International Journal of Medical Informatics 139 (2020) 104158

Contents lists available at ScienceDirect

International Journal of Medical Informatics

journal homepage: www.elsevier.com/locate/ijmedinf

A new approach to integrating patient-generated data with expert knowledge for personalized goal setting: A pilot study

Marissa Burgermaster[a,b,*], Jung H. Son[b], Patricia G. Davidson[c], Arlene M. Smaldone[d], Gilad Kuperman[b,e], Daniel J. Feller[b], Katherine Gardner Burt[f], Matthew E. Levine[b], David J. Albers[b,g], Chunhua Weng[b], Lena Mamykina[b]

[a] Nutritional Sciences & Population Health, University of Texas at Austin, Austin, TX, USA
[b] Biomedical Informatics, Columbia University, New York, NY, USA
[c] Nutrition, West Chester University, West Chester, PA, USA
[d] School of Nursing & College of Dental Medicine, Columbia University, New York, NY, USA
[e] Memorial Sloan Kettering Cancer Center, New York, NY, USA
[f] Health Sciences, Lehman College, Bronx, NY, USA
[g] Pediatrics & Informatics, University of Colorado, Aurora, CO, USA

ARTICLE INFO

Keywords:
Patient-generated health data
Knowledge representation
Expert system
Suggestion system
Personalized nutrition

ABSTRACT

Introduction: Self-monitoring technologies produce patient-generated data that could be leveraged to personalize nutritional goal setting to improve population health; however, most computational approaches are limited when applied to individual-level personalization with sparse and irregular self-monitoring data. We applied informatics methods from expert suggestion systems to a challenging clinical problem: generating personalized nutrition goals from patient-generated diet and blood glucose data.
Materials and methods: We applied qualitative process coding and decision tree modeling to understand how registered dietitians translate patient-generated data into recommendations for dietary self-management of diabetes (i.e., knowledge model). We encoded this process in a set of functions that take diet and blood glucose data as an input and output diet recommendations (i.e., inference engine). Dietitians assessed face validity. Using four patient datasets, we compared our inference engine's output to clinical narratives and gold standards developed by expert clinicians.
Results: To dietitians, the knowledge model represented how recommendations from patient data are made. Inference engine recommendations were 63 % consistent with the gold standard (range = 42 %–75 %) and 74 % consistent with narrative clinical observations (range = 63 %–83 %).
Discussion: Qualitative modeling and automating how dietitians reason over patient data resulted in a knowledge model representing clinical knowledge. However, our knowledge model was less consistent with gold standard than narrative clinical recommendations, raising questions about how best to evaluate approaches that integrate patient-generated data with expert knowledge.
Conclusion: New informatics approaches that integrate data-driven methods with expert decision making for personalized goal setting, such as the knowledge base and inference engine presented here, demonstrate the potential to extend the reach of patient-generated data by synthesizing it with clinical knowledge. However, important questions remain about the strengths and weaknesses of computer algorithms developed to discern signal from patient-generated data compared to human experts.

1. Introduction

Incorporating patient-generated health data (PGHD) into clinical systems will promote precision methods for population health [1]. With the wide-scale adoption of wearable health trackers [2] and over 325,000 health apps published in Google Play and Apple App stores [3], these new technologies have increased the volume of PGHD – "data created, recorded, or gathered by and from patients to help address a health concern." [4] PGHD include data about behaviors, such as diet, as well as clinical markers, such as blood glucose. When integrated into

* Corresponding author at: 1400 Barbara Jordan Blvd, Austin, TX 78723, USA.
E-mail address: marissa.burgermaster@austin.utexas.edu (M. Burgermaster).

https://doi.org/10.1016/j.ijmedinf.2020.104158
Received 25 October 2019; Received in revised form 19 February 2020; Accepted 23 April 2020

Table 1
Summary of method to develop and evaluate knowledge model and inference engine.

Step	Participants/Data	Analysis/Product
Developing the knowledge model and knowledge base	1 Transcripts of RDNs (n = 10) "thinking aloud" as they made diet recommendations for two patients (P1, P2) based on 30-days of PGHD (diet and BG) 2 RDNs (n = 2) were recontacted to assess face validity of decision tree	Qualitative Analysis: 1 Process coding, Decision tree modeling 2 Member checking Product: Decision tree
Developing the inference engine	n/a	Product: Decision tree translated into machine readable form in R
Evaluation	CDEs (n = 2) participated in multiple interviews to reach consensus observations and recommendations for four patients (P1-P4) based on 30-days of PGHD (diet and BG)	Products: Narrative clinical observations, Gold standard recommendations

Notes: RDN = registered dietitan nutritionist; PGHD = patient generated health data; BG = blood glucose; CDE = certified diabetes educator (i.e., a clinician who has completed specialized training and hours in counseling patients with diabetes to earn certification). Neither CDE who participated in the evaluation was a RDN whose data were used in the qualitative analysis.

clinical care, PGHD have potential to positively influence care delivery, patient-provider communication, and health outcomes [5,6]. In particular, integrating *personalized goal setting based on PGHD* from home monitoring of blood pressure [7], blood glucose [8], and physical activity [9] into clinical decision making has been demonstrated to improve patient outcomes.

Despite these benefits, integrating PGHD in clinical practice presents many challenges. Providing clinicians with direct access to these data during clinical encounters is time consuming [10] and can lead to information overload; furthermore, human analysis of data is prone to cognitive biases, including anchoring and confirmation bias [11]. New methods for computational data analysis enable discovery using data, including PGHD [12]. However, the majority of traditional statistical machine learning methods require large volumes of dense data. These approaches have been successful when applied to populations using electronic health record (EHR) data [13–15]. Yet, they may not work well in contexts where decisions need to be made for each patient individually, using sparse and irregular data collected with self-monitoring. Furthermore, computational analysis of clinical data often involves "black box" approaches, which may lead to lack of trust and lack of adoption [16]. Developing true precision approaches in this context requires combining data-driven discovery with expert knowledge in a way that allows clinicians to inspect decision rules and modify them if necessary.

In this research, we investigated an approach to integrating expert knowledge and patient generated data by modeling the process of expert decision making using PGHD. Our approach builds upon informatics methods derived from expert suggestion systems, which combine patient data with a knowledge base in an inference engine that mimics expert decision-making. Initially developed to handle complex intensive care unit (ICU) cases [17], suggestion systems have been effective in clinical scenarios with multiple and complex variables to consider [18–21]. However, suggestion systems have not been extensively applied to PGHD. Furthermore, few studies conducted thus far explicitly examined how clinicians reason about PGHD, yet such analysis is foundational to the development of suggestion systems in this context.

