JMIR Diabetes

Emerging Technologies, Medical Devices, Apps, Sensors, and Informatics to Help People with Diabetes
Volume 7 (2022), Issue 3 ISSN 2371-4379 Editors-in-Chief: Ricardo Correa, MD, EdD; Sheyu Li, MD

Contents

Reviews

Original Papers

Review

Diabetes Self-management Apps: Systematic Review of Adoption Determinants and Future Research Agenda

Hessah Alaslawi[1], MSc, PhD; Ilhem Berrou[2], PhD; Abdullah Al Hamid[3], PhD; Dari Alhuwail[4], PhD; Zoe Aslanpour[1], PhD

[1]Department of Clinical and Pharmaceutical Sciences, University of Hertfordshire, Hatfield, United Kingdom

[2]School of Health & Social Wellbeing, University of the West of England, Bristol, United Kingdom

[3]Saudi Ministry of Health, Najran, Saudi Arabia

[4]Department of Information Science, College of Computing Sciences and Engineering, Kuwait University, Kuwait, Kuwait

Corresponding Author:
Ilhem Berrou, PhD
School of Health & Social Wellbeing
University of the West of England
2B03 Glenside Campus
Bristol, BS16 1DD
United Kingdom
Phone: 44 1173284053 ext 4053
Email: ilhem.berrou@uwe.ac.uk

Abstract

Background: Most diabetes management involves self-management. Effective self-management of the condition improves diabetes control, reduces the risk of complications, and improves patient outcomes. Mobile apps for diabetes self-management (DSM) can enhance patients' self-management activities. However, they are only effective if clinicians recommend them, and patients use them.

Objective: This study aimed to explore the determinants of DSM apps' use by patients and their recommendations by health care professionals (HCPs). It also outlines the future research agenda for using DSM apps in diabetes care.

Methods: We systematically reviewed the factors affecting the adoption of DSM apps by both patients and HCPs. Searches were performed using PubMed, Scopus, CINAHL, Cochrane Central, ACM, and Xplore digital libraries for articles published from 2008 to 2020. The search terms were *diabetes*, *mobile apps*, and *self-management*. Relevant data were extracted from the included studies and analyzed using a thematic synthesis approach.

Results: A total of 28 studies met the inclusion criteria. We identified a range of determinants related to patients' and HCPs' characteristics, experiences, and preferences. Young female patients were more likely to adopt DSM apps. Patients' perceptions of the benefits of apps, ease of use, and recommendations by patients and other HCPs strongly affect their intention to use DSM apps. HCPs are less likely to recommend these apps if they do not perceive their benefits and may not recommend their use if they are unaware of their existence or credibility. Young and technology-savvy HCPs were more likely to recommend DSM apps.

Conclusions: Despite the potential of DSM apps to improve patients' self-care activities and diabetes outcomes, HCPs and patients remain hesitant to use them. However, the COVID-19 pandemic may hasten the integration of technology into diabetes care. The use of DSM apps may become a part of the new normal.

(JMIR Diabetes 2022;7(3):e28153) doi:10.2196/28153

KEYWORDS

diabetes self-management; mobile apps; mobile health; mHealth adoption; mobile phone

Introduction

Background

Diabetes prevalence continues to increase worldwide, affecting 1 in 11 people [1]. Persistent hyperglycemia leads to the development of microvascular and macrovascular complications and increases the risk of death; this risk is highest in the young age group [2]. The management of diabetes-induced cardiovascular disease and chronic kidney disease requires heavy health care resource consumption and up to a 4-fold increase in health care costs [3]. Type 2 diabetes is the most prevalent form of this condition and is characterized by persistent hyperglycemia and insulin resistance. Most patients are managed in primary care settings, and given the increasing prevalence, health care settings are experiencing unprecedented demands for clinical appointments and input from health care professionals (HCPs). This often means that patients have limited time with clinicians to discuss diabetes management and optimize treatment [4]. Diabetes self-management (DSM) can improve glycemic control and reduce the risk of complications [5].

Most diabetes management is thought to involve self-management [6]. The term self-management is often used interchangeably with self-care. Self-care refers to behaviors and activities undertaken to manage acute illnesses or injuries, with a focus on treatment [7]. Self-management is a more appropriate term when describing the strategies that patients use to cope with the emotional and practical issues encountered while living with a long-term illness [7]. For patients living with type 2 diabetes, DSM entails adherence to prescribed medication, maintaining a healthy diet, regular physical activity, routine foot checks, frequent monitoring of blood glucose levels if using insulin or sulfonylureas, and managing symptoms of low or very high glucose levels [8]. Patients also have to cope with the reality of diabetic microvascular and macrovascular complications [9] and an increased risk of disability and death [10]. Therefore, DSM education and support is paramount, especially at the point of diagnosis, to influence patients' behaviors and enhance their engagement with diabetes care [11]. When first diagnosed, patients usually receive DSM education and support from HCPs, followed by ongoing support from other practitioners and community resources [11].

HCPs are increasingly supporting autonomous DSM given the current strain on health care resources [5] and the fact that face-to-face consultations and education courses may not work for everyone. Digital technology has been shown to encourage autonomy and improve diabetes outcomes [12]. Digital and wireless technologies are widely available to support lifestyle and treatment interventions as well as diabetes medical devices, such as blood glucose meters, continuous glucose monitoring devices, and smart insulin pens and pumps [13]. However, mobile health (mHealth) apps for diabetes management are at the forefront of innovations that support DSM. A range of diabetes health apps are available, including nutrition, physical activity, glucose monitoring, insulin titration and delivery, and artificial pancreas systems [13].

Mobile apps have been shown to reduce the barriers to self-management activities, as they provide diabetes education, data logging and trend viewing, and connecting and transferring data to HCPs [14]. Furthermore, mobile apps can be useful elements in effectively modifying lifestyles [15]. The use of apps can lead to a significant reduction in hemoglobin A_{1c} levels among patients with type 2 diabetes [16], improve communication with HCPs, and facilitate remote disease monitoring [17].

Objectives

Several studies have reported factors that affect patients' adoption (use) of diabetes management apps, including patients' characteristics and experiences, app characteristics and functions, and recommendations by HCPs and other patients [18]. Various theoretical lenses have been used to explore app adoption, including the technology acceptance model and the diffusion of innovation theory [19], theory of reasoned action, and unified theory of acceptance and use of technology [20]. However, very few studies examined the antecedents influencing HCPs' recommendation of DSM apps to their patients and integrating them into their practice [21]. Although many studies have explored the factors that affect patients' adoption of DSM mobile apps using varying study designs and sample sizes, a systematic overview of these factors and their importance remains missing. Thus, this paper aimed to systematically review the determinants of DSM app adoption by HCPs and patients, highlighting their significance in facilitating or hindering their use. The term adoption will be used throughout to indicate patients' use of DSM apps and HCPs recommendation of these apps or integrating them in their practice.

This review makes 3 main contributions. First, it provides a comprehensive and systematic review of all studied determinants of DSM app adoption by HCPs and patients. Second, this review highlights the significance of each of these determinants based on the frequency of reporting and the type and sample size of the reporting studies. This will inform commissioners and diabetes app developers of what patients and HCPs look for in DSM apps and the circumstances in which they decide to adopt or reject their use. Third, this review combined patients' and HCPs' perspectives on the determinants of DSM app adoption. This is critical because DSM apps can only be effective if HCPs recommend them, and patients use them.

Methods

Data Sources and Searches

We searched PubMed, Scopus, CINAHL, ACM digital library, IEEE Xplore digital library and Cochrane Central using the terms "*adoption (uptake, acceptance, use, implement)*," "*mobile apps (apps, mHealth, smartphones, digital health intervention)*," and "*T2DM (diabetes mellitus, type 2, chronic conditions, long-term conditions)*." We also checked the references of the selected studies and the references of systematic reviews exploring the use of mobile apps for DSM. Multimedia Appendix 1 [22-49] lists the search strategy used for PubMed. The search strategy for PubMed was adapted to search other databases.

Eligibility Criteria

We included original studies published between 2008 (when the main app stores, iOS and Android, were launched) and February 2020, which reported on the factors affecting the adoption of self-management apps for diabetes care, involving patients with type 2 diabetes, and HCPs, or stakeholders, or caregivers dealing with patients with diabetes, using quantitative, qualitative, or mixed methods. We did not exclude studies involving patients with type 2 and type 1 diabetes, patients with type 2 diabetes and other comorbidities, or patients who did not specify their diabetes type. This was done to ensure the inclusion of all relevant studies involving patients with type 2 diabetes.

Adoption refers to the decision to proceed with the full or partial implementation of an innovation [50]. In this study, the term adoption specifically refers to patients' use of DSM apps and HCPs' recommendation of these apps and integrating them in their practice. Mobile apps are defined as "software applications that can be executed on a mobile platform or a web-based software application that is tailored to a mobile platform but is executed on a server" [51]. Studies on health informatics or digital health intervention or health information technology or telemedicine or telehealth or mHealth have been included in this review if the use of mobile diabetes apps is clearly highlighted. We excluded studies reporting on digital health interventions that did not involve the use of a mobile app, including the use of other mobile functions (eg, calls and SMS).

In all, 2 reviewers (HA and AA) independently screened the titles and abstracts and then full texts to select eligible studies. Reviewers resolved disagreements through discussion or, if necessary, through discussion with an arbitrator (IB).

Data Extraction and Quality Assessment

Data extraction and quality assessment were performed by HA and verified by IB, and any disagreements were resolved through discussion within the review team. For studies reporting on mHealth in general, including mobile apps, and eHealth in general, including mobile apps, careful extraction of data relating to mobile apps was performed whenever possible. Critical appraisal skill program tools [52] were used for the quality assessment of qualitative studies, cohort studies, and case-control studies. To cover the quality assessment of cross-sectional studies, the Joanna Briggs Institute critical tools for observational studies were used [53]. The quality of the included studies was independently assessed by HA and DA. The reviewers resolved the discrepancies through discussion.

Data Synthesis and Analysis

To generate new insights from the included studies, the thematic synthesis methodology of Thomas and Harden (2008) [54] was used, as it provides a clear process for synthesizing qualitative data reported in different study designs. This process of data synthesis follows 3 steps: line-by-line coding, organization of *free codes* to build *descriptive* themes and the development of *analytical* themes.

Descriptive data related to the study design, participant type and age, sample size, types of mobile apps used, and study outcomes were extracted. Data pertaining to the factors affecting participants' use of mobile apps for DSM were independently coded by 2 reviewers (HA and IB). Discrepancies in coding were resolved through discussion and the coding frame was modified accordingly. Similarities between codes were highlighted, and codes were stratified into (descriptive) themes to describe data patterns. This was followed by synthesizing or interrogating descriptive themes to develop analytical themes. Although this method is mainly used to synthesize evidence from qualitative studies, it remains a useful approach for synthesizing qualitative data that can be reported in quantitative studies. In their review of systematic reviews, Hong et al [55] noted that data-based convergent synthesis design was commonly used, where data from qualitative and quantitative studies were analyzed using the same synthesis method, and the results are presented together.

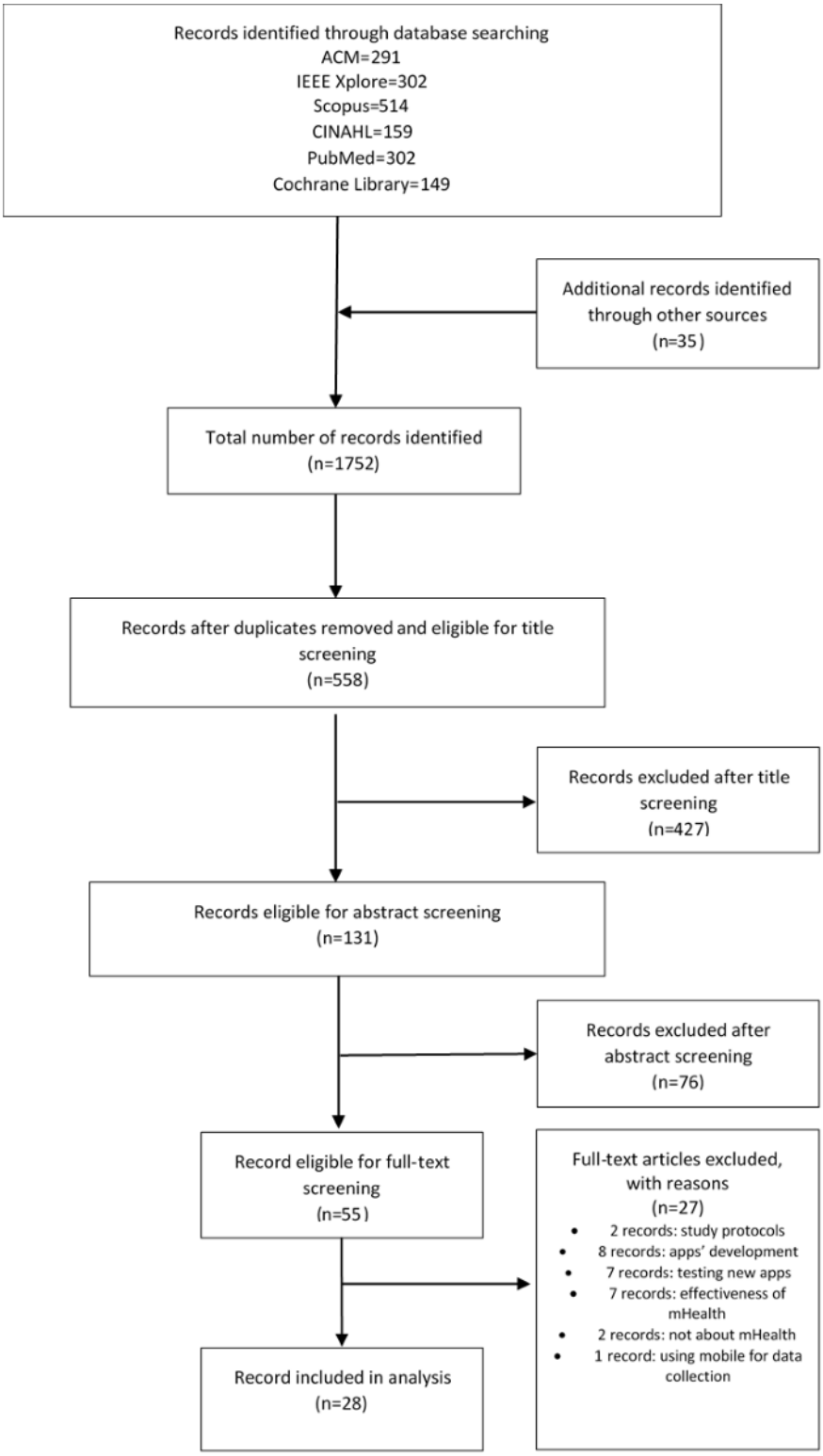
Results

Characteristics of the Included Studies

A total of 28 studies met the inclusion criteria. Figure 1 illustrates the study selection process. We identified 1752 citations from 6 databases (291 articles from ACM, 302 from IEEE Xplore, 514 from Scopus, 302 from PubMed, 149 from Cochrane Library, and 159 from CINAHL). A total of 131 articles passed title screening, and 55 articles passed the abstract screening. From the 55 articles, 27 (49%) articles were eliminated during full-text screening: 2 records were not about mHealth, 2 records were study protocols, 8 records were about app development, 7 records about testing new apps, 7 records were about the impact of mobile apps on diabetes self-management (DSM), and 1 record was about using mobile apps as tools for collecting data. All retrieved articles were published between 2015 and 2019. Most studies (10/28, 36%) were conducted in the United States [21-24,50-55], followed by Canada (3/28, 11%) [25-27] and the United Kingdom (3/28, 11%) [28-30]. In addition, (2/28, 7%) studies were conducted in each of the following countries: Australia [31,32], Saudi Arabia [33,34], and Germany [35,36]. Furthermore, of 28 studies, 1 (4%) study was conducted in each of the following countries: Peru [37], Denmark [38], Rwanda [39], New Zealand [40], Norway [41], and China [42].

The study design of the retrieved papers included qualitative design in 50% (14/28) of the studies [25,26,28,30-32,34,36-38,43-46,48], cross-sectional design in 43% (12/28) of the studies [22,23,27,29,33,35,36,39-42,47,49], cohort design in 4% (1/28) of the studies [24], and mixed methods (cross-sectional design and qualitative design) in 4% (1/28) of the studies [36]. Most studies were primary (26/28, 92%). The data in one study was reported from app entries [24], and another study used secondary data from a national survey [27]. The quality of most included studies was moderate to high (11 and 12, respectively). In all, 18% (5/28) of the studies were of low quality (Multimedia Appendix 1). Most studies were rated as valuable, despite the quality assessment score.

Figure 1. Study selection flow chart.



The Participants' Characteristics

The participants in 36% (10/28) of the studies included patients with type 2 diabetes mellitus (T2DM) only [26,29,32-34,37-39,45,48], 18% (5/28) of the studies included patients with type 1 diabetes mellitus and T2DM [22,35,43,46,47], and 7% (2/28) of the studies included patients with diabetes mellitus without specifying the type [25,41]. In 11% (3/28) of the studies, patients had chronic conditions, including diabetes [24,27,31], and 11% (3/28) of the studies included patients with diabetes mellitus and cardiovascular disease [30,42,44]. In addition, 14% (4/28) of the studies included patients and HCPs [36,44,47,49]; 4% (1/28) of the studies included patients with diabetes, HCPs, and research assistants [30] and 4% (1/28) of the studies were conducted exclusively with HCPs [23]. The HCPs included in the studies were dietitians, nurses, diabetes educators, community pharmacists, physicians, and podiatrists. A study included HCPs

and decision makers [40], and another study included patients with prediabetes or T2DM and family, friends, and HCPs [28].

Most of the included studies (20/28, 71%) recruited <100 participants, 14% (4/28) of the studies had 100 to 500 participants [25,35,41,47], 7% (2/28) of the studies had 500 to 1000 participants [24,39], and 11% (3/28) of the studies recruited >1000 participants [27,42,49].

All studies involved patients aged >18 years, except for a study that involved patients aged <18 years [41]. On average, the patients taking part in the included studies were in their 30s in one study [46], 40s [27] in another study, 50s in studies (9/26, 35%) [25,31,33,34,37,42,45,47,49], and 60s in studies (7/26, 27%) [22,25,29,39,43,44,48]. A total of 4 studies did not report the patients' age [28,30,35,36], and 3 studies reported a range of patient ages [24,38,41]. For the studies involving HCPs, a study reported the mean age of 38 (SD 6.2) years [44], 4 studies only provided the participants' age range [23,33,47,49] and one study did not report the age of the participants [36].

mHealth Interventions

Various mHealth interventions were explored in the reviewed studies. A total of 21 studies examined mHealth apps for diabetes, and 4 studies explored mHealth interventions for diabetes, including mobile apps [22,35,37,40]. In addition, 3 studies explored eHealth interventions for diabetes, including mHealth mobile apps [31,33,45].

Multimedia Appendix 2 [22-49] summarizes the study design, participant characteristics, mHealth interventions used, key outcomes, and determinants of app adoption reported in the included studies.

Factors Affecting the Adoption of DSM Apps

This part is organized into two main sections: (1) factors affecting patients' use of DSM apps and (2) factors affecting HCPs' recommendation of DSM apps. Each section is further divided into subsections. The included studies identified many factors that were facilitators or barriers to adoption, which were weighed against the study design and sample size to highlight the prevalence of the reported factors.

Factors Affecting Patients' Use of DSM Apps

The patients' sociodemographic and diabetes characteristics, perceptions and experiences, and desired app characteristics determine the likelihood of app adoption.

The Patient's Sociodemographic and Diabetes Characteristics

A total of 33% (9/27) of studies found that younger patients were more likely to use DSM apps [22,35,39,41,42,45,47,49]. In addition, 3 studies reported that female patients [35,41,42] and those with a higher level of education were more likely to engage in DSM app use [41,42,49]. Ernsting et al [42] reported that health app users have a higher level of eHealth literacy (the ability to use information technology for health); the higher the eHealth literacy, the more likely patients will adopt DSM apps. A large cross-sectional study by Zhang et al [49], involving 1276 patients revealed that patients with a higher monthly income are more likely to adopt diabetes apps.

Technology use also affects patients' adoption of DSM apps. A total of 3 studies showed that smartphone users are more likely to use health apps [22,24,35]. Furthermore 8 studies reported that patients who do not know how to use apps or find apps difficult to use were less likely to use DSM apps [25,26,38,39,43-46]. Finally, 5 studies reported that training patients on how to use apps improves their adoption [34,39,41,43,44].

The duration of diagnosis, frequency of blood glucose monitoring and physical activity, and diabetes control affect patients' adoption of DSM apps. A total of 3 studies reported that newly diagnosed patients were more likely to use DSM apps [32,33,39]. In addition, patients who regularly monitor their blood glucose levels [39] and undertake regular physical activity [42] were more likely to adopt DSM apps. Patients whose diabetes is adequately controlled and who are not experiencing diabetic complications are less likely to adopt DSM apps [38,44]. Table 1 presents the patients' sociodemographic and diabetes characteristics that affected their use of DSM apps.

Table 1. Patients' sociodemographic and diabetes characteristics (N=5396).

Themes, factors, and definitions	Sample size (participants), n (%)	Study type	Reference
Patients' characteristics			
Age: younger patients are more likely to use DSM[a] apps			
	12 (0.22)	Qualitative	[45]
	189 (3.5)	Cross-sectional	[47]
	233 (4.32)	Cross-sectional	[35]
	44 (0.82)	Cross-sectional	[33]
	1500 (27.8)	Cross-sectional	[42]
	60 (1.11)	Cross-sectional	[22]
	796 (14.75)	Cross-sectional	[39]
	355 (6.58)	Cross-sectional	[41]
	1276 (23.65)	Cross-sectional	[49]
Gender: female patients are more likely to use DSM apps			
	233 (4.32)	Cross-sectional	[35]
	1500 (27.8)	Cross-sectional	[42]
	355 (6.58)	Cross-sectional	[41]
Education: the higher the level of education, the more engaged is the patient in app use			
	1500 (27.8)	Cross-sectional	[42]
	355 (6.58)	Cross-sectional	[41]
	1276 (23.65)	Cross-sectional	[49]
eHealth literacy: health app users had higher levels of eHealth literacy	1500 (27.8)	Cross-sectional	[42]
Monthly income: patients with higher income are more likely to use DSM apps	1276 (23.65)	Cross-sectional	[49]
Technology use			
Smartphone users are more interested in using health apps			
	233 (4.32)	Cross-sectional	[35]
	60 (1.11)	Cross-sectional	[22]
	503 (9.32)	Cohort	[24]
Patients with difficulties in using new technology are less likely to use DSM apps			
	29 (0.54)	Qualitative	[44]
	30 (0.56)	Qualitative	[38]
	21 (0.34)	Qualitative	[46]
	12 (0.22)	Qualitative	[45]
	287 (5.32)	Qualitative	[25]
	18 (0.33)	Qualitative	[26]
	16 (0.3)	Qualitative	[43]
	796 (14.75)	Cross-sectional	[39]
Training on how to use an app improves its adoption			
	29 (0.54)	Qualitative	[44]
	11 (0.2)	Qualitative	[34]
	16 (0.3)	Qualitative	[43]
	355 (6.58)	Cross-sectional	[41]

Themes, factors, and definitions	Sample size (participants), n (%)	Study type	Reference
	796 (14.75)	Cross-sectional	[39]
Diabetes characteristics			
Length of diagnosis: newly diagnosed patients are more likely to use DSM apps			
	16 (0.3)	Qualitative	[32]
	44 (0.82)	Cross-sectional	[33]
	796 (14.75)	Cross-sectional	[39]
Frequent monitoring of blood glucose levels: patients who frequently monitor sugar levels are more likely to use DSM apps	796 (14.75)	Cross-sectional	[39]
Being active: physically active patients are more likely to use DSM apps	1500 (27.8)	Cross-sectional	[42]
Controlled patients: patients not experiencing problems with diabetes are less likely to use DSM apps			
	29 (0.54)	Qualitative	[44]
	30 (0.56)	Qualitative	[38]

[a]DSM: diabetes self-management.

The Patients' Perceptions and Experiences

A total of 10 studies reported that patients were confident in their DSM without the need for apps, and they did not perceive or were uncertain of the benefits of DSM apps [26,27,32,34,36,38,39,43,47,48]. Interestingly, in 2 smaller qualitative studies, patients reported that they would not use DSM apps, as this puts them in full control of their diabetes and makes them accountable for their behaviors [26,45].

In addition, 2 studies reported that patients would not use DSM apps because they preferred direct and in-person services and interactions [22,45]. However, 5 studies reported that patients are more likely to use DSM apps if recommended by HCPs [26,30,38,41,49], other patients, or the media [49].

Other barriers to the use of DSM apps relate to patients' experiences with the apps. Patients are less likely to use DSM apps if data entry is onerous [26,32,36,37,43,48] or patients could not integrate the app with daily activities, creating time constraints [26,32,36,43,44]. Patients are less likely to use DSM apps if they are not aware of their existence [26,36,38,39,47]. Table 2 presents the perceptions and experiences that affect patients' use of DSM apps.

Table 2. Patients' perceptions and experiences (N=3027).

Themes, factors, and definitions	Sample size (participants), n (%)	Study type	Reference
Patients' perceptions			
No perceived benefit: patients are confident without using apps and do not perceive and are uncertain of the benefits of the app in DSM[a]			
	16 (0.53)	Qualitative	[32]
	30 (0.99)	Qualitative	[38]
	9 (0.3)	Qualitative	[36]
	11 (0.36)	Qualitative	[34]
	16 (0.53)	Qualitative	[43]
	18 (0.6)	Qualitative	[26]
	24 (0.79)	Qualitative	[48]
	189 (6.24)	Cross-sectional	[47]
	163 (5.38)	Cross-sectional	[27]
	796 (26.3)	Cross-sectional	[39]
Taking charge and accountability: patients worry that apps put them in full control of their diabetes and make them accountable for their behavior			
	12 (0.4)	Qualitative	[45]
	18 (0.6)	Qualitative	[26]
Direct contact: patients prefer in-person services			
	12 (0.4)	Qualitative	[45]
	60 (1.98)	Cross-sectional	[22]
Recommendation			
Patients are more likely to use DSM apps if recommended by HCPs[b]			
	30 (0.99)	Qualitative	[38]
	18 (0.6)	Qualitative	[26]
	8 (0.26)	Qualitative	[30]
	355 (11.73)	Cross-sectional	[41]
	1276 (42.15)	Cross-sectional	[49]
Patients are more likely to use DSM apps if recommended by other patients	1276 (42.15)	Cross-sectional	[49]
Patients are more likely to use DSM apps if recommended by media	1276 (42.15)	Cross-sectional	[49]
Lack of awareness of existing apps: patients do not know of existing DSM apps			
	30 (0.99)	Qualitative	[38]
	9 (0.3)	Qualitative	[36]
	18 (0.6)	Qualitative	[26]
	189 (6.24)	Cross-sectional	[47]
	796 (26.3)	Cross-sectional	[39]
Patients' experiences			
Data entry: patients find data entry burdensome			
	16 (0.53)	Qualitative	[45]
	9 (0.3)	Qualitative	[36]
	15 (0.5)	Qualitative	[37]
	18 (0.6)	Qualitative	[26]
	16 (0.53)	Qualitative	[43]

Themes, factors, and definitions	Sample size (participants), n (%)	Study type	Reference
	24 (0.79)	Qualitative	[48]
	355 (11.73)	Cross-sectional	[41]
Time constraint: patients could not integrate the app with daily activities			
	29 (0.96)	Qualitative	[44]
	16 (0.53)	Qualitative	[32]
	9 (0.3)	Qualitative	[36]
	18 (0.6)	Qualitative	[26]

[a]DSM: diabetes self-management.

[b]HCP: health care professional.

The Desired App Characteristics

Other factors that affect patients' use of DSM apps relate to the functions and features of these apps. The studies included in this review either evaluated DSM apps with specific functions or reported on patients' preferred app functions and features that would encourage them to adopt the DSM app and integrate it into their self-management routines. The functions and features are presented in Tables 3 and 4, respectively.

Functions related to nutrition and diet have been reported in 73% (19/26) of studies (tracking diet, calorie counting, and healthy meal recipes) [22,26,27,29,32-35,37-39,41-44,46-49], followed by blood glucose monitoring functions (diaries and reminders to check blood glucose levels) reported in 58% (15/26) of studies [22,26,29,32,33,35,38,39,41,43,46-49], and physical activity functions (tracking, pedometer functions, and reminders to exercise) reported in 54% (14/26) studies [22,27,29,34,35,37-39,41,42,44,46,48,49].

Patients also prefer DSM apps to include medicine management functions such as insulin calculators, tracking medications, and medication reminders, as reported in 13 studies [22,29-31,35,37,38,41,43,44,46,47,49]. Weight management functions were reported in 11 studies [22,27,29,35,37-39,41-43,46], followed by mental health functions in 7 studies, including stress management and emotional support [27,32,37,39,42,44,46]. Appointment reminder preferences were reported in 4 studies [31,38,46,47], and sleep pattern functions were reported in 2 studies [29,42].

Patients are more likely to use DSM apps if they facilitate communication with HCPs (12/26, 46%) [26,30,31,33,34,36,38,41,43,44,48,49] and patients (7/26, 27%) [28,31,35-37,44,49], are visually appealing (10/26, 39%) [26,32,35-38,43,44,46,48], are easy to use (8/26, 31%) [26,30,34,37,38,41,48,49], are easy to understand (1/26, 4%) [43] and easy to access (1/26, 4%) [48], ensure privacy and security (7/26, 27%) [25,30,35,36,41,43,46], provide instant feedback (5/26, 19%) [32,34,37,42,48] and personalized information (2/26, 8%) [26,44], enable goal setting (4/26, 15%) [26,37,42,46], are not costly (5/26, 19%) [24,38,43,48,49], and are available in the patients' native language (1/26, 4%) [46]. In addition, patients are more likely to use DSM apps if they provide relevant information about diabetes, latest research, and trends (8/26, 31%) [26,31,36-38,43,46,48], increase access to patients' medical history and notes (3/26, 12%) [22,31,47], and provide information on how to detect and manage hypoglycemia (2/26, 8%) [39,46]. Patients are less likely to use DSM apps if they experience technical problems that cause frequent app crashes (4/26, 15%) [35,38,43,44].

Table 3. The desired diabetes self-management apps' functions (N=21).

App function	Studies, n (%)	References
Nutrition and diet; for example, carbohydrates counting, diet plans, and reference of nutritional values on dishes in restaurants	19 (90.5)	[22,26,27,29,32-35,37-39,41-44,46-49]
Blood glucose monitoring; for example, diabetes diary, blood sugar test reminder, and monitoring hypoglycemia symptoms	15 (71.43)	[22,26,29,32,33,35,38,39,41,43,46-49]
Physical activity; for example, tracking physical activity and exercise plan	14 (66.67)	[22,27,29,34,35,37-39,41,42,44,46,48,49]
Medicines management; for example, insulin dose calculator and medication reminders	13 (61.9)	[22,29-31,35,37,38,41,43,44,46,47,49]
Weight management; for example, tracking weight and weight loss plans	11 (52.38)	[22,27,29,35,37-39,41-43,46]
Mental health; for example, monitoring mood and well-being and social support	7 (33.33)	[27,32,37,39,42,44,46]
Appointments reminders	4 (19.05)	[31,38,46,47]
Sleep pattern	2 (9.53)	[29,42]

Table 4. The desired diabetes self-management (DSM) apps' features (N=5524).

Theme (apps' features): factors and definitions	Sample size (participants) n (%)	Study type	Reference
Ease of use			
Patients are more likely to use DSM apps if they are easy to use			
	15 (0.27)	Qualitative	[37]
	30 (0.54)	Qualitative	[38]
	18 (0.33)	Qualitative	[26]
	11 (0.2)	Qualitative	[34]
	8 (0.15)	Qualitative	[30]
	24 (0.43)	Qualitative	[48]
	355 (6.43)	Cross-sectional	[41]
	1276 (23.1)	Cross-sectional	[49]
Patients are more likely to use DSM apps if they are easy to understand	16 (0.29)	Qualitative	[43]
Patients are more likely to use DSM apps if they are easy to access	24 (0.43)	Qualitative	[48]
Communication			
Patients are more likely to use DSM apps if they enable communication with HCPs[a]			
	29 (0.52)	Qualitative	[44]
	30 (0.54)	Qualitative	[38]
	9 (0.16)	Qualitative	[36]
	18 (0.33)	Qualitative	[26]
	11 (0.2)	Qualitative	[34]
	16 (0.29)	Qualitative	[43]
	8 (0.15)	Qualitative	[30]
	24 (0.43)	Qualitative	[48]
	53 (0.96)	Qualitative	[31]
	44 (0.8)	Cross-sectional	[33]
	355 (6.43)	Cross-sectional	[41]
	1276 (23.1)	Cross-sectional	[49]
Patients are more likely to use DSM apps if they enable communication and knowledge sharing with other patients			
	29 (0.52)	Qualitative	[44]
	15 (0.27)	Qualitative	[37]
	9 (0.16)	Qualitative	[36]
	31 (0.56)	Qualitative	[28]
	53 (0.96)	Qualitative	[31]
	233 (4.22)	Cross-sectional	[35]
	1276 (23.1)	Cross-sectional	[49]
Patients are more likely to use DSM apps if they have a social media component			
	31 (0.56)	Qualitative	[28]
	8 (0.15)	Qualitative	[30]
	233 (4.22)	Cross-sectional	[35]
Feedback: patients are more likely to use DSM apps if they get real-time feedback			
	16 (0.29)	Qualitative	[32]
	15 (0.27)	Qualitative	[37]

Theme (apps' features): factors and definitions	Sample size (participants) n (%)	Study type	Reference
	11 (0.2)	Qualitative	[34]
	24 (0.43)	Qualitative	[48]
	1500 (27.15)	Cross-sectional	[42]
Customization: patients are more likely to use DSM apps if they provide personalized or tailored information			
	29 (0.52)	Qualitative	[44]
	18 (0.33)	Qualitative	[26]
Presentation			
Patients are more likely to use DSM apps if they include visual aids or visual effects			
	29 (0.52)	Qualitative	[44]
	16 (0.29)	Qualitative	[32]
	30 (0.54)	Qualitative	[38]
	21 (0.38)	Qualitative	[46]
	9 (0.16)	Qualitative	[36]
	15 (0.27)	Qualitative	[37]
	18 (0.33)	Qualitative	[26]
	16 (0.29)	Qualitative	[43]
	24 (0.43)	Qualitative	[48]
	233 (4.22)	Cross-sectional	[35]
Patients prefer a clear layout of apps and a suitable font size	30 (0.54)	Qualitative	[38]
Goal setting: patients are more likely to use DSM apps if they set up goals			
	21 (0.38)	Qualitative	[46]
	15 (0.27)	Qualitative	[37]
	18 (0.33)	Qualitative	[26]
	1500 (27.15)	Cross-sectional	[42]
Privacy and security: patients are more likely to use DSM apps if they ensure data privacy and security			
	21 (0.38)	Qualitative	[46]
	9 (0.16)	Qualitative	[36]
	287 (5.2)	Qualitative	[25]
	16 (0.29)	Qualitative	[43]
	8 (0.15)	Qualitative	[30]
	233 (4.22)	Cross-sectional	[35]
	355 (6.43)	Cross-sectional	[41]
Cost: patients consider the cost of apps when deciding to use DSM apps			
	503 (9.11)	Cohort	[24]
	30 (0.54)	Qualitative	[38]
	16 (0.29)	Qualitative	[43]
	24 (0.43)	Qualitative	[48]
	1276 (23.1)	Cross-sectional	[49]
Technical problems: patients are less likely to use DSM apps if they experience technical problems or app crashes			
	29 (0.52)	Qualitative	[44]
	30 (0.54)	Qualitative	[38]
	16 (0.29)	Qualitative	[43]
	233 (4.22)	Cross-sectional	[35]

Theme (apps' features): factors and definitions	Sample size (participants) n (%)	Study type	Reference
Language: patients are more likely to use apps if they are in their native language in addition to English	21 (0.38)	Qualitative	[46]
Information			
Information about diabetes and the latest research findings			
	30 (0.54)	Qualitative	[38]
	21 (0.38)	Qualitative	[46]
	9 (0.16)	Qualitative	[36]
	15 (0.27)	Qualitative	[37]
	18 (0.33)	Qualitative	[26]
	16 (0.29)	Qualitative	[43]
	24 (0.43)	Qualitative	[48]
	53 (0.96)	Qualitative	[31]
Patient information, medical history, and medical notes			
	53 (0.96)	Qualitative	[31]
	189 (3.42)	Cross-sectional	[47]
	60 (1.09)	Cross-sectional	[22]
Information about symptoms of hypoglycemia and its management			
	21 (0.38)	Qualitative	[46]
	796 (14.41)	Cross-sectional	[39]

[a]HCP: health care professional.

