the problem-identifying tasks. For example, the problem-identifying tasks "check the amount of carbohydrate intake from the previous meal" and "calculate the carbohydrates on board" are complementary and compose the higher-level task "check the amount of carbohydrates", which can characterize a hyperglycemic event.

The first process in the reasoning engine is *Hypotheses Generation*. In our model, a hypothesis represents the inferred candidate result of a task that the reasoning engine validates or invalidates. For example, the hypothesis "there is no insulin registration before or after a meal" may be a candidate answer to the task "check if the patient forgot to take insulin before or after a meal". This process generates a current plan case composed of a sequence of tasks with associated hypotheses to

test based on the plan and the Plan Rules of the Plan Case Base (Figure 7, no. 1) and on the System Generated Context (current context). The process uses the results of previously tested hypotheses to update the active case plan if necessary (Figure 7, no. 5b). For example, if the hypothesis "patient has hyperglycemia" is true, the process updates the plan and adds 18 hypotheses according to the rules, such as "the latest insulin intake was lower than the insulin needed defining by the sensitivity factor for reaching 5.5 mmol/L". The outcome of the Hypotheses Generation is a sequence of hypotheses to validate (or refute), each for the accomplishment of a specific task constituting the plan.

The second process is *Hypothesis Activation*. The hypotheses generation process initiates this process for each hypothesis listed in the current plan case (Figure 7, no. 2). Hypothesis Activation requires the Activation Rules from the Plan Case Base (Figure 7, no. 2c) and the current context from Patients, EHRs or both (Figure 7, no. 2b). The *Hypothesis Activation* process ensures that the required context for evaluating a hypothesis is available. For example, the hypothesis "patient has hyperglycemia" requires Blood Glucose registrations from the Patient entity. If required context is not available for a hypothesis listed in the current plan case, the system flags the concerned hypothesis as NA. If the required context is available, the system activates the hypothesis. The activation of a hypothesis automatically initiates its evaluation (Figure 7, no. 3).

Figure 8. Example of hierarchy of plans (P) and tasks (T). P1 contains P2 and two tasks, P1T1 and P1T2.
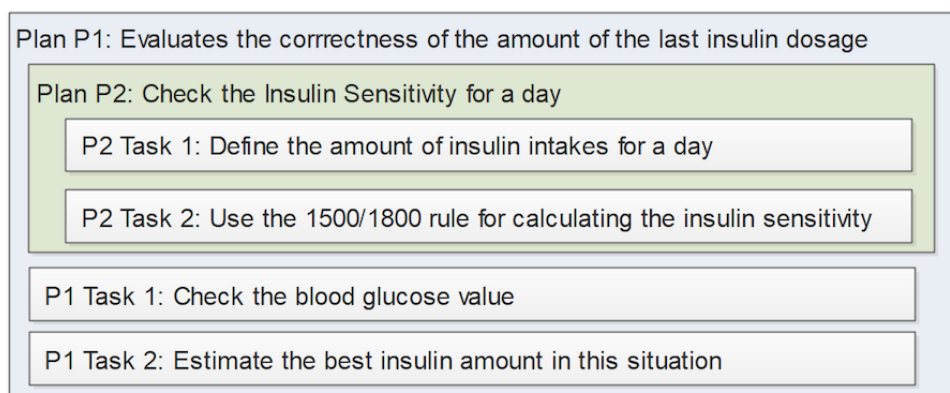
The *Hypothesis Evaluation* process validates or invalidates the claim proposed by the hypothesis. To do so, this process uses the Evaluation Rules of the Plan Case Base (Figure7, no. 3c) and the current context from Patients, EHRs or both (Figure7, no. 3b). The output of this process is a hypothesis result (Figure7, no. 4), which could be true, false, or NA. This output is then stored with the other hypotheses results (Figure7, no. 5a) and sent back to the Hypothesis Generation process (Figure7, no. 5b) for potential current plan case updates.

Once the Hypotheses Generation activated all hypotheses in its current plan case, it triggers the Interpretation process (Figure7, no. 6). This process uses the Relations between problem-identifying Tasks and their Explanations from the Explanation Case Base (Figure7, no. 6b) as well as the hypotheses results (Figure7, no. 6a) to create a textual interpretation of the results of the execution of the reasoning

engine to allow users to consult it. The textual interpretation is the final context generated by the system (Figure7, no. 7). The system then displays the context to the users.

Hypotheses List

Figure 9 describes all the hypotheses used by the KBM at this stage. We organized the hypotheses per type and per order of execution (ie, from top to bottom), according to the Explanation Case Base and of the Plan Case Base. The interpretation of the hypotheses defines them, instead of their internal identification code, for better clarity. For simplicity, we omitted the context requirements for their activation and generation in this paper. For example, the generation of the hypothesis "there is not enough insulin" requires that the hypothesis "patients have hyperglycemia" be true and its activation requires the registration of insulin self-collected health data.

Data Reliability

The first type of hypothesis relates to the *data reliability* of patients' self-collected health data. The first hypothesis "data is not reliable" is automatically activated. The output of the evaluation process of this hypothesis is an impact factor of reliability, which defines how much the results of other hypotheses and the self-collected data can be trusted based on a scale of 0-50, from distrust to trust. The trust level is calculated by subtracting the sum of the value (or grade) of each sub-hypothesis evaluated to true by the system listed in the plan case of data reliability. For example, if the HbA_{1c} value calculated by the module (ie, based on blood glucose self-measurements) deviates by more than 5% (ie, based on the approximation of the translation of A1C to estimated average blood glucose by Nathan et al [24] and the inaccuracy of the blood-glucose monitoring systems for self-testing [25]) of the HbA_{1c} value determined by laboratory tests, the trust level decreases by 10 points. There are several types of sub-hypothesis. For example, "No [data type] registered" indicates that the most relevant data type is missing from the patient's data: blood glucose, carbohydrates, insulin, and physical activity. Several sub-hypotheses compose this hypothesis: one per data type. For each hypothesis validated by the evaluation process (eg, "no blood glucose registered" is true), the interpretation process displays a message to users proposing that they register a new type of data with the support of examples. For example, if the patient is using insulin and the hypothesis "no carbohydrates registered" is true, the system displays "registering carbohydrate intakes will permit a better estimation of your insulin correction dosage as well as …and could help you reduce variation, ie, highs and lows of your blood glucose values".

"Error values in [data type]" means that the registered values for a specific data type are probably incorrect. For example, a blood glucose value of 1.1 mmol/L is probably due to error either in the registration or measurement process. Importantly, blood glucose levels less than 1.1 mmol/l provoke neurological damages [26]. However, the KBM conveys a specific message to users regarding these events, in addition to grading the trust level of the data, for them to validate the origin of these values. Currently, the module focuses only on blood glucose, carbohydrates, and insulin values for this sub-hypothesis.

"Not enough data registrations" focuses on the minimal number of registrations per type of data and per day to calculate trends. For example, patients should check their blood glucose at least 5 times a day for this sub-hypothesis to be false. The National Institute for Health and Care Excellence (NICE) recommends self-testing blood glucose level at least four times a day [27], but we increased this number for better accuracy. The interpretation process also displays a motivational message to encourage patients to register data more often if some hypotheses are true.

