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Digital Interventions in Type 2 Diabetes Mellitus

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Abstract

Introduction: *Type 2 diabetes mellitus (T2DM) is a highly prevalent chronic disease with an increasing mortality rate over the last decade. Diabetes self-management education (DSME) programs have been reported as essential to improve survival; however, patient adherence rates are very low. Therefore, digital devices have been created to deliver DSME at a distance and enhance program attendance. This study aims to assess the effects of digitally delivered DSME programs on the glycosylated hemoglobin (HbA1C) of patients with prediabetes and T2DM.*
Methods: *We researched PUBMED databases for randomized controlled trials (RCT) and observational studies (OS) published between 2012-2022 in English, Portuguese, or Spanish. The selected articles tested digital DSME interventions against treatment as usual (TAU) on adults (>18 years) previously diagnosed with T2DM or prediabetes. The result was measured by determining the HbA1c levels.*
Results: *Out of 261 articles, 14 RCTs were selected based on eligibility criteria. Digital DSME technologies have different objectives, including monitoring glycemic fluctuation, insulin titration, nutritional guidance, sleeping assessment, enhancement of physical activity, control of comorbidities, relevant task notifications, personalized treatment recommendations, educational content, and patient/medical staff remote interaction. Some of the technologies combined machine learning techniques for different functions, including detecting adverse glycemic events, physical activity, and blood pressure, among others. Although the level of adherence varied among the various trials, 4 of the 14 RCTs analyzed reported a significant reduction of HbA1c levels using these digital devices compared to TAU.*
Discussion: *Programs providing digital DSME education is a potentially cost-effective tool to improve diabetes care worldwide by overcoming distance barriers, facilitating physician-patient communication, and reducing HbA1c levels. Future improvements in implementing these technologies could enhance user compliance and contribute effectively to diabetes management.*

Introduction

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disease with a global prevalence of 10.5% among adults (Sun et al., 2022). Diabetes-related mortality has been increasing in the last decade, especially in developing countries (WHO, 2016).

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The American Diabetes Association (ADA) strongly recommends a diabetes self-management education (DSME) program for patients with T2DM to achieve the skills needed for self-care management and decision-making (American Diabetes Association Professional Practice Committee, 2022b). Although this method has been demonstrated to improve the quality of life of these patients and to reduce glycosylated hemoglobin (HbA1c) levels, mortality risk, and health care costs (American Diabetes Association Professional Practice Committee, 2022b; Li et al., 2018); adherence rate is approximately 10% (Coningsby et al., 2022).

Recently, new digital instruments have been engineered to deliver DSME programs remotely cost-effectively, facilitating attendance and motivating more people with diabetes to participate in these activities (Bassi et al., 2021). Furthermore, these technologies have shown similar or even greater results regarding HbA1C reduction and patient engagement than in-person methods (American Diabetes Association Professional Practice Committee, 2022b). However, a comprehensive analysis of the available DSME programs still needs to be improved. Therefore, our objective is to review the effectiveness of the leading digital DSME tools in relation to HbA1c levels in adults with prediabetes or T2DM.

Materials and Methods

Eligibility Criteria

Randomized controlled trials (RCTs) or observational studies (OSs) that gathered all the following criteria were included in the analysis: 1) comparing a digital DSME device against in-person treatment as usual (TAU); 2) in adults (>18 years) diagnosed with T2DM or pre-diabetes according to ADA's guidelines; 3) using HbA1c as an outcome; 4) and being written in English, Portuguese, or Spanish. Studies were excluded if they involved children or patients diagnosed with non-T2DM.

Design and Data Sources

This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2020). Digital Intervention was defined as using digital and technology resources to educate the patients about their disease, such as cellphones, tablets, telehealth, or other forms of web-based conferencing or interface for exchanging information about disease or health behaviors.