Factors Affecting HCPs' Recommendation of DSM Apps

Only a small number of studies involved HCPs [23,28,30,40,44,47,49], despite their role in promoting and facilitating DSM. Table 5 presents the relevant findings.

Some factors identified by patients as determinants of DSM app adoption have also been reported by HCPs. These include patients' characteristics, beliefs, and experiences. HCPs reported that patients who find it difficult to use or access technology are less likely to use DSM apps, and HCPs will be reluctant to recommend DSM apps to those patients [23,30,44]. Furthermore, HCPs are more likely to recommend DSM apps if they are easy to use [23,30], easy to access [23], provide prompt real-time feedback [30], improve communication between patients and HCPs [49], are free of charge [23,49], and are available in the patients' language [23]. HCPs also reported in the study by Zhang et al [49] that patients do not trust diabetes apps, and hence, will not be using them and that patients are less likely to use DSM apps if they require onerous and time-consuming data entry tasks.

Similar to patients' reports, HCPs would recommend DSM apps if they provide information about diabetes and the latest research findings [30]. Other similar factors include the desired functions, features, and information of the apps. Similar to patients, HCPs would recommend DSM apps if they include nutrition and diet functions [23,47], blood glucose monitoring [23,49], physical activity tracking [23], medicines' management [47], and weight management [23].

HCPs characteristics, beliefs, and awareness of existing DSM apps also affect their recommendation to patients. A study reported that HCPs aged between 40 and 49 years are most likely to recommend DSM apps, and awareness of diabetes apps increases with the HCP's age [49]. Moreover, HCPs with Master of Science degrees, those registered as dietitian nutritionists [23], and those working in tertiary care settings [49] are more likely to recommend apps to patients. HCPs who routinely use apps are more likely to recommend apps to their patients. Those who are not *technology savvy* are likely to require training sessions on how to use apps before recommending them [23]. Zhang et al [49] suggested that HCPs are not convinced of the impact of DSM apps on blood glucose levels; therefore, they may be reluctant to recommend them. Furthermore, HCPs' lack of awareness of existing or appropriate DSM apps hinders their recommendations to patients [23,49].

Other factors that may hinder HCPs' recommendation of app use are related to work pressure. A total of 3 studies highlighted that the heavy workload of HCPs would prevent them from recommending apps, given that they lack the time needed to train patients on how to use the app [23,30,44,49]. HCPs reported in the study by Zhang et al [49] that they may not recommend diabetes apps to patients, as it is not clear if it is legal to provide diabetes care through apps and how to bill the patient for this internet-based care.

Table 5. Summary of the factors affecting health care professionals' (HCPs) recommendations of diabetes self-management (DSM) apps (N=1297).

Themes, factors, and definitions	Sample size (participants), n (%)	Study type	Reference
Patients' characteristics—technology use: HCPs report that patients who face difficulties in using or accessing to technology are less likely to use DSM apps and less likely to recommend apps for them			
	5 (0.39)	Qualitative	[44]
	6 (0.46)	Qualitative	[30]
	583 (44.95)	Cross-sectional	[23]
Patients' beliefs—patients' distrust: HCPs reported that the main obstacle to use apps is patients' distrust of the apps	608 (46.88)	Cross-sectional	[49]
Patients' experiences			
Data entry: HCPs report that the patients may find data entry burdensome	6 (0.46)	Qualitative	[30]
Time constraint: HCPs report that using apps could be time consuming for patients	583 (44.95)	Cross-sectional	[23]
HCPs characteristics			
Age: HCPs awareness about apps increases with age; HCPs aged between 40 and 49 years are more likely to recommend apps for patients	608 (46.88)	Cross-sectional	[49]
Educational levels: HCPs with masters' degree and registered dietician nutritionists are more likely to recommend apps for patients	583 (44.95)	Cross-sectional	[23]
Clinical settings: HCPs in tertiary care are more likely to recommend and use DSM apps for patients	608 (46.88)	Cross-sectional	[49]
Technology use: HCPs who are not technology savvy require more training about apps			
	5 (0.39)	Qualitative	[44]
	583 (44.95)	Cross-sectional	[23]
HCPs beliefs—no perceived benefits: HCPs are less likely to recommend apps because of the lack of evidence about their effectiveness	608 (46.88)	Cross-sectional	[49]
HCPs awareness—lack of awareness			
HCPs do not know of the existing apps			
	95 (7.32)	Cross-sectional	[36]
	608 (46.88)	Cross-sectional	[49]
HCPs do not know about the suitable apps to recommend	608 (46.88)	Cross-sectional	[49]
Work pressures			
Legal issues: HCPs are less likely to recommend apps for managing diabetes because they do not know if it is legal to use apps to manage patients	608 (46.88)	Cross-sectional	[49]
Workload: workload and workflow challenges are the main barriers to recommend DSM apps			
	5 (0.39)	Qualitative	[44]
	6 (0.46)	Qualitative	[30]
	608 (46.88)	Cross-sectional	[49]
Billing issues: uncertainty on how to bill the patients about health care provided through the apps	608 (46.88)	Cross-sectional	[49]
Apps features			
Ease of use			
HCPs are more likely to recommend DSM apps to patients if they are easy to use			
	6 (0.46)	Qualitative	[30]
	583 (44.95)	Cross-sectional	[23]
HCPs are more likely to recommend DSM apps to patients if it they are easy to access	583 (44.95)	Cross-sectional	[23]

Themes, factors, and definitions	Sample size (participants), n (%)	Study type	Reference
Feedback: HCPs are more likely to recommend DSM apps to patients if they provide real-time feedback	6 (0.46)	Qualitative	[30]
Communication: HCPs are more likely to recommend DSM apps to patients if they improve communication with HCPs	608 (46.88)	Cross-sectional	[49]
Cost: HCPs are more likely to recommend DSM apps to patients if apps are free of charge			
	583 (44.95)	Cross-sectional	[23]
	608 (46.88)	Cross-sectional	[49]
Multi-language: HCPs are less likely to recommend DSM apps for patients if apps are not available in the patients' language	583 (44.95)	Cross-sectional	[23]
Apps' information provision: HCPs would like the apps to have information about diabetes and new research findings	6 (0.46)	Qualitative	[30]

Discussion

Principal Findings

This study systematically reviewed the determinants of DSM app use by patients and their recommendations by HCPs, highlighting their prevalence and significance in facilitating and hindering their uptake. To our knowledge, this is the first review exploring the prevalence and determinants of use by patients with T2DM and HCPs' recommendations of mobile apps for DSM.

Patients' sociodemographic characteristics are determinants of app use in DSM. Age has been consistently reported to be a key influencing factor. Younger [56-59], female [60,61] patients were more likely to use DSM apps. Older patients are less likely to engage in digital technologies and health apps [62]. However, the current COVID-19 pandemic highlights that, when necessary, older patients can effectively interact with mobile apps that are beneficial and meet their needs, such as social networking apps and digital health apps [63]. Older patients are an important population to target to improve DSM behaviors [64], given the high prevalence of this condition among this group. Notably, the literature often focuses on biological age as a factor and the assumed decline in cognitive function, sight, hearing, and motor skills over time. However, when considering technology adoption, the concept of age should be expanded to incorporate the *technological age* of patients; people who are aged 60 years in 2020 have had at least 20 years of familiarity or experience with digital technology [65].

Patients' use of DSM apps is also influenced by their level of education, eHealth literacy, perceptions and digital experiences, and technical skills [56,66-71]. Interestingly, the duration of diagnosis also affected the use of DSM apps. Newly diagnosed patients are more likely to use DSM apps, as shown in the qualitative study by Baptista et al [71]. The authors further clarified that patients may become frustrated with the *basic* content of the apps as they become more experienced with diabetes management.

Direct recommendations by health professionals have been suggested as a significant influencer of patients' use of DSM apps [72]. However, only a few studies have explored diabetes HCPs' recommendation of DSM apps and their integration into care pathways. Clinicians are still apprehensive about recommending DSM apps, especially that consensus regarding the strength of their evidence base and evaluation methods is yet to be reached [73].

Several determinants related to DSM apps reported in our review were also postulated as constructs of the main adoption theories; for example, diffusion of innovation theory [74], technology acceptance model [75], and the unified theory of acceptance and use of technology [76]. These include the relative advantages of apps in DSM, compatibility with daily schedules, and ease of use.

It was found that patients with type 2 diabetes prefer interactive apps with functions that aid them in maintaining a healthy lifestyle, reducing weight, and managing their medicines. Privacy, security, and costs also affect use. These are in line with the findings of the review by Adu et al [77] for developing diabetes apps and the review of diabetes-related applications by Doyle-Delgado and Chamberlain [78], as well as the reviews for other health conditions such as hypertension [79], gestational diabetes [80], and chronic conditions [81]. Interestingly, mental health functions were desired to be part of diabetes apps rather than separate or generic apps, which highlights the importance patients assign to integrated mental and diabetes health care.

Studies exploring HCPs' use and recommendations of DSM apps are scarce. Our review identified similar factors affecting HCPs' recommendations of DSM to their patients. HCPs are a diverse group of technology users, and their own characteristics and experiences with mobile apps affect their likelihood of recommending these apps [82]. This highlights the need to integrate digital health education into health care curricula [82]. Furthermore, workload pressures [19,66,67] have also been reported to hinder HCPs' recommendation of apps, especially if time is required to train patients. It is important to consider that because of the lack of regulatory frameworks, digital health clinical guidelines, institutional review, and validation of available apps, HCPs are likely to hesitate to recommend them [13,83].

Future Research

Looking forward, there are a few issues to consider, especially that digital health apps are likely to be one of the legacies of the COVID-19 pandemic, disrupting traditional health care delivery models [84]. First, researchers have investigated the

role and effectiveness of these apps as stand-alone or complementary resources. Efforts should be dedicated to investigate how DSM apps can be integrated into care pathways [83,85], and to explore the roles and responsibilities of health care organizations, HCPs, and patients in a system where DSM apps put the patient in *the driver seat* of managing their condition, the HCP holding the *map* and providing feedback and monitoring, and health care organizations ensuring *road safety* and clinical governance. Furthermore, it is important to explore the impact of ethnicity and race on engagement with and access to diabetes care when mHealth apps and technologies are integrated into care pathways. Mobile apps and technologies may improve access but may also exacerbate inequalities [56]. Answering this question is paramount for designing effective, efficient, and equitable services. It is also important to fully investigate the impact of health care delivery, via mobile apps, on clinical and patient outcomes and how reimbursement and remuneration can be claimed [86].

Second, several ethical issues must be explored when integrating health technologies such as mobile apps into care pathways. One of the most frequently reported barriers to mobile app adoption in health care is the fear of losing human interaction between the patient and the HCP, but at the same time, patients and HCPs see the potential for mobile apps to increase their contact and meaningful input, albeit internet-based. Research could explore how mobile apps can be integrated into care pathways without dehumanizing patients or HCPs [87]. This may warrant investigating how to affect cultural change, especially in relation to the management of long-term conditions and where health technologies fit in the new normal. Privacy is another issue that is often reported when digital technologies are used to deliver health care services. Research could explore the required legal changes, depending on culture and context, to facilitate a safe transfer of information between patients, health care organizations, and relevant stakeholders (and who those stakeholders might be) [88].

Third, regulatory, clinical, and professional bodies' evaluation and support of apps is a key facilitator to encourage health care organizations and HCPs to recommend apps for patient care and for patients to engage with the recommended apps [13]. Research could develop evaluation and implementation frameworks and inform the development of clinical and care guidelines that integrate mobile apps into disease management pathways.

Study Strengths and Limitations

This is the first systematic review to present a synthesis of the determinants that affect patients' use of DSM apps and HCPs recommending them. It also highlights the features and functions required for DSM apps. It draws from a range of studies with qualitative and quantitative designs to improve our understanding of the significance of these factors when deciding to use or recommend a DSM app. However, several potential limitations should be considered when interpreting the findings of this study. First, we included only studies published in peer-reviewed journals, and some of which were of poor quality. Further insights may be reported in conference proceedings and gray literature resources, which were excluded from this study. Second, we included studies that reported on the use of DSM apps in type 2 diabetes, even if those studies reported other types of diabetes or other long-term conditions. This meant that, occasionally, it was not possible to separate data relating to type 2 diabetes from data relating to type 1 diabetes, cardiovascular disease, and other comorbidities. Third, considering the factors reported in this review were not always explicitly highlighted in the included studies, our identification, interpretation, and coding techniques may have affected the review findings. Finally, several of the reported factors are based on what would influence patients and HCPs' *hypothetical* adoption of DSM apps rather than actual use. Therefore, hypothetical bias must be considered when interpreting the findings of our review.

Conclusions

DSM is paramount for improving diabetes outcomes and reducing the risk of complications. Mobile apps can facilitate self-management activities if patients use them and HCPs recommend them. Addressing the technology, patient, and HCP factors that may hinder the use of DSM apps can improve their role in diabetes care, especially if these apps are integrated into diabetes care pathways.

Authors' Contributions

HA and IB conceptualized the study. HA, IB, and ZA designed the methodology. HA, AAH, and IB performed data collection, and the data were validated by HA and IB. Formal analysis was performed by HA and IB, and investigation, by SA and IB. The original draft was written by HA, IB, and ZA and was reviewed and edited by HA, IB, ZA, AAH, and DA. Visualization was performed by HA and IB. The study was supervised by IB, ZA, and DA, and HA and IB were involved in project administration. Funding acquisition was done by HA. All the authors have read and agreed to the published version of the manuscript. This research is a part of PhD studentship of HA. The PhD studentship of HA is funded by the Kuwaiti Ministry of Health (Kuwait).

Conflicts of Interest

None declared.

Multimedia Appendix 1
PubMed search strategy and the results of the quality assessment of the included studies.
[DOCX File , 104 KB - diabetes_v7i3e28153_app1.docx]

Multimedia Appendix 2
Summary and characteristics of the included studies.
[DOCX File , 41 KB - diabetes_v7i3e28153_app2.docx]

References

1. IDF Diabetes Atlas. International Diabetes Federation. 2019. URL: https://diabetesatlas.org/upload/resources/material/20200302_133351_IDFATLAS9e-final-web.pdf [accessed 2020-04-06]
2. Wou C, Unwin N, Huang Y, Roglic G. Implications of the growing burden of diabetes for premature cardiovascular disease mortality and the attainment of the Sustainable Development Goal target 3.4. Cardiovasc Diagn Ther 2019 Apr;9(2):140-149 [FREE Full text] [doi: 10.21037/cdt.2018.09.04] [Medline: 31143635]
3. Nichols G, Ustyugova A, Deruaz-Luyet A, Brodovicz K. 16-OR: contributions of chronic kidney disease and cardiovascular disease to medical costs of type 2 diabetes. Diabetes 2019;68(Supplement_1) [FREE Full text] [doi: 10.2337/db19-16-OR]
4. 15-minute minimum consultations, continuity of care through 'micro-teams', and an end to isolated working: this is the future of general practice. Royal College of General Practitioners. URL: https://www.rcgp.org.uk/about-us/news/2019/may/15-minute-minimum-consultations-continuity-of-care.aspx [accessed 2020-06-14]
5. Lee A, Piette J, Heisler M, Janevic M, Rosland AM. Diabetes self-management and glycemic control: the role of autonomy support from informal health supporters. Health Psychol 2019 Feb;38(2):122-132 [FREE Full text] [doi: 10.1037/hea0000710] [Medline: 30652911]
6. Funnell MM, Anderson RM. The problem with compliance in diabetes. JAMA 2000 Oct 04;284(13):1709. [doi: 10.1001/jama.284.13.1709-jms1004-6-1]
7. Self care. Royal College of Nursing. URL: https://www.rcn.org.uk/clinical-topics/public-health/self-care [accessed 2020-03-03]
8. Shrivastava SR, Shrivastava PS, Ramasamy J. Role of self-care in management of diabetes mellitus. J Diabetes Metab Disord 2013 Mar 05;12(1):14 [FREE Full text] [doi: 10.1186/2251-6581-12-14] [Medline: 23497559]
9. Papatheodorou K, Banach M, Bekiari E, Rizzo M, Edmonds M. Complications of diabetes 2017. J Diabetes Res 2018;2018:3086167-3086164 [FREE Full text] [doi: 10.1155/2018/3086167] [Medline: 29713648]
10. Lin X, Xu Y, Pan X, Xu J, Ding Y, Sun X, et al. Global, regional, and national burden and trend of diabetes in 195 countries and territories: an analysis from 1990 to 2025. Sci Rep 2020 Sep 08;10(1):14790 [FREE Full text] [doi: 10.1038/s41598-020-71908-9] [Medline: 32901098]
11. Powers M, Bardsley J, Cypress M, Duker P, Funnell MM, Fischl AH, et al. Diabetes self-management education and support in type 2 diabetes. Diabetes Educ 2017 Feb;43(1):40-53 [FREE Full text] [doi: 10.1177/0145721716689694] [Medline: 28118121]
12. Greenwood DA, Gee PM, Fatkin KJ, Peeples M. A systematic review of reviews evaluating technology-enabled diabetes self-management education and support. J Diabetes Sci Technol 2017 Sep;11(5):1015-1027. [doi: 10.1177/1932296817713506] [Medline: 28560898]
13. Fleming G, Petrie J, Bergenstal R, Holl R, Peters A, Heinemann L. Diabetes digital app technology: benefits, challenges, and recommendations. A consensus report by the European Association for the Study of Diabetes (EASD) and the American Diabetes Association (ADA) diabetes technology working group. Diabetes Care 2020 Jan;43(1):250-260 [FREE Full text] [doi: 10.2337/dci19-0062] [Medline: 31806649]
14. Basilico A, Marceglia S, Bonacina S, Pinciroli F. Advising patients on selecting trustful apps for diabetes self-care. Comput Biol Med 2016 Apr 01;71:86-96. [doi: 10.1016/j.compbiomed.2016.02.005] [Medline: 26897071]
15. Beck J, Greenwood D, Blanton L, Bollinger ST, Butcher MK, Condon JE, et al. 2017 national standards for diabetes self-management education and support. Diabetes Educ 2017 Jul 28;43(5):449-464 [FREE Full text] [doi: 10.1177/0145721717722968]
16. Wu Y, Yao X, Vespasiani G, Nicolucci A, Dong Y, Kwong J, et al. Mobile app-based interventions to support diabetes self-management: a systematic review of randomized controlled trials to identify functions associated with glycemic efficacy. JMIR Mhealth Uhealth 2017 Mar 14;5(3):e35 [FREE Full text] [doi: 10.2196/mhealth.6522] [Medline: 28292740]
17. Fatehi F, Gray LC, Russell AW. Mobile health (mHealth) for diabetes care: opportunities and challenges. Diabetes Technol Ther 2017 Jan;19(1):1-3. [doi: 10.1089/dia.2016.0430] [Medline: 28099051]
18. Zhang Y, Liu C, Luo S, Xie Y, Liu F, Li X, et al. Factors influencing patients' intentions to use diabetes management apps based on an extended unified theory of acceptance and use of technology model: web-based survey. J Med Internet Res 2019 Aug 13;21(8):e15023 [FREE Full text] [doi: 10.2196/15023] [Medline: 31411146]
19. Gagnon M, Ngangue P, Payne-Gagnon J, Desmartis M. m-Health adoption by healthcare professionals: a systematic review. J Am Med Inform Assoc 2016 Jan;23(1):212-220 [FREE Full text] [doi: 10.1093/jamia/ocv052] [Medline: 26078410]
20. Maniam A, Dhillon J, Baghaei N. Determinants of patients' intention to adopt diabetes self-management applications. In: Proceedings of the 15th New Zealand Conference on Human-Computer Interaction. 2015 Presented at: CHINZ 2015: 15th New Zealand Conference on Human-Computer Interaction; Sep 3 - 4, 2015; Hamilton New Zealand URL: https://doi.org/10.1145/2808047.2808059 [doi: 10.1145/2808047.2808059]

21. Byambasuren O, Beller E, Glasziou P. Current knowledge and adoption of mobile health apps among Australian general practitioners: survey study. JMIR Mhealth Uhealth 2019 Jun 03;7(6):e13199 [FREE Full text] [doi: 10.2196/13199] [Medline: 31199343]
22. Humble JR, Tolley EA, Krukowski RA, Womack CR, Motley TS, Bailey JE. Use of and interest in mobile health for diabetes self-care in vulnerable populations. J Telemed Telecare 2016 Jan;22(1):32-38. [doi: 10.1177/1357633X15586641] [Medline: 26026179]
23. Karduck J, Chapman-Novakofski K. Results of the clinician apps survey, how clinicians working with patients with diabetes and obesity use mobile health apps. J Nutr Educ Behav 2018 Jan;50(1):62-9.e1 [FREE Full text] [doi: 10.1016/j.jneb.2017.06.004] [Medline: 29325664]
24. North F, Chaudhry R. Apple HealthKit and health app: patient uptake and barriers in primary care. Telemed J E Health 2016 Jul;22(7):608-613. [doi: 10.1089/tmj.2015.0106] [Medline: 27172297]
25. Ofili EO, Pemu PE, Quarshie A, Mensah EA, Rollins L, Ojutalayo F, et al. Democratizing discovery health with N=Me. Trans Am Clin Climatol Assoc 2018;129:215-234. [Medline: 30166716]
26. Peng W, Yuan S, Holtz B. Exploring the challenges and opportunities of health mobile apps for individuals with type 2 diabetes living in rural communities. Telemed J E Health 2016 Sep;22(9):733-738 [FREE Full text] [doi: 10.1089/tmj.2015.0180] [Medline: 26982017]
27. Robbins R, Krebs P, Jagannathan R, Jean-Louis G, Duncan DT. Health app use among US mobile phone users: analysis of trends by chronic disease status. JMIR Mhealth Uhealth 2017 Dec 19;5(12):e197 [FREE Full text] [doi: 10.2196/mhealth.7832] [Medline: 29258981]
28. Surkan PJ, Mezzanotte KS, Sena LM, Chang LW, Gittelsohn J, Trolle Lagerros Y, et al. Community-driven priorities in smartphone application development: leveraging social networks to self-manage type 2 diabetes in a low-income African American neighborhood. Int J Environ Res Public Health 2019 Jul 30;16(15):2715 [FREE Full text] [doi: 10.3390/ijerph16152715] [Medline: 31366047]
29. Tanenbaum ML, Bhatt HB, Thomas VA, Wing RR. Use of self-monitoring tools in a clinic sample of adults with type 2 diabetes. Transl Behav Med 2017 Jun;7(2):358-363. [doi: 10.1007/s13142-016-0418-4] [Medline: 27270913]
30. Thies K, Anderson D, Cramer B. Lack of adoption of a mobile app to support patient self-management of diabetes and hypertension in a federally qualified health center: interview analysis of staff and patients in a failed randomized trial. JMIR Hum Factors 2017 Oct 03;4(4):e24 [FREE Full text] [doi: 10.2196/humanfactors.7709] [Medline: 28974481]
31. Zulman DM, Jenchura EC, Cohen DM, Lewis ET, Houston TK, Asch SM. How can ehealth technology address challenges related to multimorbidity? Perspectives from patients with multiple chronic conditions. J Gen Intern Med 2015 Aug;30(8):1063-1070. [doi: 10.1007/s11606-015-3222-9] [Medline: 25691239]
32. Desveaux L, Shaw J, Saragosa M, Soobiah C, Marani H, Hensel J, et al. A mobile app to improve self-management of individuals with type 2 diabetes: qualitative realist evaluation. J Med Internet Res 2018 Mar 16;20(3):e81 [FREE Full text] [doi: 10.2196/jmir.8712] [Medline: 29549070]
33. Dobson KG, Hall P. A pilot study examining patient attitudes and intentions to adopt assistive technologies into type 2 diabetes self-management. J Diabetes Sci Technol 2015 Mar;9(2):309-315. [doi: 10.1177/1932296814560395] [Medline: 25427965]
34. Pludwinski S, Ahmad F, Wayne N, Ritvo P. Participant experiences in a smartphone-based health coaching intervention for type 2 diabetes: a qualitative inquiry. J Telemed Telecare 2016 Apr 21;22(3):172-178. [doi: 10.1177/1357633X15595178] [Medline: 26199275]
35. Conway N, Campbell I, Forbes P, Cunningham S, Wake D. mHealth applications for diabetes: user preference and implications for app development. Health Informatics J 2016 Dec;22(4):1111-1120 [FREE Full text] [doi: 10.1177/1460458215616265] [Medline: 26635324]
36. Kayyali R, Peletidi A, Ismail M, Hashim Z, Bandeira P, Bonnah J. Awareness and use of mHealth apps: a study from England. Pharmacy (Basel) 2017 Jun 14;5(2):A [FREE Full text] [doi: 10.3390/pharmacy5020033] [Medline: 28970445]
37. Kelly L, Jenkinson C, Morley D. Experiences of using web-based and mobile technologies to support self-management of type 2 diabetes: qualitative study. JMIR Diabetes 2018 May 11;3(2):e9 [FREE Full text] [doi: 10.2196/diabetes.9743] [Medline: 30291098]
38. Jeffrey B, Bagala M, Creighton A, Leavey T, Nicholls S, Wood C, et al. Mobile phone applications and their use in the self-management of Type 2 Diabetes Mellitus: a qualitative study among app users and non-app users. Diabetol Metab Syndr 2019;11:84 [FREE Full text] [doi: 10.1186/s13098-019-0480-4] [Medline: 31636719]
39. Trawley S, Baptista S, Browne JL, Pouwer F, Speight J. The use of mobile applications among adults with type 1 and type 2 diabetes: results from the second miles-Australia (miles-2) study. Diabetes Technol Ther 2017 Dec;19(12):730-738. [doi: 10.1089/dia.2017.0235] [Medline: 29028442]
40. Alanzi T. mHealth for diabetes self-management in the Kingdom of Saudi Arabia: barriers and solutions. J Multidiscip Healthc 2018;11:535-546 [FREE Full text] [doi: 10.2147/JMDH.S174198] [Medline: 30349285]
41. Rafiullah M, David SK. Health apps usage and preferences among Saudi patients with diabetes: a survey. Int J Clin Pract 2019 May 17;73(5):e13345. [doi: 10.1111/ijcp.13345] [Medline: 30884059]

42. Ernsting C, Stühmann LM, Dombrowski SU, Voigt-Antons J, Kuhlmey A, Gellert P. Associations of health app use and perceived effectiveness in people with cardiovascular diseases and diabetes: population-based survey. JMIR Mhealth Uhealth 2019 Mar 28;7(3):e12179 [FREE Full text] [doi: 10.2196/12179] [Medline: 30920383]
43. Scheibe M, Reichelt J, Bellmann M, Kirch W. Acceptance factors of mobile apps for diabetes by patients aged 50 or older: a qualitative study. Med 2 0 2015 Mar 02;4(1):e1 [FREE Full text] [doi: 10.2196/med20.3912] [Medline: 25733033]
44. Brandt LR, Hidalgo L, Diez-Canseco F, Araya R, Mohr DC, Menezes PR, et al. Addressing depression comorbid with diabetes or hypertension in resource-poor settings: a qualitative study about user perception of a nurse-supported smartphone app in Peru. JMIR Ment Health 2019 Jun 18;6(6):e11701 [FREE Full text] [doi: 10.2196/11701] [Medline: 31215511]
45. Mathiesen AS, Thomsen T, Jensen T, Schiøtz C, Langberg H, Egerod I. The influence of diabetes distress on digital interventions for diabetes management in vulnerable people with type 2 diabetes: a qualitative study of patient perspectives. J Clin Transl Endocrinol 2017 Sep;9:41-47 [FREE Full text] [doi: 10.1016/j.jcte.2017.07.002] [Medline: 29067269]
46. Kabeza CB, Harst L, Schwarz PE, Timpel P. Assessment of Rwandan diabetic patients' needs and expectations to develop their first diabetes self-management smartphone application (Kir'App). Therapeutic Advances Endocrinol 2019 Apr 26;10:204201881984531. [doi: 10.1177/2042018819845318]
47. Boyle L, Grainger R, Hall RM, Krebs JD. Use of and beliefs about mobile phone apps for diabetes self-management: surveys of people in a hospital diabetes clinic and diabetes health professionals in New Zealand. JMIR Mhealth Uhealth 2017 Jun 30;5(6):e85 [FREE Full text] [doi: 10.2196/mhealth.7263] [Medline: 28666975]
48. Torbjørnsen A, Ribu L, Rønnevig M, Grøttland A, Helseth S. Users' acceptability of a mobile application for persons with type 2 diabetes: a qualitative study. BMC Health Serv Res 2019 Sep 06;19(1):641 [FREE Full text] [doi: 10.1186/s12913-019-4486-2] [Medline: 31492176]
49. Zhang Y, Li X, Luo S, Liu C, Xie Y, Guo J, et al. Use, perspectives, and attitudes regarding diabetes management mobile apps among diabetes patients and diabetologists in China: national web-based survey. JMIR Mhealth Uhealth 2019 Feb 08;7(2):e12658 [FREE Full text] [doi: 10.2196/12658] [Medline: 30735147]
50. Fixsen D, Naoom S, Blase K, Friedman R, Wallace F. Implementation Research: A Synthesis of the Literature. Tampa, FL: University of South Florida, Louis de la Parte Florida Mental Health Institute, The National Implementation Research Network; 2005.
51. Understanding mobile apps. Federal Trade Commission. URL: https://www.consumer.ftc.gov/articles/0018-understanding-mobile-apps [accessed 2020-03-26]
52. CASP checklist. CASP. URL: https://casp-uk.net/casp-tools-checklists/ [accessed 2022-07-03]
53. Systematic reviews of etiology and risk. In: JBI Manual for Evidence Synthesis. Adelaide, South Australia: JBI; 2020.
54. Thomas J, Harden A. Methods for the thematic synthesis of qualitative research in systematic reviews. BMC Med Res Methodol 2008 Jul 10;8:45 [FREE Full text] [doi: 10.1186/1471-2288-8-45] [Medline: 18616818]
55. Hong QN, Pluye P, Bujold M, Wassef M. Convergent and sequential synthesis designs: implications for conducting and reporting systematic reviews of qualitative and quantitative evidence. Syst Rev 2017 Mar 23;6(1):61 [FREE Full text] [doi: 10.1186/s13643-017-0454-2] [Medline: 28335799]
56. Bol N, Helberger N, Weert JC. Differences in mobile health app use: a source of new digital inequalities? Inf Soc 2018 Apr 26;34(3):183-193. [doi: 10.1080/01972243.2018.1438550]
57. Shen C, Wang MP, Chu JT, Wan A, Viswanath K, Chan SS, et al. Health app possession among smartphone or tablet owners in Hong Kong: population-based survey. JMIR Mhealth Uhealth 2017 Jun 05;5(6):e77 [FREE Full text] [doi: 10.2196/mhealth.7628] [Medline: 28583905]
58. Gardner M, Jenkins S, O'Neil D, Wood D, Spurrier B, Pruthi S. Perceptions of video-based appointments from the patient's home: a patient survey. Telemed J E Health 2015 Apr;21(4):281-285 [FREE Full text] [doi: 10.1089/tmj.2014.0037] [Medline: 25166260]
59. Nymberg V, Bolmsjö BB, Wolff M, Calling S, Gerward S, Sandberg M. 'Having to learn this so late in our lives…' Swedish elderly patients' beliefs, experiences, attitudes and expectations of e-health in primary health care. Scand J Prim Health Care 2019 Mar;37(1):41-52 [FREE Full text] [doi: 10.1080/02813432.2019.1570612] [Medline: 30732519]
60. Lupton D, Maslen S. How women use digital technologies for health: qualitative interview and focus group study. J Med Internet Res 2019 Jan 25;21(1):e11481 [FREE Full text] [doi: 10.2196/11481] [Medline: 30681963]
61. Bidmon S, Terlutter R. Gender differences in searching for health information on the internet and the virtual patient-physician relationship in Germany: exploratory results on how men and women differ and why. J Med Internet Res 2015 Jun 22;17(6):e156 [FREE Full text] [doi: 10.2196/jmir.4127] [Medline: 26099325]
62. Isaković M, Sedlar U, Volk M, Bešter J. Usability pitfalls of diabetes mHealth apps for the elderly. J Diabetes Res 2016;2016:1604609 [FREE Full text] [doi: 10.1155/2016/1604609] [Medline: 27034957]
63. Banskota S, Healy M, Goldberg E. 15 smartphone apps for older adults to use while in isolation during the COVID-19 pandemic. West J Emerg Med 2020 Apr 14;21(3):514-525. [doi: 10.5811/westjem.2020.4.47372] [Medline: 32302279]
64. Paiva JO, Andrade RM, de Oliveira PA, Duarte P, Santos IS, Evangelista AL, et al. Mobile applications for elderly healthcare: a systematic mapping. PLoS One 2020 Jul 30;15(7):e0236091 [FREE Full text] [doi: 10.1371/journal.pone.0236091] [Medline: 32730266]

65. Harris M, Cox K, Musgrove C, Ernstberger K. Consumer preferences for banking technologies by age groups. Int J Bank Market 2016;34(4):587-602 [FREE Full text] [doi: 10.1108/IJBM-04-2015-0056]
66. O'Connor S, Hanlon P, O'Donnell CA, Garcia S, Glanville J, Mair F. Understanding factors affecting patient and public engagement and recruitment to digital health interventions: a systematic review of qualitative studies. BMC Med Inform Decis Mak 2016 Sep 15;16(1):120 [FREE Full text] [doi: 10.1186/s12911-016-0359-3] [Medline: 27630020]
67. Alvarado MM, Kum H, Gonzalez Coronado K, Foster MJ, Ortega P, Lawley MA. Barriers to remote health interventions for type 2 diabetes: a systematic review and proposed classification scheme. J Med Internet Res 2017 Feb 13;19(2):e28 [FREE Full text] [doi: 10.2196/jmir.6382] [Medline: 28193598]
68. Kampmeijer R, Pavlova M, Tambor M, Golinowska S, Groot W. The use of e-health and m-health tools in health promotion and primary prevention among older adults: a systematic literature review. BMC Health Serv Res 2016 Sep 05;16 Suppl 5(S5):290 [FREE Full text] [doi: 10.1186/s12913-016-1522-3] [Medline: 27608677]
69. Hahn RA, Truman BI. Education improves public health and promotes health equity. Int J Health Serv 2015;45(4):657-678. [doi: 10.1177/0020731415585986] [Medline: 25995305]
70. Guo SH, Hsing H, Lin J, Lee C. Relationships between mobile eHealth literacy, diabetes self-care, and glycemic outcomes in Taiwanese patients with type 2 diabetes: cross-sectional study. JMIR Mhealth Uhealth 2021 Feb 05;9(2):e18404 [FREE Full text] [doi: 10.2196/18404] [Medline: 33544088]
71. Baptista S, Wadley G, Bird D, Oldenburg B, Speight J, My Diabetes Coach Research Group. User experiences with a type 2 diabetes coaching app: qualitative study. JMIR Diabetes 2020 Jul 17;5(3):e16692 [FREE Full text] [doi: 10.2196/16692] [Medline: 32706649]
72. Rossmann C, Riesmeyer C, Brew-Sam N, Karnowski V, Joeckel S, Chib A, et al. Appropriation of mobile health for diabetes self-management: lessons from two qualitative studies. JMIR Diabetes 2019 Mar 29;4(1):e10271 [FREE Full text] [doi: 10.2196/10271] [Medline: 30924786]
73. The Transformative Power of Mobile Medicine Leveraging Innovation, Seizing Opportunities and Overcoming Obstacles of MHealth. Amsterdam, Netherlands: Elsevier Science; 2019.
74. Rogers E. Diffusion of Innovations, 5th Edition. New York: Free Press; 2003.
75. Davis FD. User acceptance of information technology: system characteristics, user perceptions and behavioral impacts. Int J Man Machine Stud 1993 Mar;38(3):475-487. [doi: 10.1006/imms.1993.1022]
76. Venkatesh V, Davis FD. A theoretical extension of the technology acceptance model: four longitudinal field studies. Manag Sci 2000 Feb;46(2):186-204. [doi: 10.1287/mnsc.46.2.186.11926]
77. Adu MD, Malabu UH, Malau-Aduli AE, Malau-Aduli BS. Users' preferences and design recommendations to promote engagements with mobile apps for diabetes self-management: multi-national perspectives. PLoS One 2018 Dec 10;13(12):e0208942 [FREE Full text] [doi: 10.1371/journal.pone.0208942] [Medline: 30532235]
78. Doyle-Delgado KJ, Chamberlain JJ. Use of diabetes-related applications and digital health tools by people with diabetes and their health care providers. Clin Diabetes 2020 Dec;38(5):449-461 [FREE Full text] [doi: 10.2337/cd20-0046] [Medline: 33384470]
79. Alessa T, Abdi S, Hawley MS, de Witte L. Mobile apps to support the self-management of hypertension: systematic review of effectiveness, usability, and user satisfaction. JMIR Mhealth Uhealth 2018 Jul 23;6(7):e10723 [FREE Full text] [doi: 10.2196/10723] [Medline: 30037787]
80. Chen J, Gemming L, Hanning R, Allman-Farinelli M. Smartphone apps and the nutrition care process: current perspectives and future considerations. Patient Educ Couns 2018 Apr;101(4):750-757. [doi: 10.1016/j.pec.2017.11.011] [Medline: 29169863]
81. Birkhoff SD, Smeltzer SC. Perceptions of smartphone user-centered mobile health tracking apps across various chronic illness populations: an integrative review. J Nurs Scholarsh 2017 Jul;49(4):371-378. [doi: 10.1111/jnu.12298] [Medline: 28605151]
82. Machleid F, Kaczmarczyk R, Johann D, Balčiūnas J, Atienza-Carbonell B, von Maltzahn F, et al. Perceptions of digital health education among European medical students: mixed methods survey. J Med Internet Res 2020 Aug 14;22(8):e19827 [FREE Full text] [doi: 10.2196/19827] [Medline: 32667899]
83. Gordon W, Landman A, Zhang H, Bates DW. Beyond validation: getting health apps into clinical practice. NPJ Digit Med 2020;3:14 [FREE Full text] [doi: 10.1038/s41746-019-0212-z] [Medline: 32047860]
84. Securing a positive health care technology legacy from COVID-19. The Health Foundation. URL: https://www.health.org.uk/publications/long-reads/securing-a-positive-health-care-technology-legacy-from-covid-19 [accessed 2021-06-10]
85. Ramdani B, Duan B, Berrou I. Exploring the determinants of mobile health adoption by hospitals in China: empirical study. JMIR Med Inform 2020 Jul 14;8(7):e14795 [FREE Full text] [doi: 10.2196/14795] [Medline: 32459630]
86. Esser M, Boreham A, Ring C, Schreier J. PNS100 The New Reimbursement Route for Digital Health Applications (DIGA) in Germany: critical appraisal and first evaluation of the possible effect on the German Healthcare System. Value Health 2020 Dec;23:S658-S659. [doi: 10.1016/j.jval.2020.08.1544]
87. Botrugno C. Information technologies in healthcare: enhancing or dehumanising doctor-patient interaction? Health (London) 2021 Jul 18;25(4):475-493. [doi: 10.1177/1363459319891213] [Medline: 31849239]

88. Grundy Q, Chiu K, Held F, Continella A, Bero L, Holz R. Data sharing practices of medicines related apps and the mobile ecosystem: traffic, content, and network analysis. BMJ 2019 Mar 20;364:l920 [FREE Full text] [doi: 10.1136/bmj.l920] [Medline: 30894349]

Abbreviations

DSM: diabetes self-management
HCP: health care professional
mHealth: mobile health
T2DM: type 2 diabetes mellitus

Edited by K Mizokami-Stout; submitted 01.03.21; peer-reviewed by N Gordon, L Nelson, C Della Vecchia, S Li; comments to author 24.04.21; revised version received 30.06.21; accepted 24.03.22; published 28.07.22.