We applied our approach to a relevant clinical question: What specific dietary changes would have the most impact for a specific patient with type 2 diabetes (T2D)? This is a relevant context in which to assess our approach because inter-individual variability in blood glucose response to the same meals [22–24] suggests that personalized diet goals are needed. Furthermore, guidelines for diabetes self-management education indicate clinicians should work with patients to develop individualized dietary self-management goals and plans [25,26]. Self-monitoring data, including dietary records and records of blood glucose levels, can help to inform and personalize self-management goals; however, the volume and complexity of such data makes identifying relevant trends and developing goals difficult, even for experts [27]. Yet, individually collected dietary and blood glucose records are typically insufficient to identify robust trends using traditional machine learning methods [28]. Further, similar to the ICU data used in traditional suggestion systems, patient-generated diet and blood glucose data are complex, and there are currently no clinical guidelines or validated processes by which nutrition experts (i.e., registered dietitian nutritionists; RDNs) transform these data into personalized diet recommendations.

Thus, the goal of this research was to examine applicability of the suggestion system approach to providing data-driven decision support in the context of personalizing nutritional recommendations for individuals with T2D using PGHD. In order to achieve this goal, we studied decision making of RDNs who consult individuals with T2D and used a mixed methods approach to formalize a set of expert decisions in a knowledge model. We used a combination of qualitative and quantitative methods to 1) develop two essential building blocks of a suggestion system in personalized nutritional counseling: a knowledge model that represents RDNs' recommendation-making process, and a knowledge base of formal rules that recommend personalized diet goals based on diet and blood glucose self-monitoring data; 2) encode these rules to automatically generate recommendations from patient data sets (i.e., the inference engine); and 3) evaluate the output of the system.

2. Methods

We developed a method to achieve our objectives that is summarized in Table 1 and described in detail below.

2.1. Developing the knowledge model and knowledge base

To analyze how RDNs use PGHD to generate personalized diet recommendations, we applied a qualitative method called process coding [29]. We used this method to conduct the secondary analysis of data collected during our previous research that involved observing RDNs as they analyzed self-monitoring data collected by individuals with T2D: Ten RDNs with graduate degrees in nutrition and experience counseling patients with T2D examined two datasets collected in our prior research [27]. These datasets were recorded by two individuals with T2D who self-monitored their diet and blood glucose levels in the context of their daily lives for 30 days (i.e., P1, P2 in Table 2). Datasets consisted of PGHD collected via smartphone application including the following elements: meal photos and brief descriptions, mealtime labels (i.e., breakfast, lunch, dinner), meal ingredients, and pre- and 2 -h-post-meal blood glucose readings. RDNs separate from those involved in this study preprocessed the PGHD with a standard protocol that leveraged the USDA Food Composition Database [30] to calculate calorie and macronutrient (i.e., carbohydrate, fat, protein, fiber) composition of each recorded meal. Both raw and preprocessed information were provided to the ten study RDNs. These datasets are summarized in the first two columns of Table 2. We recorded the RDNs as they "thought aloud" about their recommendations and transcribed these recordings. The

Table 2
Description of Patient (n = 4) 30-Day Meal Data Sets Used in Developing and Evaluating the Knowledge Model.

	P1 mean ± SD	P2 mean ± SD	P3 mean ± SD	P4 mean ± SD
Meals	66	72	40	31
BG change in mg/dl	16.5 ± 22.3	27.9 ± 37.6	22.5 ± 21.5	22.0 ± 33.6
Meals with excursions	9%	26 %	15 %	19 %
Breakfast				
Meals	23	24	12	10
Excursions	2	0	0	2
% Carb	30 ± 10 %	14 ± 4%	33 ± 10 %	44 ± 31 %
Fiber in grams	6.4 ± 2	3.0 ± 1.5	3.3 ± 2.2	3.1 ± 3
% Protein	43 ± 9%	25 ± 2%	32 ± 13 %	11 ± 7%
% Fat	27 ± 9%	60 ± 3%	35 ± 17 %	36 ± 28 %
Lunch				
Meals	20	22	14	11
Excursions	2	14	1	4
% Carb	21 ± 11 %	25 ± 8%	31 ± 13 %	36 ± 19 %
Fiber in grams	7.2 ± 4.6	7.7 ± 1.7	8.3 ± 4	2.5 ± 2.1
% Protein	58 ± 11 %	23 ± 6%	26 ± 11 %	22 ± 10 %
% Fat	22 ± 8%	52 ± 6%	44 ± 19 %	42 ± 16 %
Dinner				
Meals	23	26	14	10
Excursions	2	5	5	0
% Carb	24 ± 9%	22 ± 8%	24 ± 12 %	25 ± 13 %
Fiber in grams	9.6 ± 3.6	10.6 ± 3.3	5.4 ± 3.5	5.1 ± 2.1
% Protein	57 ± 14 %	23 ± 8%	28 ± 7%	23 ± 7%
% Fat	20 ± 10 %	55 ± 9%	48 ± 9%	52 ± 12 %

Notes: BG = blood glucose; Excursion = BG change ≥ 50 mg/dl; acceptable macronutrient distribution ranges (AMDR): carbohydrate = 45–65 %, fat = 20–35 %, protein = 10–35 % and recommended fiber intake of 25 – 30 grams/day [39]).

Columbia University Medical Center IRB approved this study.

We extracted information about specific observable or conceptual actions from the transcripts, thus identifying the series of processes by which RDNs analyzed each patient's data and arrived at a recommendation, coding each with a gerund (i.e., an "action word" ending in –ing) [29]. This established a set of cognitive actions taken when RDNs reason about self-monitoring data (e.g., "*Reducing* the data set into high and low impact meals using blood glucose data"). Interviews were coded until saturation (i.e., no new codes were arising from the data) [31]. Then, we synthesized the process codes into process themes that represented similar actions across multiple RDNs.

We formalized the process themes into a knowledge base representing key decision rules by adapting a qualitative method called decision tree modeling in which the analyst builds a composite model of the decision-making process by iteratively condensing actions into the logical order of steps taken to arrive at a decision [32]. We ordered the process themes from the process coding to sequentially represent key decision points in the RDNs' counseling process.

We shared a visual representation of key decision points (i.e., the knowledge base) with two of the RDNs via interviews. In these member-checking interviews, we asked the RDNs to assess face validity of the decision tree and the potential usefulness of an automated decision tree in clinical practice. These evaluation methods are common for early assessment of computational methods for clinical data analysis, such as computational phenotyping [15,33,34]. Together with these participants, we specified numeric values for key decision points.

2.2. Developing the inference engine

We then encoded these rules to build an inference engine that automatically generates diet recommendations using individuals' self-monitoring data. We translated the revised decision tree model into machine-readable form via a series of functions that represented each key decision point and transformed meal and blood glucose data into personalized recommendations (e.g., "At breakfast, eat more protein"). Functions were written in R Version 3.0.7 (The R Foundation for Statistical Computing, Vienna, Austria).