Figure 9. List of hypotheses organized per type used by the knowledge-based module (KBM).
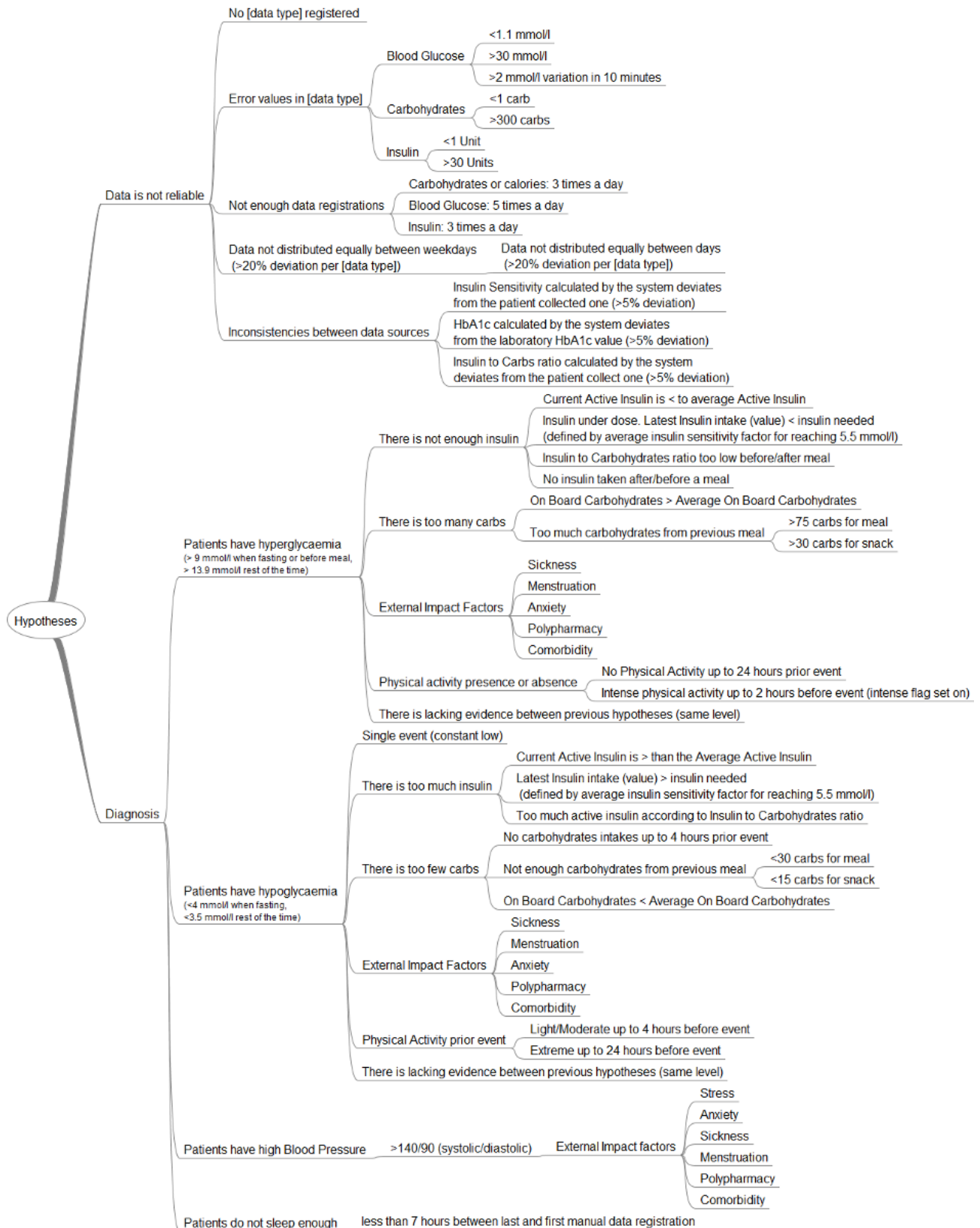
"Data not distributed equally between days" concentrates on the regularity of the total number of registrations per day and per type of data for the whole data self-collection period. The participants suggested allowing 20% deviation in the number of registrations and days. The "Data not distributed equally between weekdays" follows the same principle but organizes the day per weekdays instead (eg, Monday, Tuesday.). These 2 hypotheses ensure that patients register data regularly and that the registrations are not impacted by their lifestyles (eg, working during the week and performing outdoor activities on the weekend).

"Inconsistencies between data source" is another hypothesis where the system checks the difference in the value of the same data type from different sources and allows 5% deviation between them. The module implements 3 sub-hypotheses. The first is checking the HbA_{1c} value calculated by the module itself against the same value determined by a laboratory test as explained previously. The second is checking the insulin sensitivity calculated by the module against the same value reported by the patient, and the last is checking the Insulin to Carbohydrates ratio (I:C) calculated by the module against the same value reported by the patient. The system alerts the user to this deviation with warning messages.

The evaluation of the previous hypotheses gives (1) an indication about the accuracy and the reliability of the self-collected health data for the clinicians, and (2) recommendations for improving the reliability of the data for the patients.

Medical Problem Identification

The second type of hypotheses relates to *medical problem identification*. The activation of these hypotheses depends on the value of the patients' self-collected data and concerns hyperglycemia, hypoglycemia, high blood pressure events, and short sleeping patterns. The time of the highest blood glucose value in a continuous hyperglycemic event (6 hours maximum—suggested by the participants) and the time of the lowest blood glucose value in a continuous hypoglycemic event define a reference time where the possible causes could be easier to detect by the module.

Hyperglycaemia

In the case of hyperglycemia, Hypotheses Generation activates the hypothesis and set its result to true if it detects one or more blood glucose values greater than 9 mmol/L when fasting or before a meal (ie, if the information is available) or 13.9 mmol/L at other times of the day during a single continuous event. A single event is a continuous hyperglycemic event without blood glucose levels returning to the normal range. We chose a higher hyperglycemic level than the standard ones (eg, greater than 7mmol/L when fasting [27]) based the input of the co-design (see section "Relevance of the " for more details).

Once a hyperglycemia event is detected, the system updates the plan case automatically and adds 5 sub-hypotheses. The first is "there is not enough insulin," whose result is true by default and which the module tries to invalidate. To do so, the Hypotheses Generation activates 4 sub-hypotheses and all of them should be false or NA to invalidate the parent hypothesis. This includes the current active insulin is less than the average active insulin. Active insulin, or insulin on board (IOB), is the amount of insulin remaining active at a time in the body. The IOB calculation follows the Open Artificial Pancreas System (OpenAPS) approach [28]. A current IOB lower than the average IOB means that less insulin is present at this time, which could be a factor of the hyperglycemic event. Next, the dose of the last insulin shot was insufficient: the amount of the last insulin intake was insufficient for bringing the blood glucose value to 5.5 mmol/L. This is the mean value of the recommended range of blood glucose values defined by several guidelines [27,29]. The hypothesis evaluation process calculates how many units

of insulin are necessary to bring the blood glucose value to this level based on the insulin sensitivity factor. If the insulin sensitivity factor is not provided by the patient, it is calculated by using the 1500/1800 rule [22,23]. Then, the I:C is too low if a meal was taken up to 4 hours (ie, one hour more than the time needed for the serum glucose level to return to near-fasting values in healthy patients [30]) prior to the hyperglycemic event. The hypothesis evaluation process checks if the amount of carbohydrates consumed are "covered" by a shot of insulin using the I:C provided by the patient. If unavailable, the hypothesis evaluation process uses the daily I:C calculated from the total carbohydrates and total rapid-acting insulin of the same day. If the patient did not register carbohydrate intakes, the system uses the 500/450 rule [23,31]. Finally, no insulin taken after or before a meal. The hypothesis evaluation process checks if there was an insulin injection before or after the meal (ie, 30 minutes window—decided by the participants) to compensate for the carbohydrate intake.

The second sub-hypothesis is "there are too much carbohydrates". As with the last hypothesis, this hypothesis is true unless all sub-hypotheses are false or NA. First, there are greater carbohydrates on board (COB) than the average COB. COB is the amount of carbohydrates remaining unabsorbed at a time. The COB uses the carbohydrate absorption rate reported by the patient. Too much unabsorbed carbohydrates can lead to a hyperglycemic event. Second, for patients not following a low-carb diet, the last carbohydrate intake was greater than the recommendation: more than 75 carbs for a meal and more than 30 carbs for a snack [32]. The module uses standards mealtime by default (eg, lunchtime from 11:00 to 13:00) but patients can report them as well. As with the previous one, a too-high carbohydrate intake could lead to a hyperglycemic event if not planned.

The third sub-hypothesis is the presence of external factors, such as menstruation or polypharmacy. External factors can greatly affect the patient's metabolism and render calculations difficult [33]. The system currently flags their presence in case other hypotheses fail to find potential causes of the hyperglycemic event.

The fourth sub-hypothesis is addressing the lack of physical activity to explain the hyperglycemic event and is set to true if patients did not engage in any physical activity up to 24 hours before the noticeable event happened (ie, blood glucose levels can be impacted by physical activity 24 hours after it ended [34]).

The last sub-hypothesis is "lack of evidence". The hypothesis evaluation process checks if the module has identified possible causes of the hyperglycemic event based on the results of other hypotheses. If the system detects a possible cause, the hypothesis is false. However, it is true if all other hypotheses have false or NA results. Having a true result for this hypothesis means that a potential *information gap* is present at the time of this event, and the system informs the user and invites them to investigate the data around the time of this event.