Please cite as:
Alaslawi H, Berrou I, Al Hamid A, Alhuwail D, Aslanpour Z
Diabetes Self-management Apps: Systematic Review of Adoption Determinants and Future Research Agenda
JMIR Diabetes 2022;7(3):e28153
URL: https://diabetes.jmir.org/2022/3/e28153
doi:10.2196/28153
PMID:35900826

Original Paper

Association Between Mobile Health App Engagement and Weight Loss and Glycemic Control in Adults With Type 2 Diabetes and Prediabetes (D'LITE Study): Prospective Cohort Study

Su Lin Lim[1], PhD; Melissa Hui Juan Tay[1], BSc; Kai Wen Ong[1], BSc; Jolyn Johal[1], BND; Qai Ven Yap[2], BSc; Yiong Huak Chan[2], PhD; Genevieve Kai Ning Yeo[1], BA; Chin Meng Khoo[3,4], MBBS, PhD; Alison Yaxley[5], PhD

[1]Department of Dietetics, National University Hospital, Singapore, Singapore

[2]Biostaistics Unit, Yong Loo Lin School of Medicine, National University Singapore, Singapore, Singapore

[3]Division of Endocrinology, Department of Medicine, National University Hospital, Singapore, Singapore

[4]Yong Loo Lin School of Medicine, National University Singapore, Singapore, Singapore

[5]Nutrition and Dietetics, College of Nursing and Health Sciences, Flinders University, Adelaide, Australia

Corresponding Author:
Su Lin Lim, PhD
Department of Dietetics
National University Hospital
5 Lower Kent Ridge Road
Singapore, 119074
Singapore
Phone: 65 67724580
Fax: 65 67791938
Email: su_lin_lim@nuhs.edu.sg

Abstract

Background: Mobile health apps are increasingly used as early intervention to support behavior change for diabetes prevention and control, with the overarching goal of lowering the overall disease burden.

Objective: This prospective cohort study conducted in Singapore aimed to investigate app engagement features and their association with weight loss and improved glycemic control among adults with diabetes and prediabetes from the intervention arm of the Diabetes Lifestyle Intervention using Technology Empowerment randomized controlled trial.

Methods: Diabetes and prediabetes participants (N=171) with a median age of 52 years, BMI of 29.3 kg/m^2, and glycated hemoglobin (HbA_{1c}) level of 6.5% and who were being assigned the Nutritionist Buddy Diabetes app were included. Body weight and HbA_{1c} were measured at baseline, 3 months, and 6 months. A total of 476,300 data points on daily app engagement were tracked via the backend dashboard and developer's report. The app engagement data were analyzed by quartiles and weekly means expressed in days per week. Linear mixed model analysis was used to determine the associations between the app engagements with percentage weight and HbA_{1c} change.

Results: The median overall app engagement rate was maintained above 90% at 6 months. Participants who were actively engaged in ≥5 app features were associated with the greatest overall weight reduction of 10.6% from baseline (mean difference −6, 95% CI −8.9 to −3.2; *P*<.001) at 6 months. Adhering to the carbohydrate limit of >5.9 days per week and choosing healthier food options for >4.3 days per week had the most impact, eliciting weight loss of 9.1% (mean difference −5.2, 95% CI −8.2 to −2.2; *P*=.001) and 8.8% (mean difference −4.2, 95% CI −7.1 to −1.3; *P*=.005), respectively. Among the participants with diabetes, those who had a complete meal log for >5.1 days per week or kept within their carbohydrate limit for >5.9 days per week each achieved greater HbA_{1c} reductions of 1.2% (SD 1.3%; SD 1.5%), as compared with 0.2% (SD 1%; SD 0.6%). in the reference groups who used the features <1.1 or ≤2.5 days per week, respectively.

Conclusions: Higher app engagement led to greater weight loss and HbA_{1c} reduction among adults with overweight or obesity with type 2 diabetes or prediabetes.

Trial Registration: Australian New Zealand Clinical Trials Registry (ANZCTR) ACTRN12617001112358; https://anzctr.org.au/Trial/Registration/TrialReview.aspx?ACTRN=12617001112358

(JMIR Diabetes 2022;7(3):e35039) doi:10.2196/35039

KEYWORDS

engagement; diabetes; prediabetes; mobile health; mHealth; mobile apps; weight loss; glycemic control; glycated hemoglobin; HbA1c change; mobile phone

Introduction

Background

Globally, 374 million people are at an increased risk of developing type 2 diabetes [1]. With the increasingly urbanized and aging population, these numbers are expected to increase to 700 million by 2045 [1]. In Singapore, diabetes accounts for 8.6% of the total disease burden [2]. The prevalence of diabetes in Singapore increased from 8.2% in 2004 to 8.8% in 2017, with the latest prevalence at 9.5% in 2020 [3]. Of greater concern, 1 in 3 patients with diabetes has poor control of their condition and is at increased risk of a host of diabetes-related complications [4]. In addition, people with prediabetes who make up 14.4% of the Singapore population have a one-third chance of developing diabetes in the next 8 years [4]. Therefore, preventing the progression from prediabetes to diabetes and slowing the progression of diabetes are of utmost importance.

Weight reduction is associated with prevention and slowing of diabetes progression in patients with overweight or obesity with prediabetes or diabetes [5]. A 5% weight loss is associated with improved insulin sensitivity, better glycemic control, and reduced need for diabetes medications [5,6]. A 1% decrease in glycated hemoglobin (HbA_{1c}) has been found to decrease death by 21%, myocardial infarction by 14%, and microvascular complications by 37% [7].

Apart from receiving medical care from health care providers, self-management (eg, monitoring of food intake, weight, and blood glucose) is an integral part of diabetes management to achieve sustainable health outcomes. In line with the self-regulation theory, patients with good self-management practices showed better management of their diabetes compared with patients who were simply prescribed medications [8]. In addition, good self-management practices can help patients to lose weight and improve hypertension and hyperlipidemia, which are key cardiovascular risk factors [9].

Numerous mobile apps have been developed to promote diabetes self-management. A meta-analysis with follow-up periods of approximately 6 months revealed a significant HbA_{1c} reduction (mean difference 0.49%, 95% CI 0.30-0.68) through diabetes self-management via mobile phone interactions [8]. Similarly, another meta-analysis of diabetes apps specifically designed to improve self-management practices reported a statistically significant reduction in body weight (mean difference 0.84 kg, 95% CI 0.17-1.51) among participants with diabetes [9].

There is limited research assessing users' app engagement and the association with weight and HbA_{1c} changes in people with diabetes. App engagement studies were not focused on diabetes or had limited description on how engagement data were derived [10]. The question remains as to which app engagement features are associated with weight loss and improved glycemia to replicate similar findings in the real-world application. This prospective cohort study would add insight to the effectiveness of key app engagement functions associated with metabolic benefits among a group of individuals with diabetes risk and non–insulin-dependent diabetes.

Objective

The primary Diabetes Lifestyle Intervention using Technology Empowerment (D'LITE) study has shown that both participants with prediabetes or diabetes achieved significant weight loss with a mean difference of −3.1 kg (95% CI −4.5 to −1.7; $P<.001$) and −2.4 kg (95% CI −3.5 to −1.3; $P<.001$) at 6 months, respectively, when compared with the control group [11,12]. The participants with prediabetes were 2.1 times likely to achieve normoglycemia (defined as $HbA_{1c}<5.7\%$) than in the control group ($P<.018$). Participants with diabetes also experienced a significant decrease in HbA_{1c} levels (mean change −0.7%, SD 1.2% vs −0.3%, SD 1.0%; $P<.01$) [11]. This further accentuates the need for investigating the various engagement levels within the app and its association with weight and HbA_{1c} reduction.

Therefore, the primary aim of our study was to investigate the association between participant engagement with a diabetes app and weight change and glycemic control in adults with diabetes and prediabetes. The findings of this study would provide insights on how diabetes apps could be used effectively to facilitate positive behavioral changes to improve health outcomes.

Methods

Study Design

This prospective cohort study included prespecified subgroup analysis of all participants from the intervention arm of the D'LITE study (N=171) who were assigned the Nutritionist Buddy Diabetes (nBuddy Diabetes) app [11,12]. A full description of the D'LITE study and the intervention details for both diabetes and prediabetes groups have previously been published [11,12].

The conceptualization of the nBuddy Diabetes app was based on behavioral science and the app was built with an extensive local food database and culturally appropriate automated cues [11]. In brief, the nBuddy Diabetes app comprises multiple features intended to support a participant's self-management efforts including self-monitoring features of meal logging, calorie (CAL) and carbohydrate (CHO) limit alerts, and step tracking, which relies on the phone's built-in pedometer and syncing with the user's mobile phone. CAL and CHO limits were autocalculated by the app and individualized based on the participants' input of their current weight, age, gender, and activity level in the app. When the CAL or CHO limit is reached per meal or per day, the automated cues designed with

behavioral science embedded in the app algorithm will send a real-time prompt to remind participants to make a healthier meal choice. In addition, the app provides outcome tracking features such as weight charting and self-monitoring of blood glucose (SMBG), fasting and random blood glucose (RBG), to be inputted by the participants. A chat function involving 2-way communication between the dietitian and participants to facilitate individual lifestyle modification and coaching were made available within the app. Educational videos were uploaded onto the app and participants were notified upon upload via the chat function. Automated suggestions of healthier and culturally appropriate food alternatives and reminders for participants to engage with the app were also included.

At baseline, participants were taught to download and use the nBuddy Diabetes app to facilitate weight loss and glycemic control. Participants were advised to track their food and exercise daily while measuring their body weight twice weekly. During the first 3 months, participants were advised to measure their blood glucose 2 days per week. Participants were provided with a glucometer (FreeStyle Optium Neo) and a digital weighing scale (Omron HN-289). They were encouraged to achieve daily step count goals starting with an initial 3000 steps in the first week, 7000 in the second week, and 10,000 by the third week. Participants were advised to keep within the individualized CAL and CHO limits that were automatically calculated by the app based on the users' profile.

Setting and Participants

The study recruitment was conducted at government polyclinics, general practitioner clinics, health screening facilities, and hospital outpatient clinics in Singapore from October 2017 to September 2019. The inclusion criteria were adults who were 21 to 75 years of age, were literate in English, had a diagnosis of type 2 diabetes or prediabetes, had a BMI of ≥23 kg/m^2, had a smartphone, and had provided written informed consent. Patients were excluded if they had been diagnosed with heart failure, advanced kidney disease, type 1 diabetes, severe cognitive or psychological disabilities, untreated hypothyroidism, thalassemia, or blood disorders or were pregnant. In addition, participants with insulin use, noncompliance to prescribed medications, and anemia were also excluded.

Outcome Variables

Participants were assessed at baseline, 3 months, and 6 months from enrollment. The outcomes of interest were percentage changes in weight and HbA_{1c} levels from baseline to 3 months and 6 months. Body weight was measured using a calibrated digital weighing scale (Omron HN-289) at the clinic, while blood samples were obtained by a research assistant to determine HbA_{1c} levels following the standard methods of testing at National University Hospital Department of Laboratory Medicine and National Healthcare Group Diagnostics (both accredited by the College of American Pathologists). Reductions of 0.5% of HbA_{1c} levels and weight loss of ≥5% are considered clinically meaningful improvements associated with a decrease in cardiovascular risk in patients with diabetes in 12 months [13,14]. As such, the cut-offs of ≥5% weight loss and ≥0.5% HbA_{1c} reduction were chosen for use in interpretation of the data.

Data Sources

App engagement data during the intervention period were tracked via the app's backend dashboard and developer's report. A total of 476,300 data points from the 171 participants were extracted. To coincide with the outcome measurements, the data were analyzed at 2 separate periods from baseline to 3 months and baseline to 6 months.

App engagement was defined as actively using the individual app features. For example, actively using the app features such as entering a body weight value was considered an app engagement while browsing or scrolling through the app was not. With the exception of videos watched, engagement data of all app features were tracked daily and the weekly mean days were derived for baseline to 3 months and baseline to 6 months. Videos watched, on the other hand, were calculated out of 22 videos that were uploaded via the app across 6 months. The exact definitions and derivations of the respective app engagements are presented in Table 1. The app engagement data were categorized into quartiles for comparison and analysis purposes.

Table 1. App engagement definitions.

App engagement	Definitions
Complete meal log	Considered complete if breakfast, lunch, and dinner were logged for the day. However, during Ramadan (Muslim fasting month), breakfast and dinner logged were considered the complete meal log for Muslim participants. The result is presented as the number of days participants had a complete meal log per week.
Any meal log (include incomplete meal log)	Number of days participants keyed in at least 1 food entry per week.
Within carbohydrate limit	Number of days participants kept within their carbohydrate limit as set by the app (only among the participants who had complete meal log) per week.
Within calorie limit	Number of days participants kept within their calorie limit as set by the app per week (only among the participants who had complete meal log).
Choosing healthier food options	Number of days participants consistently selected food choices labeled as healthier choices by the app per week.
Fasting blood glucose measurement	Number of days fasting blood glucose readings were recorded per week.
Random blood glucose measurement	Number of days random blood glucose readings were recorded per week.
Weight charting	Number of days weight was charted per week.
Achieving step count goal	Number of days participants achieved their step count goal per week.
Communication with dietitian	Number of days participants messaged the dietitian in the app per week.
Videos watched	Total number of videos watched during the 6 months.
Overall app use	Number of days participants actively use ≥1 features of the app per week.
App features with ≥75% uptake	App features (any meal log, within carbohydrate limit, within calorie limit, consistent healthier food choices, fasting blood glucose measurement, random blood glucose measurement, weight charting, achieving step count goal, communication with dietitian, and videos watched) with ≥75% uptake across 6 months.

The number of app engagement features with ≥75% uptake was also calculated. With 75% being considered a common and realistic uptake as reiterated by similar mobile health (mHealth) studies in the literature, it was used as a cut-off for more meaningful comparison of data with pre-existing literature [15]. On the basis of the cross-tabulation analysis, the results from 5 features and beyond rendered no additional effect and was taken as the minimal cut-off point for the test of significance.

Statistical Methods

All analyses were performed using SPSS for Windows (version 26.0; SPSS Inc). Descriptive data for continuous variables were presented as median (IQR) or frequencies and percentages for categorical variables. Differences in continuous variables were assessed using the 2-sample *t* test when normality and homogeneity assumptions were satisfied; otherwise, the Mann-Whitney *U* test was used. The chi-square or Fisher exact test was used for categorical variables. The primary unit of analyses was the percentage change in weight and absolute HbA_{1c} levels at months 3 and 6 from baseline. Associations among app engagement behaviors, overall app use rate, and app features with ≥75% uptake on the outcomes were assessed using the Linear Mixed Model analysis to account for the clustering effect of recruitment sources as a random factor, adjusting for demographic and relevant covariates. Subgroup analyses of participants with diabetes and prediabetes were performed to investigate the associations. The app engagement data were categorized into quartiles for comparison and analysis purposes. The lowest quartile of app engagement was used as the reference category. Statistical significance was set at $P<.05$ (2-sided). Data were analyzed using the on-treatment approach, with missing data assumed as noncompliance to the intervention.

Ethics Approval

The study was approved by the National Health care Group Domain Specific Review Board in Singapore (2017/00397), conducted in accordance with the Declaration of Helsinki and aligned with the Strengthening the Reporting of Observational Studies in Epidemiology guidelines [16].

Results

Participants' Descriptive Data

Table 2 describes the baseline characteristics of the participants. A total of 171 participants were assigned to the mobile app group. Of the 171 participants, there were 99 (57.9%) participants with diabetes and 72 (42.1%) participants with prediabetes. At 6 months, 5 participants from the prediabetes group, 5 from the diabetes group, and an additional participant from the diabetes group who missed his 6-month outcome measurements were considered lost to follow up. Of 171, there were 109 (63.7%) males.

Table 2. Demographics of study participants at baseline (N=171).

Characteristics	All participants	Participants with DM[a] (n=99)	Participants with PreDM[b] (n=72)
Age (years), median (IQR)	52 (44-59)	52 (44-59)	52 (46-59)
Sex, n (%)			
Male	109 (63.7)	66 (66.7)	43 (59.7)
Female	62 (36.3)	33 (33.3)	29 (40.3)
Ethnicity, n (%)			
Chinese	123 (71.9)	66 (66.7)	57 (79.2)
Malay	25 (14.6)	18 (18.2)	7 (9.7)
Indian	18 (10.5)	11 (11.1)	7 (9.7)
Others	5 (2.9)	4 (4)	1 (1.4)
Clinical variables, median (IQR)			
Weight (kg)	82.6 (74.2-90.3)	82.6 (75.6-90.8)	82.0 (73.0-89.4)
BMI (kg/m^2)	29.3 (27.1-32.4)	29.8 (27.4-32.4)	28.9 (26.9-32.4)
HbA_{1c}[c] (%)	6.5 (5.9-7.5)	7.3 (6.6-8.0)	5.9 (5.7-6.2)
Fasting blood glucose (mmol/L)	6.8 (5.9-7.9)	7.8 (6.6-8.7)	6.0 (5.7-6.6)
Comorbidity, n (%)			
Hypertension	119 (69.6)	62 (62.6)	57 (79.2)
Hyperlipidemia	120 (70.2)	62 (62.6)	58 (80.6)
Years of diagnosis, mean (SD)	N/A[d]	5.2 (4.1)	2.3 (2.5)

[a]DM: diabetes.

[b]PreDM: prediabetes.

[c]HbA_{1c}: glycated hemoglobin.

[d]N/A: not applicable.

Engagement Rates of nBuddy Diabetes App Features

The overall app use was high for the first 3 months and maintained throughout the 6 months (Table 3). Median overall app engagement rate remained high at above 90% over the course of the intervention. The most used features included step tracking (95.6%), meal logging (76.6%), and communication with the dietitian within the app's chat system (50%). The least used features were RBG monitoring (18%), fasting blood glucose monitoring (19%), and weight charting (26%). This was anticipated owing to prior instructions given to the participants on the frequency (twice a week) of weight charting and SMBG. The trends in the app engagement were similar at baseline to 3 months and 6 months.

Table 3. Engagement rates of the nBuddy[a] Diabetes app features (N=171).

App features engagement	Baseline to 3 months (%)	Baseline to 6 months (%)
Overall app use		
Values, median (IQR)	97.8 (78.9-100.0)	91.7 (60.0-100.0)
Value, range	8.9-100.0	9.4-100.0
Meal logging		
Value, median (IQR)	76.6 (54.0-98.0)	71.0 (30.0-94.0)
Value, range	10.0-100.0	6.0-100.0
Step tracking		
Values, median (IQR)	95.6 (77.8-100.0)	90.0 (59.4-98.9)
Value, range	14.4-100.0	8.3-100.0
FBG[b] monitoring		
Values, median (IQR)	19.0 (8.0-30.0)	12.0 (4.0-19.0)
Value, range	0-86.0	0-69.0
RBG[c] monitoring		
Values, median (IQR)	18.0 (7.0-30.0)	11.0 (3.0-17.0)
Value, range	0-96.0	0-79.0
Weight charting		
Values, median (IQR)	26.0 (16.0-68.0)	18.0 (11.0-54.0)
Value, range	3.0-97.0	2.0-98.0
Communication with dietitian		
Values, median (IQR)	50.0 (29.0-67.0)	43.0 (23.0-63.0)
Value, range	8.0-123.0	4.0-105.0
Videos watched		
Values, median (IQR)	N/A[d]	32.0 (5.0-64.0)
Value, range	N/A	0-100.0

[a]nBuddy: nutritionist buddy.

[b]FBG: fasting blood glucose.

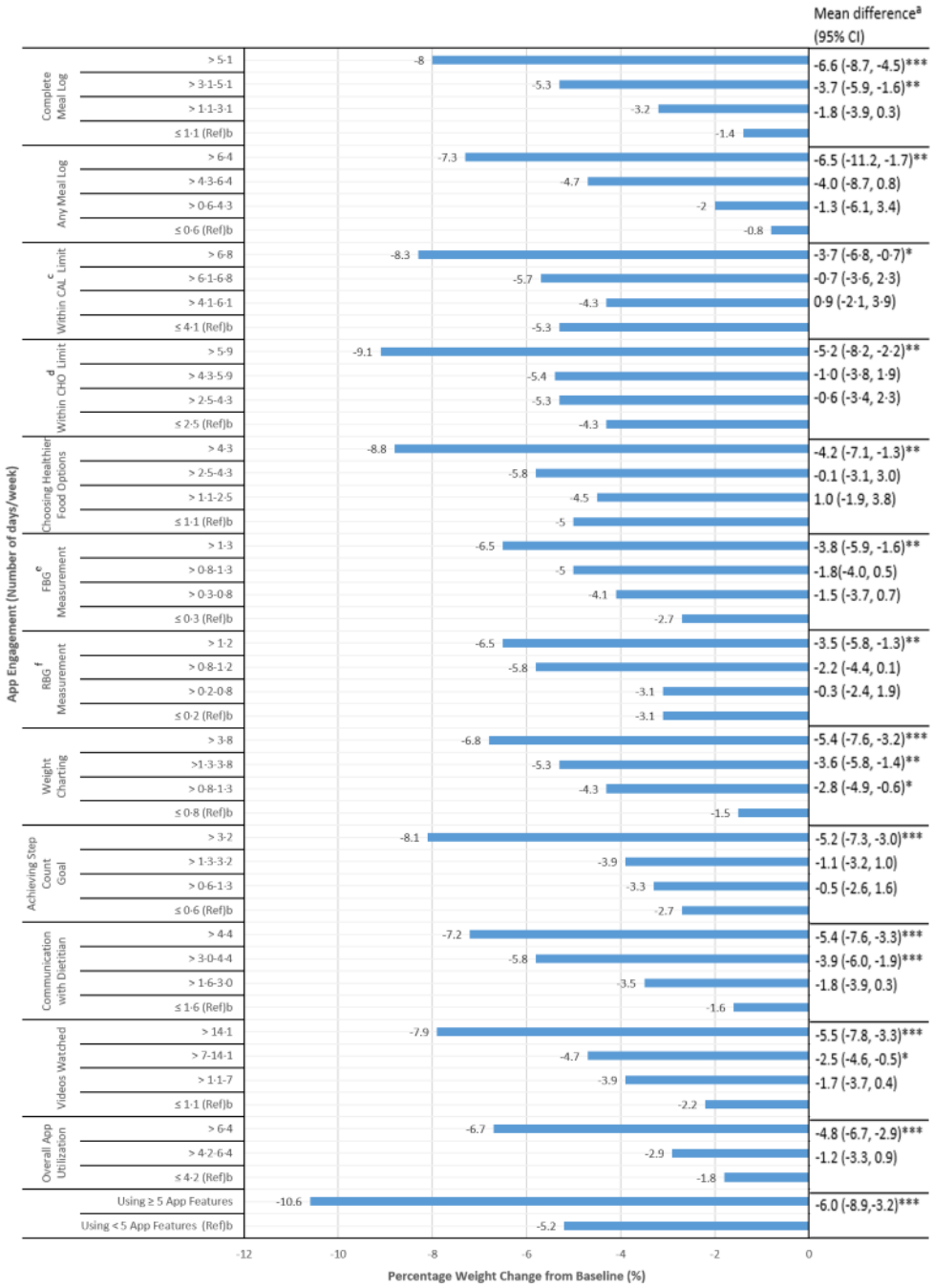
[c]RBG: random blood glucose.

[d]N/A: not applicable.

Associations Between App Engagement and Weight Change

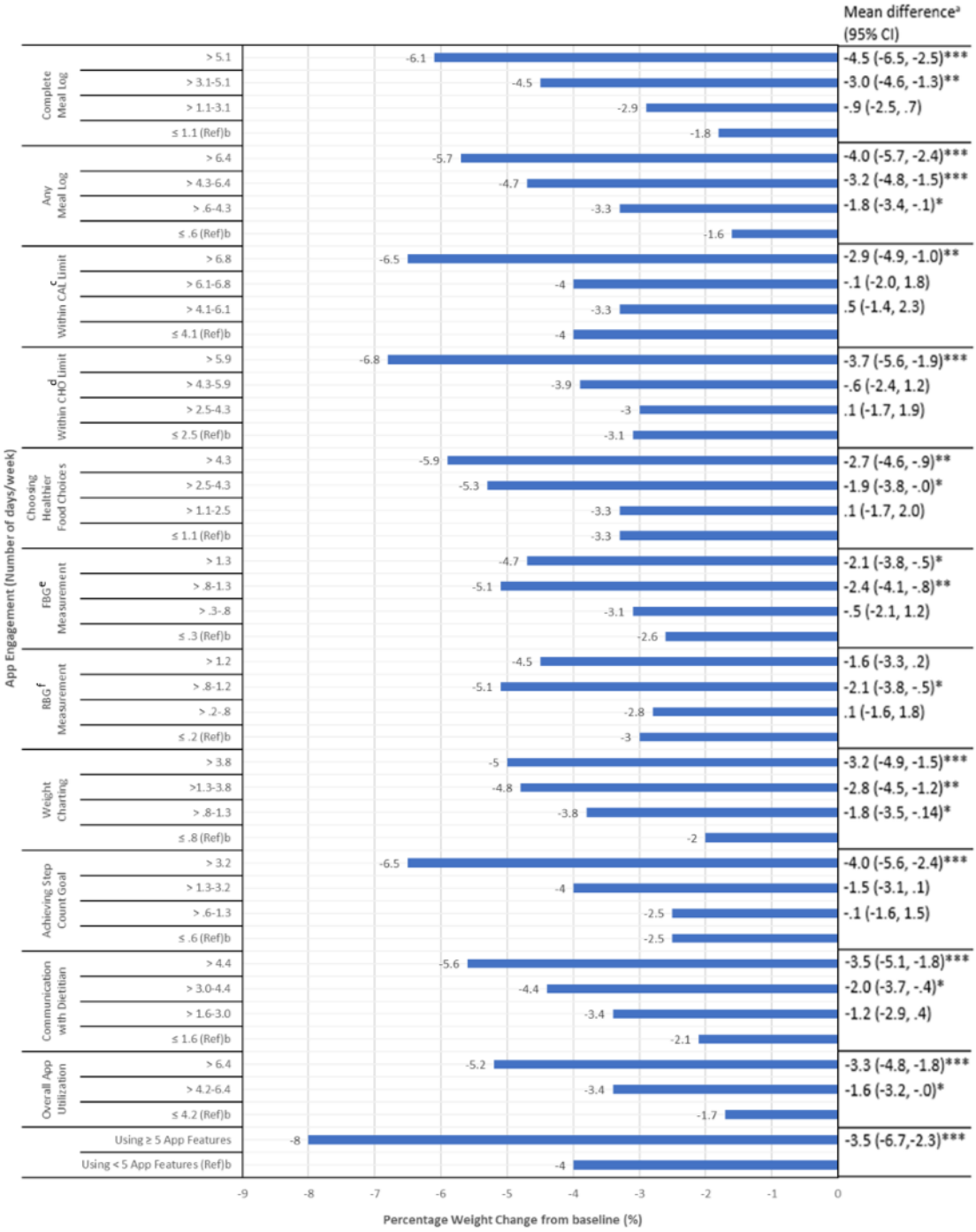
Figure 1 shows the association between app engagement and weight reduction among all participants at 6 months. The top quartiles of all app engagements achieved significantly greater weight loss at 6 months. The same weight loss trend was observed at 3 months, with the exception of RBG measurements (Figure 2). Among all the app features, the highest quartiles of within CHO limits and choosing healthier food options were associated with the greatest weight reductions of 9.1% and 8.8%, respectively (mean difference −5.2, 95% CI −8.2 to −2.2; *P*=.001; mean difference −4.2, 95% CI −7.1 to −1.3; *P*=.005; Figure 1). The overall use of the app for >6.4 days per week could elicit a weight loss of 6.7% (mean difference −4.8, 95% CI −6.7 to −2.9; *P*<.001), as compared with using the app for ≤4.2 days per week. Similarly, engaging in ≥5 app features with ≥75% uptake was significantly associated with a weight loss of 10.6% from baseline (mean difference −6; 95% CI −8.9 to −3.2; *P*<.001).

Figure 1. Association between app engagement and percentage weight change from baseline for all participants at 6 months (n=171). *P<.05. **P<.01. ***P<.001.



[a]Mean percentage weight difference when compared to reference quartiles
[b]Ref: Reference group.
[c]CAL: Calorie.
[d]CHO: Carbohydrate.
[e]FBG: Fasting blood glucose measured in the morning before food or water.
[f]RBG: Random blood glucose measured two hours following ingestion of breakfast, lunch or dinner.

Figure 2. Association between app engagement and percentage weight change from baseline for all participants at 3 months (n=171). *P<.05. **P<.01. ***P<.001.



[a]Mean percentage weight difference when compared to reference quartiles
[b]Ref: Reference group.
[c]CAL: Calorie.
[d]CHO: Carbohydrate.
[e]FBG: Fasting blood glucose measured in the morning before food or water.
[f]RBG: Random blood glucose measured two hours following ingestion of breakfast, lunch or dinner.

Among participants with prediabetes or diabetes, the highest quartiles of app engagement for all the app features led to ≥5% weight loss at 6 months (Multimedia Appendix 1). This trend was observed as early as 3 months whereby the highest quartile engagement levels of almost all the app features led to ≥5% weight loss (Multimedia Appendix 2). Complete meal log, keeping within CAL and CHO limits and choosing healthier food options, elicited the greatest weight loss of ≥8% when these app features were used most frequently (Multimedia Appendix 1).

In addition, overall use of the app for >6.4 days per week led to a greater weight loss of 6.8% compared with 2.1% weight loss for app use of ≤4.2 days per week (P=.009) among the prediabetes group at 6 months (Multimedia Appendix 1). A similar trend was observed in the diabetes group. Engaging in ≥5 app features with ≥75% uptake elicited an overall weight

loss of 9.8% and 11.9% among the participants with diabetes and prediabetes, respectively.

Upon examining the app engagements efficiency, the app features that stood out for weight loss among the participants with prediabetes were complete meal log, within the CHO limit, RBG measurement, achieving step count goal, and communication with the dietitian (P<.05; Multimedia Appendix 1). Meanwhile, among the participants with diabetes, to attain both weight loss and HbA_{1c} reduction, the features that stood out were complete or any meal log, RBG measurement, weight charting, communication with dietitian, and videos watched (P<.01; Multimedia Appendices 1 and 3).

Associations Between App Engagement and HbA_{1c} Change

Multimedia Appendices 3 and 4 illustrate that the higher the app engagement quartiles, the greater the HbA_{1c} reduction. As expected, HbA_{1c} reduction was more pronounced among participants with diabetes (P<.05) than participants with prediabetes among all app engagement. Among the participants with diabetes, all app engagements at the highest quartiles had clinically meaningful HbA_{1c} reduction of between 0.9% and 1.4% at 3 months and 6 months (P<.05 for all; Multimedia Appendices 3 and 4). Among the app features, meal logging, keeping within CAL and CHO limits, choosing healthier food options, fasting blood glucose and RBG measurements, weight charting, and achieving step count goal elicited the greatest impact on HbA_{1c} reduction of ≥1.2%, when used most frequently (Multimedia Appendix 3).

Participants with diabetes who had a complete meal log for >5.1 days per week or kept within their CHO limit of >5.9 days per week each achieved greater HbA_{1c} reductions of 1.2% (SD 1.5%) versus 0.2% (SD 0.6%) in those who logged their meals ≤1.1 days or kept within CHO ≤2.5 days per week (Multimedia Appendix 3). Overall app use of >6.4 days was associated with greater HbA_{1c} reduction (1.1% vs 0.3%) when compared with using the app for ≤4.2 days per week.