2.3. Evaluation

As with other suggestion system evaluations [35], we compared our inference engine's output to experts'. Two certified diabetes educators (CDEs), one an RDN and one an RN, both with doctoral degrees and extensive experience in counseling patients with T2D and training clinicians to counsel patients, developed the expert gold standard. For each of four patients with T2D (the two patients whose data were used in the RDN interviews, P1 and P2, and data from two additional patients, P3 and P4), each CDE reviewed the patient's data and developed an initial set of observations. Datasets were developed from 30-days of PGHD. Datasets were organized in an excel spreadsheet and included information about meals and blood glucose as described above and summarized in Table 2. Only meals with full data were used; snacks were excluded. Then, both CDEs participated in a 60 – 90-min meeting with either the first or senior author to develop a consensus set of observations. First, CDEs developed a consensus set of narrative clinical observations about each patient, similar to what they might say to a patient in their counseling practice (e.g., "For breakfasts, meals that have over 40 % of protein, and about 35 % of carbs have mild impact"). Later, the CDEs revisited the data to develop a gold standard, selecting specific recommendations from a list including "eat more," "maintain," or "eat less" of each macronutrient (e.g., "At breakfast, maintain protein"), resolving differences by consensus.

We qualitatively compared the inference engine's output to the narrative observations. We coded each observation by meal and macronutrient. We discarded observations that could not be matched to inference engine output because they were not related to macronutrients (e.g. "texture of carbohydrates has an impact on blood glucose;" n = 4). We then determined if each inference engine recommendation did or did not align with one or more of the CDE observations, referring to the summary statistics for the patient. In two instances, two of the CDEs' observations that applied to a macronutrient and/or meal time implied different recommendations and we rated the recommendations both consistent and inconsistent. We then calculated percent agreement based on these ratings. We also calculated percent agreement between the inference engine's output and the CDE's gold standard selections.

3. Results

3.1. Knowledge model and knowledge base

With the goal of developing formalized decision rules, we used decision tree modeling to synthesize the process themes from the 10 RDN interviews into four logical, sequential steps clinical experts take to transform patient-generated diet and blood glucose data into personalized diet recommendations:

1) Reduce the dataset by splitting it into high and low blood glucose impact meals based on blood glucose data;
2) Compare macronutrient composition of meals in low impact and high impact datasets to guidelines;
3) Compare alignment with guidelines between the low and high impact meals;
4) Present a goal based on differences in macronutrient distributions between low and high impact meals for each mealtime.

We validated the knowledge base with two RDNs who

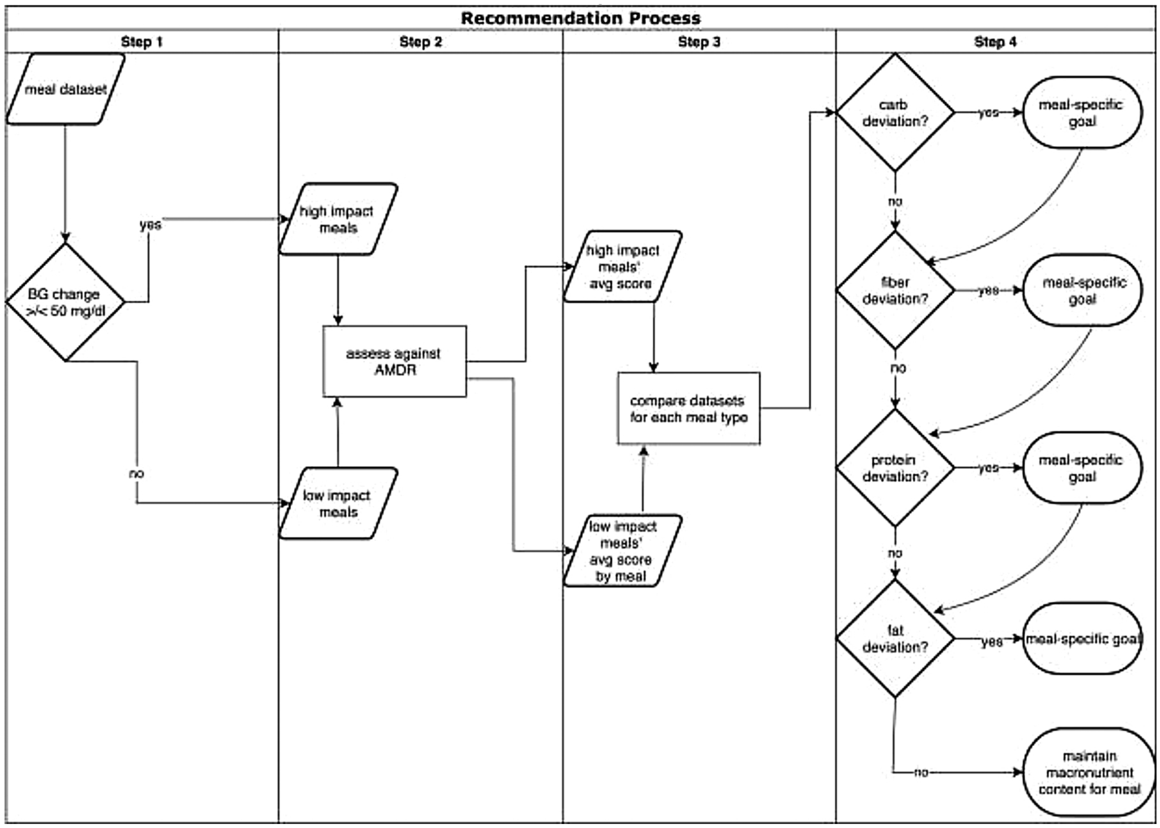

Fig. 1. Decision Tree Model for Personalized Diet Recommendations for Patients with T2D Based on Diet and Blood Glucose Self-Monitoring Data.
Notes: This figure formalizes the four key steps clinical experts take when transforming patient-generated diet and blood glucose data into personalized diet recommendations for patients with T2D: 1) Dividing the data set by impact; 2) Estimating macronutrient content of meals; 3) comparing macronutrients in high and low impact datasets; 4) generating a meal- and macronutrient-specific diet recommendation; T2D = type 2 diabetes, BG = blood glucose, AMDR = acceptable macronutrient distribution range.

independently determined that it appropriately represented a process for determining dietary goals for patients with T2D. Furthermore, they provided numeric values to more precisely define the decision rules. For step one, the RDNs defined a "high impact meal" as a meal is accompanied by a post- minus pre-meal blood glucose change of 50 mg/dl or more. For step 2, the RDNs clarified that they would use acceptable macronutrient distribution ranges (AMDR; i.e., carbohydrate = 45–65 %, fat = 20–35 %, protein = 10–35 % and fiber = 25 − 30 grams/day [36]) to identify the macronutrient composition of a meal and compare, on average, between high and low impact meals.