The following search strategy was conducted on 9th September 2022, using Medline database: (diabetes[Title]) AND ((Digital[tw]) OR (Digital platform-based[tw]) OR (Digital health tools[tw]) OR (Digital health intervention[tw]) OR (Digital health profession[tw]) OR (digital media[tw]) OR (Digital intervention self-management education[tw]) OR (Digital communication[tw]) OR (Digital educationassisted[tw]) OR (Digital education[tw]) OR (Digital education methods[tw]) OR (Digital technology[Mesh])). Filters: Clinical Study. Sort by: Most Recent.

Data collection

Two reviewers (LS and KPB) independently screened and reviewed the articles and extracted study data. A third author (CVM) resolved any disagreements. Data were generated by reporting the digital DSME interventions' characteristics, their role in T2DM prevention, and their impact on HbA1c reduction and patient adherence. All data were organized into a table (table 1) and a narrative description.

Data Extraction

From the included studies, data on HbA1c was extracted as the primary outcome.

Synthesis methods

A qualitative systematic synthesis was performed using a critical interpretive method based on the studies' key concepts, such as DSME technologies' characteristics, effectiveness, and intervention adherence. The included articles are summarized in Table 1. The assessment of the risk of bias was evaluated by applying the Risk of Bias 2 (RoB2) tool, which is displayed in Figure 2. 58,3% of articles showed a low risk of bias, 16,7% raised some concerns, and 25% classified as at high risk. The features that represented an increased risk of bias were those related to the outcome analysis (measurement of the outcome and missing data) or a possible selection of the reported results.

Results

The study selection process is displayed in Figure 1, a flow diagram adapted from PRISMA´s guidelines. The initial search displayed 261 studies. Two authors (LS and KPB) reviewed the titles and abstracts of all 261 articles, excluding 208, for the following reasons: they were not related to diabetes (n = 146), were about gestational diabetes (n = 9), assessed type 1 Diabetes (n = 16), or did not evaluate digital interventions for DSME (n = 37). The same two authors (LS and KPB) excluded one report because of restricted access to the full text. Moreover, these two authors reviewed the full text of the 53 remaining articles, excluding 39 articles for the following reasons: they were protocols or ongoing trials (n = 16), did not assess the outcome of interest (n = 26), the control group did not receive in-person TAU (n = 2), there was no control arm (n = 1), the target population was not correct (n = 1), or did not assess digital interventions for DSME (n = 2). A third author (CVM) resolved any discrepancies. A total of 14 articles were eligible for full-text screening (Christensen et al., 2022; Farmer et al., 2021; Fortmann et al., 2017; Frias et al., 2017; Gong et al., 2020; Hilmarsdóttir et al., 2020; Kassavou et al., 2020; Katula et al., 2022;