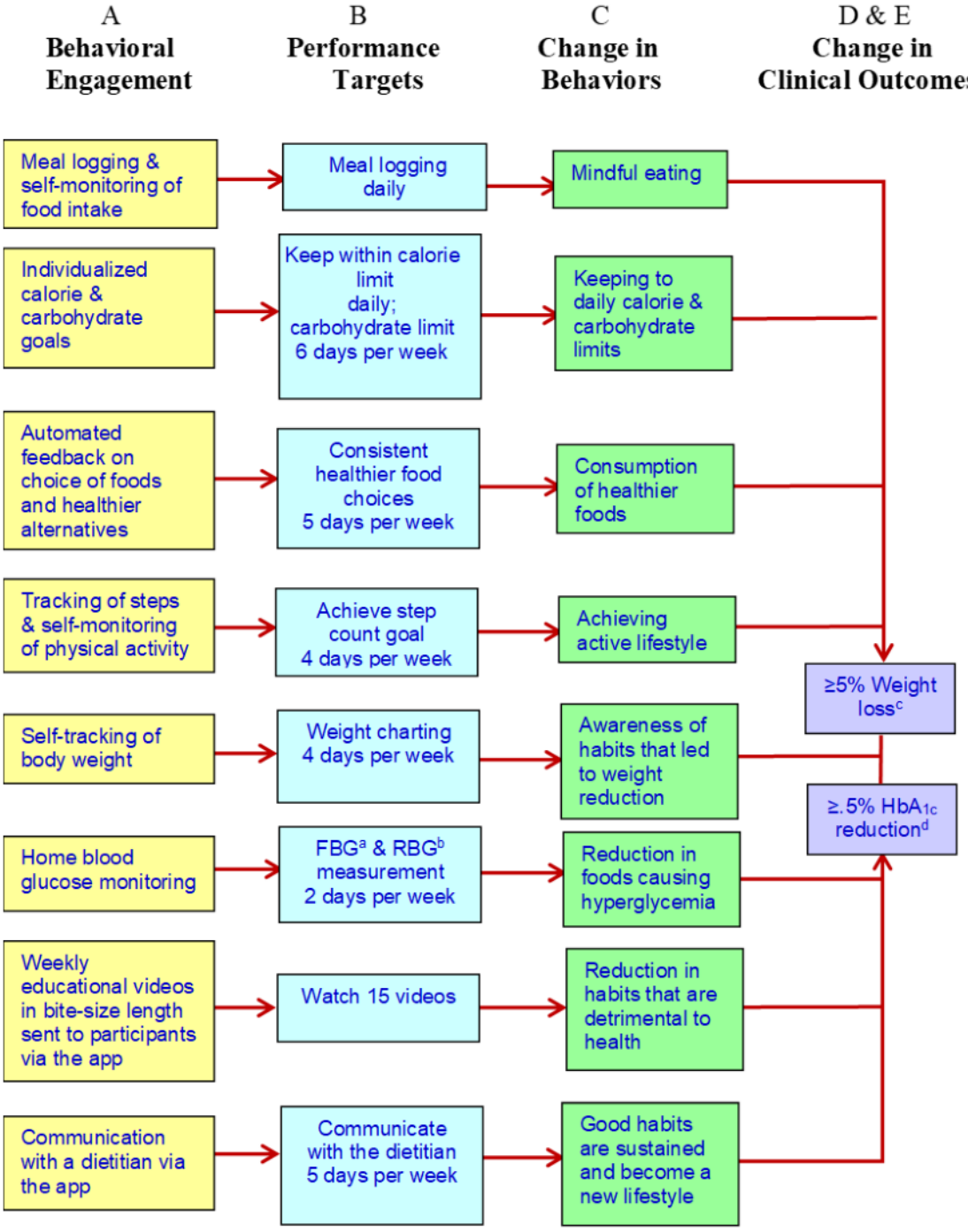
Discussion

Principal Findings

Our prospective study is significant in reporting the association between a diabetes app engagement and weight loss and HbA_{1c} change in adults with diabetes and prediabetes. Engaging with ≥5 app features with ≥75% uptake was associated with a substantial weight loss of 10.6% from baseline. Among participants with diabetes, greater app engagements led to higher improvement in glycemic control with HbA_{1c} reduction of between 1.0% and 1.4%. Our study results demonstrated that diabetes self-management through mobile phone app engagement was effective and sustainable at 6 months.

Past weight loss studies have reported better health outcomes with higher app engagement [17], emphasizing that higher app engagement is the primary determinant in successful weight loss [10]. Our findings are consistent with Painter et al [17] who found that a higher frequency of food log days, self-weighing entry days, or higher step counts per week was significantly associated with greater weight loss among participants with overweight and obesity. Our study revealed that the higher frequency of app use, the higher likelihood of achieving weight loss and HbA_{1c} reduction at 6 months. Moreover, the top quartiles of overall app use among all participants were significantly associated with a greater weight loss and HbA_{1c} reduction. We postulate that the more time spent on the app, the participants are more likely to engage with learning, self-monitoring, and health improvement behaviors that in turn lead to better self-management capability and commitment [18]. The self-regulation theory also states that self-monitoring and evaluation of one's behaviors will lead to self-reinforcements, which in turn support behavior change toward attaining better health outcomes [17]. As the nBuddy Diabetes app was conceptualized based on a theoretical behavioral model [11], the results of this study provide evidence of the degree of app engagement for achieving clinically meaningful weight and HbA_{1c} reduction within 6 months. Figure 3 describes how our study findings align with the self-regulation theory to bring positive changes in behavior and health outcomes.

Figure 3. Effective behavioral treatment strategies in the nBuddy Diabetes App to optimize blood glucose control and weight loss (adapted from Lim et al [11]).



[a]FBG: Fasting blood glucose.
[b]RBG: Random blood glucose.
[c]Clinically meaningful 5% weight reduction among all participants.
[d]Clinically meaningful 0.5% HbA1c reduction among participants with DM.

Meal logging has been identified as a commonly used feature among diabetes mHealth apps [19]. It is well-known that meal logging and tracking facilitate healthy dietary modifications [20]. Similarly, meal logging is one of the most used features in this study. Our study findings further strengthened the evidence of the link between meal logging via the app and improvements in weight and glycemic control [21]. Finally, Ingels et al [20] emphasized the importance of frequent and consistent dietary tracking for successful long-term weight loss. Taken together, meal logging should be made part of routine monitoring, similar to SMBG, not just to guide management for patients with diabetes during clinic visits but also as an important behavioral intervention.

It is also important to note that participants communicated with the dietitian through the app every other day. This feature provides an avenue for the user to clarify and ask questions

pertaining to diabetes or weight control. It has been shown that SMBG with education and proper feedback improves diabetes control [22]. The 2-way communication with a dietitian could empower participants to make immediate changes based on the SMBG readings, meal log, and physical activity. Indeed, the engagement with the dietitian through the app was associated with a significant reduction in body weight and HbA_{1c} levels.

Apart from being one of the most used features, step counting was associated with clinically meaningful and statistically significant weight and HbA_{1c} reductions. Step counters with predetermined goals have been effective in forming good walking habits [5,23]. Our study findings agree with a meta-analysis that highlighted the benefits of pedometer use on weight loss among adults with overweight and obesity with diabetes [23]. Contrary to our findings, a meta-analysis and systematic review reported inconclusive glycemic effect and relationship around step count goals among patients with diabetes [24].

A study on diabetes apps found that inclusion of approximately 6 features led to both short- and long-term weight loss [25]. The use of a combination of features is also akin to the concepts of health care bundles consisting of 3 to 5 evidence-based practices to manage health care conditions [26]. Moreover, this study showed a greater HbA_{1c} reduction with ≥75% uptake of ≥5 app features at 3 and 6 months compared with using ≤5 features. In addition, our study emphasized complete meal log, within CHO limit, RBG measurement, achieving step count goal, and communication with dietitian for attaining weight loss among participants with prediabetes. On the other hand, complete meal log or any meal log, RBG measurement, weight charting, communication with the dietitian, and videos watched were crucial for participants with diabetes. Furthermore, Painter et al [17] highlighted the importance of self-monitoring features for better outcomes, and Van Rhoon et al [27] recommended a mixture of passive and interactive features. A recently published meta-analysis and systematic review echoed a similar conclusion as the authors concluded that the inclusion of an app to multicomponent usual care leads to greater weight loss [28].

The decline in app use over time was expected and has been commonly cited in mHealth app interventions [27]. However, the overall high app use was sustainable in our study at 3 months and 6 months. This could be attributed to the design features of the app, such as prompts that served as reminders for participants to use the app, and the chat function that was among the most used features in this study. The presence of a dietitian or health coach support could have assisted in optimal health information acquisition, learning, and application [29]. Moreover, the chat function has the potential to address patient lapses through reminders and deliver real-time tailored and dynamic behavioral interventions to support patient compliance with dietary and exercise recommendations [30]. This is also supported by past studies that reported significant associations between physician-patient communication and weight loss and HbA_{1c} reduction [29]. Several diabetes apps have not only echoed the importance of the 2-way chat communication but also highlighted its effectiveness in influencing behavior change [25].

Strengths and Limitations

With the COVID-19 pandemic, the adoption of this locally contextualized app-based intervention, such as the nBuddy Diabetes app, could help practitioners facilitate better care and improve patients' self-management in diabetes at the population level. The strengths of this study are the prospective tracking of health outcomes and the large number of app engagement data sets that enabled us to study the individual effect of specific app features on achieving desirable weight loss and blood glucose control. Similar to findings from the literature [28,31], our low attrition rate also illustrated that facilitating communication with a dietitian in the app could lead to greater and sustained engagement in diabetes self-management.

A limitation of this study is that participants who were willing to participate in this study displayed some degree of readiness for change with digital health literacy, and hence, the effect on unmotivated participants without digital health literacy remains unexamined. Participants may have also sought external input such as engaging in other health interventions or using other health apps, making it difficult to attribute success in weight loss and glycemic control solely to the app.

Conclusions

In conclusion, engagement with the nBuddy Diabetes self-management app could elicit meaningful weight loss and HbA_{1c} reduction among individuals with overweight or obesity with prediabetes or diabetes. The greater the engagement with the app, the greater the weight loss and HbA_{1c} reduction.

Acknowledgments

The study was funded by the Singapore Ministry of Health's National Medical Research Council under its Health Services Research Grant (NMRC/HSRG/0063/2016).

Authors' Contributions

SLL and CMK conceived the idea, developed the study design, and supervised the project. MHJT, JJ, KWO, and GKNY carried out the project. QVY and YHC provided statistical expertise and contributed to the interpretation of the results. SLL took the lead in writing the manuscript. AY cosupervised this project, contributed to the interpretation of results, and played an instrumental role in drafting the manuscript. All authors provided critical feedback and approved the final version of the manuscript.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Associations between app engagement and percentage weight change at 6 months for prediabetes or diabetes.
[DOCX File , 36 KB - diabetes_v7i3e35039_app1.docx]

Multimedia Appendix 2
Associations between app engagement and percentage weight change at 3 months for prediabetes or diabetes.
[DOCX File , 44 KB - diabetes_v7i3e35039_app2.docx]

Multimedia Appendix 3
Associations between app engagement and glycated hemoglobin change at 6 months for prediabetes or diabetes.
[DOCX File , 36 KB - diabetes_v7i3e35039_app3.docx]

Multimedia Appendix 4
Associations between app engagement and glycated hemoglobin change at 3 months for prediabetes or diabetes.
[DOCX File , 37 KB - diabetes_v7i3e35039_app4.docx]

References

1. International Diabetes Federation. 2021 Dec 9. URL: https://www.idf.org/aboutdiabetes/what-is-diabetes/facts-figures.html [accessed 2020-11-09]
2. Disease burden. Ministry of Health Singapore. 2019. URL: https://www.moh.gov.sg/resources-statistics/singapore-health-facts/disease-burden [accessed 2020-11-09]
3. National Population Health Survey 2020. Singapore: Epidemiology & Disease Control Division, Ministry of Health, Republic of Singapore; 2020.
4. Information paper on diabetes in Singapore. National Registry of Disease Office. URL: https://www.nrdo.gov.sg/docs/librariesprovider3/default-document-library/diabetes-info-paper-v6.pdf?sfvrsn=0 [accessed 2020-11-09]
5. American Diabetes Association. 8. Obesity management for the treatment of type 2 diabetes: standards of medical care in diabetes-2020. Diabetes Care 2020 Jan;43(Suppl 1):S89-S97. [doi: 10.2337/dc20-S008] [Medline: 31862751]
6. Ryan DH, Yockey SR. Weight loss and improvement in comorbidity: differences at 5%, 10%, 15%, and over. Curr Obes Rep 2017 Jun 28;6(2):187-194 [FREE Full text] [doi: 10.1007/s13679-017-0262-y] [Medline: 28455679]
7. Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, Cull CA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ 2000 Aug 12;321(7258):405-412 [FREE Full text] [doi: 10.1136/bmj.321.7258.405] [Medline: 10938048]
8. Hou C, Carter B, Hewitt J, Francisa T, Mayor S. Do mobile phone applications improve glycemic control (HbA1c) in the self-management of diabetes? A systematic review, meta-analysis, and GRADE of 14 randomized trials. Diabetes Care 2016 Nov;39(11):2089-2095. [doi: 10.2337/dc16-0346] [Medline: 27926892]
9. Cai X, Qiu S, Luo D, Wang L, Lu Y, Li M. Mobile application interventions and weight loss in type 2 diabetes: a meta-analysis. Obesity (Silver Spring) 2020 Mar 22;28(3):502-509. [doi: 10.1002/oby.22715] [Medline: 31965748]
10. Serrano KJ, Coa KI, Yu M, Wolff-Hughes DL, Atienza AA. Characterizing user engagement with health app data: a data mining approach. Transl Behav Med 2017 Jun;7(2):277-285 [FREE Full text] [doi: 10.1007/s13142-017-0508-y] [Medline: 28616846]
11. Lim SL, Ong KW, Johal J, Han CY, Yap QV, Chan YH, et al. Effect of a smartphone app on weight change and metabolic outcomes in Asian adults with type 2 diabetes: a randomized clinical trial. JAMA Netw Open 2021 Jun 01;4(6):e2112417 [FREE Full text] [doi: 10.1001/jamanetworkopen.2021.12417] [Medline: 34081137]
12. Lim SL, Ong KW, Johal J, Han CY, Yap QV, Chan YH, et al. A smartphone app-based lifestyle change program for prediabetes (D'LITE Study) in a multiethnic Asian population: a randomized controlled trial. Front Nutr 2021 Jan 24;8:780567 [FREE Full text] [doi: 10.3389/fnut.2021.780567] [Medline: 35141265]
13. Little RR, Rohlfing CL. The long and winding road to optimal HbA1c measurement. Clin Chim Acta 2013 Mar 15;418:63-71 [FREE Full text] [doi: 10.1016/j.cca.2012.12.026] [Medline: 23318564]
14. Franz MJ, Boucher JL, Rutten-Ramos S, VanWormer JJ. Lifestyle weight-loss intervention outcomes in overweight and obese adults with type 2 diabetes: a systematic review and meta-analysis of randomized clinical trials. J Acad Nutr Diet 2015 Sep;115(9):1447-1463. [doi: 10.1016/j.jand.2015.02.031] [Medline: 25935570]
15. Lim SL, Johal J, Ong KW, Han CY, Chan YH, Lee YM, et al. Lifestyle intervention enabled by mobile technology on weight loss in patients with nonalcoholic fatty liver disease: randomized controlled trial. JMIR Mhealth Uhealth 2020 Apr 13;8(4):e14802 [FREE Full text] [doi: 10.2196/14802] [Medline: 32281943]

16. von Elm E, Altman D, Egger M, Pocock S, Gøtzsche PC, Vandenbroucke J, STROBE Initiative. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. Int J Surg 2014 Dec;12(12):1495-1499 [FREE Full text] [doi: 10.1016/j.ijsu.2014.07.013] [Medline: 25046131]
17. Painter SL, Ahmed R, Hill JO, Kushner RF, Lindquist R, Brunning S, et al. What matters in weight loss? An in-depth analysis of self-monitoring. J Med Internet Res 2017 May 12;19(5):e160 [FREE Full text] [doi: 10.2196/jmir.7457] [Medline: 28500022]
18. Schoeppe S, Alley S, Van Lippevelde W, Bray NA, Williams SL, Duncan MJ, et al. Efficacy of interventions that use apps to improve diet, physical activity and sedentary behaviour: a systematic review. Int J Behav Nutr Phys Act 2016 Dec 07;13(1):127 [FREE Full text] [doi: 10.1186/s12966-016-0454-y] [Medline: 27927218]
19. Böhm AK, Jensen ML, Sørensen MR, Stargardt T. Real-world evidence of user engagement with mobile health for diabetes management: longitudinal observational study. JMIR Mhealth Uhealth 2020 Nov 06;8(11):e22212 [FREE Full text] [doi: 10.2196/22212] [Medline: 32975198]
20. Ingels J, Misra R, Stewart J, Lucke-Wold B, Shawley-Brzoska S. The effect of adherence to dietary tracking on weight loss: using HLM to model weight loss over time. J Diabetes Res 2017;2017:6951495 [FREE Full text] [doi: 10.1155/2017/6951495] [Medline: 28852651]
21. Porter J, Huggins CE, Truby H, Collins J. The effect of using mobile technology-based methods that record food or nutrient intake on diabetes control and nutrition outcomes: a systematic review. Nutrients 2016 Dec 17;8(12):815 [FREE Full text] [doi: 10.3390/nu8120815] [Medline: 27999302]
22. Goyal S, Morita P, Lewis GF, Yu C, Seto E, Cafazzo JA. The systematic design of a behavioural mobile health application for the self-management of type 2 diabetes. Can J Diabetes 2016 Feb;40(1):95-104. [doi: 10.1016/j.jcjd.2015.06.007] [Medline: 26455762]
23. Cai X, Qiu SH, Yin H, Sun ZL, Ju CP, Zügel M, et al. Pedometer intervention and weight loss in overweight and obese adults with Type 2 diabetes: a meta-analysis. Diabet Med 2016 Aug 25;33(8):1035-1044 [FREE Full text] [doi: 10.1111/dme.13104] [Medline: 26926674]
24. Hall KS, Hyde ET, Bassett DR, Carlson SA, Carnethon MR, Ekelund U, et al. Systematic review of the prospective association of daily step counts with risk of mortality, cardiovascular disease, and dysglycemia. Int J Behav Nutr Phys Act 2020 Jun 20;17(1):78 [FREE Full text] [doi: 10.1186/s12966-020-00978-9] [Medline: 32563261]
25. Zhang Y, Li X, Luo S, Liu C, Xie Y, Guo J, et al. Use, perspectives, and attitudes regarding diabetes management mobile apps among diabetes patients and diabetologists in China: national web-based survey. JMIR Mhealth Uhealth 2019 Feb 08;7(2):e12658 [FREE Full text] [doi: 10.2196/12658] [Medline: 30735147]
26. Lavallée JF, Gray TA, Dumville J, Russell W, Cullum N. The effects of care bundles on patient outcomes: a systematic review and meta-analysis. Implement Sci 2017 Nov 29;12(1):142 [FREE Full text] [doi: 10.1186/s13012-017-0670-0] [Medline: 29187217]
27. Van Rhoon L, Byrne M, Morrissey E, Murphy J, McSharry J. A systematic review of the behaviour change techniques and digital features in technology-driven type 2 diabetes prevention interventions. Digit Health 2020 Mar 24;6:2055207620914427 [FREE Full text] [doi: 10.1177/2055207620914427] [Medline: 32269830]
28. Ang SM, Chen J, Liew JH, Johal J, Dan YY, Allman-Farinelli M, et al. Efficacy of interventions that incorporate mobile apps in facilitating weight loss and health behavior change in the Asian population: systematic review and meta-analysis. J Med Internet Res 2021 Nov 16;23(11):e28185 [FREE Full text] [doi: 10.2196/28185] [Medline: 34783674]
29. Saffari M, Ghanizadeh G, Koenig HG. Health education via mobile text messaging for glycemic control in adults with type 2 diabetes: a systematic review and meta-analysis. Prim Care Diabetes 2014 Dec;8(4):275-285. [doi: 10.1016/j.pcd.2014.03.004] [Medline: 24793589]
30. Chen J, Lieffers J, Bauman A, Hanning R, Allman-Farinelli M. Designing health apps to support dietetic professional practice and their patients: qualitative results from an international survey. JMIR Mhealth Uhealth 2017 Mar 31;5(3):e40 [FREE Full text] [doi: 10.2196/mhealth.6945] [Medline: 28363882]
31. Meyerowitz-Katz G, Ravi S, Arnolda L, Feng X, Maberly G, Astell-Burt T. Rates of attrition and dropout in app-based interventions for chronic disease: systematic review and meta-analysis. J Med Internet Res 2020 Sep 29;22(9):e20283 [FREE Full text] [doi: 10.2196/20283] [Medline: 32990635]

Abbreviations

CAL: calorie
CHO: carbohydrate
D'LITE: Diabetes Lifestyle Intervention Using Technology Empowerment
HbA_{1c}: glycated hemoglobin
mHealth: mobile health
nBuddy: Nutritionist Buddy
RBG: random blood glucose
SMBG: self-monitoring of blood glucose

Edited by YK Lin; submitted 22.02.22; peer-reviewed by M Zheng, H Ranjani; comments to author 10.05.22; revised version received 04.07.22; accepted 15.07.22; published 30.09.22.

Please cite as:
Lim SL, Tay MHJ, Ong KW, Johal J, Yap QV, Chan YH, Yeo GKN, Khoo CM, Yaxley A
Association Between Mobile Health App Engagement and Weight Loss and Glycemic Control in Adults With Type 2 Diabetes and Prediabetes (D'LITE Study): Prospective Cohort Study
JMIR Diabetes 2022;7(3):e35039
URL: https://diabetes.jmir.org/2022/3/e35039
doi:10.2196/35039
PMID:36178718

Original Paper

Effectiveness of a Diabetes-Focused Electronic Discharge Order Set and Postdischarge Nursing Support Among Poorly Controlled Hospitalized Patients: Randomized Controlled Trial

Audrey White[1], MD; David Bradley[2], MD; Elizabeth Buschur[2], MD; Cara Harris[2], DNP, APRN-CNP, CDCES; Jacob LaFleur[3], BS; Michael Pennell[4], PhD; Adam Soliman[3], BS; Kathleen Wyne[2], MD, PhD; Kathleen Dungan[2], MPH, MD

[1]Internal Medicine, University of Virginia, Charlottesville, VA, United States

[2]Division of Endocrinology, Diabetes & Metabolism, The Ohio State University, Columbus, OH, United States

[3]College of Medicine, The Ohio State University, Columbus, OH, United States

[4]Division of Biostatistics, Department of Biostatistics, The Ohio State University College of Public Health, Columbus, OH, United States

Corresponding Author:
Kathleen Dungan, MPH, MD
Division of Endocrinology, Diabetes & Metabolism
The Ohio State University
517 McCampbell Hall
1581 Dodd Drive
Columbus, OH, 43210
United States
Phone: 1 614 685 3333
Email: kathleen.dungan@osumc.edu

Abstract

Background: Although the use of electronic order sets has become standard practice for inpatient diabetes management, there is limited decision support at discharge.

Objective: In this study, we assessed whether an electronic discharge order set (DOS) plus nurse follow-up calls improve discharge orders and postdischarge outcomes among hospitalized patients with type 2 diabetes mellitus.

Methods: This was a randomized, open-label, single center study that compared an electronic DOS and nurse phone calls to enhanced standard care (ESC) in hospitalized insulin-requiring patients with type 2 diabetes mellitus. The primary outcome was change in glycated hemoglobin (HbA_{1c}) level at 24 weeks after discharge. The secondary outcomes included the completeness and accuracy of discharge prescriptions related to diabetes.

Results: This study was stopped early because of feasibility concerns related to the long-term follow-up. However, 158 participants were enrolled (DOS: n=82; ESC: n=76), of whom 155 had discharge data. The DOS group had a greater frequency of prescriptions for bolus insulin (78% vs 44%; *P*=.01), needles or syringes (95% vs 63%; *P*=.03), and glucometers (86% vs 36%; *P*<.001). The clarity of the orders was similar. HbA_{1c} data were available for 54 participants in each arm at 12 weeks and for 44 and 45 participants in the DOS and ESC arms, respectively, at 24 weeks. The unadjusted difference in change in HbA_{1c} level (DOS – ESC) was −0.6% (SD 0.4%; *P*=.18) at 12 weeks and −1.1% (SD 0.4%; *P*=.01) at 24 weeks. The adjusted difference in change in HbA_{1c} level was −0.5% (SD 0.4%; *P*=.20) at 12 weeks and −0.7% (SD 0.4%; *P*=.09) at 24 weeks. The achievement of the individualized HbA_{1c} target was greater in the DOS group at 12 weeks but not at 24 weeks.

Conclusions: An intervention that included a DOS plus a postdischarge nurse phone call resulted in more complete discharge prescriptions. The assessment of postdischarge outcomes was limited, owing to the loss of the long-term follow-up, but it suggested a possible benefit in glucose control.

Trial Registration: ClinicalTrials.gov NCT03455985; https://clinicaltrials.gov/ct2/show/NCT03455985

(JMIR Diabetes 2022;7(3):e33401) doi:10.2196/33401

KEYWORDS

type 2 diabetes; discharge; order set

Introduction

Scope and Impact of Diabetes

Type 2 diabetes mellitus (T2D) is a major public health problem that is prevalent in 37.3 million US adults and has been steadily increasing [1]. Diabetes is known to lead to considerable morbidity and mortality, with 39% developing chronic kidney disease, 12% reporting severe vision loss, and nearly 290,000 deaths annually [1]. As the prevalence of diabetes increases, complications can occur and hospitalizations are expected to follow. Diabetes is present in at least 25% of hospitalized patients [2], and hospitalizations for hyperglycemic crises have increased over time [3].

Many complications of diabetes are preventable with comprehensive care, including glycemic control [4]. However, despite the increasing availability of numerous therapeutic classes of medications, the proportion of individuals achieving a glycated hemoglobin (HbA_{1c}) level of <7% has declined over time [5]. The reasons for this finding are complex and multifactorial, including changes in demographics, practice patterns, health care policy, and the social and economic context [6].

Challenges With Hospital Transitions of Care

Hospitalization presents an opportunity to identify potentially vulnerable patients with diabetes and to impact their glucose control, but additional system-based barriers may also occur. During hospitalization, expert guidelines generally recommend the discontinuation of preadmission therapies in favor of an insulin regimen that contains basal, prandial, and correction components [7,8]. In addition, patients receiving insulin before admission often undergo an adjustment in dose owing to changes in oral intake or illness-related factors, and the type of insulin may differ owing to restrictions in hospital formularies. In patients on non–insulin-based regimens who do not achieve glycemic goals, intensification of insulin therapy at discharge may be required. These changes in therapy that occur during hospitalization can magnify the treatment gaps during the transition from hospital to home.

Consequences of Ineffective Diabetes Discharge Procedures

Unfortunately, effective hospital discharge programs for patients with diabetes are understudied [9-11]. In particular, patients who initiate or intensify insulin therapy have the greatest benefit in glycemic control [10,12]. However, these patients are also particularly vulnerable to transitions in care for a variety of reasons, including the complexity of therapy, differences in dosing and administration in the hospital compared with home, inconsistent or inadequate education in the hospital setting, differences in patient and provider expectations, and insufficient resources and access to care [13,14]. Disruption of insulin therapy following hospitalization is associated with higher HbA_{1c} levels after discharge, shorter survival, and increased frequency of readmission and medical costs [15]. Insulin therapy could be interrupted intentionally or more likely via unintentional means, including missing prescriptions or associated supplies, unclear instructions for use, or other barriers, such as cost and coverage issues, medication complexity, low health literacy, and limited access to care.

Role of Discharge Order Sets

In a Society of Hospital Medicine Survey, only one-fourth of hospitals were supported by written protocols to standardize medication, education, equipment, and follow-up instructions for hospitalized patients with diabetes [16]. Despite being the most frequently used task-specific order set during hospitalization [17], order sets have not been used to guide insulin use at hospital discharge [18]. Preliminary studies at our institution demonstrated that a switch to a new electronic medical record (EMR) platform resulted in an increase in unclear prescriptions for insulin at the time of discharge, in part owing to the use of a free text field in insulin prescriptions [19]. This study assessed whether a diabetes-focused inpatient discharge order set (DOS) with nurse follow-up calls can improve postdischarge outcomes compared with enhanced standard care (ESC) among hospitalized patients with insulin-requiring T2D.

Methods

Design and Participants

This was a single center, 24-week randomized open-label parallel group controlled trial. The inclusion criteria were hospitalized patients aged 25 to 75 years with T2D for at least a 3-month duration, an HbA_{1c} level of >8.5% (69 mmol/mol) within 3 months before enrollment, requiring at least 10 units of basal insulin per day while in the hospital, and able to provide informed consent. The age 25 years was chosen to minimize the possibility of inadvertently including type 1 diabetes [20,21], while the age 75 years was chosen to minimize the inclusion of patients who were less likely to discharge home [22]. Participants were required to have access to a phone or electronic messaging post discharge. Exclusion criteria included inmates, pregnancy, inability to consent, or patients with an expected need for skilled nursing facility stay greater than 2 weeks.

Participants were identified through daily screening of inpatient medical and surgical services throughout the institution and were enrolled between January 5, 2018, and April 3, 2020. Permission was obtained from the attending physician of the inpatient service by the study coordinator before approaching the patient in person.

Sample Size

We estimated a sample size of 111 individuals per group to achieve 80% power to detect a treatment difference of 0.8% in HbA_{1c} levels, adjusting for baseline clinical factors (age, insulin dose at discharge, and whether the patient was new to insulin), assuming 20% attrition, σ=2.2% (SD of HbA_{1c} levels), ρ=.25 (correlation between HbA_{1c} levels at baseline and at 24 weeks),

and R^2=0. 5 (squared correlation between baseline factors and the outcome) [23]. However, study enrollment was halted in March 2020 owing to the COVID-19 pandemic crisis and concerns about the feasibility of continuing to enroll and conduct study visits.

Intervention

Randomization to the DOS or ESC was performed in a 1:1 ratio using a random number generator program within an electronic data capture system (REDCap [Research Electronic Data Capture; Vanderbilt University]) and was stratified by admission insulin therapy.

The DOS was developed with the consultation of a multidisciplinary team that included feedback from Hospital Medicine and diabetes specialists of the hospital. Before the development of the DOS, discharge orders were not specifically tailored to the patient with diabetes. In the DOS, the following orders are accompanied by preselected options with additional cascading options to enhance decision support (Table S1 in Multimedia Appendix 1):

- Diet: there are multiple choices from regular to enteral feeding. The DOS presents 2 separate choices, one for a consistent carbohydrate diet and the other for a flexible carbohydrate diet intended for the patient with carbohydrate counting skills. The goal is to help link the patient's insulin regimen to their diet.
- Follow-up appointments or referrals: prepopulated choices for primary care, endocrinology, and diabetes education, with prompts to consider outside referrals for patients living outside the catchment area to increase the likelihood of follow-up.
- Medications: for hospitalized patients, neither the preadmission order nor the hospital order for insulin is typically appropriate for a patient at discharge. Moreover, such orders are often complex, and ancillary orders such as pen needles or syringes may be omitted. Thus, insulin options in the DOS are presented via a pick list with linked panels containing a prefilled quantity of pen needles or syringes as appropriate, and default text with decision support that assists the prescriber in choosing the appropriate dose adjustments (eg, basal insulin titration or short or rapid acting correction scale) if indicated.
- Glucose monitoring: these supplies are rarely addressed in admission or discharge orders. The testing supplies in the DOS are bundled (monitor, test strips, and lancets) with default instructions and prefilled quantities, according to the frequency of glucose monitoring.
- Additional supplies: glucagon orders and ketone strips are presented as options with default prescribing instructions.
- Education: additional instructions, including glucose targets and insulin administration, are provided as preselected options.

No modifications were made to the DOS during the study period. The DOS is embedded within the discharge navigator of the EMR (Epic). The DOS also provided instructions to the patients for basal insulin dose self-titration. Default instructions advised patients to increase the dose of insulin glargine 300 U/mL (Gla-300) by 2 units every 4 days for fasting glucose greater than 130 mg/dL, provided no values were less than 80 mg/dL. These instructions could be amended by the discharge team or the primary care provider. Other than Gla-300, no additional prescriptions were pended. In the DOS arm, the primary team was instructed to verify and complete the DOS launched by the study team.

All participants in both treatment groups received a phone call at 2 and 6 weeks following discharge, in which data related to ambulatory and inpatient encounters, glucose monitoring, and insulin use were collected. Basal insulin adherence was defined as >80% of the doses taken in the previous week, and the participants in the DOS received follow-up telephone calls by the study nurse to facilitate ongoing basal insulin dose titration and hospital follow-up. The nurse had a basic understanding of diabetes but was not a certified diabetes care and education specialist. In the ESC group, follow-up telephone calls and visits were conducted on the same schedule as in the ESC group but were conducted by the study coordinator for the purposes of information gathering only. In-person visits at 12 and 24 weeks were conducted by the coordinator in the ESC group and by the nurse with or without the coordinator in the DOS group. During in-person visits, HbA_{1c} and point-of-care glucose levels were collected, in addition to data collected during telephone visits. Patient retention efforts included face-to-face visits with a study investigator before all enrollments to confirm the willingness to complete all study visits, identifying multiple methods of contacting the patient, identifying emergency contacts, and performing study visits during hospitalization when a patient was readmitted.

Background Therapy and Procedures

All participants received Gla-300 (provided at no cost to the participant) plus additional background therapy (noninsulin and prandial insulin therapies) as part of standard care, as determined by the hospital discharge team. A basic description of Gla-300 was provided to hospital teams using a standard template, recommending that Gla-300 be administered in 1 or 2 injections per day at the same time of day (only pens with 1 unit dosing increments were available). A 1:1 initial dosing conversion from in-hospital administration of glargine 100 U/mL or detemir to outpatient Gla-300 was recommended. The Diabetes Consult Service provided input only when requested by the primary service.

All patients received standard discharge instructions using the EMR, which features medication reconciliation, prescription generation, disease-specific instructions, and follow-up appointments. Hospital discharge was coordinated by the primary team and case manager, who arranged follow-up and any additional needs, such as transportation before discharge. A discharge summary is sent to the primary care provider of the records per routine practice. All patients were instructed to maintain a standardized study diary that recorded glucose levels and insulin dose by the time of day, as well as any hypoglycemic events and associated symptoms.

Analysis

The primary outcome was the change in HbA_{1c} levels from baseline to 24 weeks post discharge.

Secondary outcomes related to hospital discharge included the proportion of patients with prescriptions for insulin and related supplies, and clear patient instructions (including correct frequency, no jargon or technical terms, correct quantity dispensed, and refills) using the following definitions:

- Jargon: any medical abbreviation or terms (introduced via use of free text fields for bolus insulins during medication reconciliation or prescription generation) that inappropriately appear in patient discharge instructions. Examples include “CIR,” “ICR,” “CF,” “ISF,” “QAC,” “HS,” “SQ,” “Q,” “TID,” “1:50>150,” “SS,” “SSI,” and “subcutaneous.”
- Quantity: the appropriate quantity was determined from the dose or number required for at least a 30-day supply. The frequency of glucose testing was assumed to be 3 or more times per day, because all patients required insulin.
- Refills: present if any refill was provided.
- Bolus error: this refers to omission or incorrect frequency or quantity, lack of refill for a given bolus prescription, or use of jargon or technical terms or abbreviations in the discharge instructions.
- Any error: this refers to any error (such as use of jargon, incorrect frequency, or quantity) in, or omission of any insulin, syringes, pen needles, or testing equipment.
- Carbohydrate counting refers to the adjustment of the bolus insulin dose based on the carbohydrate to insulin ratio.

The study investigator (KD) confirmed after the study coordinators (JL and AS) collected these data. All study staff received training using a standardized slide set and in-person instructions.