Both RDNs were enthusiastic about the prospect of using an automated system to identify meal-blood glucose patterns in their own practice. Specifically, they suggested that outsourcing PGHD analysis to an expert system would allow them to focus on counseling patients about how to achieve these goals rather than spending appointment time to identify recommendations. This was consistent with sentiments expressed by the RDNs during the interviews and the CDEs during the consensus recommendation meetings.

We used this information to transform the decision tree into formal rules for our knowledge base, which is presented in Fig. 1. The four steps include:

1) Split the patient data set into "high impact" meals, defined as having a ≥ 50 mg/dl change in blood glucose from pre to post meal readings, and "low impact" meals, defined as having < 50 mg/dl change in blood glucose from pre to post meal readings.
2) Determine which macronutrient(s), based on AMDR, are candidates for adjustment to improve blood glucose. Using the thresholds set out in the AMDR, each macronutrient is assigned a score for each meal: high (+1), low (-1), or in range (0). Fiber recommendations suggest 25 − 30 grams/day, rather than a proportional range that can be applied on a per meal basis. Considering the typical American's under-consumption of fiber, we therefore set the threshold for fiber at ≥ 8 g/meal and categorized a meal as high (1) or low (-1) fiber.
3) Identify the target macronutrient to be adjusted to improve blood glucose response by comparing deviations from the guidelines between the low and high impact meals. Within the high and low impact groups, meals are grouped by meal type and average high/low score is calculated for each macronutrient and rounded to the nearest whole number. Then, for each macronutrient at each mealtime, the average score for high impact meals is subtracted from the average score for low impact meals in order to determine the magnitude of the deviation for each macronutrient at each mealtime.
4) Present a meal-specific goal for each macronutrient based on the direction of the deviation. If the deviation score is positive, meaning low impact meals had more of the macronutrient, a goal is generated to eat more of that macronutrient at that mealtime; if the deviation score is negative, meaning high impact meals had more of the macronutrient, a goal is generated to eat less of the macronutrient at that mealtime; if the deviation score is zero, meaning there was no difference in the macronutrient in high and low impact meals at that mealtime, the system suggests that no change be made for that macronutrient at that mealtime. This step translates deviations between low and high impact meals into meal-specific human-readable goals (e.g., "At breakfast eat more carbohydrate," "At dinner eat less fat," or "At lunch maintain fiber").

Table 3
Comparison of Inference Engine (IE) Recommendations to Certified Diabetes Educator (CDE) Gold Standard.

	P1		P2		P3		P4	
	IE	CDE	IE	CDE	IE	CDE	IE	CDE
Breakfast								
Carb	increase	maintain	maintain	increase	maintain	maintain	maintain	maintain
Fiber	maintain	increase	maintain	maintain	maintain	increase	maintain	increase
Protein	maintain	maintain	maintain	maintain	maintain	maintain	maintain	increase
Fat	maintain	reduce	maintain	reduce	maintain	maintain	maintain	maintain
Lunch								
Carb	maintain	increase	maintain	maintain	maintain	maintain	maintain	maintain
Fiber	maintain	increase	maintain	maintain	increase	maintain	maintain	increase
Protein	maintain	maintain	maintain	maintain	maintain	maintain	maintain	increase
Fat	maintain	maintain	maintain	reduce	maintain	maintain	maintain	maintain
Dinner								
Carb	maintain	maintain	maintain	maintain	maintain	maintain	maintain	maintain
Fiber	reduce	maintain	maintain	maintain	maintain	increase	maintain	maintain
Protein	maintain	maintain	maintain	maintain	maintain	maintain	maintain	maintain
Fat	reduce	maintain	maintain	reduce	maintain	maintain	maintain	maintain
Percent agreement		42 %		67 %		75 %		67 %

3.2. Inference engine

To automatically generate nutrition recommendations using individuals' self-monitoring data, we developed computable logic and a set of functions to reason over the knowledge representation (available github.com/plasmak11/GluCopilot). The input for the R functions was a data frame that consisted of one row per meal and columns for meal type (i.e., breakfast, lunch, dinner), blood glucose change, proportion of calories from carb, proportion of calories from protein, proportion of calories from fat, and grams of fiber. The output was a list of recommendations for each meal. The recommendations for the four patient datasets are presented in Table 3.

3.3. Evaluation

The inference engine recommendations aligned with CDE narrative observations 74 % of the time (63 % of the recommendations for P1, 75 % of recommendations for P2, 75 % of recommendations for P3, and 83 % of recommendations for P4, See Supplementary Table 1). In some cases, the CDEs found it difficult to identify the problem nutrient. For example, in one case they observed, "There does not appear to be a significant connection between macronutrients and changes in blood glucose levels."

Comparing the inference engine output to the CDE gold standard, our inference engine made recommendations for 8% of meal-macronutrient cases while CDEs made a recommendation in 31 % of cases. Inference engine output and the CDE gold standard were 63 % consistent (42 % consistent for P1, 67 % consistent for P2, 75 % consistent for P3, and 67 % consistent for P4, see Table 3).

4. Discussion

Though the ubiquity of health apps has made PGHD readily available, transforming these data into actionable insight for patients and providers is challenging. This is particularly evident in the case of personalized diet goals for T2D where individual data are complex and difficult to interpret and sparse data limit purely computational analysis. Yet, given the worldwide burden of rising T2D prevalence [37–39] and the link between dietary management of T2D and improved outcomes [26,40–43], solutions to this problem have high potential for clinical impact. To address this challenge, we developed and validated a new approach to modeling expert clinical knowledge that automates the synthesis of diet and blood glucose self-monitoring data into suggested personalized dietary goals for individuals with T2D. We extended previous work in personalizing diet recommendations by demonstrating the feasibility of qualitatively modeling and then automating how clinical experts in nutrition (i.e., RDNs) reason over PGHD. As the health system increasingly emphasizes personalized approaches, this approach to developing a knowledge model and inference engine is potentially generalizable to other use cases for synthesizing PGHD to support personalized goal setting.

In this work, we examined applicability of qualitative modeling of clinical reasoning and decision making to the development of a suggestion system that can generate personalized nutritional recommendations using individuals' diet and blood glucose self-monitoring data. The study provided preliminary evidence for the feasibility of this approach and suggested several new directions for future work. First, the process encoding method used in this study produced a decision tree that was acceptable to our RDN clinical experts; this suggests that process coding may be used to model clinical decisions in other settings, together with other cognitive modeling approaches, such as concept maps [44]. However, despite this alignment between the decision tree and decision process of expert clinicians, the automatic inference engine's suggestions were mixed compared to expert output. While the inference engine output was consistent with the narrative clinical observations made by the CDEs, there was less consistency between the inference engine's output and CDEs' gold standard set of recommendations. For some patients, when compared to an expert-developed gold standard, our inference engine performed comparably to other suggestion systems [21,45]; however, for P1 in particular, it performed unacceptably. Finally, the CDEs made more recommendations than the inference engine. This suggests that the knowledge base represented clinical knowledge, yet it encountered challenges translating this knowledge into personalized nutritional suggestions.