Hypoglycemia

Regarding hypoglycemic events, the system follows the same approach. It activates the hypothesis and sets its result to true if it detects one or more blood glucose values lower than 4 mmol/L when fasting (ie, if the information is available) or 3.5 mmol/L at others time of the day during a single continuous event. We chose a lower hypoglycemic level than the standard ones (ie,less than 4 mmol/L when not fasting [27]) based on the input of the co-design session. See section "Relevance of the " for more details. Once a hypoglycemia event is detected, the system further activates 5 sub-hypotheses automatically. The first is "there is too much insulin," whose result is true by default and which the module attempts to invalidate. To do so, it activates 3 more sub-hypotheses and all of them should be false or NA to invalidate the parent hypothesis. First, the current active insulin is greater than the average active insulin. Having a high amount of insulin could be the cause of a hypoglycemic event. Second, the last insulin injection was too high: the amount of the last insulin intake was greater than the requirements (based on the insulin sensitivity factor) for bringing the blood glucose value to 5.5 mmol/L (mean value of the recommended range of blood glucose values defined by several guidelines [27,29]). Third, the current active insulin is greater than required according to the I:C.

The second hypothesis is "there are too few carbohydrates". This hypothesis is also true by default until invalidated by processing 2 sub-hypotheses. First, there was no carbohydrate intake up to 4 hours prior to the hypoglycemic event. This is one hour more than the time needed for the blood glucose level to return to near-fasting values in healthy patients [30]. Second, for patients not following a low-carb diet, the last carbohydrate intake was lower than the recommendation of less than 30 carbs for a meal or less than 15 carbs for a snack [32].

The third hypothesis concerns the presence of external factors and functions the same way as the hyperglycemic event.

The fourth hypothesis is about physical activity prior to the hypoglycemic event. The module automatically activates and process 2 sub-hypotheses. First, the patient engaged in light to moderate physical activity up to 4 hours prior to the hypoglycemic event. Light to moderate physical activity intensity can be expressed with an intensity tag (ie, text), in time (ie, less than 60 minutes—defined by the participants), in steps (ie, less than 3000 steps [35]) or in Metabolic Equivalent of Task unit (ie, less than 6 METs [36]). Second, the patient engaged in extreme physical activity up to 24 hours prior to the hypoglycemic event [34].

The last hypothesis activated addresses the lack of evidence for finding possible causes of a hypoglycemic event and functions in the same manner as its counterpart for a hyperglycemic event.

Regarding high blood pressure events, a hypothesis is activated and set to true automatically when high blood pressure is detected (ie, greater than 140/90 (systolic/diastolic) [37]). The sub-hypotheses then checks the presence or absence of external factors and function in the same manner as that for the hyperglycemia and hypoglycemic events.

The last hypothesis concerns the patient's sleeping pattern. One hypothesis per night is activated and focuses on identifying the time elapsed between 2 registrations performed manually by the patient (ie, not done automatically by sensors). The hypothesis is set to true if there is less than the recommended 7-hour sleep period [38].

After a discussion, the designers decided to discard patient-defined target values as input for the hypotheses. For example, the detection of hyperglycemia and hypoglycemic events could rely on patient-defined goals focusing on maintaining a blood glucose range between 3.5-12 mmol/L instead of the value the module currently uses. However, these values override medical standards already defining these events and could potentially induce errors in medical workers. The designers discarded other contextual information such as ketones and heart rate for the first version of the module, as patients rarely measure ketones themselves compared to the other data, and heart rate not being available on the Diabetesdagboka or Mysgr applications.

The presence or absence of information gaps also evaluates the relevance of the data for the clinicians (ie, no information gap means reliable data). The identification of the potential causes of a problem could provide conversational topics for clinicians and a retrospective review of medical events for patients and clinicians.

Testing

The goal of the testing phase was to ensure that the designed KBM module works, does not affect the performance of FullFlow and that participants of the workshops find the module useful during a consultation. All conditions were met, and the module was integrated into the FullFlow project.

Testing the relevance of the medical outcome of the module was out of scope at this stage and will be performed during the clinical study of the FullFlow project. The discussion section presents more details on the situation.

Technical Implementation and Performance Assessment

The implementation of the KBM relied on the reasoning engine model described in Figure 7 and follows the same processes and sequences. Black and white unit tests were performed against the KBM (see Methods section) to ensure that the KBM provides the services defined in the Knowledge base and reasoning engine section. The assessment of the performance of the KBM showed that the execution time is lower than 30 milliseconds with a typical load of data and, therefore, does not affect the performance of FullFlow. Details about the technical implementation, the tests performed and an excerpt of the results of one instance of the KBM are provided in Multimedia Appendix 1.

Relevance of the Module

We asked the participants of the clinician workshops and the co-design (ie, clinicians and patients) the same question: "do you think the module could be relevant during a consultation, especially for identifying potential problems?" and all of them answered yes. Then we showed the findings of the KBM within a FullFlow report to the participants. The findings are the results

of a run of the KBM against self-collected health data provided by the in-house researcher. The results contained the noticeable events, their potential causes, and explanation, as well as their distributions through time, along with the reliability of the data (Figures 10, 11, 12, and 13 in the next section for more details).

There were 2 patients that preferred to have this module connected to their self-management solutions to (1) obtain suggestions on why serious medical events occur, and (2) to prepare for the consultation. The participants appreciated the concept of presenting the module between the overall view and the more detailed graphs in FullFlow because it permits faster identification of problems without having to examine the data. We discussed the KBM findings with the participants and how they felt about them. Based on these discussions the following actions were taken. First, we removed the data reliability grade from the visual display because it did not mean anything concrete to the participants. According to them, an alert stating the potential problems would be sufficient. Second, we changed the standards of hypoglycemia (ie, less than 5 mmol/L when fasting and less than 4 mmol/L at other times of the day) and hyperglycemia ie, greater than 7 mmol/L when fasting or before meals and greater than 9 mmol/L at other times) defined by the NICE [27] and the Norwegian Directorate of Health [29] to high hyperglycemia (ie, greater than 9 mmol/L when fasting or before meals and greater than 13.9 mmol/L) and low hypoglycemia (ie, less than 4 mmol/L when fasting and less than 3.5 mmol/L at other times) because the patients preferred to discuss the more serious events with their medical workers rather than all events outside the recommended range. Third, we updated the text displaying the feedback regarding medical events to be more nuanced (eg, "this event *may* have been due to…") because the patients took for granted the findings of the

module. However, in real life, we believe that medical workers also play a role here by limiting the impact on the patients.

Other than these points, the participants appreciated the module because it permitted them to obtain possible explanations for why events occurred and what they could improve.

Figure 10 shows an example of an Interpretation of the KBM regarding a hypoglycemic event. It this case, 4 potential causes were identified for explaining this event: (1) higher active insulin than average, (2) higher insulin to carbohydrates ratio, (3) presence of moderate or extreme physical activity before the event, and (4) a low-carbohydrates meal. The system provides justifications for all potential causes (ie, italic and smaller font text in the figure). Figure 11 shows an example of a representation of an information gap concerning a hypoglycemic event. Figure 12 shows a summary of noticeable events found by the KBM. It summarizes the number of hypoglycemic and hyperglycemic events (ie, 10 and 4 respectively) and the number of their potential main causes (eg, 9 hypoglycemic events may have been caused by having too much insulin). A single noticeable event can have multiple potential causes (eg, 14 potential causes are linked to 10 hypoglycemic events in the figure). The summary also contains a distribution per hour and per weekdays of the noticeable events. It can help clinicians identifying trend regarding daily or weekly routines followed by the patients.

Figure 13 shows a reliability grading of the self-collected health data. For example, the figure shows that there is a significant difference regarding the Blood Glucose registrations during the week, with a deviation of almost 6 registrations, while the rules allow a deviation of almost 3 registrations.