Data collection was conducted using REDCap, which features branching logic relative to each discharge order as relevant. Each patient was interviewed at enrollment to determine the supplies needed at the time of discharge. Post discharge, self-reported insulin dosing and hypoglycemia were solicited by the study coordinator.

Secondary outcomes also included HbA_{1c} at 12 weeks; fasting glucose at 12 and 24 weeks; and the proportion of participants achieving an HbA_{1c} level of <7% (53 mmol/mol), an HbA_{1c} level of <6.5% (48 mmol/mol), or an individualized HbA_{1c} target, defined using the Health Care Effectiveness Data and Information Set (HEDIS) criteria [24]. HbA_{1c} levels and health care use data were collected at study visits or extracted from the EMR (when available) for participants with missing data.

All secondary outcomes were prespecified, except for hospital readmission, which was considered an exploratory outcome.

All outcomes were assessed according to the group originally assigned. Follow-up data, including primary and secondary outcomes, were analyzed using generalized linear mixed models. Continuous outcomes were analyzed using linear mixed models, assuming an unstructured covariance matrix for residual errors, and binary outcomes were analyzed using logistic regression models containing random subject-specific intercepts. For some binary outcomes, we could not fit mixed models because of small cell counts. In these cases, data were analyzed cross-sectionally using separate logistic regression models fitted to the data at each time point or Fisher’s exact test, depending on the number of events. All models were adjusted for potential confounders, which we defined as any factors measured at baseline related to the outcome (P<.10) that differed by a meaningful amount across treatment arms (difference in proportions of 10% or more, difference in means of 0.5 SDs or more) at any follow-up visit (Table S2 in Multimedia Appendix 1). In the primary analysis (change in HbA_{1c}), we also adjusted for risk factors identified a priori (age, insulin dose at discharge, and whether the patient was new to insulin) to increase the precision of our treatment effect estimate. In secondary analyses, the Holm method [24] was used to account for multiple comparisons performed at 2, 6, 12, and 24 weeks [25]. Differences in the components ordered at discharge were analyzed using the Fisher Exact Test. Analyses were performed using SAS (version 9.4) and JMP 13.1 (SAS Inc).

Ethics Approval

This study was approved by the Ohio State University Institutional Review Board (2017H0354), and all patients provided informed consent.

Results

Overview

A total of 158 patients signed a consent form (Multimedia Appendix 2). Three patients did not receive the study intervention owing to a withdrawal of consent (2 patients, 1 in each study arm) or no longer qualified owing to a switch to U500 insulin before discharge (1 patient who was randomized to the DOS arm did not receive the intervention (Gla-300) because the patient was treated with U500 insulin, a regimen that does not require basal insulin). The participants had a mean age of 52 (SD 10.2) years, a median duration of diabetes of 11 years, and 81.9% (127/155) were on insulin therapy before hospital admission. Baseline characteristics of each group are presented in Table 1. The treatment groups were similar except for an imbalance in diabetes duration, marital status, and neuropathy.

Table 1. Patient characteristics (number of patients overall: N=158; patients in the enhanced standard care [ESC] arm: n=76; patients in the discharge order set [DOS] arm: n=82).

	Overall	ESC	DOS
Age (years), mean (SD)	51.7 (10.2)	51.4 (10.5)	52 (10.1)
Male, n (%)	68 (43)	33 (43.3)	35 (42.7)
White,[a,b] n (%)	74 (46.8)	34 (44.7)	40 (48.8)
Hispanic, n (%)	3 (1.9)	1 (1.3)	2 (2.4)
Diabetes duration (years), median (IQR)	11 (7-20)	14 (7-20)	10 (6-15)
BMI (kg/m^2), mean (SD)	38.2 (9.5)	38.1 (8.7)	38.4 (10.1)
Past medical history, n (%)			
Hypertension	134 (84.8)	64 (84.2)	70 (85.4)
Hyperlipidemia	98 (62)	45 (59.2)	53 (64.6)
Coronary artery disease	44 (27.9)	18 (23.7)	26 (31.7)
Heart failure	37 (23.4)	17 (22.4)	20 (24.4)
Cerebrovascular disease	21 (13.3)	12 (15.8)	9 (11)
Peripheral vascular disease	14 (8.9)	5 (6.6)	9 (11)
Retinopathy	28 (17.7)	16 (21.1)	12 (14.6)
Nephropathy	39 (24.7)	19 (25)	20 (24.4)
Neuropathy	81 (51.3)	45 (59.2)	36 (43.9)
Estimated glomerular filtration rate (mL/min/1.73 m^2), mean (SD)			
>60	109 (69)	51 (67.1)	58 (70.7)
30-60	39 (24.7)	21 (27.6)	18 (22)
<30	107 (6.3)	4 (5.3)	6 (7.43)
Charlson Comorbidity Index (total score), median (IQR)	3 (2-5)	3 (2-4.75)	3 (2-5)
Education, n (%)			
Less than high school	15 (9.5)	10 (13.2)	5 (6.1)
High school or equivalent	118 (74.7)	55 (72.4)	63 (76.8)
Bachelor’s degree	25 (15.8)	11 (14.5)	14 (17.1)
Marital status, n (%)			
Single, never married	46 (29.1)	22 (30)	24 (29.3)
Married or domestic partnership	66 (41.8)	25 (32.9)	41 (50)
Divorced, separated, or widowed	46 (29.1)	29 (38.2)	17 (20.7)
Work status, n (%)			
Employed	63 (39.9)	33 (43.4)	30 (36.6)
Unemployed	23 (14.6)	11 (14.5)	12 (14.6)
Retired	21 (13.3)	10 (13.2)	11 (13.4)
Unable to work	51 (32.3)	22 (29)	29 (35.4)
Home ownership, n (%)			
Own	58 (36.7)	28 (36.8)	30 (36.6)
Other	100 (63.3)	48 (63.1)	52 (63.4)
Insurance, n (%)			
None	11 (7)	7 (9.2)	4 (4.9)
Private	52 (32.9)	22 (29.0)	30 (36.7)
Medicare	35 (22.1)	18 (23.7)	17 (20.7)

	Overall	ESC	DOS
Medicaid	60 (38)	29 (38.2)	31 (37.8)
Primary reason for admission, n (%)			
Cardiovascular	40 (25.3)	21 (27.6)	19 (23.2)
Gastrointestinal	16 (10.1)	8 (10.5)	8 (9.8)
Infectious disease	28 (17.7)	12 (15.8)	16 (19.5)
Other	74 (46.8)	35 (46.1)	39 (47.6)
Admission service, n (%)			
General medicine	33 (20.9)	16 (21.1)	17 (20.7)
Family medicine	5 (3.2)	3 (4)	2 (2.4)
Cardiology	23 (14.5)	15 (19.7)	8 (9.8)
Surgery	6 (3.8)	2 (2.6)	4 (4.9)
Admission severe hyperglycemia,[c] n (%)	19 (12.1)	8 (10.5)	11 (13.6)
Hospital length of stay (days), median (IQR)	5 (3-8)	5 (3-8)	5 (3-8)
Diabetes consult, n (%)	62 (39.2)	26 (34.2)	36 (43.9)
Education consult, n (%)	29 (18.4)	11 (14.5)	18 (22)
Admission diabetes medications, n (%)			
Any insulin	127 (80.9)	63 (82.9)	64 (79)
Basal insulin	126 (80)	64 (84.2)	62 (76.5)
Premix insulin	1 (0.64)	1 (1.3)	0 (0)
Bolus insulin	82 (52.2)	40 (52.6)	42 (51.9)
Metformin	53 (33.5)	25 (32.9)	28 (34.2)
Sulfonylurea or glinide	12 (7.6)	7 (9.2)	5 (6.1)
SGLT2[d] inhibitor	11 (7)	4 (5.3)	7 (8.5)
DPP-4[e] inhibitor	6 (3.8)	4 (5.3)	2 (2.4)
GLP-1[f] receptor agonist	26 (16.5)	14 (18.4)	12 (14.6)
Other	1 (0.63)	0 (0)	1 (1.2)
Other admission medications, n (%)			
Statin	120 (76)	57 (75)	63 (76.8)
ACEI[g] or ARB[h]	80 (50.6)	41 (54)	39 (47.6)
β-blocker	73 (46.2)	37 (46.7)	36 (43.9)
Glucocorticoids	5 (3.2)	1 (1.3)	4 (4.9)
Aspirin	84 (53.2)	42 (55.3)	42 (51.2)
Discharge diabetes medications			
Total insulin dose (unit), median (IQR)	68 (42-115)	74 (43-116)	68 (37.8-112.5)
Total insulin dose (unit/kg/day), median (IQR)	0.61 (0.38-1.03)	0.59 (0.39-1.03)	0.69 (0.39-1.03)
Basal insulin	41 (30, 75)	50 (30, 74)	41 (30, 78.7)
Bolus insulin	123 (79)	63 (79)	60 (80)
Metformin, n (%)	56 (36.1)	26 (34.7)	30 (37.5)
Sulfonylurea or glinide, n (%)	6 (3.8)	3 (4)	3 (3.8)
SGLT2-inhibitor, n (%)	5 (3.2)	5 (6.7)	0 (0)
DPP-4 inhibitor, n (%)	10 (6.5)	6 (8)	4 (5)
GLP-1 receptor agonist, n (%)	24 (15.5)	14 (18.7)	10 (12.5)

	Overall	ESC	DOS
Diabetes empowerment scale [26], median (IQR)	4.4 (4-4.8)	4.4 (4-4.8)	4.3 (3.9-4.8)
Functional health literacy [27], median (IQR)	4 (2-6)	4 (2-6)	5 (3-6)
Multidimensional scale of perceived social support [28], median (IQR)	6 (4.9-6.8)	6.1 (5-6.8)	5.9 (4.7-6.8)

[a]Race was categorized as White (46.5%), Black (52.3%), Asian (0.65%), or other (0.65%).

[b]Chi-square analysis could not be performed owing to insufficient cell count.

[c]Admission for diabetic ketoacidosis, nonketotic hyperglycemic hyperosmolar state, or diabetes as the primary indication for admission.

[d]SGLT2: sodium-glucose cotransporter-2.

[e]DPP-4: dipeptidyl peptidase-4.

[f]GLP-1: glucagon-like peptide-1.

[g]ACEI: angiotensin-converting enzyme inhibitor-1.

[h]ARB: angiotensin receptor blocker.

Discharge Orders

Discharge data were available in 75 participants in the ESC arm and 80 participants in the DOS arm. Analysis of discharge orders is shown in Table 2. Among patients reporting an insufficient supply, those in the DOS arm were more likely to receive prescriptions for bolus insulin (21/27, 78%, vs 12/27, 44%; *P*=.01), needles and syringes (18/19, 95%, vs 15/24, 63%; *P*=.03), and glucometers (24/28, 86%, vs 9/25, 36%; *P*<.001). During hospitalization, most participants reported sufficient home supplies of bolus insulin (78/119, 66%), lancets (80/155, 52%), and a glucometer (102/155, 66%). However, needles and syringes were sufficient in only 7% (3/46) of patients, and test strips were sufficient in only 43% (66/155). No continuous or intermittently scanned glucose monitors were used. Overall, the errors in discharge orders were similar between the arms (44/80, 55%, in DOS vs 51/75, 68%, in ESC). Among patients in need of a bolus insulin prescription, errors occurred in 53% (9/17) of the DOS group and 79% (19/24) of the ESC group (*P*=.10). Medical jargon was present in 29% (5/17) of the DOS group and 38% (9/24) of the ESC group (*P*=.74). Patients in the DOS arm were more likely to receive needles or syringes in the correct quantity (17/19, 89%, vs 14/24, 58%; *P*=.04). The number of participants reporting a need for test strips or lancets who received both was 79% (27/34) in the DOS group and 59% (23/46) in the standard of care group (*P*=.08). For those who were prescribed bolus insulin and who reported needing supplies at baseline, 94.1% (16/17) in the DOS and 57.1% (12/21) in the standard of care received both prescriptions (*P*=.01).

Table 2. Discharge order set.

	Overall		Enhanced standard care		Discharge order set		*P* value[a]
	n (%)	N	n (%)	N	n (%)	N	
Bolus insulin							
Bolus insulin at discharge	123 (79.4)	155	60 (80)	75	63 (78)	80	.99
Home supply sufficient	78 (65.6)	119	33 (58)	57	45 (73)	62	.13
Prescription provided[b]	33 (61.1)	54	12 (44)	27	21 (78)	27	*.01*
Jargon present[b]	14 (34.1)	41	9 (38)	24	5 (29)	17	.74
Any bolus error present[b,c]	28 (68.3)	41	19 (79)	24	9 (53)	24	.10
Carbohydrate counting[d]	8 (5.3)	152	5 (7)	73	3 (4)	79	.48
Basal insulin							
Correct basal insulin ordered	100 (64.9)	155	44 (59)	75	56 (71)	80	.13
Needles and syringes							
Home supply sufficient	3 (6.5)	46	2 (8)	26	1 (5)	20	.99
Prescription provided[b]	33 (76.7)	43	15 (63)	24	18 (95)	19	*.03*
Correct quantity[b]	31 (72.1)	43	14 (58)	24	17 (89)	19	*.04*
Glucometer							
Glucometer at home	102 (65.8)	155	50 (67)	75	52 (65)	80	.87
Prescription provided[b]	33 (62.3)	53	9 (36)	25	24 (86)	28	*<.001*
Test strips							
Home supply sufficient	66 (42.6)	155	32 (43)	75	34 (43)	80	.99
Prescription provided[b]	59 (66.3)	89	25 (58)	43	34 (74)	46	.12
Correct quantity[b]	59 (66.3)	89	25 (58)	43	34 (74)	46	.12
Lancets							
Home supply sufficient	80 (51.6)	155	35 (47)	75	45 (56)	80	.26
Prescription provided[b]	48 (64.9)	74	21 (54)	39	27 (77)	35	.05
Correct quantity[b]	48 (64.9)	74	21 (54)	39	27 (77)	35	.05
Any error	95 (61.3)	155	51 (68)	75	44 (55)	80	.10

[a]*P* values with statistical significance are italicized.

[b]Among patients with insufficient supply and in need of a prescription.

[c]Bolus error refers to any error in frequency or quantity or the use of jargon, technical terms, or abbreviations in the discharge instructions.

[d]Adjusting bolus insulin dose based on the carbohydrate to insulin ratio.

HbA_{1c} and Glucose

HbA_{1c} and glucose measurements are shown in Table 3. HbA_{1c} was available in 54 participants in each arm at 12 weeks, and 44 and 45 participants in the DOS and ESC arms, respectively, at 24 weeks. The remaining participants were lost to follow-up. There was no difference in baseline characteristics according to HbA_{1c} availability at weeks 12 or 24 (Table S3 in Multimedia Appendix 1). The change in HbA_{1c} at 12 weeks was −2% (SD 0.3%; 22, SD 3.3 mmol/mol) vs −1.4% (SD 0.3%; 15, SD 3.3 mmol/mol) at 12 weeks and −2.1% (SD 0.3%; 23, SD 3.3 mmol/mol) vs −1.0% (SD 0.3%; 11, SD 3.3 mmol/mol) at 24 weeks in the DOS and ESC arms, respectively. The differences between the groups were not significant after adjustment for age, neuropathy, total daily insulin dose, and reason for hospitalization. The proportions of participants achieving a target HbA_{1c} level of <7% (53 mmol/mol) or <6.5% (48 mmol/mol) were similar. Participants in the DOS arm were more likely to achieve an HbA_{1c} level below their HEDIS target at 12 weeks (22/54, 41%, vs 9/54, 17%; odds ratio [OR] 3.29, 95% CI 1.32-8.13; *P*=.01); although this association did not persist for 24 weeks (16/45, 36%, vs 9/45, 20%; OR 2.10, 95% CI 0.80-5.55; *P*=.13). Fasting glucose levels were similar between the groups at the 12- and 24-week study visits.

Table 3. Follow-up glucose and glycated hemoglobin (HbA_{1c}) data.

	12 weeks			24 weeks		
	Enhanced standard care	Discharge order set	*P* value[a]	Enhanced standard care	Discharge order set	*P* value[a]
HbA_{1c}[b]						
Number at discharge	n=73	n=79	N/A[c]	N/A	N/A	N/A
Discharge HbA_{1c} (%), median (IQR)	10.9 (9.8-12)	10.7 (9.5-11.9)	N/A	N/A	N/A	N/A
Discharge HbA_{1c} (mmol/mol), median (IQR)	96 (67-108)	93 (80-107)	N/A	N/A	N/A	N/A
Number at follow-up	n=54	n=54	N/A	n=45	n=44	N/A
Observed data (%), median (IQR)	8.9 (8.1-11.3)	8.7 (7.2-10.1)	N/A	9.5 (7.8-12.2)	8.3 (7.5-10)	N/A
Observed data (mmol/mol), median (IQR)	74 (65-100)	72 (55-87)	N/A	80 (62-110)	67 (58-86)	N/A
Change from baseline (%),[d] mean (SE)	−1.4 (0.3)	−2 (0.3)	N/A	−1.0 (0.3)	−2.1 (0.3)	N/A
Change from baseline (mmol/mol),[d] mean (SE)	15 (3)	22 (3)	N/A	11 (3)	23 (3)	N/A
Difference in change,[d,e] mean (SE)	Reference	−0.6 (0.4)	.18	Reference	−1.1 (0.4)	.01
Adjusted difference in change,[d,e,f] mean (SE)	Reference	−0.5 (0.4)	.20	Reference	−0.7 (0.4)	.09
HbA_{1c} <7% (53 mmol/mol),[g] n (%)	2 (3.7)	7 (13.0)	.16	2 (4.4)	3 (6.8)	.68
HbA_{1c} <6.5% (48 mmol/mol),[g] n (%)	1 (1.9)	4 (7.4)	.36	0 (0)	3 (6.8)	.12
HbA_{1c} <HEDIS[h] target, n (%)	9 (16.7)	22 (40.7)		9 (20)	16 (36.4)	
HbA_{1c} <HEDIS target,[i] OR[j] (95% CI)	Reference	3.29 (1.32-8.13)	.01	Reference	2.1 (0.8-5.55)	.13
Point-of-care glucose						
Fasting only	n=27	n=27	N/A	n=21	n=20	N/A
Observed data, median (IQR)	212 (149-258)	166 (142-239)	N/A	209 (129.5-234)	152.5 (127.3-247.3)	N/A
Adjusted difference,[e] mean (SE)	Reference	−18 (23)	.44	Reference	−26.5 (30.3)	.39
Any	n=40	n=45	N/A	n=33	n=33	N/A
Observed data, median (IQR)	209.5 (133.8-258)	179 (150.5-144.5)	N/A	209 (136.5-295)	161 (134-230)	N/A
Adjusted difference[k]	Reference	−23.9 (20.8)	.25	Reference	−30.4 (21.9)	.17

[a]Estimated using a linear mixed model.

[b]Data for follow-up HbA_{1c} levels were collected at study visits and, when possible, extracted from the electronic medical records. All other data were obtained during the study visits. One death occurred at 24 weeks in the DOS group.

[c]N/A: not applicable.

[d]Change from baseline in discharge order set; change from baseline in enhanced standard care.

[e]Adjusted for age, work status, insurance, and functional health literacy scores. Two participants were excluded from the analysis because of missing functional health literacy scores.

[f]Adjusted for age, neuropathy, total daily insulin dose, insulin before admission, reason for hospitalization, and metformin use at discharge.

[g]Mixed models could not be fit owing to small cell sizes; Fisher Exact Tests were performed instead.

[h]HEDIS: Health Care Effectiveness Data and Information Set (target is <8% if age ≥65 years or known history of ischemic vascular disease, heart failure, advanced kidney disease [estimated glomerular filtration rate of <30 mL/min/1.73 m^2], dementia, proliferative retinopathy or blindness, advanced neuropathy [history of ulcer or amputation], or history of severe hypoglycemia; otherwise, goal is <7%).

[i]Estimate (95% CI). From separate logistic regression models fitted to data at each time point, odds ratios adjusted for baseline HbA_{1c} but not for confounders, owing to small cell counts.

[j]OR: odds ratio.

[k]Adjusted for marital status, insurance, and bolus insulin use at admission.

Health Care Use

Readmissions within 30 days (exploratory outcome) occurred in 17 (13%) of the participants. Among all participants, primary care follow-up was 55%, 74%, and 87% at 2, 6, and 12 weeks while endocrinology visits occurred in 23%, 27%, and 52% of participants at 2, 6, and 12 weeks, respectively. Emergency department visits, readmission rates, primary care, and endocrinology follow-up visits were similar between the groups (Table S4 in Multimedia Appendix 1).

Diabetes Medications and Hypoglycemia

The basal insulin dose and initiation of glucose-lowering medications were similar between the groups at follow-up (Tables S4 and S5 in Multimedia Appendix 1). At the 2- and 24-week follow-ups, changes in basal insulin dose were similar. However, patients in the DOS arm were significantly more likely to have an increase in basal insulin dose at 12 weeks (25/45, 53%, vs 8/38, 21%; OR 4.70, 95% CI 1.63-13.52), and the difference at 6 weeks was marginally significant (16/34, 49%, vs 8/9, 23%; OR 3.53, 95% CI 1.18-10.62). Patients in the DOS group were also more likely to have a *decrease* in basal insulin dose at 12 weeks (13/45, 28%, vs 1/38, 3%; *P*=.009), but not at other time points (Table S4 in Multimedia Appendix 1). Basal insulin adherence was similar at all follow-up time points (Table S4 in Multimedia Appendix 1). Hypoglycemic events were similar between the groups (Table S4 in Multimedia Appendix 1).

Discussion

Principal Findings

In this study, an insulin-specific DOS was developed to address barriers to prescribing insulin and to improve hospital transition of care among persons with T2D. The DOS resulted in improvements in prescriptions for bolus insulin, needles, and testing supplies, but did not improve order clarity. Follow-up data were available for a subset of patients for whom there were favorable trends in adjusted HbA_{1c} levels, despite early discontinuation of study recruitment. These data from the first study to implement a dedicated DOS among hospitalized patients with T2D requiring insulin provide important insights for optimizing hospital diabetes discharge programs.

Discharge Orders

Medication reconciliation is a cognitively demanding task, particularly when insulin is involved. Despite the readily available electronic medication reconciliation functionality, there is still an opportunity to improve discharge orders for insulin. In this study, a DOS improved the frequency of missing prescriptions for insulin and glucose monitoring supplies. This is of critical importance, because disruption of insulin therapy is a known predictor of hospital readmission, higher HbA_{1c} levels, and increased costs [15]. Moreover, the omission of preadmission diabetes therapies at discharge is associated with higher readmission and mortality rates [15,29,30]. These findings are novel in that proposed interventions to date have included individual provider education, traditional quality improvement initiatives, or hiring pharmacists rather than enhancing electronic decision support [31-34]. Although not an integral component of the DOS studied here, we observed no significant change in the proportion of patients who were prescribed metformin and other noninsulin therapies from admission to discharge. Future iterations should also consider the optimization of noninsulin therapies, particularly to reduce cardiorenal risk [34].

However, there are opportunities to improve the clarity of insulin instructions in the EMR. Dosing fields are typically inadequate, resulting in the need to use free text fields or provide discharge instructions via a separate workflow that is external to the electronic medication reconciliation process [11]. Additional customization could include fields that account for oral intake, glucose level, or time of day, guide patient self-titration, or calculate the quantity dispensed. In particular, decision support could provide guidance for converting flexible meal dosing (the standard practice at the study institution) to fixed meal dosing, which is more appropriate for many patients. Additional benefits could be achieved by implementing a remote monitoring program postdischarge and device integration (smart insulin pen and glucose monitor) within the EMR. Ironically, one artifact may have been introduced by the multifaceted intervention itself, which required a switch in basal insulin at discharge, often late in hospitalization and possibly after other discharge orders were populated. Following the closure of the study and after obtaining feedback from the institution's multidisciplinary inpatient Glucose Management Committee, additional revisions to the DOS were made, including presenting pens as the preferred choice and adding concentrated and premixed insulin orders.

Follow-up Data

In this study, HbA_{1c} reduction was evident in both groups, likely owing to the provision of insulin therapy (at least, in part). The individualized HEDIS goal was reached by more patients in the DOS group at 3 months, but there was a waning of effect from 3 to 6 months as the intervention intensity decreased. This phenomenon has been previously described and underscores the need for ongoing high frequency care [10]. The HbA_{1c} reduction was similar to or somewhat smaller in magnitude compared with other prospective nonrandomized studies of recently hospitalized patients [35,36].

A greater proportion of participants had an increase in the basal insulin dose in the DOS group at 6 and 12 weeks but not at 2 weeks, compared with the ESC group. This emphasizes the utility of early hospital follow-ups to review any prescription needs, assess the patient's understanding of the diabetes regimen, obtain a history of hyperglycemia or hypoglycemia, and remind patients to perform self-titration where relevant. Moreover, early visits could address the need for prandial insulin (to avoid overreliance on basal insulin) if not already prescribed and noninsulin therapies. At the 12-week time point, it is important to establish a plan for continued frequent contact (such as monthly visits by a pharmacist or nurse) to maintain early success.

Despite a favorable trend in HbA_{1c} levels, hypoglycemia was similar in both the groups. While the total daily dose of insulin was reasonable at 0.61 unit/kg, patients tended to have

basal-heavy regimens and might have benefited from a dose reduction at discharge to further reduce the frequency of hypoglycemia [36].

While the study population was generalizable owing to the broad inclusion criteria, the limited follow-up data greatly impacted the ability to assess the external validity of the postdischarge component of the intervention. This study was not designed to address many barriers to successful transitions of care, including clinical inertia, as well as patient-specific factors such as mental health, physical disability, literacy, financial hardship, social factors, and lack of transportation [14,37]. While formal diabetes education is of tremendous value in helping prepare patients for hospital discharge [12,38], it is not widely available or reimbursable in the hospital setting. Comprehensive models that incorporate bedside nurses, dietitians, care managers, and pharmacists, possibly in combination with video or web-based education resources with timely feedback may help to bridge the gap in education [12,38,39]. Specially trained navigators, caseworkers, or community health workers can help address other barriers. Finally, multilevel interventions should incorporate frequent contact, target the highest-risk patients, and span multiple domains of care [40,41]. Access to and quality of care should improve as telehealth visits and remote glucose monitoring become mainstream.

Limitations

As noted in the previous paragraph, the limitations of the study relate to loss to follow-up, even within the context of specifically dedicated study staff and other enhancements. The COVID-19 pandemic presented the largest barrier to carrying out study procedures, as dropout was more common among patients who were enrolled in the 6 months before the start of the pandemic. Unfortunately, we were able to address this issue only partially with telehealth or minimal contact strategies; this highlights the overall vulnerability of our patient population. Furthermore, it is unknown whether similar results would be achieved in other populations (type 1 diabetes, noninsulin requiring, and broader age range). As with other multicomponent interventions, it is difficult to discern which components of the discharge instruction or nursing support were the primary determinants of success. Finally, while the DOS increased the completeness of diabetes medications at discharge, it was launched by the study team to understand its utility under optimal use. Thus, an additional study of the usability, acceptability, and implementation of the DOS is needed. For example, it would have been useful to quantify the time saved through the use of the order set owing to the presence of prefilled fields and decision support.

Conclusions

An intervention that included electronic DOS plus postdischarge nurse phone calls resulted in more complete discharge prescriptions for insulin and related supplies. However, there is an opportunity to improve the clarity of the instructions. Post discharge HbA_{1c} levels showed favorable trends, but interpretation of data is limited owing to loss of follow-up amid COVID-19 pandemic restrictions. More intensive interventions are needed to optimize postdischarge care.

Acknowledgments

This investigator-sponsored study was funded by Sanofi. The authors wish to thank Amber Anaya and Angela Hoffman for their contributions to this project. This project was supported in part by award number UL1TR001070 from the National Center for Advancing Translational Sciences. The content is solely the responsibility of the authors and does not represent the views of the National Center for Advancing Translational Sciences or National Institutes of Health. The full protocol is available upon request to the corresponding author (KD).

The Diabetes Empowerment scale was supported by grant number P30DK020572 (Michigan Diabetes Research Center) from the National Institute of Diabetes and Digestive and Kidney Diseases.

Conflicts of Interest

KD discloses research support from Novo Nordisk, Sanofi, Viacyte, Abbott, and Dexcom; consulting with Eli Lilly, Novo Nordisk, Boehringer-Ingelheim, Dexcom, and Tolerion; and honorarium from UptoDate and Elsevier. MP discloses research support from Pfizer. EB discloses research support from Dexcom and the Juvenile Diabetes Research Foundation. KW discloses research support from Sanofi and Allergan, consulting with Novo Nordisk, and honorarium from Nova Biomedical.

Multimedia Appendix 1
Supplemental data.
[DOCX File , 39 KB - diabetes_v7i3e33401_app1.docx]

Multimedia Appendix 2
CONSORT (Consolidated Standards of Reporting Trials) diagram (patient flow diagram).
[PPTX File , 36 KB - diabetes_v7i3e33401_app2.pptx]

Multimedia Appendix 3
CONSORT-eHEALTH checklist (V 1.6.1).

[PDF File (Adobe PDF File), 4438 KB - diabetes_v7i3e33401_app3.pdf]

References

1. National Diabetes Statistics Report. Centers for Disease Control and Prevention. URL: https://www.cdc.gov/diabetes/data/statistics-report/index.html [accessed 2022-04-11]
2. American Diabetes Association. Economic costs of diabetes in the U.S. in 2017. Diabetes Care 2018 May;41(5):917-928 [FREE Full text] [doi: 10.2337/dci18-0007] [Medline: 29567642]
3. Benoit SR, Hora I, Pasquel FJ, Gregg EW, Albright AL, Imperatore G. Trends in emergency department visits and inpatient admissions for hyperglycemic crises in adults with diabetes in the U.S., 2006-2015. Diabetes Care 2020 May;43(5):1057-1064. [doi: 10.2337/dc19-2449] [Medline: 32161050]
4. American Diabetes Association Professional Practice Committee, Draznin B, Aroda VR, Bakris G, Benson G, Brown FM, et al. 6. Glycemic targets: standards of medical care in diabetes-2022. Diabetes Care 2022 Jan 01;45(Suppl 1):S83-S96. [doi: 10.2337/dc22-S006] [Medline: 34964868]
5. Fang M, Wang D, Coresh J, Selvin E. Trends in diabetes treatment and control in U.S. adults, 1999-2018. N Engl J Med 2021 Jun 10;384(23):2219-2228 [FREE Full text] [doi: 10.1056/NEJMsa2032271] [Medline: 34107181]
6. Gregg EW, Hora I, Benoit SR. Resurgence in diabetes-related complications. JAMA 2019 May 21;321(19):1867-1868. [doi: 10.1001/jama.2019.3471] [Medline: 30985875]
7. American Diabetes Association Professional Practice Committee, American Diabetes Association Professional Practice Committee:, Draznin B, Aroda VR, Bakris G, Benson G, et al. 16. Diabetes care in the hospital: standards of medical care in diabetes-2022. Diabetes Care 2022 Jan 01;45(Suppl 1):S244-S253. [doi: 10.2337/dc22-S016] [Medline: 34964884]
8. Umpierrez GE, Hellman R, Korytkowski MT, Kosiborod M, Maynard GA, Montori VM, Endocrine Society. Management of hyperglycemia in hospitalized patients in non-critical care setting: an endocrine society clinical practice guideline. J Clin Endocrinol Metab 2012 Jan;97(1):16-38. [doi: 10.1210/jc.2011-2098] [Medline: 22223765]
9. Cook CB, Seifert KM, Hull BP, Hovan MJ, Charles JC, Miller-Cage V, et al. Inpatient to outpatient transfer of diabetes care: planing for an effective hospital discharge. Endocr Pract 2009 Apr;15(3):263-269. [doi: 10.4158/EP.15.3.263] [Medline: 19364697]
10. Wexler DJ, Beauharnais CC, Regan S, Nathan DM, Cagliero E, Larkin ME. Impact of inpatient diabetes management, education, and improved discharge transition on glycemic control 12 months after discharge. Diabetes Res Clin Pract 2012 Nov;98(2):249-256 [FREE Full text] [doi: 10.1016/j.diabres.2012.09.016] [Medline: 23036785]
11. Donihi AC. Practical recommendations for transitioning patients with type 2 diabetes from hospital to home. Curr Diab Rep 2017 Jul;17(7):52. [doi: 10.1007/s11892-017-0876-1] [Medline: 28573408]
12. Dungan K, Lyons S, Manu K, Kulkarni M, Ebrahim K, Grantier C, et al. An individualized inpatient diabetes education and hospital transition program for poorly controlled hospitalized patients with diabetes. Endocr Pract 2014 Dec;20(12):1265-1273. [doi: 10.4158/EP14061.OR] [Medline: 25100371]
13. Kimmel B, Sullivan MM, Rushakoff RJ. Survey on transition from inpatient to outpatient for patients on insulin: what really goes on at home? Endocr Pract 2010;16(5):785-791. [doi: 10.4158/EP10013.OR] [Medline: 20350914]
14. Wheeler K, Crawford R, McAdams D, Robinson R, Dunbar VG, Cook CB. Inpatient to outpatient transfer of diabetes care: perceptions of barriers to postdischarge followup in urban African American patients. Ethn Dis 2007;17(2):238-243. [Medline: 17682352]
15. Wu EQ, Zhou S, Yu A, Lu M, Sharma H, Gill J, et al. Outcomes associated with insulin therapy disruption after hospital discharge among patients with type 2 diabetes mellitus who had used insulin before and during hospitalization. Endocr Pract 2012;18(5):651-659. [doi: 10.4158/EP11314.OR] [Medline: 22440990]
16. Rodriguez A, Magee M, Ramos P, Seley JJ, Nolan A, Kulasa K, et al. Best practices for interdisciplinary care management by hospital glycemic teams: results of a society of hospital medicine survey among 19 U.S. hospitals. Diabetes Spectr 2014 Aug;27(3):197-206 [FREE Full text] [doi: 10.2337/diaspect.27.3.197] [Medline: 26246780]
17. Wright A, Feblowitz JC, Pang JE, Carpenter JD, Krall MA, Middleton B, et al. Use of order sets in inpatient computerized provider order entry systems: a comparative analysis of usage patterns at seven sites. Int J Med Inform 2012 Nov;81(11):733-745 [FREE Full text] [doi: 10.1016/j.ijmedinf.2012.04.003] [Medline: 22819199]
18. Schnipper JL, Liang CL, Ndumele CD, Pendergrass ML. Effects of a computerized order set on the inpatient management of hyperglycemia: a cluster-randomized controlled trial. Endocr Pract 2010;16(2):209-218. [doi: 10.4158/EP09262.OR] [Medline: 20061280]
19. Shaw IT, Deiter R, Dungan KM. Prolonged glucose lowering therapy in post-cardiac surgery-induced stress hyperglycemia. In: Proceedings of the 2013 Annual Conference of Endocrine Society. 2013 Presented at: Endo '13; June 15-18, 2013; San Francisco, CA, USA p. 822.
20. Turner R, Stratton I, Horton V, Manley S, Zimmet P, Mackay IR, et al. UKPDS 25: autoantibodies to islet-cell cytoplasm and glutamic acid decarboxylase for prediction of insulin requirement in type 2 diabetes. UK Prospective Diabetes Study Group. Lancet 1997 Nov 01;350(9087):1288-1293. [doi: 10.1016/s0140-6736(97)03062-6] [Medline: 9357409]
21. Tuomi T, Carlsson A, Li H, Isomaa B, Miettinen A, Nilsson A, et al. Clinical and genetic characteristics of type 2 diabetes with and without GAD antibodies. Diabetes 1999 Jan;48(1):150-157. [doi: 10.2337/diabetes.48.1.150] [Medline: 9892237]