Our inference engine was more consistent with CDE-generated narrative observations than with the gold standard that included more formal recommendations. There exist several possible explanations for this drop in accuracy. First, it may suggest that personalized dietary recommendations for T2D based on PGHD remain an imprecise "art." Narrative observations were more flexible; there was typically more than one narrative observation for each mealtime for each patient dataset and some were "both" consistent and inconsistent with the inference engine output. When forced to formulate a single discrete recommendation in the gold standard, CDEs may have been limited in their ability to limit their choice to only one. Indeed, they made numerous comments regarding the difficulty of identifing a stable dietary pattern. Our past research showed that identifying data-driven insights can be challenging even for experienced clinicians [27]. Future research could examine ways to develop gold standards for tasks that may be challenging to human experts.

Second, this discrepancy could indicate that CDEs used their expert knowledge to infer factors that may have influenced individuals' BG levels beyond those available in the dataset, which led to a higher number of suggestions. While a meal's macronutrient composition has an undeniable effect on post-prandial blood glucose, medications, physical activity, and even the extended effects of previous meals, can also affect blood glucose [46]. Yet, our knowledge base and inference engine prioritized individuals' diet as the main contributor to changes in individuals' BG levels. Future research could expand our approach to incorporate data regarding other factors influencing BG, including medication, sleep, and physical activity. However, this expansion of the scope may present a new challenge: incorporating additional data streems may require more complex computational data science methods, which may be more difficult to inspect and interpret than the knowledge base and decision tree developed in this work. In contrast to previous work on clinician acceptance of expert systems [47], our RDN participants had a positive reaction to the prospect of CDS for personalized dietary recommendations based on PGHD. Synergistic approaches that blend data science with human intuition, experience, and intelligence should be explored.

Additionally, the datasets used in this study had relatively few blood glucose excursions (i.e., post meal changes > 50 mg/dl), thus limiting variability in the meals used to generate recommendations. In particular, P1, for whom the evaluation was least consistent, only experienced blood glucose excursions in 9% of meals. Given that over 40 % of patients with T2D have uncontrolled diabetes [48], future research could evaluate the inference engine's output compared to the gold standard with PGHD input from patients with more blood glucose excursions.

While further research is needed to provide stronger evidence for the proposed approach, this initial study has several implications for new clinical decision support systems (CDSS) that integrate clinical reasoning and decision making with patient self-monitoring data. A CDSS for personalized nutrition could reduce time needed for processing and analyzing data during clinical encounters, thus leaving more time for counseling and potentially improving patients' success in achieving dietary self-management goals. This is important, given the concerns regarding increased workload associated with using CDSS [10], particularly when including PGHD [27,49]. The experts who generated recommendations for this study had unlimited time and multiple meetings to discuss the data and develop consensus, whereas a typical clinical encounter is 15 min. Furthermore, it can help to ameliorate cognitive biases identified in previous studies of clinicians' reasoning with PGHD [50]. This suggests that CDSS based on this type of knowledge base could become a useful part of clinical workflow [51].

RDNs, the healthcare providers who are the experts in nutrition therapy for chronic disease management, responded positively to the idea of a CDSS that transforms patient-generated meal and blood glucose data into macronutrient and meal-based recommendations. This positive feedback is encouraging as it suggests a direction for the design of future CDSS that may inspire adoption by clinicians. In its focus on providing support for data-analytic aspects of a patient encounter, our solution allowed providers to focus on the part of the patient encounter they enjoyed the most – a conversation and shared decision making with a patient. We avoided common problems related to knowledge engineering, namely clinician confidence in their own decision-making capabilities without CDSS tools [51,52] and the need to encode a vast amount of information to produce useful decision support [53]. As noted in the literature on expert systems, CDSS for personalized nutrition may facilitate the translation of research to practice as new scientific knowledge arises [53]. Such systems could further support integration of PGHD into clinical encounters beyond dietetics, including primary care and subspecialties, thereby improving the quality of nutrition advice, which often relies heavily on personal experience, bias, and habit. In addition to strengthening the knowledge base, future work to support PGHD-driven CDSS would include new research to feasibly integrate them with clinical workflow and acceptability by non-nutrition-expert clinicians who counsel patients on T2D self-management (e.g., primary care providers). Complimentary work is needed to support integration of nutrition-related PGHD with clinical systems, for example via SMART on FHIR [49,54]. Initial steps have been taken to include "wellness" PGHD (i.e., BG, blood pressure, and BMI) in existing FHIR resources [55]; however, interoperability [6] and controlled terminologies remain significant technical challenges [56].

Our findings also suggest that our knowledge base and inference engine could be useful in the area of personal informatics and digital health. Achieving and maintaining health behavior change is a known challenge [57]. People tend to be more successful when they lay out a specific plan for achieving a goal. While our inference engine is limited in that suggests changes in macronutrient consumption, which can be difficult to translate into behavior changes, existing resources could be leveraged to support more actionable recommendations, such as a knowledge base for diabetes problem solving action plans [58], or a commercially available food ontology. People also tend to be more successful in changing health behavior when interventions consider their context. Future iterations of our knowledge base could incorporate other contextual data generated along with meal data in order to deliver "just in time" interventions [59] to help patients overcome barriers to achieving their dietary goals.

4.1. Limitations

It is important to note several limitations in the design and evaluation of the work presented here. First, our inference engine relies on PGHD. Self-monitoring diet and blood glucose are particularly burdensome for patients to collect. Furthermore, these data are often prone to social desirability bias as individuals are less likely to record activities that would meet with disapproval from their healthcare providers. Though patient-generated diet data are not bias-free, technologies for dietary self-monitoring can provide a more comprehensive picture of a patient's eating patterns those traditionally used in dietetics, (e.g., 3-day food records, 24-h dietary recalls) [60]. Likewise, smartphone-based blood glucose logging has been demonstrated to be feasible and effective [61].

Second, this study focused on feasibility of the proposed approach and was small in its scope. The knowledge modeling phase included only 10 RDNs, and may be missed important aspects of the clinicians' decision making in this context. Furthermore, the evaluation was conducted with a limited number of experts (n = 4). In addition, the evaluation included only 4 datasets; while these datasets were collected by real individuals with T2DM, they are unlikely to represent a broad spectrum of patterns in changes in BG levels. In addition, the data used here represent patients with few glucose excursions and may therefore be influenced by selection bias. Finally, our knowledge base was validated qualitatively on proximal outcomes. Though we avoided circularity by evaluating the inference engine on additional datasets that were not used in developing the knowledge representation [47], we were not able to calculate an error rate or ROC to evaluate the system because no objective measure of truth exists. Furthermore, as our prototype has not yet been developed into CDS or deployed in a field trial, we did not evaluate its effect on clinician or patient behavior [47] or health outcomes [62].