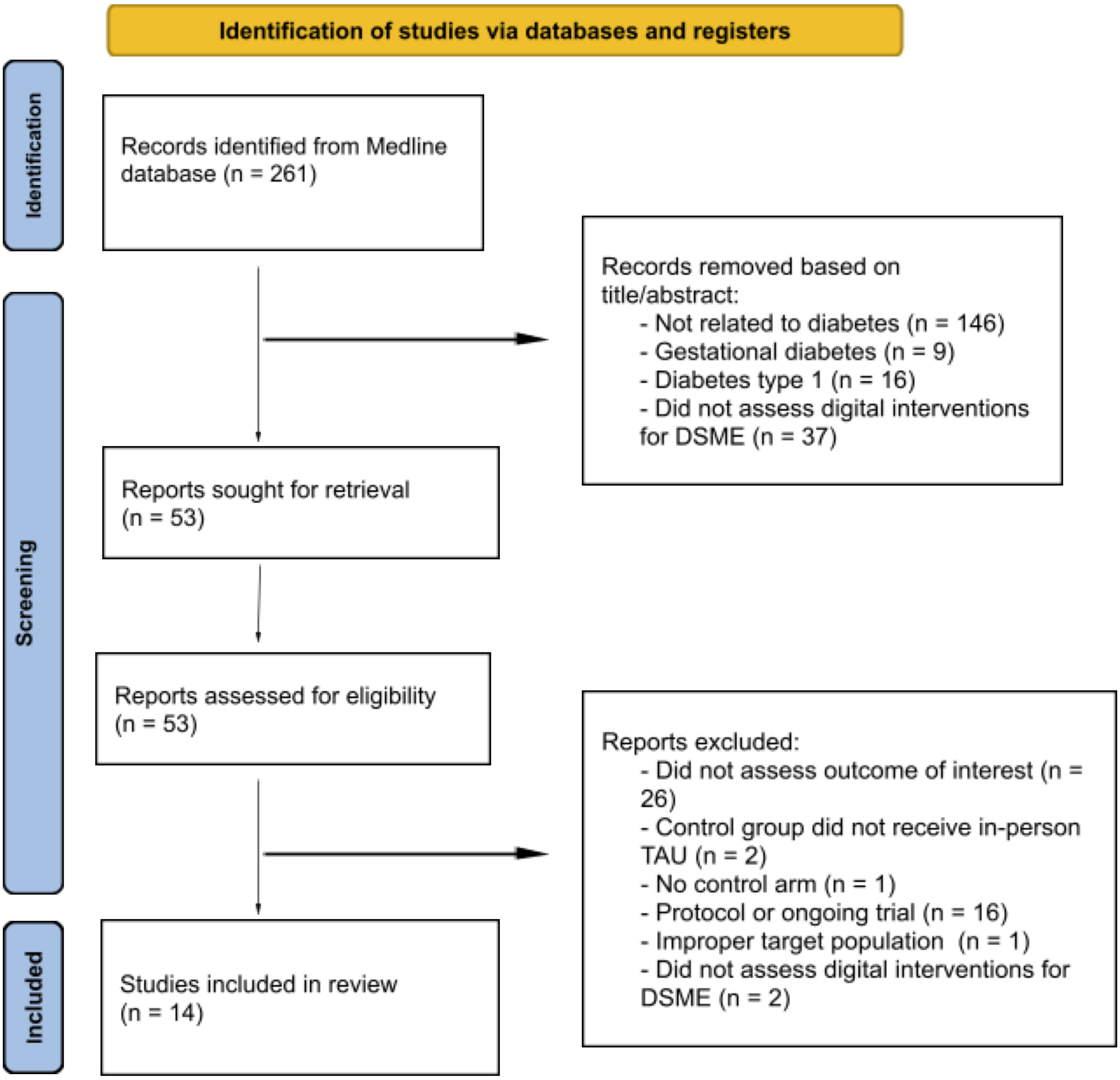

Figure 1: *Flowchart adapted from the PRISMA flow diagram template.*

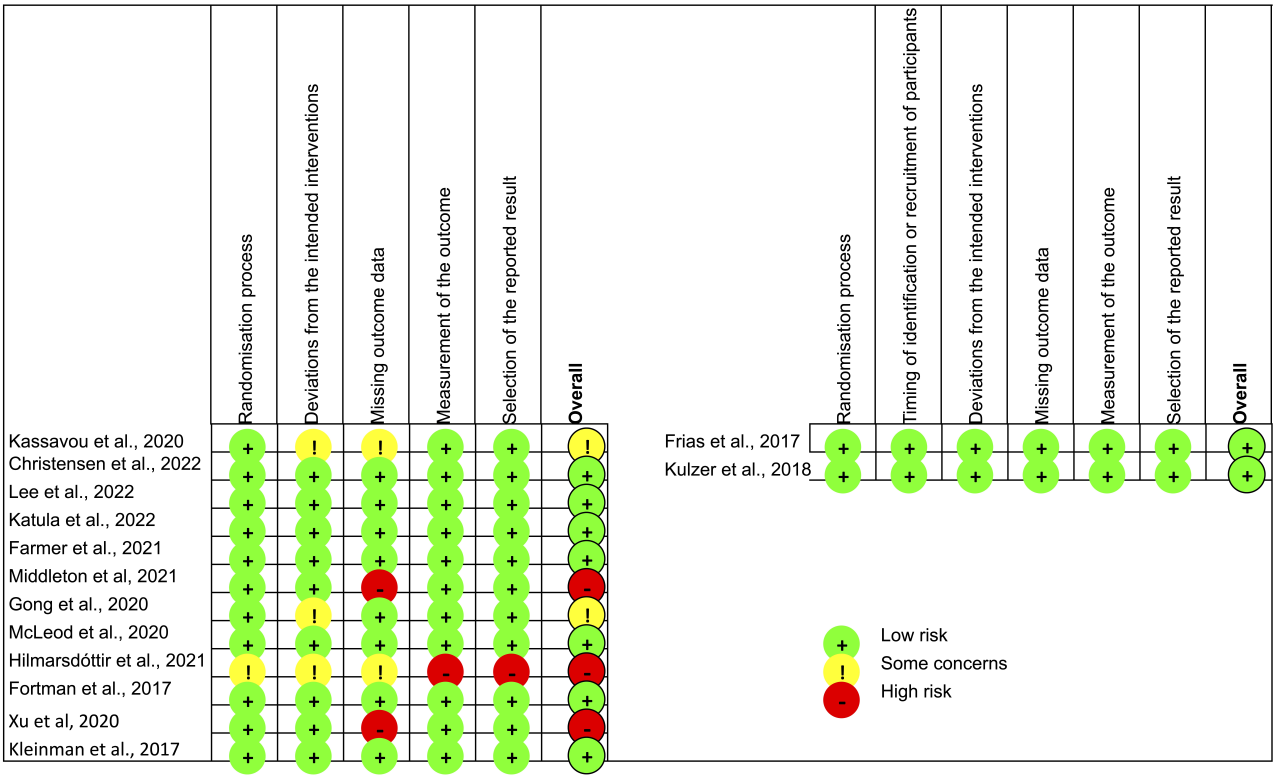

Figure 2: *For randomized (left) and cluster randomized trials (right). RoB2 applicative is available at: https://www.riskofbias.info/welcome.*

Kleinman et al., 2017; Kulzer et al., 2018; Lee et al., 2022; McLeod et al., 2020; Middleton et al., 2021; Xu et al., 2020).

Discussion

Cases of T2DM have been increasing globally, resulting in higher costs. Management and follow-up of patients with chronic conditions such as T2DM solely based on direct patient interaction with their primary care physician can hinder the overall control and progression of the disease. They may result in insufficient management of the patient's needs entirely. Using new technologies can result in better follow-up and control, resulting in patient compliance and adherence to the established treatments by their primary care physicians.

It is possible to extend the services offered by a healthcare system through digital health interventions. One clear example is the DSME interventions that can be achieved through the digital strategies discussed in this review.

DSME technologies have been reported to help manage patients with type 2 diabetes and cardiovascular risk factors. Although the management of glycemic levels has been reported to decrease the incidence of microvascular complications, macrovascular outcomes were not significantly different in patients with better glycemic control (King et al., 1999). In recent years, the strategy of reducing cardiovascular risk to reduce mortality and microvascular complications has received further attention (American Diabetes Association Professional Practice Committee, 2022b). Additionally, novel medications such as Liraglutide and, more recently, the Sodium-Glucose Co-Transporter 2 (SGLT2) inhibitors have reduced mortality by interfering with other biological pathways and moving beyond just the glycemic control (Lopaschuk & Verma, 2020; Marso et al., 2016). But all these pharmacological or non-pharmacological life-saving interventions only work if the patients adhere to the treatment regimen. Previous studies suggest that DSME is part of the multidisciplinary management required by the patients, which empowers them to participate in their disease monitoring actively.

Technology and data monitoring devices have been studied in patients with T2DM treated with insulin. These studies suggest that such devices facilitate personalized diabetes-care models, helping the physician in decision-making and encouraging patient communication with the healthcare team (Heinemann et al., 2020). However, most apps lack reinforcers for improving medication adherence (Huang et al., 2019).