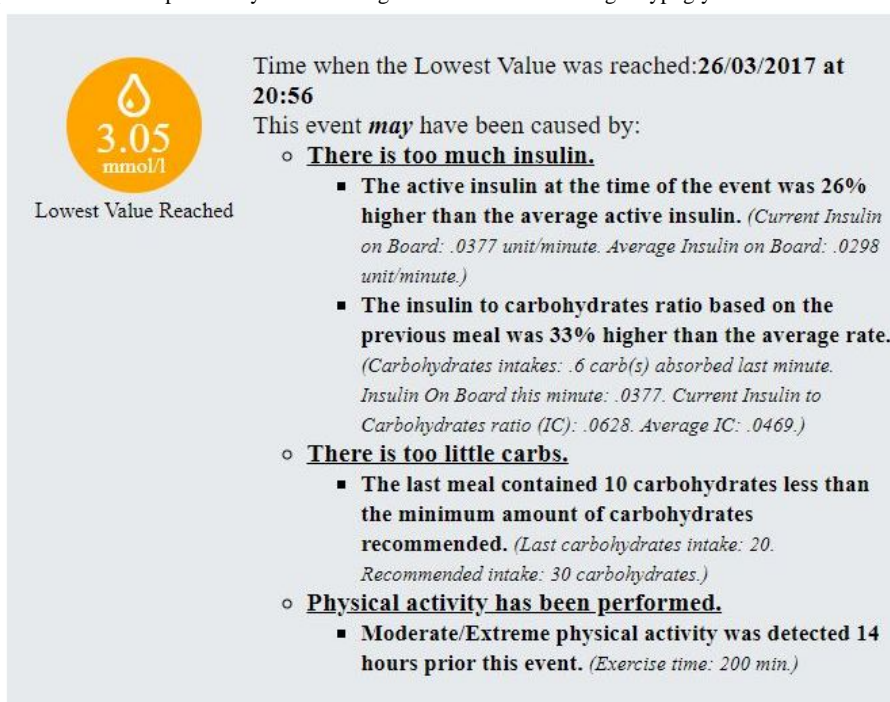**Figure 10.** Example of potential causes expressed by the knowledge-based module of a single hypoglycaemic event.

Figure 11. Example of information gap expressed by the KBM of a single hypoglycaemic event.
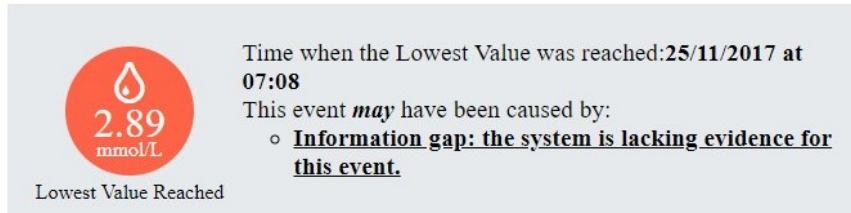

Figure 12. Summary of noticeable events detected by the knowledge-based module, their main potential main causes (top) and their distribution per hour and per weekdays (bottom).
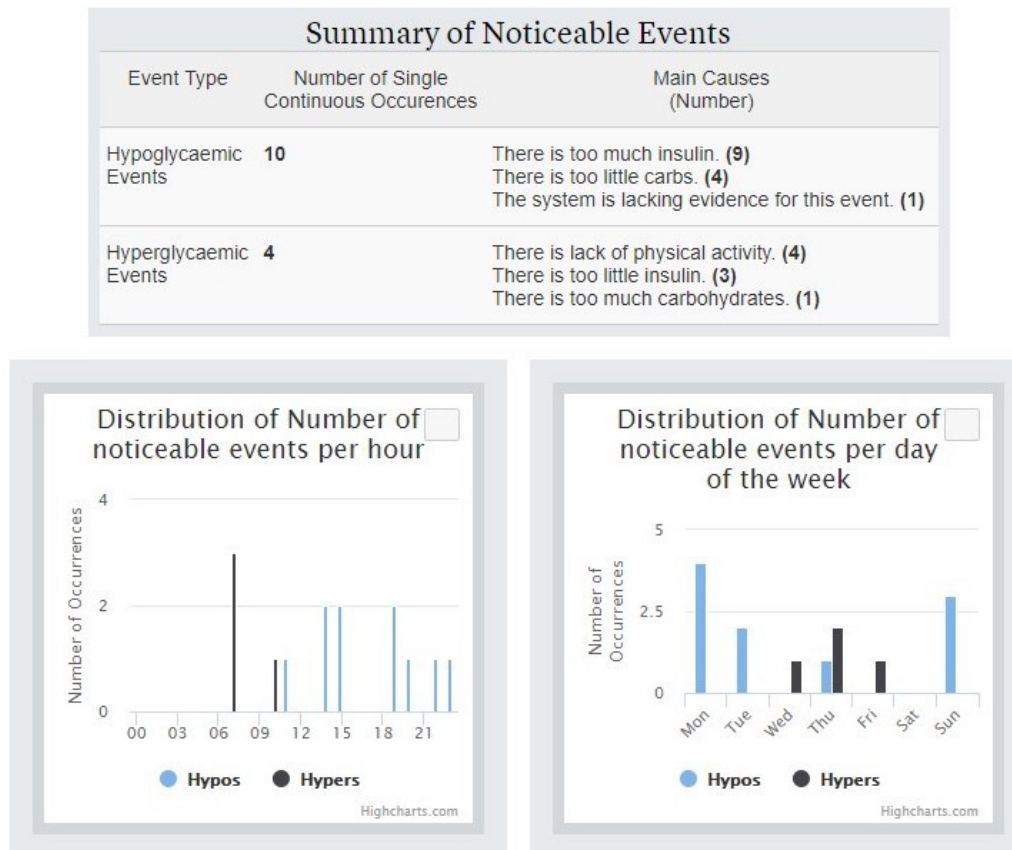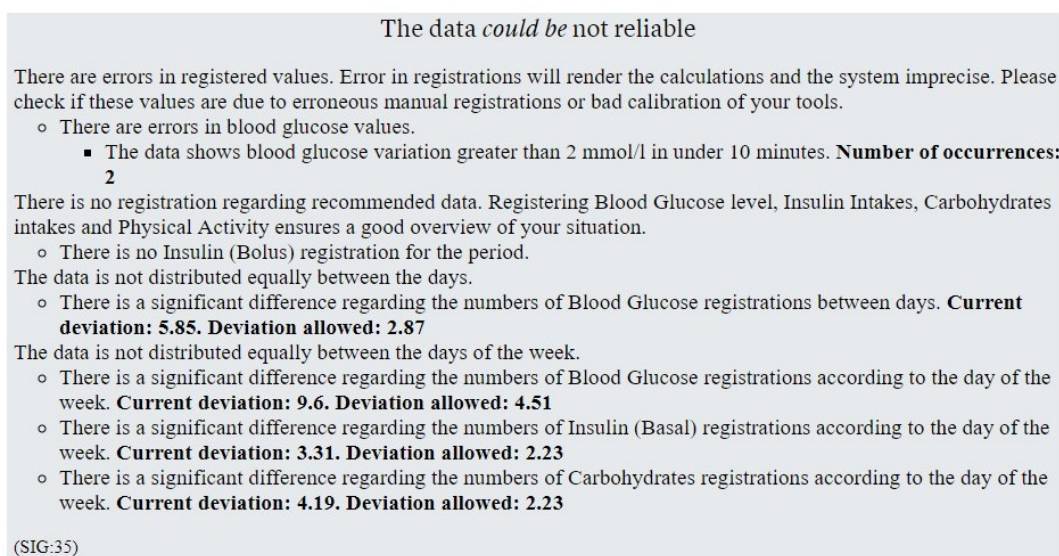

Figure 13. Summary of the data reliability issues found by the knowledge-based module.

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In 1 out of 14 (8%) noticeable events, the module lacked evidence to explain why a specific event occurred, which define an information gap. When discussing this with the patient concerned, he suggested that this could have been due to factors such as that he did not register, or estimated incorrectly carbohydrate intakes, for example.

The discussion showed that the module has a potential to improve the consultation between patients and clinicians and has, therefore, be integrated into the FullFlow.

Discussion

Demonstrated Potential

This paper demonstrated how a KBM using a hypothesize-and-test strategy fed with context may pinpoint the presence of information gaps in patient self-collected health data and identify relevant health information. It could address the barriers of acceptance regarding the introduction of patient self-collected health data into consultation: defining the reliability of the data and identify information gaps and reducing the necessary time for extracting the relevant information from the data. The recommendation of actions to follow to improve the self-collected data provided by the system could also motivate and empower patients by allowing them to be more aware of the possibilities offered by the technology. The suggestion of medical subjects related to the causes of medical events could also help steer the consultation and improve its efficiency.