5. Conclusion

We developed a new approach to using informatics methods to support patient-generated data-driven decision making about personalized nutrition goals. The knowledge base and inference engine presented here demonstrate the potential to extend the reach of PGHD by synthesizing it with clinical knowledge. Our results raise important questions in the area of PGHD and CDS about whether human experts or computer algorithms are better suited to discerning signal from PGHD.

Funding sources

This work was funded in part by the National Library of Medicine (NLM007079) and the Robert Wood Johnson Foundation (RWJF 73070).

Summary points

- Patient-generated health data (PGHD) can help to identify personalized health goals
- Sparse self-monitoring data presents challenges to traditional machine learning
- A suggestion system can mitigate these challenges by modeling expert decision making
- Our knowledge base and inference engine were face valid and demonstrated potential utility
- A suggestion system approach can extend potential for precision health by combining PGHD with clinical knowledge

Contributorship statement

MB, LM, CW conceived and designed the study. MB, JHS, LM, MEL, DJA contributed to the design of the system. MB and JHS implemented the system. MB, DJF collected the data. MB performed the analysis. MB, LM, GK, AMS, PGD, KGB contributed to the interpretation of the study findings. MB wrote the first draft of the manuscript. LM, GK contributed to the content of the manuscript. MB, PGD, AMS, KGB contributed nutrition and diabetes education expertise. GK, CW contributed knowledge representation and clinical decision support expertise. All authors revised the manuscript and approved the final version.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] T.H. Payne, S. Corley, T.A. Cullen, T.K. Gandhi, L. Harrington, G.J. Kuperman, J.E. Mattison, D.P. McCallie, C.J. McDonald, P.C. Tang, W.M. Tierney, C. Weaver, C.R. Weir, M.H. Zaroukian, Report of the AMIA EHR-2020 task force on the status and future direction of EHRs, J. Am. Med. Inform. Assoc. 22 (2015) 1102–1110, https://doi.org/10.1093/jamia/ocv066.

[2] P. Harrop, J. Hayward, R. Das, G. Holland, Wearable Technology 2015-2025: Technologies, Markets, Forecasts, IDTechEx Rep, (2015).

[3] mHealth Economics 2017 - Current Status and Future Trends in Mobile Health, Research2guidance. (n.d.). https://research2guidance.com/product/mhealth-economics-2017-current-status-and-future-trends-in-mobile-health/ (Accessed 11 June 2018).

[4] Patient-Generated Health Data | HealthIT.gov, (n.d.). https://www.healthit.gov/topic/scientific-initiatives/patient-generated-health-data (Accessed 11 June 2018).

[5] A.M. Lai, P.-Y.S. Hsueh, Y.K. Choi, R.R. Austin, Present and future trends in consumer health informatics and patient-generated health data, Yearb. Med. Inform. 26 (2017) 152–159, https://doi.org/10.15265/IY-2017-016.

[6] F. Greaves, R. Rozenblum, Social and consumer informatics, Key Adv. Clin. Inform. Elsevier, 2017, pp. 257–278, https://doi.org/10.1016/B978-0-12-809523-2.00018-2.

[7] N. Lv, L. Xiao, M.L. Simmons, L.G. Rosas, A. Chan, M. Entwistle, Personalized hypertension management using patient-generated health data integrated with electronic health records (EMPOWER-H): six-month pre-post study, J. Med. Internet Res. 19 (2017) e311.

[8] P.C. Tang, J.M. Overhage, A.S. Chan, N.L. Brown, B. Aghighi, M.P. Entwistle, S.L. Hui, S.M. Hyde, L.H. Klieman, C.J. Mitchell, Online disease management of diabetes: engaging and motivating patients online with enhanced resources-diabetes (EMPOWER-D), a randomized controlled trial, J. Am. Med. Inform. Assoc. 20 (2012) 526–534.

[9] D.M. Mann, J. Palmisano, J.J. Lin, A pilot randomized trial of technology-assisted goal setting to improve physical activity among primary care patients with prediabetes, Prev. Med. Rep. 4 (2016) 107–112.

[10] C.M. Danis, Incorporating patient generated health data into chronic disease management: a human factors approach, Healthc. Inf. Manag. Syst. Springer, Cham, 2016, pp. 177–188, https://doi.org/10.1007/978-3-319-20765-0_10.

[11] G. Saposnik, D. Redelmeier, C.C. Ruff, P.N. Tobler, Cognitive biases associated with medical decisions: a systematic review, BMC Med. Inform. Decis. Mak. 16 (2016), https://doi.org/10.1186/s12911-016-0377-1.

[12] P.M. Desai, E.G. Mitchell, M.L. Hwang, M.E. Levine, D.J. Albers, L. Mamykina, Personal Health Oracle: Explorations of Personalized Predictions in Diabetes Self-Management, in: ACM, 2019: p. 370.

[13] D.J. Albers, N. Elhadad, E. Tabak, A. Perotte, G. Hripcsak, Dynamical phenotyping: using temporal analysis of clinically collected physiologic data to stratify populations, PLoS One 9 (2014) e96443.

[14] D.J. Albers, N. Elhadad, J. Claassen, R. Perotte, A. Goldstein, G. Hripcsak, Estimating summary statistics for electronic health record laboratory data for use in high-throughput phenotyping algorithms, J. Biomed. Inform. 78 (2018) 87–101.

[15] R. Pivovarov, A.J. Perotte, E. Grave, J. Angiolillo, C.H. Wiggins, N. Elhadad, Learning probabilistic phenotypes from heterogeneous EHR data, J. Biomed. Inform. 58 (2015) 156–165, https://doi.org/10.1016/j.jbi.2015.10.001.

[16] D.S. Watson, J. Krutzinna, I.N. Bruce, C.E. Griffiths, I.B. McInnes, M.R. Barnes, L. Floridi, Clinical applications of machine learning algorithms: beyond the black box, BMJ 364 (2019), https://doi.org/10.1136/bmj.l886.

[17] E.S. Berner, T.J.L. Lande, Overview of clinical decision support systems, Clin. Decis. Support Syst. Springer, Cham, 2016, pp. 1–17, https://doi.org/10.1007/978-3-319-31913-1_1.

[18] P.J. Haug, R.M. Gardner, R.S. Evans, B.H. Rocha, R.A. Rocha, Clinical decision support at intermountain healthcare, Clin. Decis. Support Syst. Springer, New York, NY, 2007, pp. 159–189, https://doi.org/10.1007/978-0-387-38319-4_8.

[19] R.S. Evans, D.C. Classen, S.L. Pestotnik, H.P. Lundsgaarde, J.P. Burke, Improving empiric antibiotic selection using computer decision support, Arch. Intern. Med. 154 (1994) 878–884, https://doi.org/10.1001/archinte.1994.00420080076008.