There are some limitations in our study. Although

	Reference	Country	Study design (n)	Subjects	Study outcomes	Intervention (duration)	Results
1	Kassavou et al., 2020	United Kingdom	RCT (135)	Adults > 18 years with either or both poorly controlled BP and glucose levels.	Changes in: medication adherence, SBP, HbA1c (secondary outcome)	Highly tailored text message and interactive voice response intervention (12 weeks).	The HbA1c in the intervention group was 4.5 mmol/mol lower compared to the control group (95% CI -13.099 to 4.710). However, this study was not powered to detect significant between-group differences of HbA1c.
2	Christensen et al., 2022	Denmark	RCT (170)	Patients aged 18–70 years (mean age of 56 years) with T2DM and a BMI between 30 and 45 kg/m2.	Variations in: body weight, HbA1c (secondary outcome), BMI, lipid profile, SBP, DBP	*LIVA 2.0 (long-term Lifestyle change InterVention and eHealth Application)*: an individualized digital lifestyle coaching program that consists in a first face-to-face meeting with an individual health coach, which is followed by weekly synchronous visual online meetings. Each patient and their health coach agree the lifestyle goals for that participant; who uses LIVA 2.0 to complete daily goal records, and to send comments to their personal health coach (6 months).	Of those patients with elevated HbA1c at baseline, 24 out of 62 (39%) adults from the intervention group normalized their HbA1c < 6.5% at six months, compared to 8 out of 40 (20%) in the control group (p = 0.047). However, the reduction of HbA1c wasn't statistically significant.
3	Lee et al., 2022	South korea	RCT (269)	Adults aged 19-74 years (mean age of 52.5 years) with T2DM, who also had HbA1c level of ≥7.5% and a BMI of ≥18.5 kg/m2.	Changes in: HbA1c (primary outcome), FBG, lifestyle behavior, body weight, BP, lipid profile, frequency of hypoglycemia, HOMA-IR and HOMA-β. In addition, the program satisfaction and adherence were assessed.	*iCareD system*: electronic medical record–integrated mobile app that records patients' self-care data (SMBG, dietary habits, and step count), and sends automated text messages (educational, behavioral, and motivational messages) from the iCareD system to the participants' mobile phones (6 months).	The change in HbA1c levels did not differ significantly at 26 weeks (primary outcome) among the 3 groups [usual care (UC), mobile diabetes self-care (MC), and MC with personalized feedback]. However, the reduction in HbA1c levels at 12 weeks was significantly different among the 3 groups (UC vs MC vs MC+personalized feedback: −0.49% vs −0.86% vs −1.04%; P=.02).
4	Katula et al., 2022	USA	RCT (599)	Pre-diabetic volunteers (HbA1c 5.7%–6.4% [39–46 mmol/mol]) aged ≥19 years (mean age of 55.4 years).	Changes in: HbA1c (primary outcome), body weight, cardiovascular risk factors.	*The Omada Health Program* is a digital Diabetes Prevention Program (d-DPP), recognized by the CDC Diabetes Prevention Recognition Program. This is an asynchronous program that includes 12 months of novel interactive lessons, messages with a lifestyle health coach, virtual peer group discussions, and monitoring of meal, physical activity and weight (13 months).	At 12 months, the d-DPP group reduced significantly the HbA1c by an average of −0.23% (95% CI= −0.26, −0.20), compared with −0.16% (95% CI= −0.19, −0.12) for the control group (p=0.001) (primary endpoint).
5	Farmer et al., 2021	South Africa, Malawi	RCT (1186)	Adults > 18 years (mean age of 57.1 years) with T2DM.	Differences in the levels of: HbA1c (primary endpoint), BP, lipid profile.	Motivational and educational text messages, three to four times per week (12 months).	SMS text messages did not significantly improve glycemic control.
6	Middleton et al., 2021	Australia	RCT (40)	Patients (mean age of 32.7 years) with young-onset T2DM (age of onset 18-40 years).	Variations in: HbA1c (secondary outcome), lipid profile, SMBG data availability, and psychosocial well-being. Also, the attendance at scheduled clinical appointments was assessed.	*Enhanced SMS Text Message–Based Support and Reminder Program:* 1-8 supportive and/or informative text messages per month, individualized for each subject depending on baseline characteristics like gender and smoking status (12 months).	There were no between-group significant differences in HbA1c, BMI, lipids, or SMBG data.
7	Gong et al., 2020	Australia	RCT (187)	Adults aged ≥18 years (mean age of 57 years) with T2DM for less than 10 years.	Variations in HbA1c and health-related quality of life (HRQoL) (primary endpoints).	*My Diabetes Coach* (MDC) program consists in an interaction with the software assistant, Laura, which checks their blood glucose and additional information (12 months).	Although the HbA1c mean decreased in both arms at 12 months, there were not statistically significant differences between both groups (−0.04%, 95% CI −0.45 to 0.36; P=.83).