22. Tian W. An All-Payer View of Hospital Discharge to Postacute Care, 2013. HCUP Statistical Brief #205. Agency for Healthcare Research and Quality. Rockville, MD, USA: Agency for Healthcare Research and Quality; 2016 May. URL: http://www.hcup-us.ahrq.gov/reports/statbriefs/sb205-Hospital-Discharge-Postacute-Care.pdf [accessed 2022-05-31]
23. Oakes JM, Feldman HA. Statistical power for nonequivalent pretest-posttest designs. The impact of change-score versus ANCOVA models. Eval Rev 2001 Feb;25(1):3-28. [doi: 10.1177/0193841X0102500101] [Medline: 11205523]
24. Comprehensive Diabetes Care (CDC). National Committee for Quality Assurance. 2020. URL: https://www.ncqa.org/hedis/measures/comprehensive-diabetes-care/ [accessed 2021-01-25]
25. Holm S. A simple sequentially rejective multiple test procedure. Scand J Stat 1979;6(2):65-70 [FREE Full text]
26. Anderson RM, Fitzgerald JT, Gruppen LD, Funnell MM, Oh MS. The Diabetes Empowerment Scale-Short Form (DES-SF). Diabetes Care 2003;26(5):1641-1642. [doi: 10.2337/diacare.26.5.1641-a] [Medline: 12716841]
27. Weiss BD, Mays MZ, Martz W, Castro KM, DeWalt DA, Pignone MP, et al. Quick assessment of literacy in primary care: the newest vital sign. Ann Fam Med 2005;3(6):514-522. [doi: 10.1370/afm.405] [Medline: 16338915]
28. Zimet GD, Dahlem NW, Zimet SG, Farley GK. The Multidimensional Scale of Perceived Social Support. J Pers Assess 1988;52(1):30-41. [doi: 10.1207/s15327752jpa5201_2]
29. Lipska KJ, Wang Y, Kosiborod M, Masoudi FA, Havranek EP, Krumholz HM, et al. Discontinuation of antihyperglycemic therapy and clinical outcomes after acute myocardial infarction in older patients with diabetes. Circ Cardiovasc Qual Outcomes 2010 May;3(3):236-242. [doi: 10.1161/CIRCOUTCOMES.109.887620] [Medline: 20354220]
30. Montejano L, Vo L, McMorrow D. Transitions of care for people with type 2 diabetes: utilization of antihyperglycemic agents pre- and post-hospitalization. Diabetes Ther 2016 Mar;7(1):91-103 [FREE Full text] [doi: 10.1007/s13300-015-0148-5] [Medline: 26659004]
31. Turchin A, Sosina O, Zhang H, Shubina M, Desai SP, Simonson DC, et al. Ambulatory medication reconciliation and frequency of hospitalizations and emergency department visits in patients with diabetes. Diabetes Care 2018 Aug;41(8):1639-1645. [doi: 10.2337/dc17-1260] [Medline: 29891639]
32. Shah N, Kulasa K. Diabetes medication reconciliation at hospital discharge. J Endocr Soc 2021 May 3;5(Suppl 1):A424. [doi: 10.1210/jendso/bvab048.866]
33. Medications at Transitions and Clinical Handoffs (MATCH) Toolkit for Medication Reconciliation. Agency for Healthcare Research and Quality. 2012 Aug. URL: https://www.ahrq.gov/sites/default/files/publications/files/match.pdf [accessed 2022-04-12]
34. American Diabetes Association Professional Practice Committee, Draznin B, Aroda VR, Bakris G, Benson G, Brown FM, et al. 9. Pharmacologic approaches to glycemic treatment: standards of medical care in diabetes-2022. Diabetes Care 2022 Jan 01;45(Suppl 1):S125-S143. [doi: 10.2337/dc22-S009] [Medline: 34964831]
35. Perez A, Carrasco-Sánchez FJ, González C, Seguí-Ripoll JM, Trescolí C, Ena J, et al. Efficacy and safety of insulin glargine 300 U/mL (Gla-300) during hospitalization and therapy intensification at discharge in patients with insufficiently controlled type 2 diabetes: results of the phase IV COBALTA trial. BMJ Open Diabetes Res Care 2020 Sep;8(1):e001518 [FREE Full text] [doi: 10.1136/bmjdrc-2020-001518] [Medline: 32928792]
36. Gianchandani RY, Pasquel FJ, Rubin DJ, Dungan KM, Vellanki P, Wang H, et al. The efficacy and safety of co-administration of sitagliptin with metformin in patients with type 2 diabetes at hospital discharge. Endocr Pract 2018 Jun;24(6):556-564 [FREE Full text] [doi: 10.4158/EP-2018-0036] [Medline: 29949432]
37. Rubin DJ, Donnell-Jackson K, Jhingan R, Golden SH, Paranjape A. Early readmission among patients with diabetes: a qualitative assessment of contributing factors. J Diabetes Complications 2014;28(6):869-873. [doi: 10.1016/j.jdiacomp.2014.06.013] [Medline: 25087192]
38. Healy SJ, Black D, Harris C, Lorenz A, Dungan KM. Inpatient diabetes education is associated with less frequent hospital readmission among patients with poor glycemic control. Diabetes Care 2013 Oct;36(10):2960-2967 [FREE Full text] [doi: 10.2337/dc13-0108] [Medline: 23835695]
39. Hardee SG, Osborne KC, Njuguna N, Allis D, Brewington D, Patil SP, et al. Interdisciplinary diabetes care: a new model for inpatient diabetes education. Diabetes Spectr 2015 Nov;28(4):276-282 [FREE Full text] [doi: 10.2337/diaspect.28.4.276] [Medline: 26600730]
40. Golden SH, Maruthur N, Mathioudakis N, Spanakis E, Rubin D, Zilbermint M, et al. The case for diabetes population health improvement: evidence-based programming for population outcomes in diabetes. Curr Diab Rep 2017 Jul;17(7):51 [FREE Full text] [doi: 10.1007/s11892-017-0875-2] [Medline: 28567711]
41. Draznin B, Kahn PA, Wagner N, Hirsch IB, Korytkowski M, Harlan DM, et al. Clinical diabetes centers of excellence: a model for future adult diabetes care. J Clin Endocrinol Metab 2018 Mar 01;103(3):809-812. [doi: 10.1210/jc.2017-02388] [Medline: 29309595]

Abbreviations

DOS: discharge order set
EMR: electronic medical record
ESC: enhanced standard care

Gla-300: insulin glargine 300 U/mL
HbA_{1c}: glycated hemoglobin
HEDIS: Health Care Effectiveness Data and Information Set
OR: odds ratio
REDCap: Research Electronic Data Capture
T2D: type 2 diabetes mellitus

Edited by YK Lin; submitted 07.09.21; peer-reviewed by G Cappon, YL Leung; comments to author 15.03.22; revised version received 10.05.22; accepted 15.06.22; published 26.07.22.

Please cite as:
White A, Bradley D, Buschur E, Harris C, LaFleur J, Pennell M, Soliman A, Wyne K, Dungan K
Effectiveness of a Diabetes-Focused Electronic Discharge Order Set and Postdischarge Nursing Support Among Poorly Controlled Hospitalized Patients: Randomized Controlled Trial
JMIR Diabetes 2022;7(3):e33401
URL: https://diabetes.jmir.org/2022/3/e33401
doi:10.2196/33401
PMID:35881437

Review

Type 1 Diabetes Hypoglycemia Prediction Algorithms: Systematic Review

Stella Tsichlaki[1], MSc; Lefteris Koumakis[2], PhD; Manolis Tsiknakis[1,2], PhD

[1]Department of Electrical & Computer Engineering, Hellenic Mediterranean University, Heraklion, Greece

[2]Institute of Computer Science, Foundation for Research and Technology-Hellas, Heraklion, Greece

Corresponding Author:
Stella Tsichlaki, MSc
Department of Electrical & Computer Engineering
Hellenic Mediterranean University
Gianni Kornarou, Estavromenos 1
Heraklion, 71004
Greece
Phone: 30 6945231917
Email: stsichlaki@gmail.com

Abstract

Background: Diabetes is a chronic condition that necessitates regular monitoring and self-management of the patient's blood glucose levels. People with type 1 diabetes (T1D) can live a productive life if they receive proper diabetes care. Nonetheless, a loose glycemic control might increase the risk of developing hypoglycemia. This incident can occur because of a variety of causes, such as taking additional doses of insulin, skipping meals, or overexercising. Mainly, the symptoms of hypoglycemia range from mild dysphoria to more severe conditions, if not detected in a timely manner.

Objective: In this review, we aimed to report on innovative detection techniques and tactics for identifying and preventing hypoglycemic episodes, focusing on T1D.

Methods: A systematic literature search following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines was performed focusing on the *PubMed*, *GoogleScholar*, *IEEEXplore*, and *ACM* Digital Library to find articles on technologies related to hypoglycemia detection in patients with T1D.

Results: The presented approaches have been used or devised to enhance blood glucose monitoring and boost its efficacy in forecasting future glucose levels, which could aid the prediction of future episodes of hypoglycemia. We detected 19 predictive models for hypoglycemia, specifically on T1D, using a wide range of algorithmic methodologies, spanning from statistics (1.9/19, 10%) to machine learning (9.88/19, 52%) and deep learning (7.22/19, 38%). The algorithms used most were the Kalman filtering and classification models (support vector machine, k-nearest neighbors, and random forests). The performance of the predictive models was found to be satisfactory overall, reaching accuracies between 70% and 99%, which proves that such technologies are capable of facilitating the prediction of T1D hypoglycemia.

Conclusions: It is evident that continuous glucose monitoring can improve glucose control in diabetes; however, predictive models for hypo- and hyperglycemia using only mainstream noninvasive sensors such as wristbands and smartwatches are foreseen to be the next step for mobile health in T1D. Prospective studies are required to demonstrate the value of such models in real-life mobile health interventions.

(JMIR Diabetes 2022;7(3):e34699) doi:10.2196/34699

KEYWORDS

type 1 diabetes; hypoglycemia; predictive models; continuous glucose monitoring; heart rate variability; artificial intelligence

Introduction

Diabetes is a recurrent condition that involves constant control and self-management of the patient's blood glucose. Improper regulation of blood glucose levels in patients with type 1 diabetes (T1D) can lead to severe problems, such as kidney and heart failure, stroke, and blindness [1]. In contrast, through appropriate care for diabetes, a patient can live a prosperous life. Nevertheless, an overly strict glycemic control can raise the likelihood of developing hypoglycemia, a rapid decrease in

blood glucose levels, which may lead to coma and potentially death if proper care is not taken immediately.

The concern of hypoglycemia is a barrier to successful hyperglycemic control, as it encourages insulin underdoing. Methods of reducing hypoglycemia occurrences include instruction and counseling to increase hypoglycemia recognition in time, as well as the development of predictive technological approaches that could reduce the occurrences of hypoglycemia. Blood glucose self-monitoring requires a blood sample to be collected on many occasions throughout the day. Currently, the use of continuous glucose monitoring (CGM) systems allows the collection of blood glucose level information in real time. In contrast, modern wearables can produce and analyze great amounts of data, which is the reason why modern technologies are frequently used in conjunction with these products to process and retrieve valuable information from the collected data. They also have several different monitoring capabilities, such as GPS, heart rate, electrocardiogram (ECG), and skin temperature, which are all important for the assessment of diabetes-related indicators [2]. Furthermore, several key indicators for the physical and mental health state of patients with T1D, such as blood glucose levels, calories, physical activity, and stress level, can be monitored by evaluating the data obtained from wearables. The main advantage of these devices is their ability to keep track of the patient's daily routine in a continuous and discreet manner without affecting their normal everyday activities.

Artificial intelligence algorithms have been widely used to predict diabetes or as diagnostic tools, especially for type 2 diabetes [3]. Machine learning models have been used to predict the near future blood glucose levels and inform patients to take appropriate actions in advance to avoid a hypo- or hyperglycemic episode [4]. An accurate predictor could improve the quality of life of patients with T1D.

The aim of this paper was to review the emerging detection methods and approaches for the identification of hypoglycemia episodes. Specifically, we investigated the methods used or invented to improve blood glucose monitoring and increase its effectiveness to estimate future glucose levels; this could contribute to the prediction process of future episodes of hypoglycemia. Overall, these methods are highly valuable based on whether they can aid the prediction process, which is critical in avoiding a potentially dangerous hypoglycemic episode that could lead to major health consequences. Finally, we discuss prediction approaches aimed at the early identification and prevention of nocturnal hypoglycemia episodes, which could lead to "dead-in-bed" syndrome if not identified early. These approaches are categorized as mentioned previously, and their proposed techniques are discussed.

Methods

Article Identification

A systematic literature search following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [5] was performed. For this research, we used *PubMed*, *GoogleScholar*, *IEEEXplore*, and *ACM* Digital Library to find articles about technologies related to hypoglycemia detection in patients with T1D. After exploring and combining many search terms to ensure having the broadest results, we used the following terms: "hypoglycemia," "prediction," "detection," "continuous glucose monitoring," "CGM," "type 1 diabetes," "T1D," "HRV," "heart rate variability," "machine learning," and "deep learning."

Inclusion and Exclusion Criteria

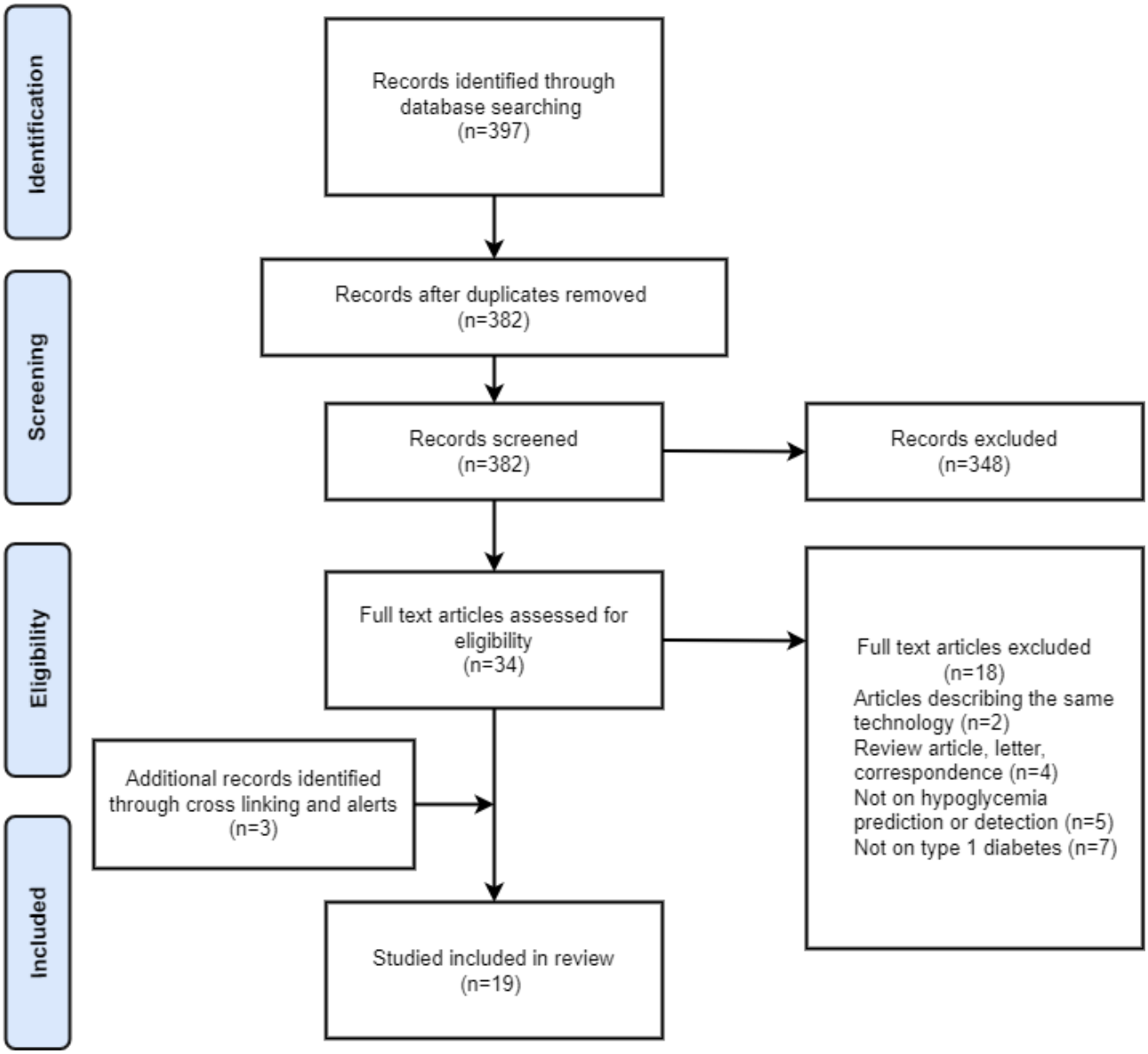
The search was performed in June 2021 and was restricted to articles from 2005 onward. In parallel, an alert was set to avoid missing articles. References of selected articles were analyzed to extract other related articles, and a complementary search in Google Scholar was used to find further information when necessary and complete the review with original works on each subtopic identified. All the authors deliberated and agreed on the inclusion and exclusion criteria. In case of disagreements, these were resolved through discussion among the authors to reach a consensus. In the first step of the screening process, journal articles and conference papers were deemed suitable for inclusion, whereas letters, correspondence, and review articles were excluded from this systematic review. Articles reporting on new glucose sensors that exhibit a linear detection range wide enough for blood or interstitial measurement were eligible. For prediction algorithms, the eligible articles had to report methods for glucose prediction and present details on the data sets used, methodology, and performance metrics. We included algorithms that predicted glucose values in a defined prediction horizon, as well as those that specifically predicted hypoglycemic events up to a maximum of 24 hours in the future. To be eligible, a study had to focus on hypoglycemia or include hypoglycemia prediction or detection techniques based on patient data. The patient group had to have T1D, whereas the trials had to have a control group. Studies that described the same methodology and technology as an already included study without significant distinction were excluded. We excluded trials that focused on the primary prevention of diabetes, those targeting gestational diabetes, those pertaining to a closed-loop or artificial pancreas system, and those that primarily focused on type 2 diabetes.

Results

Study Selection

In total, the aforementioned literature search gave 397 results. Of the 397 records, 382 (96.2%) were screened after the removal of 15 (3.8%) duplicates, and 348 (87.7%) articles were excluded as they did not meet our eligibility criteria. After reading the full text of the remaining 34 articles, complimentary alerts helped to add 3 more articles that were also evaluated based on the aforementioned screening process, resulting in the inclusion of 19 eligible articles in total. Figure 1 presents the PRISMA flow diagram [5], illustrating the search and screening procedure of this review.

Figure 1. The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram presenting the search and screening strategy followed in this systematic review.



Study Characteristics

Prediction algorithms aid in further enhancement of the quality of life of patients with T1D and their ability to avoid hypoglycemia. They enable patients to intervene early and successfully for the prevention of hypoglycemia episodes. Several of the approaches introduce novel algorithms for predicting hypoglycemia. However, only a few of them sought to assess their clinical efficacy and advantages in real-life settings. The details of each reviewed study are presented in Table 1, where we report the publication, the data set used, the technique on which the predictive model is based, and the resulting accuracy of the model.

Table 1. Summary of the reviewed hypoglycemia prediction approaches.

Study	Duration	Data set	Age (years)	Technique	Result
Mordvanyuk et al [6], 2017	500 simulated days	11 computer-generated adults through UVA-Padova T1D[a] Simulator	>18	K-nearest neighbors	• Accuracy 83.64%
Paul et al [7], 2015	6 weeks	6 patients from diabetes research in children network (DirecNet)	Mean 7 (SD 3)	Autoregressive models of higher and lower orders; state space model	• Relative error (higher autoregressive) –7% • Relative error (lower autoregressive) –24% • Relative error (state space) –12%
Jensen et al [8], 2013	2 experimental sessions for each participant	10 male patients with T1D	Mean 44 (SD 15)	SVM[b]	• AUC[c]-ROC[d] 0.962 • Sample-based sensitivity 81% • Sample-based specificity 93% • Event-based sensitivity 100%
Zhang et al [9], 2008	N/A[e]	Multiparameter Intelligent Monitoring in Intensive Care Database II	N/A	Classification tree	• Accuracy 86% • Sensitivity 89.87%
Dave et al [10], 2020	90 days	112 patients with T1D	Mean 11 (SD 10)	LR[f] and RF[g]	• Sensitivity (LR) 91.85% • Specificity (LR) 96.25% • Sensitivity (RF) 94.20% • Specificity (RF) 96.67%
Eren-Oruklu et al [11], 2010	24 hours	54 patients with T1D	Mean 12.5 (SD 5.5)	Absolute predicted glucose values; cumulative sum; exponentially weighted moving average	• Sensitivity 89%, 87.5%, and 89% • Specificity 67%, 74%, and 78%
Chase et al [12], 2010	Overnight	40 patients with T1D	Mean 21 (SD 7.5)	Linear projection; Kalman filtering; hybrid infinite impulse; statistical prediction; numerical logical algorithm	• Sensitivity 84%
Buckingham et al [13], 2013	21 nights	19 patients with T1D	≥18	Kalman Filtering	• AUC algorithm 1 71% • AUC algorithm 2 90% • AUC algorithm 3 89%
Georga et al [14], 2013	From 5 to 22 days	15 patients with T1D	Mean 42 (SD 23)	Support vector for regression	• Sensitivity (30-minute horizon) 92% • Sensitivity (60-minute horizon) 96%
Bertachi et al [15], 2018	12 weeks	10 patients with T1D	>18	SVM	• Sensitivity 78.75% • Specificity 82.15%
Vahedi et al [16], 2018	4 months	93 patients with T1D	Mean 46 (SD 38)	MLP[h] neural networks regressor	• Mean absolute percentage error RF regressor 27.9% • Mean absolute percentage error MLP regressor 29.6%
Maritsch et al [17], 2020	1 week	1 patient with T1D	N/A	Gradient boosting decision tree	• Accuracy 82.7% • Sensitivity 76.7% • Specificity 84.2%
San et al [18], 2016	10 hours overnight	15 children with T1D	<18	Deep belief neural network and restricted Boltzmann machines	• Sensitivity 80% • Specificity 50%

Study	Duration	Data set	Age (years)	Technique	Result
Kuang et al [19], 2021	8 weeks	12 patients with T1D from the OhioT1DM data set	Mean 50 (SD 30)	Deep neural networks; LSTM[i]; artificial RNN[j]	• 30-minute prediction horizon (mg/dL) RMSE[k] 19.10; MAE[l] 13.59; glucose RMSE 22.08 • 60-minute prediction Horizon (mg/dL) RMSE 32.61; MAE 24.25; glucose RMSE 38.04
Zhu et al [20], 2020	360 days (simulation) and 8 weeks (clinical trial)	10 computer-generated adults through the UVA-Padova T1D Simulator and 6 patients with T1D from the OhioT1DM data set	Mean 49 (SD 31)	Dilated RNN and transfer learning	• RMSE 20.1 mg/dL
Li, K, unpublished data, October 2019	6 months	10 computer-generated adults and 10 computer-generated children through the UVA-Padova T1D Simulator	>18 and <18	Deep reinforcement learning; double dilated RNN	• Adults: glucose TIR[m] 93% • Children: glucose TIR 83%
Munoz-Organero et al [21], 2020	10 days (simulation) and 4 days (clinical trial)	40 computer-generated adults through the AIDA Diabetes software and 9 patients with T1D from the D1NAMO Open data set	N/A	LSTM and RNN	• Computer-generated patients: RMSE <5 mg/dL • Real patients: RMSE <10 mg/dL
Ranvier et al [22], 2016	5 days	1 patient with T1D	N/A	Decision tree	• Model validation is in progress because of the lack of patient data variety
Cichosz et al [23], 2014	2 days	10 patients with T1D	Mean 44 (SD 15)	Forward selection and linear LR	• Accuracy 99% • Sensitivity 79%

[a]T1D: type 1 diabetes.
[b]SVM: support vector machine.
[c]AUC: area under the curve.
[d]ROC: receiver operating characteristic.
[e]N/A: not applicable.
[f]LR: logistic regression.
[g]RF: random forest.
[h]MLP: multilayer perceptron.
[i]LSTM: long short-term memory.
[j]RNN: recurrent neural network.
[k]RMSE: root mean square error.
[l]MAE: mean absolute error.
[m]TIR: time in target range.

Hypoglycemia Prediction Algorithms

In a study by Mordvanyuk et al [6], authors examined 11 profiles of patients with T1D using the UVA-Padova T1D Simulator, which is a system developed at the Universities of Virginia and Padova, through research purposes. In their method, they presented the use of k-nearest neighbor on patient data, along with details relevant to a sequence of meals, to forecast a possible hypoglycemic or hyperglycemic episode. Their findings indicate that the use of consecutive data can dramatically improve the results of the prediction, especially when estimates determine the type of meal (ie, breakfast, snack, and lunch). Their approach obtained a sensitivity of 88% when taking into account only carbohydrate intake, fast-acting insulin dose, and premeal blood glucose.

In terms of blood glucose prediction, the algorithms used in these studies include linear autoregressive and state space time series models, classification algorithms such as the support vector machine (SVM), classification trees, logistic regression, and random forest [7-10]. Paul et al [7] studied the use of generalized autoregressive conditional heteroscedasticity (GARCHs) models on CGM profiles of young children with T1D. They aimed to analyze glucose time series and variability, as well as the feasibility of credible blood glucose level prediction. The forecasting capabilities of the GARCH methodology were compared with those of other existing

modeling techniques, such as lower- and higher-order autoregressive models and state space models, where the GARCH method proved to be efficient in recognizing the variability of the glucose profiles and in providing a more credible prediction of short-term future blood glucose levels.

Our research was conducted specifically on patients with T1D, who have the greatest need for this type of prediction algorithm, as they are more complex because of their high sensitivity to exogenous factors and their increased blood glucose variability. In an experiment by Jensen et al [8], the authors established a pattern classification approach to enhance real-time hypoglycemia identification. They examined data from 10 patients with T1D, who experienced 17 insulin-induced hypoglycemic episodes. These episodes were then analyzed to extract characteristics, including the recent insulin intake time and the linear regression of the CGM signal, along with other measures (kurtosis and skewness), at different periods. The various combinations of features were used in an SVM model, and its performance was measured, resulting in the detection of all 17 hypoglycemic incidents, with 1 false positive and a lead time of 14 minutes.

Zhang et al [9] used a classification learning technique to forecast hypoglycemic events during a 1-hour time span. A classification tree was created using a data mining tool, and the input data comprised blood glucose measurements and insulin injection frequency. The accuracy and specificity of hypoglycemia prediction for the classification tree were 86% and 89%, respectively.

Dave et al [10] investigated 2 different approaches to effectively detect hypoglycemic episodes. These approaches comprised logistic regression and random forest. In their machine learning–based hypoglycemia detection method, they used data from 112 patients with T1D and relied on an extensive feature extraction process to identify any possible glucose patterns. Their final model was developed by considering linear and nonlinear models and combining the collected features. The proposed method correctly forecasted hypoglycemic episodes and achieved high sensitivities close to 95% and 94% and specificities of approximately 97% and 95% for prediction horizons of 0 to 15 and 15 to 30 minutes, respectively.

A few studies [11,12] incorporated different algorithms to improve the performance of their models and take advantage of the unique qualities of each algorithm. The different algorithms used in the included approaches were grouped based on their similarity and are presented in Multimedia Appendix 1.

Eren-Oruklu et al [11] examined 3 different time series–based methodologies for hypoglycemia forecasting on a data set of 54 patients with T1D. Their approach involved an exponentially weighted moving average and cumulative sum control chart, as well as the absolute values of the forecasted blood glucose levels. Each patient was fitted with a Medtronic CGM device that obtained blood glucose readings every 5 minutes. They merged the CGM's integrated alert with the estimated hypoglycemia alert, through each of the 3 aforementioned methodologies. They used a 30-minute prediction horizon, where the methodologies scored sensitivities of 89%, 87.5%, and 89%, respectively.

Some of the prediction algorithms used in these studies used linear regressions or Kalman filters, which are computational approaches that use prior data to make short-term predictions and can also be integrated into monitoring equipment. According to the Diabetes Control and Complications Trial [24], 55% of hypoglycemic events occur during sleep; hence, some studies [12,13] addressed the issue of nocturnal hypoglycemia in T1D and argued that CGM alerts may be ineffective while the patient is sleeping [12,13].

Chase et al [12] tracked 40 patients who wore GlucoWatch CGM during the night, and they discovered that 71% of the patients did not react to the alert throughout the night. They proposed that when hypoglycemia is expected, the CGM sensor sends a signal to the pump to cease injecting insulin. To anticipate hypoglycemia, they used a mathematical model that used a system that included specific prediction algorithms. These algorithms were linear projection, Kalman filtering, hybrid infinite impulse, statistical prediction, and numerical logical algorithm. Through the use of current and prior glucose levels, these algorithms forecasted hypoglycemic events. When the number of algorithms used to forecast a hypoglycemic event exceeded the specified voting threshold, the alert was activated. Specifically, when 3 algorithms were used to prompt insulin pump suspension, nocturnal hypoglycemia was avoided, with a sensitivity of 60%. Nevertheless, using only 2 of the algorithms, nocturnal hypoglycemia occurrences were prevented with a sensitivity of 84%. Finally, this study discovered that when the voting threshold increases, the prediction rate drops, although the purpose of their proposed system was to create a balanced ratio between nocturnal hypoglycemia forecasting and the probability of false alarms.

A total of 3 prediction algorithm variants were examined in a 21-night randomized study conducted by Buckingham et al [13] using a Kalman filter–based model. The experiment comprised 19 adult patients with T1D, who were already using the MiniMed Paradigm REAL-Time insulin pump and Medtronic Sof-sensor blood glucose sensor. Pump suspension events occurred on 53% of the intervention nights using the final algorithm. Preliminary effectiveness results indicated that their final algorithm reduced nighttime hypoglycemia by approximately 50%.

Algorithmic Inputs, Process, and Outputs

Through the increasing availability of equipment such as CGMs, insulin pumps, and physical activity trackers, along with the counting of carbohydrates by patients with T1D, a wide variety of data can be collected that can be used to predict blood glucose. Depending on the data gathered, their complexities, and the ultimate objective of the algorithm, a variety of methodologies were used in some of the studies, with 1 or 2 supplementary data inputs, which were typically the insulin doses, carbohydrates, or even both. The prementioned input data are conveniently available, as they are usually captured in sensor-enhanced pump trials and offer sufficient precision for modeling purposes. These 2 additional data inputs were processed by physiological models in many of the evaluated

studies [14,15,22,23] to derive additional characteristics to determine the effects and dynamics of insulin action or meals for a better interpretation by the prediction algorithms.

There is evidence that the inclusion of insulin and carbohydrate data in prediction models often increases the performance of the algorithm, even by a very small amount. However, apart from clinical trials, in which patients are deliberately selected based on their compliance with instructions and their ability (eg, to count carbohydrates), such an input into a real-life environment seems unlikely. Table 2 presents the features that were considered and analyzed in each of the reviewed studies, and Multimedia Appendix 2 presents the number of the hypoglycemia prediction references based on the year of their considered question; it is worth noting that for 2021, we have data for the first 6 months.

Table 2. Features or characteristics considered in the predictive models.

Study	CGM[a] readings	Glucose meter measurements	Insulin dosage	BMI	Carbohydrates	Meals	Activity	ECG[b]	HRV[c]	Diabetes duration	HbA_{1c}[d]
Mordvanyuk et al [6]	✓		✓		✓	✓					
Paul et al [7]	✓										
Jensen et al [8]	✓		✓	✓						✓	
Zhang et al [9]		✓	✓								
Dave et al [10]	✓		✓		✓					✓	✓
Eren-Oruklu et al [11]	✓	✓									
Chase et al [12]	✓	✓		✓						✓	✓
Buckingham et al [13]	✓										✓
Georga et al [14]	✓		✓			✓	✓				✓
Bertachi et al [15]	✓		✓				✓				
Vahedi et al [16]	✓			✓			✓			✓	
Maritsch et al [17]	✓								✓		
San et al [18]		✓						✓			
Kuang et al [19]	✓										
Zhu et al [20]	✓		✓			✓					
Li, K, unpublished data, October 2019	✓		✓			✓					
Munoz-Organero et al [21]	✓		✓			✓					
Ranvier et al [22]						✓	✓	✓			
Cichosz et al [23]	✓	✓	✓					✓	✓	✓	✓

[a]CGM: continuous glucose monitoring.

[b]ECG: electrocardiogram.

[c]HRV: heart rate variability.

[d]HbA_{1c}: hemoglobin A_{1c}.

In a study by Georga et al [14], the authors used data from a recent patient profile to provide their support vector regression model for predicting hypoglycemia incidents during sleep, as well as in the daytime, over 30- and 60-minute time spans. With a hypoglycemia threshold of 70 mg/dL, the patient profile included glucose readings, meals, insulin dosage, and physical activity along with additional elements to account for recurrent nocturnal hypoglycemia caused by previous hypoglycemia, exercise, and sleep. Their model was developed based on a data set of 15 patients with T1D in an unrestricted environment. Nocturnal hypoglycemia predictions had a sensitivity of 94% and time delays of 5.43 and 4.57 minutes, respectively. When physical activities were not considered, the sensitivities for nonnocturnal events were 92% and 96% for the 30- and 60-minute horizons, respectively, with both time delays being <5 minutes. Nevertheless, when physical activities were considered, diurnal sensitivity was reduced by 8% and 3% in each time span. In conclusion, they suggested that their method

was reliable and that both nocturnal and daytime predictions had high precision, exceeding 90%.

Activity Wearables

Another important factor influencing blood glucose levels is physical exercise. Bertachi et al [15] examined the use of physical activity monitors to gather data on heart rate, energy expenditure, and the number of steps taken to improve the prediction ability of their model. In particular, the authors investigated the prediction of nocturnal hypoglycemia in adults with T1D through a FreeStyle Libre CGM device and a physical activity monitor (Fitbit Alta HR, Fitbit). In their 12-week study, 10 adults with T1D were examined under free-living conditions at home; details about the management of T1D, CGM, and the physical activity tracker were obtained. Supervised machine learning algorithms were applied to the data, and prediction models were developed to predict the occurrence of nocturnal hypoglycemia. The authors concluded that >70% of the nocturnal hypoglycemia could be predicted using their approach. Specifically, the prediction of the SVM model produced the highest scores, with a sensitivity of 78.75% and a specificity of 82.15%.

Overall, the inclusion of a patient activity signal as an input to the algorithm can improve its predictability, which in practice indicates that many widely available activity monitoring systems are accurate enough to be used for this task. The potential issue might be more technical in terms of merging different models and examining the variability of data formats in each system during the hypoglycemia prediction process. Other relevant information, such as stress, medical treatment, and daily events in the patient's life, can be considered as potential inputs, which could be useful in differentiating these prediction models.

Vahedi et al [16] investigated the adaption of a machine learning–based model that predicts continuous glucose levels and aims to prevent hypoglycemia through using physiological and physical exercise data. They used the Medtronic MiniMed 530G insulin delivery device, along with the Enlite sensor, to collect 4 months of physiological measures, physical activity, and nutrition data from 93 individuals with T1D. Overall, their findings indicated that the model's projected glucose levels were very close to the glucose values measured with the Enlite sensor.

Another machine learning model was developed in an ongoing study by Maritsch et al [17], whose objective was to identify hypoglycemia using physiological data collected from a wearable sensor. Specifically, 1 patient with T1D participated in a 1-week study, wearing an Empatica E4 smartwatch to collect physiological data and a FreeStyle Libre CGM to gather the patient's glucose data. The reported results indicate that physiological data can indeed be used to infer hypoglycemic phases; however, frequent false-positive results were observed because of the model's high sensitivity. However, they intend to use artificial intelligence–based techniques to make the classification output comprehensible for patients and incorporate their model into wearables to alert them about impending hypoglycemic episodes.

The ability to connect CGM, insulin pumps, and activity trackers to a mobile device can allow for the application of multiple variant algorithms and complex cloud-based estimations. One of the primary aspects in common among a few of the aforementioned prediction algorithms [6,10] is that using carbohydrate consumption, insulin dosages, and activity tracking data can improve accuracy over a forecast period. Finally, integrating several models could allow for different kinds of hypoglycemia alerts, each one designed for a certain context (activity, sleep, and type of meal).