Likeliness for Use

We are aware that some patients could feel uncomfortable by a system judging them based on their disease management performance and their lifestyle. This could even be counterproductive for patients who are demotivated or make them less likely to adopt healthy self-managing routines, but using this system is intended to be voluntary and based on the patients deciding whether they want to gather and share data or not. We believe medical doctors could provide support to such patients and moderate the outcomes of modules like the one proposed during consultations. However, such patients are difficult to recruit for participation in studies for analyzing their needs, but we believe that by demonstrating the potential of such a system with examples like proposed in this paper, we will be able to recruit participants for the coming FullFlow project pilot. We also plan to organize workshops involving clinicians and psychologists focusing on motivation to address this issue.

Chosen Approach

The hypothesize-and-test strategy is only 1 approach for inductive reasoning, which is the reasoning the module uses. For example, it was possible to use pattern recognition or machine learning to achieve the same goal. The key here concerns data acquisition and data sets. We do not possess high-quality patient self-collected health data at this time: insufficient patient diversity, insufficient patients, insufficient data distributed over long periods and the quality of the data itself could be doubtful because each patient is different and is focusing on different goals and using different applications. On top of that, the data could be erroneous as well. The strategy to acquire knowledge from experts can circumvent these issues, even if it is time-consuming and financially demanding.

Limitations

First, the authors did not perform field-tests involving clinicians and patients in a real situation since the scope of this paper was to present and discuss the integration of the KBM into FullFlow.

Moreover, self-collected data represent only one source of data that could affect decision support and cannot replace other sources such as laboratory tests; above all, it cannot replace the relationship medical workers and patients have. Medical feedback concerning the module will be obtained during the clinical pilot of the FullFlow project, where patients and clinicians will be involved in a real consultation setting.

Third, we limited the focus of the KBM to patients with type 1 diabetes at this stage. However, the authors designed the reasoning engine model for supporting a multitude of medical conditions, especially patients with type 2 diabetes. An update of the knowledge base can adapt the KBM for patients with type 2 diabetes. The existing hypothesis "There is not enough insulin" can be activated only for patients with diabetes type 1 and for patients with diabetes type 2 on insulin therapy, while a new hypothesis "medication is not taken" can be created and activated for a patient with type 2 diabetes for example.

The system can exasperate medical workers if it does not support their needs or yields imprecise or erroneous information. However, as we defined the system with input from medical experts, we have reduced this risk.

The last point concerns that one patient only provided the self-collected health data. The target was to assess the relevance and usability of the module prior to possible integration into the FullFlow system, and subsequent trials will involve a larger number of patients and clinicians. The feedback provided by this patient and the participants in the workshops was used for justifying the KBM and prepare the FullFlow system for the main study.

Dynamic Knowledge Base

At this stage, we decided to limit the scope of the KBM by keeping the knowledge base static for all situations, meaning that the system cannot create and interpret rules on its own. However, the reasoning engine model is dynamic and could support other diseases with an update of the knowledge base, as illustrated in the previous section. In addition, the inputs of the rules are dynamic, meaning that patients can provide their insulin to carbohydrates ratio or their mealtime to tailor the execution of the rules relying on these data. More dynamic inputs can be considered in the future such as measurable personal goals or recommendations from clinicians for example.

For the next iteration, we plan to use patients' and clinicians' context for generating the Plan Base Case and the Explanation Case Base to provide a more tailored experience for users, by using for example comorbidity as an input for generating the rules.

Conclusion

To conclude, the hypothesize-and-test strategy is a viable approach for an inductive reasoning-based system when diverse and large and correct datasets are not available. The context-sensitive approach permits the integration of multiple factors for decision making and for simplifying the complexity and maintenance of this system.

By integrating this module to the FullFlow project, we hope to bring closer health institutions and self-managing patients, who do more on their own with seemingly less guidance from health institutions, by using the foundation for providing tailored health services during consultation: self-collected health data.

Our future clinical study will document user experience and medical outcomes through usage logs, interviews and medical and general surveys, and will help us adjust and improve this module further.

Acknowledgments

Conflicts of Interest

None declared.

Multimedia Appendix 1

Implementation of the KBM.

[PDF File (Adobe PDF File), 227KB - diabetes_v3i3e10431_app1.pdf]

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Abbreviations

API: application programming interface
COB: carbohydrates on board
EHR: electronic health record

FHIR: Fast Health care Interoperability Resources
GP: general practitioner
HbA$_{1c}$: glycated haemoglobin
IOB: insulin on board
IU: international unit
KBM: knowledge-based module
MET: Metabolic Equivalent of Task
NA: not applicable
NICE: National Institute for Health and Care Excellence
PHR: personal health record

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Review

Web-Based Interventions for Depression in Individuals with Diabetes: Review and Discussion

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Abstract

Background: Depression is twice as common in people with diabetes, and this comorbidity worsens the course of both pathologies. In clinical practice guidelines, screening and treatment of depression in patients with diabetes are highly recommended. However, depression is still both underrecognized and undertreated. To find ways to enhance their reach, psychological treatments have taken advantage of benefits of internet and technological devices as delivery formats, providing interventions that require considerably less (or even no) interaction time with therapists. Web-based treatments hold promise for effective interventions at low cost with positive results.

Objective: The objectives of this review were to describe Web-based interventions for depression in individuals with diabetes and to discuss these studies' procedures and findings in light of evidence from a wider range of interventions for depression and diabetes.

Methods: A comprehensive literature search was conducted in PsycINFO and MEDLINE electronic databases. Studies were included when they met the following selection criteria: the study was available in a peer-reviewed journal mainly publishing studies written in either English or Spanish; the studied sample comprised individuals with diabetes; the intervention targeted depression symptomatology; the intervention was accessible via the internet; and the intervention was accessible via the internet with little or no clinician support.

Results: Overall, 5 research studies were identified in the review. All studies were randomized controlled trials, and most used a wait list as a control; 4 studies reported treatment dropout, rates of which varied from 13% to 42%. Studies supported the notion that the Web-based format is a suitable psychology service delivery option for diabetic individuals with depression (effect size range for completers 0.7-0.89). Interventions varied in their characteristics but most were clinical-assisted, had a cognitive behavioral therapy approach, used diabetes-specific topics, had a weekly modular display, used homework assignments, and had some adherence management strategy. These characteristics are consistent with the intervention features associated with positive results in the literature.

Conclusions: The analyzed studies' findings and procedures are discussed in light of evidence drawn from a wider range of reviews on Web-based interventions for depression and diabetes. Consistent with previous research on depression treatment, Web-based interventions for depression among individuals with diabetes have shown positive results. Future research should contribute new evidence as to why these interventions are effective, for whom, and which particular aspects can increase patients' adherence.

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Introduction

Substantial evidence shows that depression among individuals with diabetes is associated with poorer diabetes outcomes [1] and higher levels of diabetes distress (emotional burdens, stresses, and worries associated with diabetes) [2]. When depressed, patients with diabetes show higher frequency of hypoglycemia and higher levels of glycosylated hemoglobin, their risk of developing diabetes-related complications increases [3-5]. They also show poorer adherence to self-care regimens, particularly to medications, diet, and exercise [6-7]. Congruently, diabetes comorbid depression is associated with reduced work productivity [8], reduced quality of life [9], increased medical symptom burden [10], increased functional disability [11], more health care service utilization and costs [12-13], and higher risk of mortality [14-15]. Considering that depression is twice as prevalent among people with diabetes [16], there is no doubt that interventions for depression in individuals with diabetes are crucial for both medical and economic reasons.

Fortunately, there are depression treatments for patients with diabetes [17]. Psychotherapeutic interventions, often combined with a diabetes self-management intervention, have significant effects on depressive symptoms and glycemic control [18-19]. Routine assessment, screening, and treatment of depression in patients with diabetes are recommended in clinical practice guidelines [20]. However, despite these recommendations, depression is both underrecognized and undertreated; in routine care for diabetes, depression remains untreated in 50% of patients [1]. Recently, faced with the need to enhance reach [21], some treatments have resorted to the internet and technological devices as delivery formats. Particularly interesting are interventions requiring considerably less interaction time with the therapist than face-to-face psychotherapy (guided self-help approach) or even no interaction at all (unguided self-help approach). These treatments hold promise for low-cost interventions with positive results [22-23]. They may be particularly beneficial to overcome logistical and financial obstacles burdening both health care providers and patients [24-25]. Other advantages of such interventions are flexible usage not constrained by time and place; a high level of anonymity and privacy; standardized contents, and easy translatability and cultural adaptability [26]. In the general population, effective Web-based interventions and other computerized psychological treatments for depression have been designed and tested in research and slowly but gradually in clinical settings [27]. Moreover, internet-supported therapy for depression with a guided self-help approach has proved to generate the same benefits as face-to-face therapy [28].