Table 1: *Summary of the articles included for the review.*

8	McLeod et al., 2020	New Zealand	RCT (429)	Patients aged 18–75 years (mean age of 62 years) with T2DM and prediabetes [HbA1c 41–70 mmol/mol (5.9–8.6%)], not taking insulin that were attended at the primary care level.	Differences in: HbA1c, body weight (primary outcomes), BMI, waist circumference, BP, quality of life, and scales of self-management and diabetes distress.	*BetaMe/Melon* program: It comprises four core components: (1) individual health coaching; (2) fortnightly provision of resources; (3) online peer support forum; and (4) online goal tracking. Then maintenance activities (web-based peer support and goal tracking only) complete the intervention (12 months).	HbA1c levels at 12 months did not differ between study arms.
9	Hilmarsdóttir et al., 2020	Iceland	RCT (30)	Patients aged 18-75 years (mean age of 51.2 years) with T2DM.	Variations in: HbA1c (primary outcome), blood lipids, body weight, as well as questionnaires about distress related to diabetes.	*SidekickHealth* smartphone app: a digital lifestyle program to enhance self-monitoring and the accomplishment of health goal settings in nutrition, physical activity, and stress management (12 months).	Although there were nonsignificant differences between groups, within the intervention group there was a significant decrease in HbA1c from 61 ± 21.4 to 52.7 ± 15.2 mmol/mol.
10	Xu et al., 2020	USA	RCT (65)	Patients > 18 years (mean age of 54.9 years), with T2DM and a HbA1c value of >7%.	Changes in HbA1c and FBG (primary outcomes). Also, the rates of response and engagement were measured.	*EpxDiabetes* is a telemedicine platform that provides bidirectional patient–provider communication through SMS and phone calls. It collects self-reported FBG, triaging patient data to prioritize physician action (6 months).	The absolute reduction of HbA1c in the intervention group was 0.69% (95% CI, −1.41 to 0.02, p = 0.055), versus an absolute reduction of 0.03% in the control group (95% CI, −0.88 to 0.82, p = 0.946). Of those patients with baseline HbA1c >8%, the intervention arm had a significant decrease of 1.17% (95% CI, −1.90 to −0.44, p = 0.004), versus the control group that had a 0.02% non-significant decrease (95% CI, −0.99 to 0.94, p = 0.957).
11	Kulzer et al., 2018	Germany	RCT (907)	Adults aged ≥18 years (mean age of 64 years) with T2DM and a HbA1 ≥ 7.5%, using subcutaneous insulin therapy for ≥6 months.	Between groups differences in: HbA1c levels (primary endpoint), therapy adjustments, frequency of hypoglycemic episodes and patient reported outcomes (like SMBG among others). Also, physician satisfaction was	The *integrated Personalized Diabetes Management* (*iPDM*): an iterative, 6-steps program that includes SMBG, a diabetes data management software, patient-physician communication, and support of therapeutic decision-making (12	iPDM arm had a significant greater reduction of HbA1c after 12 months versus usual care (−0.5%, p < 0.0001 versus −0.3%, p < 0.0001, which represents a difference of 0.2%, p = 0.0324).
12	Frias et al., 2017	USA	RCT (109)	Adults (mean age of 58.7 years) with SBP ≥140 mmHg and HbA1c ≥7%, failing antihypertensive (≥2 medications) and oral diabetes therapy.	Changes in: BP, HbA1c (secondary endpoint), FPG, medication adherence, physical activity and rest.	*Digital Medicine Offering (DMO)*: it measures medication adherence, physical activity, and rest using digital ingestible sensors, wearable sensor patches, and a mobile app. (12 weeks).	Although DMO group showed lower trends in HbA1c (as much as a 1% greater reduction), it had not significantly differences in the reduction of HbA1c, compared to usual care.
13	Fortmann et al., 2017.	USA	RCT (126)	Hispanic adults aged 18 to 75 years (mean age of 48.43 years), with poorly controlled T2DM.	Changes in: HbA1c levels (primary outcome), lipids, BP, and BMI. In addition, satisfaction was also assessed.	*Dulce Digital*: An m-Health text messages intervention for diabetes education and adherence (6 months).	*Dulce Digital* group achieved a significantly greater reduction in HbA1c levels compared with standard care (P = 0.03).
14	Kleinman et al., 2017	India	RCT (91)	People aged 18 to 65 years (mean age of 48.4 years) with T2DM, and levels of HbA1c between 7.5% and 12.5%.	Changes from baseline to 3 and 6 months of: HbA1c (primary outcome), BMI, waist circumference, BP, FBG, lipids, medication adherence, diabetes self-care activities, diabetes distress, and diabetes knowledge.	An m-Health platform containing a smartphone app for patients, and a website and smartphone app for providers. The platform used reminders, data visualization, and support to increase self-care behaviors. The provider website had the medical history of each participant and a set of alerts for highlighting those participants who required more attention (6	At 6 months the intervention group had a statistically significant mean HbA1c decrease of 1.5%, versus 0.8% in the usual care group (p = 0.02; 95% CI mean difference: 0.10–1.37), with no statistically significant differences after stratifying by gender, age, or length of time with