ECG‐Based Hypoglycemia Detection

In recent years, researchers have examined the effect of low blood glucose levels on the electrical activity of the heart. During hypoglycemia, studies revealed a lengthening of the QT interval (the time elapsed between the onset of the Q wave and the conclusion of the T wave), a rise in heart rate variability (HRV), and alterations in cardiac repolarization. Thus, monitoring ECG alterations can provide a noninvasive method for detecting the beginning of hypoglycemia. The emergence of novel ECG wearables permitted the effortless collection of cardiac signals and paved the path for hypoglycemia identification through ECG data and using deep learning techniques.

In a study by San et al [18], a deep belief network (DBN) was used to build a deep learning system for detecting the initiation of hypoglycemia based on a patient's ECG signal. According to the authors, the probability of hypoglycemia in individuals with T1D is most affected by QT interval prolongation, although an increase in heart rate can also influence the status of the hypoglycemic event. Specifically, their suggested DBN delivers a high classification performance with feature transformation. Through the efficiency testing of the system, 15 children with T1D participated and were monitored overnight, and the findings revealed that the suggested DBN excelled and produced higher classification performance than other current methods, with a sensitivity and specificity score of 80% and 50%, respectively.

Another deep learning framework for predicting blood glucose levels was recently developed [19], which used edge inference on a microcontroller unit. The performance of the models was evaluated based on a clinical data set acquired from 12 patients with T1D whose glucose was measured with a CGM, as well as through a long short-term memory artificial recurrent neural network. Such a system could significantly aid in T1D care and eventually be used in various diabetes management wearables, such as insulin pumps and CGMs.

Generally, machine learning and deep learning approaches demonstrate significant possibilities in terms of data analysis and prediction, and they concentrate on automatically learning behaviors and extracting characteristics from large-scale data. A deep learning model was developed [20] based on a dilated recurrent neural network (DRNN) that can anticipate future glucose levels for 30 minutes. Their DRNN model acquired a considerably wider receptive field of neurons when dilation was used, with the goal of capturing long-term relationships, and they also used a transfer learning approach to take advantage of data from various patients.

A study (Li, K, unpublished data, October 2019) suggested a dual-hormone delivery approach for patients with T1D using deep reinforcement learning and based on data from the UVA-Padova T1D Simulator [25]. In terms of the hormone delivery strategy, they used double DRNNs; input data were blood glucose and carbohydrates, and output was insulin and glucagon distribution. Overall, their findings revealed that deep reinforcement learning appeared to be helpful in developing customized hormone delivery strategies for patients with T1D.

In another deep learning–based hybrid model [21], the authors attempted to imitate the metabolic behavior of physiological blood glucose techniques based on both computer-generated and actual patient data. Furthermore, they simulated a set of differential equations for insulin and carbohydrate intake through a long short-term memory recurrent neural network. Results demonstrated that their model performs better for simulated patients because of the intricacy of the insulin and carbohydrate intake dependence on blood glucose levels, which is restricted to a specific cluster of parameters.

In a noninvasive approach, Ranvier et al [22] aimed to detect hypoglycemic events based on the continuous collection of sensed data from an off-the-shelf sensor belt; the authors based their method on 2 distinct models. The first one leveraged a physiological consequence of hypoglycemia, namely, an alteration of the user ECG's features. They additionally used the accelerometer and breathing sensor of the belt to infer the energy expenditure of the patient with T1D and correlated it with the food intake to estimate the blood glucose level. They then combined these 2 models to improve the accuracy of their prediction.

Cichosz et al [23] proposed a novel algorithm for hypoglycemia prediction, where they obtained data from 10 patients with T1D, who were observed during insulin-induced hypoglycemia, and the collected blood glucose samples were used as a reference. Their equipment involved the calculation of ECG, lead II, and a Minimed Guardian RT CGM, which generated a reading every 5 minutes. The extracted HRV patterns were incorporated into a mathematical prediction algorithm along with the CGM data. Cichosz et al [23] treated early prediction as a pattern recognition problem based on a fixed hypoglycemia level (3.9 mmol/L). Thus, measuring blood glucose from each patient was used as a reference to categorize each 5-minute reading into 2 groups: in healthy range blood glucose (Cn) or hypoglycemia (Chy). Features obtained from HRV and CGM before each blood glucose measurement were used to assess if that time point was below the hypoglycemic threshold of 3.9 mmol/L. As a result, a total of 903 samples were evaluated using the proposed algorithm, with a sensitivity of 79% and an accuracy of 99%. The algorithm was able to predict all 16 hypoglycemic events with no false positives and had a lead time of 22 minutes relative to the CGM device.

These studies indicate that ECG could be used in a free-living environment to assist patients in detecting hypoglycemic episodes. Upgraded equipment and optimized algorithms could make certain methods more precise and simpler to deploy in practice. Although patients with T1D might not be the first to benefit from these technological approaches, other non-T1D patients experiencing hypoglycemic episodes arising from other conditions, such as endocrine, hepatic, or cardiac disorders, could be positively affected by these ECG-based algorithms.

Discussion

Principal Findings

In the context of T1D hypoglycemia risk management, several hypoglycemia or blood glucose level prediction approaches were assessed in this review. Each of these approaches included different techniques and tools that were used for blood glucose level prediction. In general, hypoglycemia prediction algorithms can offer a valuable alternative to patients with T1D to prevent possible episodes, as there are many patients that experience asymptomatic hypoglycemic episodes.

Several of the approaches reviewed have already been incorporated into commercially available systems; that is, the approach proposed by Bertachi et al [15] using a FreeStyle Libre CGM device and a Fitbit Alta HR physical activity monitor, which has been shown to effectively decrease hypoglycemic episodes. A common key aspect of several of the evaluated studies is that the inclusion of carbohydrate consumption data, insulin dosages, or exercise data can enhance the accuracy of the algorithm in the context of a defined (medium- or long-term) forecast horizon. Furthermore, integrating various models could allow for several stages of hypoglycemia alerts, each of which could be tailored to a unique scenario, such as a postmeal, postactivity, or during sleep prediction [26].

Unfortunately, there can be significant variations in accuracy when predicting blood glucose levels. Data collection in these types of studies can be affected by a variety of limiting factors, including inefficient hardware, constrained health care settings, patient noncompliance with research procedures, and barriers because of extensive biomedical data records. These impediments force machine learning researchers to cope with flawed data and seek workarounds for their prediction models [27]. Furthermore, the prediction accuracy highly depends on the type of diabetes, the patient's lifestyle [28], and the existence of any other chronic disease. Some underlying mechanisms, such as age, gender, intestinal microbiota, psychological factors, and genetic traits, may also contribute to variations in outcomes [29]. In addition, we noticed that many of the previously mentioned methodologies were trained on computer-generated patients from simulators (Li, K, unpublished data, October 2019) [6,20,21] or on relatively restricted data sets involving strongly competent patients [7,17,22]. These patients strictly follow the given research guidelines or are in a monitoring environment, which abstains from everyday life where patients mostly do not monitor events, such as heart rate, regularly, which are usually essential for these methodologies. We also noticed that several methodologies used a limited number of features [7,9,11,13,18,19]. This can have a significant impact on the final results, as several factors can affect blood glucose levels, each with different severity. In contrast, some studies used a wide variety of data, such as the approach proposed by Cichosz et al [23], in which 7 different types of features were included. Specifically, they used CGM readings, glucose meter measurements, insulin dosage, ECG, HRV, diabetes duration,

and hemoglobin A_{1c} levels and achieved an accuracy of 99% and a sensitivity of 79%. In our opinion, to improve the overall efficiency of these approaches, it is necessary for researchers to obtain larger data sets and take into consideration a higher number of features in their approaches. A gold standard data set for glucose level prediction in patients with T1D would assist data analysts in experimenting, comparing, and fine-tuning their models accordingly.

CGM sensors are considered a revolution in diabetes treatment [30], are expected to enhance data-driven strategies for personalized diabetes therapy, and can provide real-time data for the creation of predictive models [31]. Clinical studies of such algorithms are projected to increase in the future as prediction approaches are integrated into CGM systems and other devices. Furthermore, the evolution of deep learning algorithms trained using streaming data provides promising results for glucose prediction [20]. The first priority for a hypoglycemia prediction model is to alert the patient before hypoglycemia occurs. Researchers attempted to predict hypoglycemic episodes at various prediction horizons in the cited studies, varying from 0 to 60 minutes. Altogether, the advantages for patients with T1D are evident, as they are empowered to make preventive decisions before their blood glucose levels reach critical points [32]. As with any new equipment, education is required to avoid the negative side effects of overreactions.

Nevertheless, the current CGM technology has drawbacks such as limited life span, skin irritation, adhesive problems, and consumable expenses, which may make it unaffordable for lifelong tracking and prediction. The challenge is to use mainstream noninvasive sensors such as wristbands and smartwatches to build reliable predictive models for hypo- and hyperglycemia following the paradigm of ECG and HR sensors available in mainstream devices and used to assist people with cardiac conditions [33].

Limitations

This review should be interpreted within the context of its limitations. We used a limited set of terms for the search of the literature. Keywords for specific algorithms were not used and we might have inadvertently omitted studies that could have contributed to the progress made in algorithms for T1D hypoglycemia prediction. We searched for articles in a limited number of databases (ie, *PubMed*, *Google Scholar*, *IEEE Xplore*, and *ACM* Digital Library), which represent the most widely used databases internationally. We did not hand search any studies reported in other reviews or the included studies, and we did not assess the interrater reliability. On the basis of our inclusion and exclusion criteria, a small number of eligible studies was included and examined in this review, which limits the generalizability of the findings.

Conclusions

In this systematic review, we included a wide range of hypoglycemia prediction algorithms and systems, some of which used specific medical or activity devices, such as CGMs and activity trackers. Nevertheless, these approaches cannot be recommended to patients on their own; they must be supported by a comprehensive plan to be effective in supporting medical care. Specifically, before deploying the right equipment or technology to aid a patient with T1D, education and medication management are required to decrease the probability of developing hypoglycemia. Overall, we conclude that other approaches to hypoglycemia prediction will be challenged compared with the commonly used CGMs in the following years, as they are restricted to event detection, and CGMs also have the potential to notify patients about their blood glucose variability.

Conflicts of Interest

None declared.

Multimedia Appendix 1
Number of algorithms used by studies categorized based on similarity.
[DOCX File , 14 KB - diabetes_v7i3e34699_app1.docx]

Multimedia Appendix 2
The number of references based on the year of their considered question.
[DOCX File , 14 KB - diabetes_v7i3e34699_app2.docx]

References

1. Rodbard D. Continuous glucose monitoring: a review of recent studies demonstrating improved glycemic outcomes. Diabetes Technol Ther 2017 Jun;19(S3):S25-S37 [FREE Full text] [doi: 10.1089/dia.2017.0035] [Medline: 28585879]
2. Banos O, Villalonga C, Bang J, Hur T, Kang D, Park S, et al. Human behavior analysis by means of multimodal context mining. Sensors (Basel) 2016 Aug 10;16(8):1264 [FREE Full text] [doi: 10.3390/s16081264] [Medline: 27517928]
3. Kavakiotis I, Tsave O, Salifoglou A, Maglaveras N, Vlahavas I, Chouvarda I. Machine learning and data mining methods in diabetes research. Comput Struct Biotechnol J 2017 Jan 8;15:104-116 [FREE Full text] [doi: 10.1016/j.csbj.2016.12.005] [Medline: 28138367]

4. Pappada SM, Cameron BD, Rosman PM. Development of a neural network for prediction of glucose concentration in type 1 diabetes patients. J Diabetes Sci Technol 2008 Sep;2(5):792-801 [FREE Full text] [doi: 10.1177/193229680800200507] [Medline: 19885262]
5. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Int J Surg 2021 Apr;88:105906. [doi: 10.1016/j.ijsu.2021.105906] [Medline: 33789826]
6. Mordvanyuk N, Torrent-Fontbona F, López B. Prediction of glucose level conditions from sequential data. In: Aguiló I, Alquézar R, Angulo C, Ortiz A, Torrens J, editors. Frontiers in Artificial Intelligence and Applications: Recent Advances in Artificial Intelligence Research and Development. Amsterdam, The Netherlands: IOS Press; 2017:227-232.
7. Paul SK, Samanta M. Predicting upcoming glucose levels in patients with type 1 diabetes using a generalized autoregressive conditional heteroscedasticity modelling approach. Int J Stats Med Res 2015 May 21;4(2):188-198. [doi: 10.6000/1929-6029.2015.04.02.4]
8. Jensen MH, Christensen TF, Tarnow L, Seto E, Dencker Johansen M, Hejlesen OK. Real-time hypoglycemia detection from continuous glucose monitoring data of subjects with type 1 diabetes. Diabetes Technol Ther 2013 Jul;15(7):538-543. [doi: 10.1089/dia.2013.0069] [Medline: 23631608]
9. Zhang Y. Predicting occurrences of acute hypoglycemia during insulin therapy in the intensive care unit. Annu Int Conf IEEE Eng Med Biol Soc 2008;2008:3297-3300. [doi: 10.1109/IEMBS.2008.4649909] [Medline: 19163412]
10. Dave D, DeSalvo DJ, Haridas B, McKay S, Shenoy A, Koh CJ, et al. Feature-based machine learning model for real-time hypoglycemia prediction. J Diabetes Sci Technol 2021 Jul;15(4):842-855 [FREE Full text] [doi: 10.1177/1932296820922622] [Medline: 32476492]
11. Eren-Oruklu M, Cinar A, Quinn L. Hypoglycemia prediction with subject-specific recursive time-series models. J Diabetes Sci Technol 2010 Jan 01;4(1):25-33 [FREE Full text] [doi: 10.1177/193229681000400104] [Medline: 20167164]
12. Buckingham B, Chase HP, Dassau E, Cobry E, Clinton P, Gage V, et al. Prevention of nocturnal hypoglycemia using predictive alarm algorithms and insulin pump suspension. Diabetes Care 2010 May;33(5):1013-1017 [FREE Full text] [doi: 10.2337/dc09-2303] [Medline: 20200307]
13. Buckingham BA, Cameron F, Calhoun P, Maahs DM, Wilson DM, Chase HP, et al. Outpatient safety assessment of an in-home predictive low-glucose suspend system with type 1 diabetes subjects at elevated risk of nocturnal hypoglycemia. Diabetes Technol Ther 2013 Aug;15(8):622-627 [FREE Full text] [doi: 10.1089/dia.2013.0040] [Medline: 23883408]
14. Georga EI, Protopappas VC, Ardigò D, Polyzos D, Fotiadis DI. A glucose model based on support vector regression for the prediction of hypoglycemic events under free-living conditions. Diabetes Technol Ther 2013 Aug;15(8):634-643. [doi: 10.1089/dia.2012.0285] [Medline: 23848178]
15. Bertachi A, Viñals C, Biagi L, Contreras I, Vehí J, Conget I, et al. Prediction of nocturnal hypoglycemia in adults with type 1 diabetes under multiple daily injections using continuous glucose monitoring and physical activity monitor. Sensors (Basel) 2020 Mar 19;20(6):1705 [FREE Full text] [doi: 10.3390/s20061705] [Medline: 32204318]
16. Vahedi MR, MacBride KB, Wunsik W, Kim Y, Fong C, Padilla AJ, et al. Predicting glucose levels in patients with type1 diabetes based on physiological and activity data. In: Proceedings of the 8th ACM MobiHoc 2018 Workshop on Pervasive Wireless Healthcare Workshop. 2018 Presented at: MobileHealth'18; June 26-25, 2018; Los Angeles, CA, USA p. 1-15. [doi: 10.1145/3220127.3220133]
17. Maritsch M, Föll S, Bérubé C, Kraus M, Feuerriegel S, Kowatsch T, et al. Towards wearable-based hypoglycemia detection and warning in diabetes. In: Extended Abstracts of the 2020 CHI Conference on Human Factors in Computing Systems. 2021 Nov Presented at: CHI EA '20; April 25-30, 2020; Honolulu, HI, USA p. 1-8. [doi: 10.1145/3334480.3382808]
18. San PP, Ling SH, Nguyen HT. Deep learning framework for detection of hypoglycemic episodes in children with type 1 diabetes. Annu Int Conf IEEE Eng Med Biol Soc 2016 Aug;2016:3503-3506. [doi: 10.1109/EMBC.2016.7591483] [Medline: 28269053]
19. Zhu T, Kuang L, Li K, Zeng J, Herrero P, Georgiou P. Blood glucose prediction in type 1 diabetes using deep learning on the edge. In: Proceedings of the 2021 IEEE International Symposium on Circuits and Systems. 2021 Presented at: ISCAS '21; May 22-28, 2021; Daegu, South Korea p. 1-5. [doi: 10.1109/iscas51556.2021.9401083]
20. Zhu T, Li K, Chen J, Herrero P, Georgiou P. Dilated recurrent neural networks for glucose forecasting in type 1 diabetes. J Healthc Inform Res 2020 Sep;4(3):308-324 [FREE Full text] [doi: 10.1007/s41666-020-00068-2] [Medline: 35415447]
21. Munoz-Organero M. Deep physiological model for blood glucose prediction in T1DM patients. Sensors (Basel) 2020 Jul 13;20(14):3896 [FREE Full text] [doi: 10.3390/s20143896] [Medline: 32668724]
22. Ranvier JE, Dubosson F, Calbimonte JP, Aberer K. Detection of hypoglycemic events through wearable sensors. In: Proceedings of the International Workshop on Semantic Web Technologies for Mobile and PErvasive Environments 2016. 2016 Presented at: CEUR '16; May 29, 2016; Heraklion, Greece p. 21-26.
23. Cichosz SL, Frystyk J, Hejlesen OK, Tarnow L, Fleischer J. A novel algorithm for prediction and detection of hypoglycemia based on continuous glucose monitoring and heart rate variability in patients with type 1 diabetes. J Diabetes Sci Technol 2014 Jul;8(4):731-737 [FREE Full text] [doi: 10.1177/1932296814528838] [Medline: 24876412]
24. Diabetes Control and Complications Trial Research Group, Nathan DM, Genuth S, Lachin J, Cleary P, Crofford O, et al. The effect of intensive treatment of diabetes on the development and progression of long-term complications in

insulin-dependent diabetes mellitus. N Engl J Med 1993 Sep 30;329(14):977-986. [doi: 10.1056/NEJM199309303291401] [Medline: 8366922]
25. Man CD, Micheletto F, Lv D, Breton M, Kovatchev B, Cobelli C. The UVA/PADOVA type 1 diabetes simulator: new features. J Diabetes Sci Technol 2014 Jan;8(1):26-34 [FREE Full text] [doi: 10.1177/1932296813514502] [Medline: 24876534]
26. Dave D, Erraguntla M, Lawley M, DeSalvo D, Haridas B, McKay S, et al. Improved low-glucose predictive alerts based on sustained hypoglycemia: model development and validation study. JMIR Diabetes 2021 Apr 29;6(2):e26909 [FREE Full text] [doi: 10.2196/26909] [Medline: 33913816]
27. Mujahid O, Contreras I, Vehi J. Machine learning techniques for hypoglycemia prediction: trends and challenges. Sensors (Basel) 2021 Jan 14;21(2):546 [FREE Full text] [doi: 10.3390/s21020546] [Medline: 33466659]
28. Johansen MY, MacDonald CS, Hansen KB, Karstoft K, Christensen R, Pedersen M, et al. Effect of an intensive lifestyle intervention on glycemic control in patients with type 2 diabetes: a randomized clinical trial. JAMA 2017 Aug 15;318(7):637-646 [FREE Full text] [doi: 10.1001/jama.2017.10169] [Medline: 28810024]
29. Cryer PE, Davis SN, Shamoon H. Hypoglycemia in diabetes. Diabetes Care 2003 Jun;26(6):1902-1912. [doi: 10.2337/diacare.26.6.1902] [Medline: 12766131]
30. Cappon G, Acciaroli G, Vettoretti M, Facchinetti A, Sparacino G. Wearable continuous glucose monitoring sensors: a revolution in diabetes treatment. Electronics 2017 Sep 05;6(3):65. [doi: 10.3390/electronics6030065]
31. Poolsup N, Suksomboon N, Kyaw AM. Systematic review and meta-analysis of the effectiveness of continuous glucose monitoring (CGM) on glucose control in diabetes. Diabetol Metab Syndr 2013 Jul 23;5:39 [FREE Full text] [doi: 10.1186/1758-5996-5-39] [Medline: 23876067]
32. Miller KM, Beck RW, Bergenstal RM, Goland RS, Haller MJ, McGill JB, T1D Exchange Clinic Network. Evidence of a strong association between frequency of self-monitoring of blood glucose and hemoglobin A1c levels in T1D exchange clinic registry participants. Diabetes Care 2013 Jul;36(7):2009-2014 [FREE Full text] [doi: 10.2337/dc12-1770] [Medline: 23378621]
33. Serhani MA, El Kassabi HT, Ismail H, Nujum Navaz A. ECG monitoring systems: review, architecture, processes, and key challenges. Sensors (Basel) 2020 Mar 24;20(6):1796 [FREE Full text] [doi: 10.3390/s20061796] [Medline: 32213969]

Abbreviations

CGM: continuous glucose monitoring
DBN: deep belief network
DRNN: dilated recurrent neural network
ECG: electrocardiogram
GARCH: generalized autoregressive conditional heteroscedasticity
HRV: heart rate variability
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
SVM: support vector machine
T1D: type 1 diabetes

Edited by K Mizokami-Stout; submitted 04.11.21; peer-reviewed by A Thongprasert, X Zhao; comments to author 23.03.22; revised version received 02.04.22; accepted 20.04.22; published 21.07.22.

Please cite as:
Tsichlaki S, Koumakis L, Tsiknakis M
Type 1 Diabetes Hypoglycemia Prediction Algorithms: Systematic Review
JMIR Diabetes 2022;7(3):e34699
URL: https://diabetes.jmir.org/2022/3/e34699
doi:10.2196/34699
PMID:35862181

Original Paper

Machine Learning–Derived Prenatal Predictive Risk Model to Guide Intervention and Prevent the Progression of Gestational Diabetes Mellitus to Type 2 Diabetes: Prediction Model Development Study

Mukkesh Kumar[1,2,3], BEng (Hons I); Li Ting Ang[1,2], BSc; Cindy Ho[1,2], BSc; Shu E Soh[4], PhD; Kok Hian Tan[5,6], MBBS, MMed, MBA; Jerry Kok Yen Chan[7,8,9], MB BCh BaO (Hons), PhD; Keith M Godfrey[10,11], BMMed (Hons), PhD; Shiao-Yng Chan[1,7], MBBS, PhD; Yap Seng Chong[1,7], MBBS, MMeD, MD; Johan G Eriksson[1,7,12,13*], MD, DMSc; Mengling Feng[3,14*], PhD; Neerja Karnani[1,2,15*], PhD

[1]Singapore Institute for Clinical Sciences, Agency for Science Technology and Research, Singapore, Singapore

[2]Bioinformatics Institute, Agency for Science Technology and Research, Singapore, Singapore

[3]Saw Swee Hock School of Public Health, National University of Singapore, National University Health System, Singapore, Singapore

[4]Department of Paediatrics, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore

[5]Division of Obstetrics and Gynecology, KK Women's and Children's Hospital, Singapore, Singapore

[6]Obstetrics and Gynecology Academic Clinical Programme, Duke-NUS Graduate Medical School, Singapore, Singapore

[7]Department of Obstetrics and Gynaecology and Human Potential Translational Research Programme, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore

[8]Department of Reproductive Medicine, KK Women's and Children's Hospital, Singapore, Singapore

[9]Cancer and Stem Cell Biology, Duke-NUS Medical School, Singapore, Singapore

[10]MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, United Kingdom

[11]National Institute for Health and Care Research Southampton Biomedical Research Centre, University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom

[12]Department of General Practice and Primary Health Care, University of Helsinki, Helsinki, Finland

[13]Folkhälsan Research Center, Helsinki, Finland

[14]Institute of Data Science, National University of Singapore, Singapore, Singapore

[15]Department of Biochemistry, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore

[*]these authors contributed equally

Corresponding Author:
Neerja Karnani, PhD
Singapore Institute for Clinical Sciences
Agency for Science Technology and Research
Brenner Centre for Molecular Medicine
30 Medical Drive
Singapore, 117609
Singapore
Phone: 65 64074041
Email: neerja_karnani@sics.a-star.edu.sg

Abstract

Background: The increasing prevalence of gestational diabetes mellitus (GDM) is concerning as women with GDM are at high risk of type 2 diabetes (T2D) later in life. The magnitude of this risk highlights the importance of early intervention to prevent the progression of GDM to T2D. Rates of postpartum screening are suboptimal, often as low as 13% in Asian countries. The lack of preventive care through structured postpartum screening in several health care systems and low public awareness are key barriers to postpartum diabetes screening.

Objective: In this study, we developed a machine learning model for early prediction of postpartum T2D following routine antenatal GDM screening. The early prediction of postpartum T2D during prenatal care would enable the implementation of

effective strategies for diabetes prevention interventions. To our best knowledge, this is the first study that uses machine learning for postpartum T2D risk assessment in antenatal populations of Asian origin.

Methods: Prospective multiethnic data (Chinese, Malay, and Indian ethnicities) from 561 pregnancies in Singapore's most deeply phenotyped mother-offspring cohort study—Growing Up in Singapore Towards healthy Outcomes—were used for predictive modeling. The feature variables included were demographics, medical or obstetric history, physical measures, lifestyle information, and GDM diagnosis. Shapley values were combined with CatBoost tree ensembles to perform feature selection. Our game theoretical approach for predictive analytics enables population subtyping and pattern discovery for data-driven precision care. The predictive models were trained using 4 machine learning algorithms: logistic regression, support vector machine, CatBoost gradient boosting, and artificial neural network. We used 5-fold stratified cross-validation to preserve the same proportion of T2D cases in each fold. Grid search pipelines were built to evaluate the best performing hyperparameters.

Results: A high performance prediction model for postpartum T2D comprising of 2 midgestation features—midpregnancy BMI after gestational weight gain and diagnosis of GDM—was developed (BMI_GDM CatBoost model: AUC=0.86, 95% CI 0.72-0.99). Prepregnancy BMI alone was inadequate in predicting postpartum T2D risk (ppBMI CatBoost model: AUC=0.62, 95% CI 0.39-0.86). A 2-hour postprandial glucose test (BMI_2hour CatBoost model: AUC=0.86, 95% CI 0.76-0.96) showed a stronger postpartum T2D risk prediction effect compared to fasting glucose test (BMI_Fasting CatBoost model: AUC=0.76, 95% CI 0.61-0.91). The BMI_GDM model was also robust when using a modified 2-point International Association of the Diabetes and Pregnancy Study Groups (IADPSG) 2018 criteria for GDM diagnosis (BMI_GDM2 CatBoost model: AUC=0.84, 95% CI 0.72-0.97). Total gestational weight gain was inversely associated with postpartum T2D outcome, independent of prepregnancy BMI and diagnosis of GDM (P=.02; OR 0.88, 95% CI 0.79-0.98).

Conclusions: Midgestation weight gain effects, combined with the metabolic derangements underlying GDM during pregnancy, signal future T2D risk in Singaporean women. Further studies will be required to examine the influence of metabolic adaptations in pregnancy on postpartum maternal metabolic health outcomes. The state-of-the-art machine learning model can be leveraged as a rapid risk stratification tool during prenatal care.

Trial Registration: ClinicalTrials.gov NCT01174875; https://clinicaltrials.gov/ct2/show/NCT01174875

(JMIR Diabetes 2022;7(3):e32366) doi:10.2196/32366

KEYWORDS

Asian populations; diabetes management; digital health; gestational diabetes mellitus; machine learning; prediction models; prenatal care; public health; risk factors; type 2 diabetes

Introduction

The prevalence of gestational diabetes mellitus (GDM) is increasing globally, with 1 in 6 pregnancies being affected [1]. GDM has long-term implications as women with a history of GDM have a 10-fold higher risk of developing type 2 diabetes (T2D) compared to those with a normoglycemic pregnancy [2]. In the Growing Up in Singapore Towards healthy Outcomes (GUSTO) study, women with GDM had a 12-fold higher risk of developing T2D 4-6 years after delivery compared with women who did not have GDM [3]. From a public health perspective, early intervention in women with GDM could contribute to tackling the rising global health burden of T2D. The T2D epidemic is of particular concern in Southeast Asia; 88 million adults are currently living with diabetes, but this is expected to increase to 153 million by 2045 [1]. Moreover, 57% of the population with diabetes in Southeast Asia are undiagnosed, increasing the risk of complications such as heart disease and stroke [1].

The American Diabetes Association guidelines recommend that women with GDM are tested 4-12 weeks postpartum using a 75 g oral glucose tolerance test (OGTT) [4]. Further testing is recommended in those with normal postpartum OGTT every 1-3 years using fasting plasma glucose, hemoglobin A_{1c} or HbA_{1c}, or an OGTT [4]. However, as GDM resolves post pregnancy, postpartum surveillance of glycemia remains low across health care systems globally. The rate of postpartum diabetes screening can be as low as 13% in Asian countries [5]. Barriers to postpartum diabetes screening include lack of structured postpartum preventive care in health care systems, lack of patient awareness of future T2D risk, and time restrictions due to maternal commitments [5,6].

Machine learning models enable predictive population risk stratification. In a prospective metabolomics study by Allalou et al [7], 21 metabolites were identified at 6-9 weeks post partum to predict the transition from GDM to T2D in women. The metabolite model using decision trees performed well with an area under the receiver operating characteristic curve (AUC) of 0.77. In another GDM to T2D transition study by Joglekar et al [8], the inclusion of circulating microRNA (miR-369-3p) at 12 weeks post partum enhanced the prediction of a clinical model (age, BMI, pregnancy fasting glucose, postpartum fasting glucose, cholesterol, and triacylglycerols) from an AUC of 0.83 to an AUC of 0.92 (logistic regression algorithm). In addition to low compliance of postpartum testing in women with GDM, the other barriers to the real-world implementation of these 2 machine learning models include the cost and access to metabolomics assay and microRNA polymerase chain reaction during routine clinical visits.

The early prediction of postpartum T2D during prenatal care would enable the implementation of effective strategies for diabetes prevention interventions. To date, there have been no

studies on using machine learning for postpartum T2D risk assessment in antenatal populations of Asian origin. In this study from Singapore, we developed a machine learning model for early prediction of postpartum T2D during routine antenatal GDM screening. Our machine learning model was implemented using the prospective GUSTO cohort study data (NCT01174875).

Methods

Ethics Approval

This study has been reviewed by the National Healthcare Group Domain Specific Review Board for ethics approval and SingHealth Centralized Institutional Review Board (CIRB/E/2019/2655).

Study Design

GUSTO is a prospective multiethnic (Chinese, Malay, and Indian ethnicities) mother-offspring cohort study. Mothers were recruited during early pregnancy from Singapore's 2 major public maternity hospitals, National University Hospital and KK Women's and Children's Hospital, between June 2009 and October 2010.

Participants of mixed ethnicity or with self-reported T2D at recruitment were excluded from model training. A total of 561 mothers had complete data on demographics, medical or obstetric history, physical measures, lifestyle information, antenatal OGTT, and postpartum OGTT 4-8 years after delivery. The World Health Organization (WHO) 1999 criteria [9] were used to diagnose GDM, and the WHO 2006 criteria [10] were used to diagnose postpartum impaired glucose tolerance (IGT), impaired fasting glucose (IFG), and T2D. The abnormal glucose metabolism (AGM) outcome comprises of IGT, IFG, and T2D diagnoses.

Feature Variables

Information on demographics (maternal age, maternal ethnicity) and medical or obstetric history (self-reported prepregnancy weight, family history of diabetes mellitus, family history of high blood pressure, family history of cardiovascular disease, previous history of GDM, previous history of gestational hypertension, and parity) were derived from first trimester questionnaires. Systolic and diastolic blood pressure were recorded at midgestation (median 26.7, IQR 26.1-27.6 weeks) and obtained from hospital case notes. Mean arterial blood pressure was derived by doubling the diastolic blood pressure and adding to the systolic blood pressure, with the composite sum divided by 3. Maternal anthropometry was measured at midgestation (median 26.9, IQR 26.4-27.6 weeks). Maternal midupper arm circumference was measured to the nearest 0.1 cm, midway between acromion process and olecranon process (using Seca 212). Maternal height was measured to the nearest 0.1 cm (using Seca 213). Maternal weight at midpregnancy was measured to the nearest 0.1 kg (using Seca 803), and BMI was derived using weight divided by height squared (kg/m^2). Total gestational weight gain was derived by subtracting first antenatal visit weight (median 9.0, IQR 7.3-11.0 weeks) from the last antenatal visit weight (median 38.1, IQR 37.3-39.1 weeks). Lifestyle information on self-reported smoking, environmental tobacco smoke exposures, and alcohol consumption were collected using questionnaires. GDM diagnosis was based on antenatal OGTT assessment (median 26.9, IQR 26.4-27.7 weeks).

Machine Learning Methodology and Statistical Analyses

Our methodological novelty lies in combining coalitional game theory concepts with machine learning. SHapley Additive exPlanations (SHAP) framework was combined with CatBoost tree ensembles for feature selection and model explainability [11,12]. The SHAP framework connects optimal credit allocation with local explanations using the classic Shapley values from cooperative game theory. Lundberg and Lee [11] have proposed SHAP as the only additive feature attribution method that satisfies 2 important properties of game theory—additivity (local accuracy) and monotonicity (consistency). In game theory, Shapley value is the average expected marginal contribution of 1 player across all possible permutation of players (ie, the average effects of team member composition and team size). Shapley value helps determine a payoff for all the game players when each player might have contributed more or less than the others when working in coalition. In machine learning, the game players are the features, and the collective payout is the model prediction. SHAP framework provides local explanations based on exact Shapley values to understand the global model structure. For each possible feature ordering, features are introduced one at a time into a conditional expectation function of the model's output, and changes in expectation are attributed to the introduced feature, averaged over all possible feature orderings in a fair manner. SHAP values represent a change in log odds ratio. Our game theoretical approach for predictive analytics enables population subtyping and pattern discovery for data-driven precision care.

The supervised machine learning models were built using Anaconda distribution of Python programming language (version 3.7.9) in JupyterLab computational environment. The predictive models were trained using the following 4 machine learning algorithms to address algorithm bias: logistic regression (generalized linear model), support vector machine (linear support vector classification), CatBoost gradient boosting (tree-based), and artificial neural network (multilayer perceptron). We used 5-fold stratified cross-validation to preserve the same proportion of AGM/T2D cases in each fold. Maximum absolute scaler was used as a preprocessor to scale each feature without destroying the sparsity. A grid search pipeline was built to evaluate the best performing hyperparameters for each machine learning model. Model performances were evaluated using the AUC with 95% CI. Implementation details of the machine learning algorithms are included in Multimedia Appendix 1.

The feature selection model using clinical features at midgestation was trained on the AGM outcome, and top predictors with SHAP value magnitudes more than zero were included in the AGM/T2D prediction models. Sensitivity analyses were performed to explore the prediction effects of

diagnosing GDM using modified 2-point International Association of the Diabetes and Pregnancy Study Groups (IADPSG) 2018 criteria [9] rather than WHO 1999 criteria (GUSTO study did not include a 1-hour glucose measurement), and the prediction effects of continuous fasting or 2-hour glucose measures and prepregnancy BMI. We also assessed the associations between total gestational weight gain and postpartum AGM and T2D outcomes. All association analyses were performed using Stata/MP software (version 16.1; StataCorp LP).

Results

The Features Significantly Associated With T2D Aligned With the Top Features From the SHAP Feature Selection Model

The relationship between all feature variables and postpartum AGM and T2D outcomes is presented in a Pearson correlation heatmap (Figures 1 and 2). Diagnosis of GDM, midupper arm circumference, and BMI are the best features for postpartum AGM/T2D machine learning model building.

Table 1 presents the univariate associations between midpregnancy features and postpartum AGM and T2D outcomes. Previous history of GDM, mean arterial blood pressure, midupper arm circumference, BMI, and diagnosis of GDM were associated with later risk of T2D. The top 4 features impacting the SHAP model outputs were midupper arm circumference, mean arterial blood pressure, BMI and diagnosis of GDM (Figure 3). The negative SHAP value for height implies that maternal height did not contribute to the prediction of AGM.