In this review, we identified Web-based interventions for depression in individuals with diabetes, addressed those interventions' efficacy, addressed differences and similarities in interventions' characteristics and study designs, and discussed studies' procedures and findings in light of evidence from a wider range of interventions for depression and diabetes.

Because psychological intervention studies are very often clinically and methodologically diverse [29], we hope that in the future, our review will be helpful for all researchers and clinicians who are willing to design Web-based interventions for depression in individuals with diabetes.

Methods

Inclusion and Exclusion Criteria

Eligible studies had to be published in English or Spanish in a peer-reviewed journal between 1990 (coinciding with introduction of the World Wide Web in 1991) and 2017.

Participants

Studies had to target adult participants (18 years or older) with a primary diagnosis of diabetes and comorbid depression. Depression was defined according to diagnostic criteria (*Diagnostic and Statistical Manual of Psychiatric Disorders*) or depressive symptomatology (on a validated self-report or clinician measure).

Web-Based Interventions

The examined Web-based interventions required the following components: program content (ie, psychoeducation and skills training guided by psychological theory); multimedia; provision of Web-based activities; and a guided or unguided self-help approach. Eligible interventions had to target depression symptomatology with the specific intent of producing emotional, behavioral, and cognitive change.

Study Design

Intervention studies with a repeated measures design, including randomized controlled trials (RCTs) and quasi experimental studies, were eligible.

Search Strategy

A literature search was conducted in the PsycINFO and MEDLINE electronic databases with the following keywords: diabetes, depression, Web-based, computer-based, internet-based, online, and psychological intervention.

Data Extraction

The following data were extracted from each study: study characteristics (eg, type of study, sample size, measures); participants' compliance (eg, dropout percentage); intervention efficacy (eg, between-group effect size in depression and diabetes-related measures); intervention characteristics (eg, delivery mode, psychotherapeutic approach, and research design); sample characteristics (eg, sample size and medical diagnosis); and treatment characteristics (eg, delivery format, therapeutic approach, therapist and peers support, and adherence management). Intervention characteristics sometimes were extracted from the study protocol paper.

Because of the small number of studies and their heterogeneity, data extracted were not statistically combined and reanalyzed. Effect sizes are presented as they were extracted from individual

papers' results sections when the between-groups difference was significant; effect size measures were either Cohen *d* or Hedges *g*.

Results

Characteristics of Included Studies

Overall, 5 studies were identified [21,30-33] and all were RCTs. A summary of reviewed articles is provided in Table 1. All studies included standardized measures to assess symptoms of depression and diabetes distress. For depression, studies used the Center for Epidemiological Studies-Depression (CES-D) measure [21,30-32] or the Patient Health Questionnaire-9 (PHQ-9) [33]. Depression inclusion criteria were established in 3 studies [21,32,33]. In Bond et al [30] and Cohn et al's [31] studies, CES-D was employed but with no established cut-off scores; their treatment groups had a mean baseline CES-D score of 12 (SD 10.4) and 16.9 (SD 11.6), respectively; 3 studies added a telephone-administered interview to confirm whether participants met a major depression episode's diagnostic criteria [21,32,33]. Newby et al [33] excluded participants with a severe profile (PHQ-9>23).

Diabetes distress was assessed with the Problem Areas in Diabetes Questionnaire (PAID) [21,30,32,33] or the Diabetes Distress Scale (DDS) [31]. All studies added at least one of the following diabetes-related measures: glycosylated hemoglobin [21,33], diabetes self-management [31,32], diabetes empowerment [30], diabetes acceptance [32], and diabetes social support [30].

In addition, 2 studies also assessed the following secondary psychological outcomes [31,33]: anxiety, psychological distress, positive and negative affect, and well-being. Only Nobis et al

[32] and Newby et al [33] included process evaluation by expectancy of benefit and intervention satisfaction. All measures were administered online.

Participants' Compliance

The percentage of enrolled participants who dropped out (treatment dropout) varied among identified studies: 41.6% (52/125) [21]; 34% (14/41) [33]; 24.0% (31/129) [32]; and 13% (4/29) [31]. Bond et al [30] did not report a treatment dropout rate.

Intervention Efficacy

Overall, 4 studies found significant reduction in depression scores in the intervention condition compared with control (effect size range 0.29-0.89 for intended-to-treat analyses and 0.70-1.00 for per protocol analyses). See Table 2 for results obtained from the study. Newby et al [33] found that the within-group effects for the intervention group (g=1.90) persisted at the 3-month follow-up. Cohn et al's [31] study showed a reduction in depression scores in the intervention condition compared with the control, although it was not significant (P=.05), and found no impact in any other measures.

Significant reduction in diabetes distress was shown in 4 studies (effect size range 0.58-0.80). Newby et al [33] reported that within-group effects for the intervention group (g=1.18) persisted at the 3-month follow-up. Positive effects were also found in diabetes social support [30] and diabetes acceptance [32]. Newby et al [33] found moderate positive differences for generalized anxiety and mental well-being that persisted at the 3-month follow-up but failed to find differences in physical well-being and somatic symptom severity. No significant differences were found for glycosylated hemoglobin [21,33] or diabetes self-management [32].

Table 1. Summary of studies included in this review.

Lead author (year)	Approach (DM[a] specific)	Depression criteria	DM type (Age target)	Participants, n	Control	Intervention length	Postassessment
Bond (2010) [30]	CBT[b] (yes)	N/A[c]	Not reported by authors (older adults)	62	Wait list	6 mo (nonmodular)	6 mo after baseline
van Bastelaar (2011) [21]	CBT (yes)	CES-D[d]>16	I and II (adults)	255	Wait list	8 modules (1 per wk)	1 mo follow-up
Cohn (2014) [31]	Positive psychology (no)	N/A	II (adults)	53	Wait list with emotion reporting	5 modules (1 per wk)	1 wk after the final module
Nobis (2015) [32]	CBT (yes)	CES-D≥23	I and II (adults)	260	Access to unguided Web-based psychoeducation	6-8 modules (1 per wk) + booster session	8 wk after randomization
Newby (2017) [33]	CBT (no)	Patient Health Questionnaire-9>5	I and II (adults)	90	Treatment as usual	6 modules (10 wk, 5 d minimum between)	1 wk after module 6 (or wk 10) 3 mo follow-up for intervention group only

[a]DM: diabetes mellitus.

[b]CBT: cognitive behavioral therapy.

[c]Not applicable.

[d]CES-D: Center for Epidemiological Studies-Depression.

Table 2. Results by intervention: Outcome measures, analysis, and effect sizes.

Lead author (year) and outcome measure	Analysis	Effect size
Bond (2010) [30]		
Center for Epidemiological Studies-Depression	Not reported	d^a=0.7
Problem Areas in Diabetes Questionnaire	Not reported	d=0.6
Diabetes Social Support Scale	Not reported	d=1.0
Diabetes Empowerment Scale	Not reported	d=0.7
van Bastelaar (2011) [21]		
Center for Epidemiological Studies-Depression	Intended-to-treat	d=0.29
Center for Epidemiological Studies-Depression	Per protocol	d=0.70
Problem Areas in Diabetes Questionnaire	Per protocol	d=0.58
Glycosylated hemoglobin	Intended-to-treat	—^{b}
Cohn (2014) [31]		
Center for Epidemiological Studies-Depression	Per protocol	—
Perceived Stress Scale	Per protocol	—
Differential Emotions Scale	Per protocol	—
Confidence in Diabetes Self-Care Scale	Per protocol	—
Diabetes Distress Scale	Per protocol	—
Nobis (2015) [32]		
Center for Epidemiological Studies-Depression	Intended-to-treat	d=0.89
Center for Epidemiological Studies-Depression	Per protocol	d=1.00
Hospital Anxiety and Depression Scale-Depression	Intended-to-treat	d=0.82
Problem Areas in Diabetes Questionnaire	Intended-to-treat	d=0.58
Acceptance and Action Diabetes Questionnaire	Intended-to-treat	d=0.22
Diabetes Self-Management Questionnaire	Intended-to-treat	d=0.07
Newby (2017) [33]		
Patient Health Questionnaire-9	Intended-to-treat	g^c=0.78
Problem Areas in Diabetes Questionnaire	Intended-to-treat	g=0.80
Kessler Psychological Distress Scale	Intended-to-treat	g=1.06
Generalized Anxiety Disorder 7-item	Intended-to-treat	g=0.72
Glycosylated hemoglobin	Intended-to-treat	—
Short form 12-item scale of mental well-being	Intended-to-treat	g=−0.66
Short form 12-item scale of physical well-being	Intended-to-treat	—
Patient Health Questionnaire physical symptoms module for somatic symptom severity	Intended-to-treat	—

^{a}Cohen d.