BMI: body mass index, **BP:** blood pressure, **CI:** confidence interval, **DBP:** diastolic blood pressure, **FBG**: fasting blood glucose, **HbA1c:** glycosylated hemoglobin, **HOMA-IR:** homeostasis model assessment for insulin resistance, **HOMA-β:** homeostasis model assessment for β-cell function, **RCT:** randomized controlled trials, **SBP:** systolic blood pressure, **SMBG:** self-monitored blood glucose, **T2DM:** Type 2 diabetes mellitus, USA: United States of America

Table 1: *Summary of the articles included for the review (continued).*

Pubmed is one of the most commonly used and ideal databases for reviewing biomedical electronic literature (Falagas et al., 2008), adding other databases would have broadened our study and included more studies. To reduce this bias, we developed a broad initial search strategy to screen many articles to be included in our review appropriately. However, another limitation is the final low number of pieces included because of our stringent criteria. Because of the high heterogeneity of the population and protocols used in this area of ongoing research, we decided to limit our scope further to increase the validity of our results. Despite including a limited number of studies, our results and conclusions are coherent with the existing literature (Mayberry et al., 2019; Pal et al., 2018; Sly et al., 2022). Finally, the use of HbA1c as a surrogate outcome might be statistically significant, although it might not reach a clinically significant improvement. Nonetheless, digital interventions that can improve HbA1c could also improve adherence, and lifestyle changes, among others; thus, the impact of an intervention with a subsequent improvement in HbA1c could also give rise to improvement in other areas outside the scope of this review.

Conclusions

Future research should focus on different patient populations to increase the adoption of diabetes self-management technologies. This is because the current technologies may not be accessible or user-friendly for everyone. Additionally, the differences in socio-cultural backgrounds and age groups among patients in different geographical locations can result in inconsistent results from various studies. Thus, the impact of these factors needs to be further investigated. Furthermore, multiple DSME technologies are designed for different purposes and approaches. However, there is currently no standard multidisciplinary approach for managing these patients. A standardized and effective intervention is needed to make DSME a viable option for healthcare providers in all income settings. In the future, randomized controlled trials that analyze specific DSME protocols as part of a comprehensive treatment plan may lead to the wider adoption of DSME in clinical practice.

Author Contributions

All the authors contributed equally to the conceptualization, methodology, systematic search, qualitative analysis, initial draft preparation, reviewing, and editing. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

The authors declare no conflict of interest.

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