[20] R.S. Evans, S.L. Pestotnik, D.C. Classen, T.P. Clemmer, L.K. Weaver, J.F. Orme, J.F. Lloyd, J.P. Burke, A computer-assisted management program for antibiotics and other antiinfective agents, N. Engl. J. Med. 338 (1998) 232–238, https://doi.org/10.1056/NEJM199801223380406.

[21] B. Kaplan, Evaluating informatics applications—clinical decision support systems literature review, Int. J. Med. Inf. 64 (2001) 15–37, https://doi.org/10.1016/S1386-5056(01)00183-6.

[22] D. Zeevi, T. Korem, N. Zmora, D. Israeli, D. Rothschild, A. Weinberger, O. Ben-Yacov, D. Lador, T. Avnit-Sagi, M. Lotan-Pompan, J. Suez, J.A. Mahdi, E. Matot, G. Malka, N. Kosower, M. Rein, G. Zilberman-Schapira, L. Dohnalová, M. Pevsner-Fischer, R. Bikovsky, Z. Halpern, E. Elinav, E. Segal, Personalized nutrition by prediction of glycemic responses, Cell 163 (2015) 1079–1094, https://doi.org/10.1016/j.cell.2015.11.001.

[23] S. Vega-López, L.M. Ausman, J.L. Griffith, A.H. Lichtenstein, Interindividual variability and intra-individual reproducibility of glycemic index values for commercial white bread, Diabetes Care 30 (2007) 1412–1417, https://doi.org/10.2337/dc06-1598.

[24] R. Vrolix, R.P. Mensink, Variability of the glycemic response to single food products in healthy subjects, Contemp. Clin. Trials 31 (2010) 5–11, https://doi.org/10.1016/j.cct.2009.08.001.

[25] M.M. Funnell, T.L. Brown, B.P. Childs, L.B. Haas, G.M. Hosey, B. Jensen, M. Maryniuk, M. Peyrot, J.D. Piette, D. Reader, L.M. Siminerio, K. Weinger, M.A. Weiss, National standards for diabetes self-management education, Diabetes Care 32 (2009) S87–S94, https://doi.org/10.2337/dc09-S087.

[26] A.B. Evert, J.L. Boucher, M. Cypress, S.A. Dunbar, M.J. Franz, E.J. Mayer-Davis, J.J. Neumiller, R. Nwankwo, C.L. Verdi, P. Urbanski, W.S. Yancy, Nutrition therapy recommendations for the management of adults with diabetes, Diabetes Care 36 (2013) 3821–3842, https://doi.org/10.2337/dc13-2042.

[27] D.J. Feller, M. Burgermaster, M.E. Levine, A. Smaldone, P.G. Davidson, D.J. Albers, L. Mamykina, A visual analytics approach for pattern-recognition in patient-generated data, J. Am. Med. Inform. Assoc. (2018), https://doi.org/10.1093/jamia/ocy054.

[28] F. Bentley, K. Tollmar, P. Stephenson, L. Levy, B. Jones, S. Robertson, E. Price, R. Catrambone, J. Wilson, Health Mashups: presenting statistical patterns between wellbeing data and context in natural language to promote behavior change, ACM Trans. Comput.-Hum. Interact. TOCHI. 20 (2013) 30.

[29] J. Saldaña, The Coding Manual for Qualitative Researchers, 2 edition, SAGE Publications Ltd, Los Angeles, 2012.

[30] J. Bodner-Montville, J.K. Ahuja, L.A. Ingwersen, E.S. Haggerty, C.W. Enns, B.P. Perloff, USDA food and nutrient database for dietary studies: released on the web, J. Food Compos. Anal. 19 (2006) S100–S107.

[31] M.Q. Patton, Qualitative Research & Evaluation Methods, 3rd edition, SAGE Publications, Inc, Thousand Oaks, Calif, 2001.

[32] M.B. Miles, A.M. Huberman, Qualitative Data Analysis: An Expanded Sourcebook,