^{b}No significance.

^{c}Hedges g.

Intervention Characteristics

Therapeutic Approach and Delivery Mode

Interventions had a cognitive behavioral therapy (CBT) [21,30,32,33] or a positive psychology [31] psychotherapeutic approach; 3 focused on relevant diabetes-specific topics [21,30,32], whereas the others used generic depression interventions. Interventions aimed to promote different skills. The amount of skills grew proportional to the number of modules presented. The most used topics were psychoeducation, cognitive restructuring, behavioral activation, coping with worries and anxiety, communication and assertiveness, problem solving, and stress management (including breathing and relaxation techniques); 2 interventions addressed relapse prevention [21,34].

Table 3. Participants' activities, clinician-patient communication, and adherence management by intervention.

Lead author (year)	Participant activities	Clinician-assisted, professional	Clinician-patient communication		Adherence management
			Synchronous	Asynchronous	
Bond (2010) [30]	Weekly discussion group & DM[a] self-management diary	Yes (nurse or psychologist or social worker)	Instant messaging, Web-based educational discussion group	Email and bulletin board	• Not reported
van Bastelaar (2011) [21]	Homework	Yes (psychologist)	N/A[b]	Semistandardized feedback on homework assignments (CNE[c])	• Message or email: Homework not received
Cohn (2014) [31]	Homework & mood or DM self-management diary	No	N/A	N/A	• Paid for: reports, questionnaires and study completion
Nobis (2015) [32]	Homework & mood diary	Yes (psychologist)	N/A	Email: personalized feedback on homework assignments	• Automated daily SMS[d] text messaging on mobile phone: reminders or motivational • Email or phone call: no logging
Newby (2017) [33]	Homework	Yes (psychologist or psychiatrist)	Phone call: patient request or deterioration	Feedback on homework assignments (CNE)	• Automated email: reminders or congratulation or no logging • Phone call: no logging

[a]DM: diabetes mellitus.

[b]Not applicable.

[c]CNE: channel not specified.

[d]SMS: short message service.

Overall, 4 interventions were distributed in modules. The amount of modules ranged from 5 to 8, and they were delivered with a minimum lapse of 5-7 days between sessions. To strengthen participants' acquired skills, one study had an optional reinforcing module ("Booster session") 4 weeks after finishing the intervention [32]. The nonmodular intervention comprised free access to a website with different resources for 6 months with weekly Web-based discussion groups [30].

All interventions provided lesson reinforcement activities and progress tracking; 4 used homework assignments to encourage patients to apply the learned skills in daily practice [21,31,32,34] and 2 added mood, thought, behavior, and diabetes self-management reporting [30,31].

Support

From Clinician

The identified interventions had important differences concerning therapist support, ranging from none [31] to highly individualized email or phone contact [32]. Bond et al [30] added a weekly discussion group delivered by a Web-based communication forum using MSN Messenger. See Table 3 for therapist support by intervention. Only one study reported clinician time spent per participant; Newby et al [33] reported that the clinician spent, on average, 27 minutes per participant for email and telephone contact over the course of the intervention.

From Peers

Only Bond et al's [30] intervention included contact with peers. This contact was both synchronous and asynchronous by instant short message service (SMS) text messaging and email. Interactions were participant-generated and not moderated by any study personnel.

Adherence Management

Two interventions incorporated automated emails or mobile SMS text messaging (integrating mobile phone support) with reminders, motivational statements, and congratulations for finishing a module [32,33]. Three addressed no logging into the website or no homework received by email (mainly standardized) or phone call [21,32,34]. Cohn et al's [31] intervention used payment as a motivation strategy; they paid US $1 for each daily report completed, US $20 for completing final questionnaires and the phone interview, and US $20 if participants completed the study within 75 days with reports on at least 75% of all days. See Table 3 for adherence management by intervention.

Discussion

Main Results and Comparisons with Previous Work

This review aimed to identify Web-based interventions for depression in individuals with diabetes and to discuss these studies' procedures and findings in light of evidence drawn

from a wider range of interventions for depression and diabetes. Overall, 5 studies met the inclusion criteria.

Studies' Characteristics

All studies were RCTs, a rigorous method proven to provide critical evidence for psychological interventions' efficacy [35]. However, most studies used a wait list as control, and literature shows than this control is more likely than many other control conditions to produce strong effect size [36]. Only one study provided an active control intended to match the intervention's nonspecific factors [32]. Future research should include active controls matched as closely as possible with the intervention under research but excluding its "active ingredient(s)" [37]. Because no-treatment controls are less costly, they can be potentially useful for novel interventions' first evaluations. When no-treatment controls are implemented, Mohr et al [36] suggest monitoring health and well-being of participants; assessing and monitoring potential threats to internal validity such as expectancies, help-seeking behavior, and other services received; and continuing assessment for patients dropping out of treatment.

Because people with depression are in need of treatment, a long follow-up period can be inappropriate when a wait list is used as a control group. However, for intervention efficacy and cost-effectiveness, assessing whether effects are long lasting is necessary. One option is to conduct within-group analyses, as performed by Newby et al [33].

All studies included standardized measures to assess depression symptoms and diabetes distress. However, there were differences in the inclusion criteria. If depression diagnosis is an inclusion criterion, it may be advisable to use cut-off scores for CES-D and PHQ-9 of ≥23 and ≥13 points, respectively; these have proven to provide an optimal balance between sensitivity and specificity in people with type 2 diabetes [38]. Nonetheless, a diagnostic interview, at least a telephone-administered diagnostic interview, is strongly recommended. This was included in 3 studies [21,32,33]. This option may indeed increase study costs, but it can also improve the precise diagnosis of depression (if diagnosis is an inclusion criterion). An even better scenario consists of a face-to-face diagnostic interview, precluding problems of not seeing the patient. A meta-analysis showed that in both controlled and uncontrolled studies, depression rates are approximately two to 3 times higher in studies that used self-report measures versus face-to-face diagnostic interviews [16]. Using Web-based questionnaires to assess depression symptomatology usually works well, but psychiatric diagnoses cannot be reliably made using self-reports solely. If face-to-face interviews cannot be conducted, a compromise solution could lie in telephone interviews to confirm the diagnosis [39].

For diabetes distress assessment, Schmitt et al's [40] recent study supported both PAID and DDS as good self-report measures of diabetes distress. They concluded that PAID was significantly more strongly associated with dysfunctional coping styles, quality of life, and depressive symptoms, whether DDS showed significantly stronger associations with diabetes self-care and metabolic outcomes; therefore, its selection should be based on study objectives. A cut-off criterion's inclusion concerning these measures should be considered, particularly for interventions with diabetes-specific content.

Because of the impact of depression-diabetes comorbidity on diabetes self-management and glycemic control [3,4,5], inclusion of these variables is desirable. Van Bastelaar et al [21] and Newby et al [33] did not find an effect on glycosylated hemoglobin, but in their studies, participants' diabetes was relatively well controlled, despite comorbid depression and high levels of diabetes distress. Face-to-face treatments for depression have shown mixed results for glycosylated hemoglobin outcomes [41] so that more evidence is needed to clarify this relationship, including its moderators and mediators. Adding recurrent glycemia monitoring can probably foster a broader understanding of the intervention effect and its relation with CBT-targets (cognition, emotion, and behavior). Newer Web platforms include emotion, thoughts and behavior registers, and sometimes graphics [42]. Glycemia data graphics could be easily integrated. This would also function as a resource itself, providing patients feedback about the relationship between depression symptomatology and glycemic control.