Figure 1. Pearson Correlation heatmap for abnormal glucose metabolism (AGM). GDM: gestational diabetes mellitus.

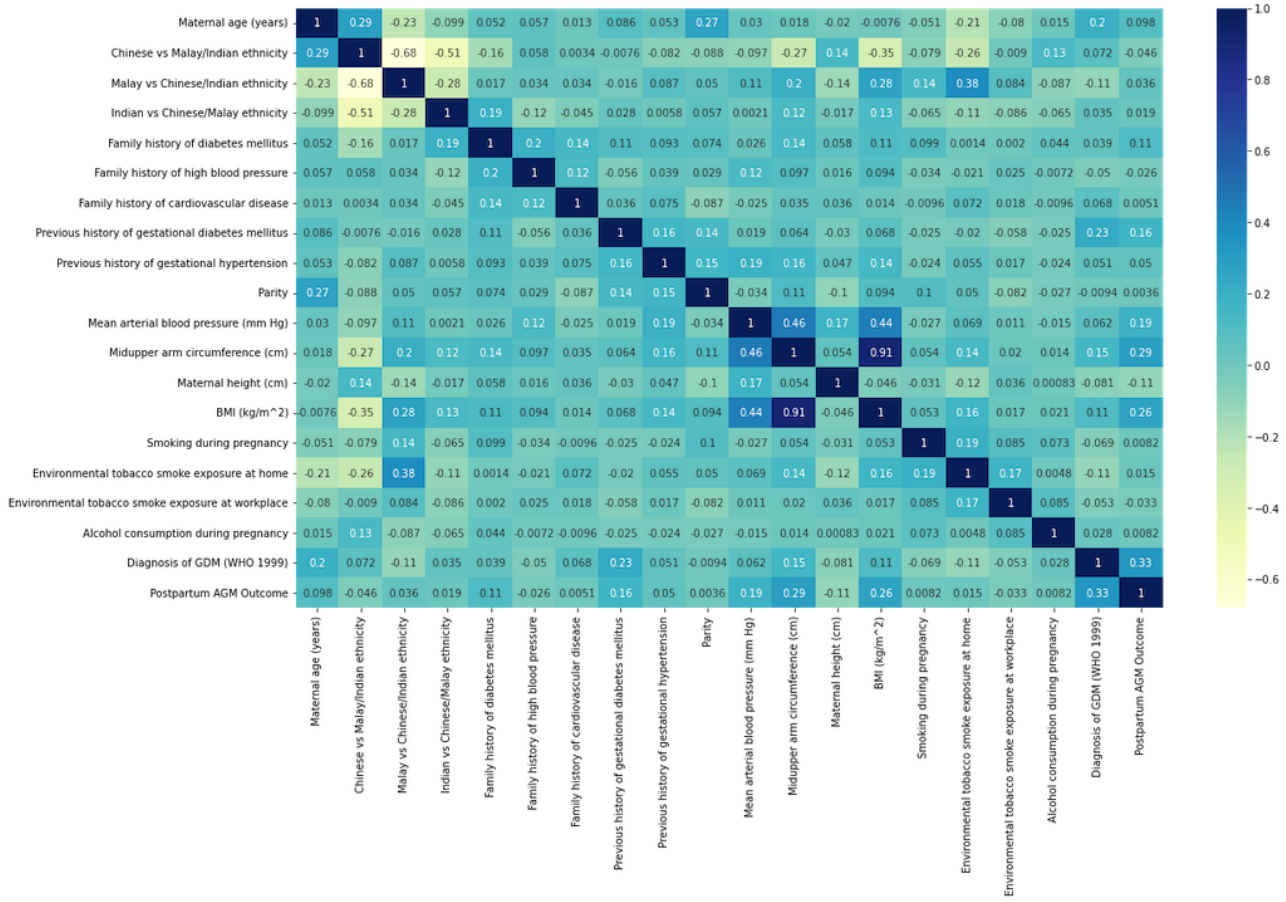


Figure 2. Pearson Correlation heatmap for type 2 diabetes (T2D). GDM: gestational diabetes mellitus.

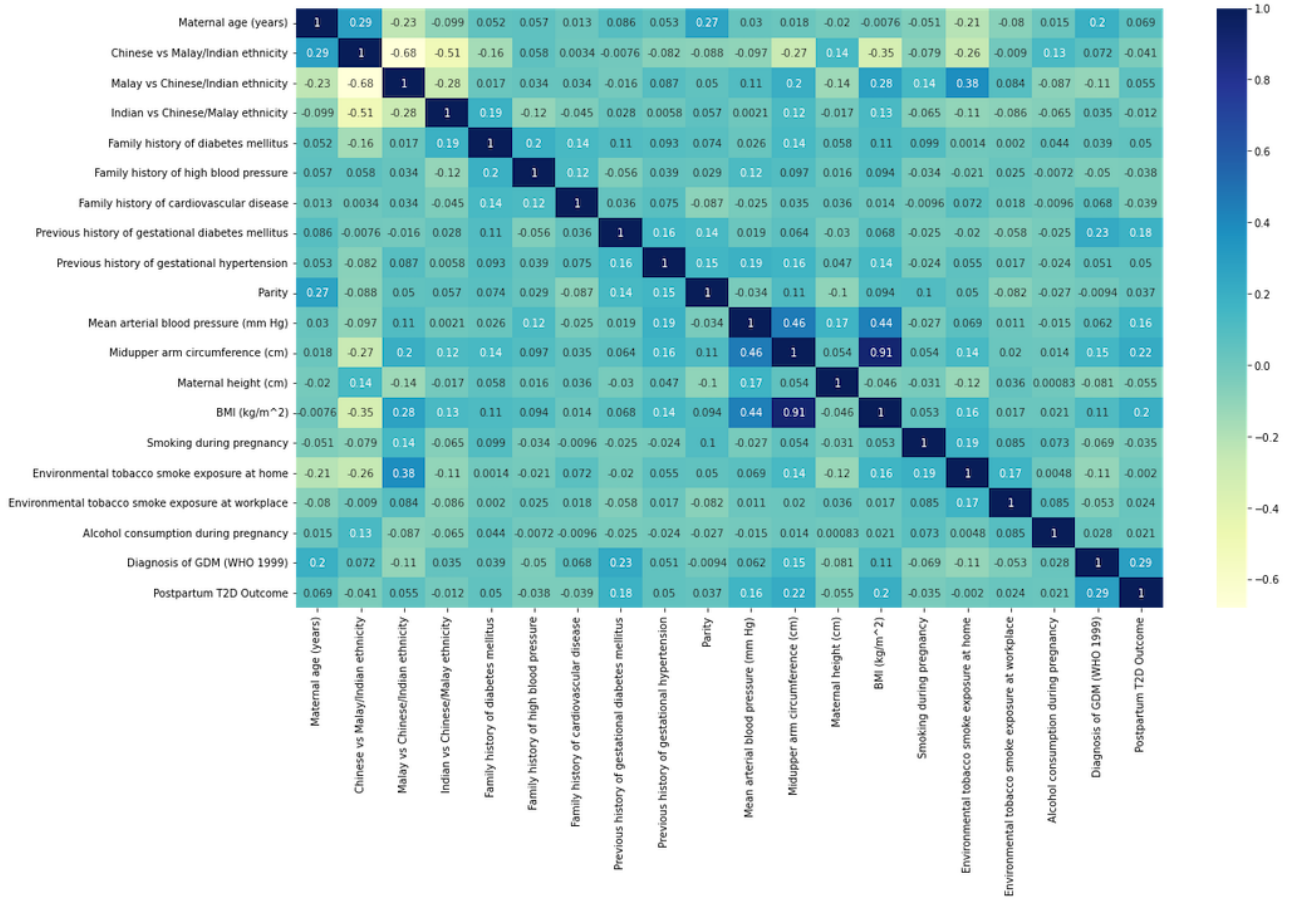


Table 1. Associations between midpregnancy characteristics and postpartum abnormal glucose metabolism (AGM) or type 2 diabetes (T2D) outcomes (4-8 years after delivery).

Characteristics	AGM (n=139)		T2D (n=32)	
	OR[a] (95% CI)	P value	OR (95% CI)	P value
Maternal age (years)	1.05 (1.01-1.09)	.02[b]	1.06 (0.99-1.14)	.10
Chinese vs Malay and Indian ethnicity	0.81 (0.55-1.19)	.28	0.71 (0.34-1.44)	.34
Malay vs Chinese and Indian ethnicity	1.20 (0.79-1.83)	.40	1.64 (0.78-3.43)	.19
Indian vs Chinese and Malay ethnicity	1.12 (0.68-1.84)	.66	0.87 (0.33-2.31)	.78
Family history of diabetes mellitus	1.72 (1.15-2.56)	.008[b]	1.55 (0.75-3.21)	.24
Family history of high blood pressure	0.88 (0.60-1.32)	.55	0.70 (0.33-1.51)	.37
Family history of cardiovascular disease	1.04 (0.57-1.90)	.90	0.51 (0.12-2.19)	.37
Previous history of gestational diabetes mellitus	5.96 (2.16-16.43)	.001[b]	7.98 (2.62-24.27)	<.001[b]
Previous history of gestational hypertension	1.86 (0.66-5.21)	.24	2.45 (0.53-11.29)	.25
Parity	1.02 (0.69-1.50)	.93	1.38 (0.66-2.89)	.39
Mean arterial blood pressure (mm Hg)	1.05 (1.03-1.07)	<.001[b]	1.07 (1.03-1.11)	<.001[b]
Midupper arm circumference (cm)	1.18 (1.12-1.25)	<.001[b]	1.23 (1.13-1.33)	<.001[b]
Maternal height (cm)	0.96 (0.92-0.99)	.01[b]	0.96 (0.90-1.02)	.10
BMI (kg/m^2)	1.14 (1.09-1.18)	<.001[b]	1.16 (1.09-1.24)	<.001[b]
Smoking during pregnancy	1.14 (0.30-4.36)	.85	N/A[c]	N/A
Environmental tobacco smoke exposure at home	1.07 (0.72-1.60)	.73	0.98 (0.46-2.08)	.96
Environmental tobacco smoke exposure at workplace	0.76 (0.38-1.51)	.43	1.37 (0.46-4.06)	.57
Alcohol consumption during pregnancy	1.14 (0.30-4.36)	.85	1.67 (0.21-13.50)	.63
Diagnosis of GDM[d] (WHO[e] 1999 criteria)	5.49 (3.51-8.58)	<.001[b]	9.57 (4.45-20.55)	<.001[b]

[a]OR: odds ratio.

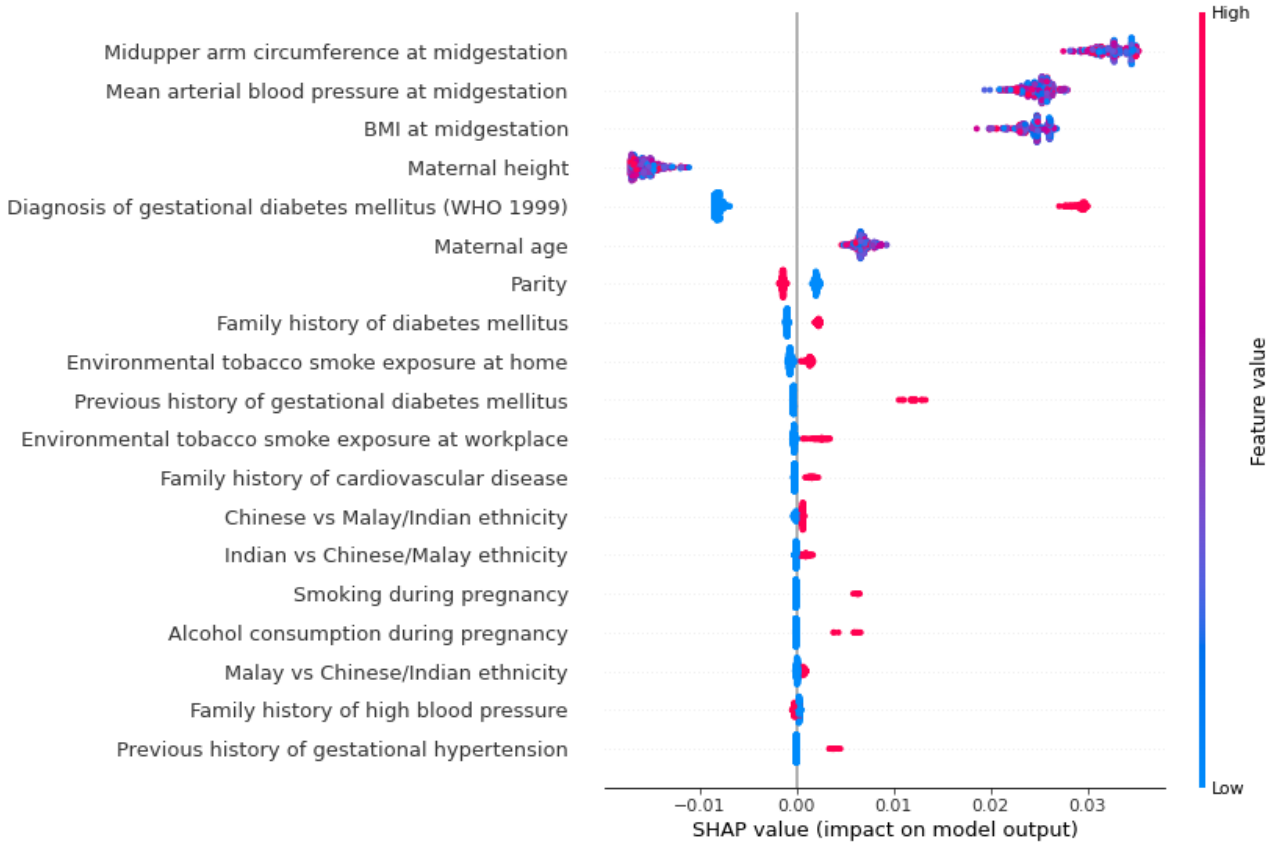
[b]Indicates statistically significant values.

[c]N/A: not applicable; fixed-effect regression estimates were not obtained as the variable did not contribute to the likelihood estimation.

[d]GDM: gestational diabetes mellitus.

[e]WHO: World Health Organization.

Figure 3. SHapley Additive exPlanations (SHAP) summery plot of feature selection model. WHO: World Health Organization.



Maternal Adiposity During Pregnancy and Metabolic Derangements Underlying GDM Signaling Future T2D Risk

Although the detailed training parameters and results for all machine learning models are shown in Tables S1-S6 (Multimedia Appendix 2), we focus on describing the results of CatBoost machine learning models as this algorithm had the best overall performance. The results for each data set of the 5-fold stratified cross-validation and the average of the cross-validation are also provided in Tables S1-S6 in Multimedia Appendix 2. Midupper arm circumference at midgestation (AUC=0.78, 95% CI 0.71-0.86) and BMI at midgestation (AUC=0.74, 95% CI 0.53-0.96) had stronger predictive performances than GDM diagnosis (AUC=0.73, 95% CI 0.51-0.95; Table S2 in Multimedia Appendix 2). The addition of GDM diagnosis improved the performance of baseline models (MUAC_GDM model: AUC=0.88, 95% CI 0.79-0.96 and BMI_GDM model: AUC=0.86, 95% CI 0.72-0.99; Table S4 in Multimedia Appendix 2). Prepregnancy BMI alone was inadequate in predicting postpartum T2D risk (AUC=0.62, 95% CI 0.39-0.86; Table S6 in Multimedia Appendix 2).

Although there is a high correlation between midupper arm circumference and BMI (r=0.91), BMI is more reliably and commonly assessed in clinical settings, and therefore, a BMI-based pregnancy model is our proposed solution (Figure 4). Table 2 summarizes the detailed training parameters of logistic regression, support vector machine, artificial neural network, and CatBoost gradient boosting algorithms, as well as the results of the proposed postpartum T2D predictive model (comprising of midpregnancy BMI after gestational weight gain and diagnosis of GDM features). Total gestational weight gain was inversely associated with postpartum AGM and T2D outcomes, independent of prepregnancy BMI and diagnosis of GDM (Table 3).

Figures 5-7 present the validation curves obtained during the training of BMI_GDM CatBoost model. The hyperparameter candidates for CatBoost model were as follows:

- Learning rate: [‘0’ - 0.00001, **‘1’- 0.0001**, ‘2’ - 0.001, ‘3’ - 0.01, ‘4’ - 0.03, ‘5’ - 0.05, ‘6’ - 0.1, ‘7’ - 0.2, ‘8’ - 0.3]
- L2 leaf regularization: [‘0’ - 1.0, ‘1’ - 2.0, ‘2’ - 3.0, ‘3’ - 4.0, **‘4’ - 5.0**, ‘5’ - 6.0]
- Random strength: [‘0’ - 1.0, ‘1’ - 2.0, ‘2’ - 3.0, ‘3’ - 4.0, **‘4’ - 5.0**, ‘5’ - 6.0]

The CatBoost model was specified with 1000 iterations, maximum depth of 6 trees, and symmetric tree growing policy. The hyperparameters tuned using grid search were learning rate of 0.0001, L2 leaf regularization of 5.0, and random strength of 5.0. The BMI_GDM CatBoost classifier is performing well under this optimal configuration.

Figure 4. SHapley Additive exPlanations (SHAP) summary plot of BMI_GDM model. WHO: World Health Organization.

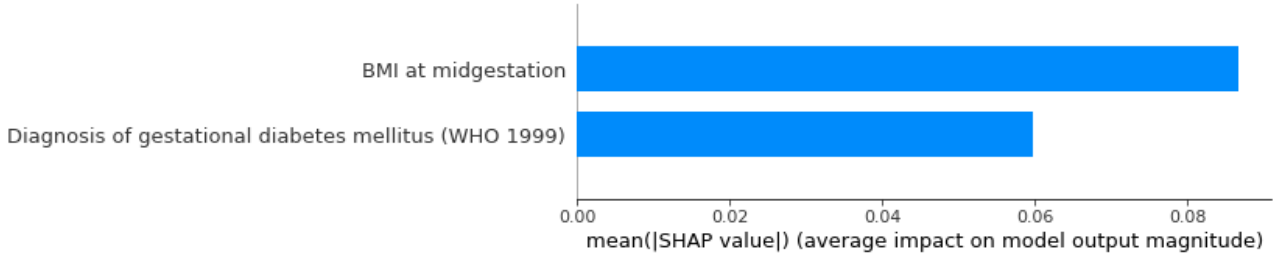


Table 2. Proposed postpartum type 2 diabetes predictive model comprising of midpregnancy BMI after gestational weight gain and diagnosis of gestational diabetes mellitus (GDM) features (based on the World Health Organization 1999 criteria).

Model specifications (BMI_GDM)	Hyperparameters tuned using grid search	Average AUC[a] (95% CI)
Logistic regression (L2 regularization penalty, stochastic average gradient descent solver)	• Inverse of regularization strength=1.0	0.85 (0.72-0.98)
Support vector machine (linear kernel, L2 regularization penalty)	• L2 regularization penalty=1.0 • Loss function='squared hinge'	0.85 (0.72-0.98)
Neural network (3 hidden layers with 10 neurons each, ReLU activation function, Adam solver, 200 iterations)	• L2 regularization penalty=0.01 • Initial learning rate=0.1	0.85 (0.73-0.97)
CatBoost[b] (1000 iterations, maximum depth of 6 trees, symmetric tree growing policy)	• L2 leaf regularization=5.0 • Learning rate=0.0001 • Random Strength=5.0	0.86 (0.72-0.99)[b]

[a]AUC: area under the receiver operating characteristic curve.

[b]Indicates the main predictive model developed in this study.

Table 3. Association between total gestational weight gain and postpartum abnormal glucose metabolism (AGM) or type 2 diabetes (T2D) outcomes (4-8 years after delivery).

Analysis	AGM (n=128)		T2D (n=31)	
	OR[a] (95% CI)	P value	OR (95% CI)	P value
Unadjusted analysis				
Total gestational weight gain (kg)	0.87 (0.82-0.91)	<.001[b]	0.79 (0.72-0.87)	<.001[b]
Adjusted analysis[c]				
Total gestational weight gain (kg)	0.93 (0.87-0.98)	.01[b]	0.88 (0.79-0.98)	.02[b]

[a]OR: odds ratio.

[b]Indicates statistically significant values.

[c]Adjusted based on maternal ethnicity, age, parity, family history of diabetes mellitus, prepregnancy BMI, and diagnosis of gestational diabetes mellitus.

Figure 5. Validation curve with CatBoost algorithm–Varying learning rate. AUC: area under the receiver operating characteristic curve.

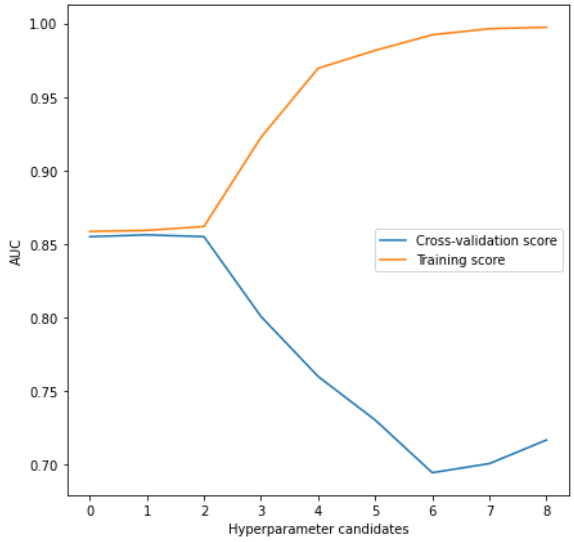


Figure 6. Validation curve with CatBoost algorithm–Varying L2 leaf regularization. AUC: area under the receiver operating characteristic curve.

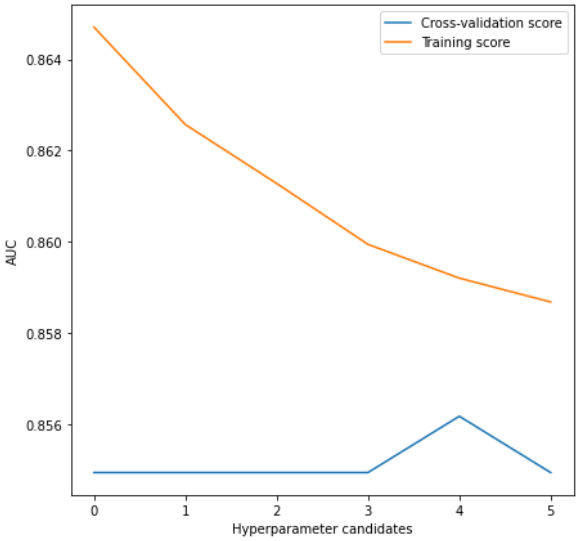
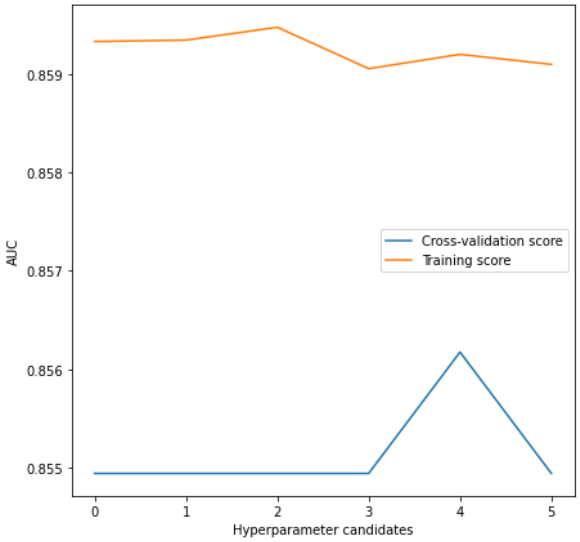


Figure 7. Validation curve with CatBoost algorithm–Varying random strength. AUC: area under the receiver operating characteristic curve.



Two-Hour Postprandial Glucose as a Stronger Predictor of Postpartum T2D Risk Compared With Fasting Glucose

When modeling antenatal glucose measures as continuous features, a 2-hour postprandial glucose (AUC=0.86, 95% CI 0.76-0.96) showed a stronger postpartum T2D risk prediction effect compared to fasting glucose (AUC=0.76, 95% CI 0.61-0.91; Table S6 in Multimedia Appendix 2). In the sensitivity analysis, predictive performance of BMI_GDM model was also robust when using the modified 2-point IADPSG 2018 criteria (AUC=0.84, 95% CI 0.72-0.97; Table S6 in Multimedia Appendix 2).

Discussion

Principal Results

We have built an effective postpartum T2D predictive model by combining game theory–based feature selection with machine learning. SHAP values recovered predictive modeling features for optimal performance, aligning model interpretability with human intuition. Our BMI_GDM model achieved an excellent AUC of 0.86 with 2 midgestation features (BMI at midgestation and diagnosis of GDM by the WHO 1999 criteria) for an early prediction of postpartum T2D risk in a Singapore population. The model was also robust when using a modified 2-point IADPSG 2018 criteria for GDM diagnosis (AUC=0.84). The BMI_GDM machine learning model can be leveraged as a risk stratification tool during routine GDM screening to identify Asian women at high risk of developing T2D, enabling early intervention. The BMI_2hour model (AUC=0.86) can be an alternative design during clinical implementation if GDM diagnosis feature is unavailable for the patient. The trained classifier can be deployed using a web application that can allow clinicians to identify women at T2D risk and develop a postpartum management plan.

The 2-feature midpregnancy BMI model (AUC=0.86) performed better in postpartum T2D prediction than a preconception BMI model (AUC=0.62), implying that midgestational weight gain effects combined with the metabolic derangements underlying GDM and fetoplacental unit signal future T2D risk. As pregnancy has a diabetogenic effect on metabolism [13], further studies will be required to examine the metabolic adaptations in pregnancy and postpartum maternal metabolic health outcomes.

In our BMI_GDM model sensitivity analysis, we observed that the 2-hour antenatal OGTT glucose peak was associated with a stronger prediction of postpartum T2D (AUC=0.86) compared with the fasting glucose (AUC=0.76) in Singaporean women. Future studies with greater statistical power will be needed to confirm whether the postpartum T2D risk is heterogenous across different thresholds of glucose tolerance for GDM diagnostic criteria.

Limitations

This study has some limitations due to the scarcity of longitudinal data. Postpartum OGTT at 4-12 weeks, and further testing in those with normal postpartum OGTT every 1-3 years were not administered in the GUSTO study, possibly underestimating the development of postdelivery dysglycemia to a certain extent and inducing bias. However, the mothers participating in GUSTO self-reported T2D status 2 years after delivery, and there were no self-reported T2D cases. Our prediction models were trained on a limited cohort of 561 pregnancies and require further validation using larger cohorts such as Electronic Health Record databases. A subcohort analyses by individual ethnic groups can be trained with larger data sets.

Comparison With Prior Work

Our early implementation of T2D risk prediction algorithm during prenatal care enables early engagement of patients and remote monitoring, compared to existing molecular biomarker-based T2D risk prediction algorithms [7,8] developed for postpartum care. The 2 midgestation clinical features (midpregnancy BMI after gestational weight gain and diagnosis of GDM) discovered from our machine learning workflow are of low cost and easily accessible during routine antenatal GDM screening. The digital biomarkers identified from our work will guide antenatal research in preventing the progression of GDM to T2D.

Conclusions

The key strength of our study lies in applying machine learning–based predictive analytics during prenatal care in the early prediction of postpartum T2D. This machine learning model can be leveraged as a risk stratification tool for preventive intervention.

Acknowledgments

We thank the GUSTO study team for their help in acquiring the research data and their crucial work with the participants. The GUSTO birth cohort study is supported by the Translational Clinical Research Flagship Program on Developmental Pathways to Metabolic Disease (awards NMRC/TCR/004-NUS/2008, NMRC/TCR/012-NUHS/2014) and Open Fund–Large Collaborative Grant (OFLCG/MOH-000504) programs, funded by the National Research Foundation and administered by the National Medical Research Council (NMRC) of Singapore. This research is supported by NMRC's Open Fund–Large Collaborative Grant, titled "Metabolic Health in Asian Women and their Children" (award OFLCG19may-0033). KMG is supported by the UK Medical Research Council (MC_UU_12011/4); the National Institute for Health Research (NIHR), NIHR Senior Investigator (NF-SI-0515-10042), and NIHR Southampton Biomedical Research Centre (IS-BRC-1215-20004); and the British Heart Foundation (RG/15/17/3174). Additional funds for data analysis were supported by the Strategic Positioning Fund and IAF-PP funds

(H17/01/a0/005) available to NK through Agency for Science, Technology and Research (A*STAR) in Singapore (award SPF 002/2013).

Data Availability

The data that support the findings of this research are available from the corresponding authors upon reasonable request. The code generated to reproduce this research is available at GitHub [14].

The postpartum T2D predictive model (CatBoost algorithm) has been deployed into a web application [15].

Authors' Contributions

Authors JGE, MF, and NK are joint senior authors of this publication.
MK contributed to research study design, data curation, machine learning modeling, statistical analyses, interpretation of results, and writing of the manuscript. LTA and CH contributed to clinical data curation. SES and SYC contributed to collection of phenotypic data in GUSTO cohort and critical reading of the manuscript. KHT, JKYC, KMG, and YSC contributed to GUSTO cohort study design, data collection, and critical reading of the manuscript. JGE contributed to interpretation of results, writing of the manuscript, and GUSTO cohort data collection. MF contributed to supervision of the study, interpretation of results, and writing of the manuscript. NK contributed to supervision of the study, interpretation of results, writing of the manuscript, and GUSTO cohort study data collection. MF and NK accept full responsibility for the work, had access to the data, and controlled the decision to publish the paper.

Conflicts of Interest

NK, KMG, SYC, and YSC are part of an academic consortium that has received research funding from Abbott Nutrition, Nestec Inc, BenevolentAI Bio Ltd, and Danone. MF was partially supported by the National Research Foundation Singapore under its AI Singapore Program (award AISG-GC-2019-001-2A). Other authors declare no conflicts of interest.

Multimedia Appendix 1
Implementation details of machine learning algorithms.
[DOCX File , 19 KB - diabetes_v7i3e32366_app1.docx]

Multimedia Appendix 2
Tables S1-S6; detailed training parameters and results for all machine learning models.
[DOCX File , 74 KB - diabetes_v7i3e32366_app2.docx]

References

1. IDF Diabetes Atlas 9th edition. International Diabetes Federation. 2019. URL: https://diabetesatlas.org/atlas/ninth-edition/ [accessed 2022-05-24]
2. Vounzoulaki E, Khunti K, Abner SC, Tan BK, Davies MJ, Gillies CL. Progression to type 2 diabetes in women with a known history of gestational diabetes: systematic review and meta-analysis. BMJ 2020 May 13;369:m1361 [FREE Full text] [doi: 10.1136/bmj.m1361] [Medline: 32404325]
3. Chen L, Soh SE, Tint M, Loy SL, Yap F, Tan KH, et al. Combined analysis of gestational diabetes and maternal weight status from pre-pregnancy through post-delivery in future development of type 2 diabetes. Sci Rep 2021 Mar 03;11(1):5021 [FREE Full text] [doi: 10.1038/s41598-021-82789-x] [Medline: 33658531]
4. American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2020. Diabetes Care 2020 Jan 20;43(Suppl 1):S14-S31. [doi: 10.2337/dc20-S002] [Medline: 31862745]
5. Nouhjah S, Shahbazian H, Amoori N, Jahanfar S, Shahbazian N, Jahanshahi A, et al. Postpartum screening practices, progression to abnormal glucose tolerance and its related risk factors in Asian women with a known history of gestational diabetes: A systematic review and meta-analysis. Diabetes Metab Syndr 2017 Dec;11 Suppl 2:S703-S712. [doi: 10.1016/j.dsx.2017.05.002] [Medline: 28571777]
6. Sanderson H, Loveman E, Colquitt J, Royle P, Waugh N, Tan BK. Improving uptake of postnatal checking of blood glucose in women who had gestational diabetes mellitus in universal healthcare settings: a systematic review. J Clin Med 2018 Dec 20;8(1):4 [FREE Full text] [doi: 10.3390/jcm8010004] [Medline: 30577481]
7. Allalou A, Nalla A, Prentice KJ, Liu Y, Zhang M, Dai FF, et al. A Predictive metabolic signature for the transition from gestational diabetes Mellitus to type 2 diabetes. Diabetes 2016 Sep 23;65(9):2529-2539 [FREE Full text] [doi: 10.2337/db15-1720] [Medline: 27338739]
8. Joglekar MV, Wong WKM, Ema FK, Georgiou HM, Shub A, Hardikar AA, et al. Postpartum circulating microRNA enhances prediction of future type 2 diabetes in women with previous gestational diabetes. Diabetologia 2021 Jul 23;64(7):1516-1526. [doi: 10.1007/s00125-021-05429-z] [Medline: 33755745]

9. Diagnostic criteria and classification of hyperglycaemia first detected in pregnancy. WHO. 2013. URL: https://apps.who.int/iris/handle/10665/85975 [accessed 2022-05-20]
10. Definition and diagnosis of diabetes mellitus and intermediate hyperglycaemia: report of a WHO/IDF consultation. WHO. 2006. URL: https://apps.who.int/iris/handle/10665/43588 [accessed 2022-05-20]
11. Lundberg SM, Erion G, Chen H, DeGrave A, Prutkin JM, Nair B, et al. From local explanations to global understanding with explainable AI for trees. Nat Mach Intell 2020 Jan;2(1):56-67 [FREE Full text] [doi: 10.1038/s42256-019-0138-9] [Medline: 32607472]
12. Prokhorenkova L, Gusev G, Vorobev A, Veronika DA, Gulin A. CatBoost: unbiased boosting with categorical features. ArXiv. Preprint posted online on June 28, 2017 2022 [FREE Full text] [doi: 10.48550/arXiv.1706.09516]
13. Zeng Z, Liu F, Li S. Metabolic adaptations in pregnancy: a review. Ann Nutr Metab 2017 Mar 16;70(1):59-65 [FREE Full text] [doi: 10.1159/000459633] [Medline: 28297696]
14. GUSTO_Type-2-Diabetes-Mellitus. GitHub. URL: https://github.com/mukkeshkumar/GUSTO_Type-2-Diabetes-Mellitus [accessed 2022-05-31]
15. Machine learning derived prenatal predictive risk model to guide intervention and prevent the progression of Gestational Diabetes Mellitus to Type 2 Diabetes. Group Mornin. URL: https://www.mornin-feng.com/all-projects-and-demos#gdm2 [accessed 2022-05-31]

Abbreviations

AGM: abnormal glucose metabolism
AUC: area under the receiver operating characteristic curve
GDM: gestational diabetes mellitus
GUSTO: Growing Up in Singapore Towards healthy Outcomes
IADPSG: International Association of Diabetes and Pregnancy Study Groups
IFG: impaired fasting glucose
IGT: impaired glucose tolerance
OGTT: oral glucose tolerance test
SHAP: SHapley Additive exPlanations
T2D: type 2 diabetes
WHO: World Health Organization

Edited by K Mizokami-Stout; submitted 26.07.21; peer-reviewed by CL Lu, A Hakemi; comments to author 09.10.21; revised version received 27.11.21; accepted 21.03.22; published 05.07.22.

Please cite as:
Kumar M, Ang LT, Ho C, Soh SE, Tan KH, Chan JKY, Godfrey KM, Chan SY, Chong YS, Eriksson JG, Feng M, Karnani N
Machine Learning–Derived Prenatal Predictive Risk Model to Guide Intervention and Prevent the Progression of Gestational Diabetes Mellitus to Type 2 Diabetes: Prediction Model Development Study
JMIR Diabetes 2022;7(3):e32366
URL: https://diabetes.jmir.org/2022/3/e32366
doi:10.2196/32366
PMID:35788016

Publisher:
JMIR Publications
130 Queens Quay East.
Toronto, ON, M5A 3Y5
Phone: (+1) 416-583-2040
Email: support@jmir.org