2nd edition, SAGE Publications, Inc, Thousand Oaks, 1994.
[33] K.M. Newton, P.L. Peissig, A.N. Kho, S.J. Bielinski, R.L. Berg, V. Choudhary, M. Basford, C.G. Chute, I.J. Kullo, R. Li, J.A. Pacheco, L.V. Rasmussen, L. Spangler, J.C. Denny, Validation of electronic medical record-based phenotyping algorithms: results and lessons learned from the eMERGE network, J. Am. Med. Inform. Assoc. 20 (2013) e147–e154, https://doi.org/10.1136/amiajnl-2012-000896.
[34] R.L. Richesson, W.E. Hammond, M. Nahm, D. Wixted, G.E. Simon, J.G. Robinson, A.E. Bauck, D. Cifelli, M.M. Smerek, J. Dickerson, R.L. Laws, R.A. Madigan, S.A. Rusincovitch, C. Kluchar, R.M. Califf, Electronic health records based phenotyping in next-generation clinical trials: a perspective from the NIH Health Care Systems Collaboratory, J. Am. Med. Inform. Assoc. 20 (2013) e226–e231, https://doi.org/10.1136/amiajnl-2013-001926.
[35] V.L. Yu, L.M. Fagan, S.M. Wraith, W.J. Clancey, A.C. Scott, J. Hannigan, R.L. Blum, B.G. Buchanan, S.N. Cohen, Antimicrobial selection by a computer. A blinded evaluation by infectious diseases experts, JAMA 242 (1979) 1279–1282, https://doi.org/10.1001/jama.1979.03300120033020.
[36] 2015-2020 Dietary Guidelines - health.gov, (n.d.). https://health.gov/dietaryguidelines/2015/guidelines/ (accessed June 12, 2018).
[37] J.P. Boyle, T.J. Thompson, E.W. Gregg, L.E. Barker, D.F. Williamson, Projection of the year 2050 burden of diabetes in the US adult population: dynamic modeling of incidence, mortality, and prediabetes prevalence, Popul. Health Metr. 8 (2010), https://doi.org/10.1186/1478-7954-8-29.
[38] W.H. Herman, The economics of diabetes prevention, Med. Clin. North Am. 95 (2011), https://doi.org/10.1016/j.mcna.2010.11.010 373–viii.
[39] J.A. Campbell, K.G. Bishu, R.J. Walker, L.E. Egede, Trends of medical expenditures and quality of life in US adults with diabetes: the medical expenditure panel survey, 2002–2011, Health Qual. Life Outcomes 15 (2017), https://doi.org/10.1186/s12955-017-0651-7.
[40] A. Emadian, R.C. Andrews, C.Y. England, V. Wallace, J.L. Thompson, The effect of macronutrients on glycaemic control: a systematic review of dietary randomised controlled trials in overweight and obese adults with type 2 diabetes in which there was no difference in weight loss between treatment groups, Br. J. Nutr. 114 (2015) 1656–1666, https://doi.org/10.1017/S0007114515003475.
[41] O. Ajala, P. English, J. Pinkney, Systematic review and meta-analysis of different dietary approaches to the management of type 2 diabetes, Am. J. Clin. Nutr. 97 (2013) 505–516, https://doi.org/10.3945/ajcn.112.042457.
[42] M.L. Wheeler, S.A. Dunbar, L.M. Jaacks, W. Karmally, E.J. Mayer-Davis, J. Wylie-Rosett, W.S. Yancy, Macronutrients, Food Groups, and Eating Patterns in the Management of Diabetes: A systematic review of the literature, 2010, Diabetes Care 35 (2012) 434–445, https://doi.org/10.2337/dc11-2216.
[43] M.J. Franz, J. MacLeod, A. Evert, C. Brown, E. Gradwell, D. Handu, A. Reppert, M. Robinson, Academy of nutrition and dietetics nutrition practice guideline for type 1 and type 2 diabetes in adults: systematic review of evidence for medical nutrition therapy effectiveness and recommendations for integration into the nutrition care process, J. Acad. Nutr. Diet. 117 (2017) 1659–1679, https://doi.org/10.1016/j.jand.2017.03.022.
[44] V.L. Patel, E.H. Shortliffe, Human-intensive techniques, Clin. Decis. Support, Elsevier, 2014, pp. 285–308.
[45] P. Ramnarayan, A.L. Tomlinson, G. Kulkarni, A. Rao, J.F. Britto, A Novel Diagnostic Aid (ISABEL): Development and Preliminary Evaluation of Clinical Performance, (2004), pp. 1091–1095.
[46] A.J. Garber, M.J. Abrahamson, J.I. Barzilay, L. Blonde, Z.T. Bloomgarden, M.A. Bush, S. Dagogo-Jack, R.A. DeFronzo, D. Einhorn, V.A. Fonseca, J.R. Garber, W.T. Garvey, G. Grunberger, Y. Handelsman, I.B. Hirsch, P.S. Jellinger, J.B. McGill, J.I. Mechanick, P.D. Rosenblit, G.E. Umpierrez, Consensus statement by the american association of clinical endocrinologists and american college of endocrinology on the comprehensive type 2 diabetes management algorithm – 2018 executive summary, Endocr. Pract. 24 (2018) 91–120, https://doi.org/10.4158/CS-2017-0153.
[47] K. Clarke, R. O'Moore, R. Smeets, J. Talmon, J. Brender, P. McNair, P. Nykanen, J. Grimson, B. Barber, A methodology for evaluation of knowledge-based systems in medicine, Artif. Intell. Med. 6 (1994) 107–121, https://doi.org/10.1016/0933-3657(94)90040-X.
[48] E. Selvin, C.M. Parrinello, D.B. Sacks, J. Coresh, Trends in prevalence and control of diabetes in the United States, 1988-1994 and 1999-2010, Ann. Intern. Med. 160 (2014) 517–525, https://doi.org/10.7326/M13-2411.
[49] T. Bergquist, R.W. Buie, Heart on FHIR: Integrating Patient Generated Data into Clinical Care to Reduce 30 Day Heart Failure Readmissions, (n.d.) 5.
[50] L. Mamykina, M.E. Levine, P.G. Davidson, A.M. Smaldone, N. Elhadad, D.J. Albers, Data-driven health management: reasoning about personally generated data in diabetes with information technologies, J. Am. Med. Inform. Assoc. 23 (2016) 526–531, https://doi.org/10.1093/jamia/ocv187.
[51] H.A. Heathfield, J. Wyatt, Philosophies for the design and development of clinical decision-support systems, Methods Inf. Med. 32 (1993) 01–08, https://doi.org/10.1055/s-0038-1634896.
[52] R.L. Engle, Attempts to use computers as diagnostic aids in medical decision making: a thirty-year experience, Perspect. Biol. Med. 35 (1992) 207–219, https://doi.org/10.1353/pbm.1992.0011.
[53] J.H. Carter, Design and implementation issues, Clin. Decis. Support Syst. Springer, New York, NY, 2007, pp. 64–98, https://doi.org/10.1007/978-0-387-38319-4_4.
[54] J.C. Mandel, D.A. Kreda, K.D. Mandl, I.S. Kohane, R.B. Ramoni, SMART on FHIR: a standards-based, interoperable apps platform for electronic health records, J. Am. Med. Inform. Assoc. 23 (2016) 899–908, https://doi.org/10.1093/jamia/ocv189.
[55] S. Pais, D. Parry, Y. Huang, Suitability of Fast Healthcare Interoperability Resources (FHIR) for Wellness Data, (2017), https://doi.org/10.24251/HICSS.2017.423.
[56] T. Kennell, J. Willig, J. Cimino, Clinical informatics researcher's desiderata for the data content of the next generation electronic health record, Appl. Clin. Inform. 08 (2017) 1159–1172, https://doi.org/10.4338/ACI-2017-06-R-0101.
[57] G.F. Dunton, Sustaining health-protective behaviors such as physical activity and healthy eating, JAMA (2018), https://doi.org/10.1001/jama.2018.6621.
[58] H.J. Cole-Lewis, A.M. Smaldone, P.R. Davidson, R. Kukafka, J.N. Tobin, A. Cassells, E.D. Mynatt, G. Hripcsak, L. Mamykina, Participatory approach to the development of a knowledge base for problem-solving in diabetes self-management, Int. J. Med. Inf. 85 (2016) 96–103, https://doi.org/10.1016/j.ijmedinf.2015.08.003.
[59] I. Nahum-Shani, S.N. Smith, A. Tewari, K. Witkiewitz, L.M. Collins, B. Spring, S. Murphy, Just in time adaptive interventions (jitais): an organizing framework for ongoing health behavior support, Methodol. Cent. Tech. Rep. (2014) (accessed May 10, 2017), http://methodology.psu.edu/media/techreports/14-126.pdf.
[60] C.M. Wharton, C.S. Johnston, B.K. Cunningham, D. Sterner, Dietary self-monitoring, but not dietary quality, improves with use of smartphone app technology in an 8-Week weight loss trial, J. Nutr. Educ. Behav. 46 (2014) 440–444, https://doi.org/10.1016/j.jneb.2014.04.291.
[61] J. Sieber, F. Flacke, M. Link, C. Haug, G. Freckmann, Improved glycemic control in a patient group performing 7-Point profile self-monitoring of blood glucose and intensive data documentation: an open-label, multicenter, observational study, Diabetes Ther. 8 (2017) 1079–1085, https://doi.org/10.1007/s13300-017-0306-z.
[62] P.S. Roshanov, N. Fernandes, J.M. Wilczynski, B.J. Hemens, J.J. You, S.M. Handler, R. Nieuwlaat, N.M. Souza, J. Beyene, H.G.C.V. Spall, A.X. Garg, R.B. Haynes, Features of effective computerised clinical decision support systems: meta-regression of 162 randomised trials, BMJ 346 (2013) f657, https://doi.org/10.1136/bmj.f657.