Assessment of other psychological outcomes (eg, anxiety) and process evaluation (eg, satisfaction with the intervention) can provide a more comprehensive assessment of the intervention's effects, identify individuals most likely to benefit, and identify adherence-related dimensions. More recent studies have tended to include these variables [31-33]. Additionally, recruitment strategies should be taken into account (eg, online) because they can lead to selection bias. The use of questionnaires to assess reasons for participating, expectancies, credibility, and patient satisfaction with the intervention are strongly suggested [32].

Participants' Compliance and Treatment Efficacy

As noted in this review, Web-based interventions often suffer from nonadherence. A systematic review of 83 Web-based interventions on lifestyle, chronic disease, and mental health (with and without therapist support) found that, on average, approximately 50% of participants adhere fully to an intervention [43]. A meta-analysis that compared adherence to Web-based and face-to-face CBT for depression (although not in a single trial) found significant differences in the percentage of treatment completers with 65% and 84%, respectively [44]. Nonetheless, authors of the meta-analysis found that in the Web-based CBT, participants completed, on average, 80% of their treatments; this does not differ significantly from the rates observed in face-to-face CBT groups. They suggest that future studies should include more detailed information on adherence, preferably both the number of completers and average number of sessions completed, and should search for factors that can explain adherence and participants' reasons for dropping out.

Interventions' impact on depressive symptoms are consistent with previous research on Web-based depression treatments in the general population with meta-analyses showing an effect size of $d=0.4$ [27] and $d=0.56$ [45] that increases to $d=0.61$ and $d=1.35$, respectively, when supported by a therapist. This lends support to the notion that Web-based interventions have potential as a psychology service delivery option for individuals with diabetes and depression.

Interventions' Characteristics

Overall, 4 interventions had a CBT only approach. Face-to-face CBT is the most extensively researched psychotherapeutic treatment for depression [46] and has shown to be effective in depression symptomatology [47] and glycemic control [48] in individuals with diabetes. CBT is also the most commonly used approach in Web-based depression interventions [45,49,50]. Furthermore, Web-based guided self-help CBT is the only approach that has been directly compared with face-to-face CBT with reported effects being similar [28]. However, all interventions are multicomponent with a number of hypothesized mechanisms (eg, behavioral activation and cognitive restructuring); therefore, determining which aspects contribute the most in psychological outcome measures is not possible. The combination of approaches may not be suggested because it makes drawing clear conclusions regarding effective ingredients even more difficult. Future studies must elucidate which skills should be promoted for stronger effect in depression and what mechanisms of change are.

The need of diabetes-specific content should be studied. An aspect that can contribute to understanding of the nondiabetic specific versus diabetic-specific debate is probably related to the presence or absence of diabetes distress. Both syndromes are closely related, but also independent, and they can co-occur or not [51]. Snoek et al [51] advanced the following 3 possible combinations of depression and diabetes among diabetic patients: with distress, but no depression; with depression, but no distress; and no depression or distress. They propose that the first 2 are more are likely to benefit from diabetes-specific depression treatment modalities. However, Newby et al's [33] nondiabetes-specific intervention showed large effects on depression *and* diabetes distress, whereas it showed no significant effects on glycemic control. In the past, both face-to-face health care and digital interventions have tended to focus on either depression or diabetes alone, despite their co-occurrence and similar behavioral treatment strategies that may call for a more holistic approach [52]. A review of Web-based interventions for comorbid depression and chronic illness showed that participants valued psychoeducation with illness-specific examples [53]. Perhaps an intervention for depression *and* diabetes, instead of *in* individuals with diabetes, may contribute to address health in a more holistic way.

Weekly modules tend to mimic face-to-face therapy sessions' frequency. Approaches like CBT normally prioritize short-term care; therefore, the average number of sessions for depression face-to-face treatment is approximately 13 [54] with brief forms containing less than 8 sessions. The ideal number of modules remains unclear, mainly because when interventions with different numbers of modules are compared, they differ in other unmeasured key variables such as the modules' content; thus, whether the impact on depression symptomatology is because of the number of modules alone remains uncertain [54]. On the other hand, evaluating the effect of the patient choosing which modules to complete and proving recommendations to participants on which modules are more suitable for them from the assessment upon registration would be interesting [42].

All interventions provided lesson reinforcement activities or progress tracking. Homework is important for helping patients to apply skills learned during sessions to various and multiple situations that arise in everyday life [55]. In face-to-face CBT for depression, the assignment of homework and homework compliance show significantly better outcomes than therapy consisting only of work during the session [54]. On the other hand, inclusion of regularly self-administered questionnaires or reports may have benefits by allowing both patients and therapists to monitor progress and deterioration of depression.

Support

Consistent with meta-analyses, a Web-based intervention's effect on depression is greater when the intervention includes therapist assistance or guidance with patients' compliance being higher [27,45]. Communication between patient and therapist in the identified studies was mainly asynchronous (personalized or semipersonalized), providing feedback on homework and other issues. Synchronous communication in the selected studies was used for adherence management after nonresponse to asynchronous strategies or for urgent cases like deterioration. Interestingly, a meta-analysis on Web-based depression interventions showed that studies providing asynchronous support yielded greater effects than studies providing synchronous support [45] perhaps because of the benefits associated with asynchronous communication such as disinhibition and more time to reflect and compose one's responses [56]. A study that compared 2 groups allocated to a Web-based CBT for depression with therapist guidance either by telephone calls or email correspondence showed significant and large symptom reductions in both groups with no significant differences between them [57]. There was no between-group difference in client-rated therapeutic alliance or treatment engagement. However, more research is needed to determine how the content, length, and frequency of therapists' feedback can affect outcomes in guided self-help treatments [58].

Newby et al's [33] intervention established a clinician's email or phone call when participants requested contact or had a depression or distress score indicating deterioration of their condition. A review of Web-based programs for depression currently available in English showed that 62% (20/32) had a crisis link defined as email addresses, phone numbers, or hotlines connected to distress centers providing counseling services to at-risk users [49]. Because of the depression's oscillating course, risk of deterioration or moments of crisis always exist; therefore, detecting them in time and determining courses of action are important.

Only one intervention incorporated peer support [30]. This reflects the small number of Web-based interventions that offer such support. A Web-based intervention for diabetic support showed that online peer support was a successful approach [42], but in interventions for depression, evidence is limited and inconsistent [59]. Future studies should bring new data to this subject.

Adherence Management

Considering that adherence is problematic in Web-based interventions [60,61] for many depressed people [45,62] and

for many people with diabetes [63] and that it is associated with treatment effectiveness [64,65], the need exists to develop and evaluate ways to increase intervention adherence. This review and the literature have shown that frequent automated reminders via email or SMS text messaging can positively influence adherence [43]. However, through studies that compare strategies, it remains necessary to determine which adherence management techniques are more effective.

Limitations

Caution is needed when drawing conclusions from efficacy results exposed by this review. In most studies, participants were well educated overall with relatively well controlled diabetes. In 2 studies [30,31], the number of participants was relatively small (25 and 31 in treatment groups), which also affects the generalizability of results. Different measures and cut-off criteria for depressive symptomatology and multicomponent interventions make comparing studies' results difficult. Finally, as mentioned above, the recruiting strategy could have led to selection bias in some cases.

This review has some limitations. We found only 5 studies that met our criteria; therefore, caution is needed when trying to generalize results. These findings may be affected by publication bias with a tendency for academic journals to publish significant findings. Because we restricted our literature search to articles written in English or Spanish, we might have missed studies eligible for inclusion but published in other languages.

Conclusions

In summary, we are optimistic about Web-based interventions for depression in people with diabetes. Our review and the literature support the idea that with the inclusion of specific features (such as some therapist support), these interventions are effective. They may enhance the therapy's reach and decrease both patient and health services costs by not only engaging in a less expensive, more accessible treatment but also preventing diabetes complications and depression deterioration. Upcoming research should continue contributing evidence on why these interventions are effective, for whom, and which aspects can increase patient adherence. We hope that, in the future, our review will be helpful for all researchers and clinicians willing to design and use Web-based interventions for depression in individuals with diabetes.

Conflicts of Interest

None declared.

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Abbreviations

CBT: cognitive behavioral therapy
CES-D: Center for Epidemiological Studies-Depression
DDS: Diabetes Distress Scale
PAID: Problem Areas in Diabetes Questionnaire
PHQ-9: Patient Health Questionnaire-9
RCT: randomized controlled trial
SMS: short message service