# Diabetes Digital App Technology:

# Benefits, Challenges, and Recommendations

## Consensus Report

European Association for the Study of Diabetes (EASD) and the
American Diabetes Association (ADA) Diabetes Technology Working Group

(Version 1.9 September 6th, 2019)

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**Conflict of interest:**

No honoraria were received by members of the ADA-EASD Diabetes Technology Committee (AEDTC) for writing this manuscript or associated meetings. Most of the members of the AEDTC work with industry as listed below; however, the industry had no impact on the manuscript and its content.

GAF is Executive Chairman of Kinexum, which advises multiple health-product companies in the fields of metabolism, cardiovascular, oncology, and dermatology. He was formerly the Group Leader of the Division of Metabolism and Endocrine Drug Products at the US Food and Drug Administration (FDA).
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RMB has conducted clinical trials, consulted, or served on the scientific advisory boards for Abbott Diabetes Care, Becton Dickinson, Bayer, Dexcom, Eli Lilly, Johnson and Johnson, Medtronic, Novo Nordisk, Roche Diabetes Care, and Sanofi. He receives no personal income from these activities, for all payment goes to the non-profit Park Nicollet Institute.
RWH coordinates the German/Austrian DPV initiative, which has been supported by Novo Nordisk, Medtronic, Roche, Boehringer-Ingelheim, and Lilly through institutional research grants. RWH did not receive any personal honoraria.
ALP has served on advisory boards for Abbott Diabetes Care, Eli Lilly, Merck, Novo Nordisk, MannKind, Lexicon, Sanofi, and Zafgen. She has received grant funding from AstraZeneca, MannKind, and Dexcom. She has been on the Speaker's Bureau for Novo Nordisk.
LH is partner of Profil Institut für Stoffwechselforschung in Neuss, Germany, and of ProSciento in San Diego, USA. He is a member of advisory boards for Roche Diagnostics, Abbott, Zense, and Medtronic.

**Acknowledgments:**
We would like to thank the following for their helpful comments: Adam Brown, John Buse, Danelle Miller, Laleh Mohajerani, Nick Riggall, Mindy Saraco, David Strasberg, and Craig Stubing. We would very much like to thank Jennifer Zhao for her excellent editorial help.

**Abbreviations:** ADA – American Diabetes Association; BGM – blood glucose monitoring; CDRH – Center for Devices and Radiological Health; CE – Conformité Européenne; CGM – continuous glucose monitoring; CMS – Centers for Medicare & Medicaid Services; DIY AID – do-it-yourself Automated Insulin Delivery; DTSec – Standard for Wireless Diabetes Device Security; DWG – DTSec Working Group; EASD – European Association for the Study of Diabetes; EMA – European Medicines Agency; EMR – electronic medical record; EU – European Union; FDA – Food and Drug Administration; FDCA – Federal Food, Drug and Cosmetic Act; GHTF – Global Harmonization Task Force on Medical Devices; GOe – Global Observatory for eHealth; HCP – health care professionals; IMDRF – International Medical Device Regulators Forum; MARS – Mobile App Rating Scale; mHealth – mobile health; NEST – National Evaluation System for health Technology; NHS – National Health Service; PDA – personal digital assistant; PPA – product performance analytics; Pre-Cert – Precertification Pilot Program; RCT – randomized control trial; RWHA – real world health analytics; RWPA – real-world performance analytics; SaMD – Software as a Medical Device; WHO – World Health Organization; UXA – user experience analytics

## Abstract

Digital health technology, especially digital and health applications (“apps”), have been developing rapidly to help people manage their diabetes. Numerous health-related apps provided on smartphones and other wireless devices are available to support people with diabetes with either lifestyle interventions or medication adjustments in response to glucose monitoring data. However, regulations and guidelines have not caught up with the burgeoning field to standardize how mobile health apps are reviewed and monitored for patient safety and clinical validity. The available evidence on the safety and effectiveness of mobile health apps, especially for diabetes, remains limited. The European Association for the Study of Diabetes and the American Diabetes Association have therefore conducted a joint review of the current landscape of available diabetes digital health technology (only standalone diabetes apps, as opposed to those that are integral to a regulated medical device, such as insulin pumps, CGM systems, and closed loop control systems) and practices of regulatory authorities and organizations. We found that across the United States and Europe, mobile apps intended to manage health and wellness are largely unregulated unless they meet the definition of medical devices for therapeutic and/or diagnostic purposes. International organizations, including the International Medical Device Regulators Forum and World Health Organization, have made strides in classifying different types of digital health technology and fitting digital health technology within the space of medical devices. As the diabetes digital health field continues to develop and become more integrated into everyday life, we wish to ensure that it is based on the best evidence for safety and efficacy. As a result, we bring to light several issues that the diabetes community, including regulatory authorities, policymakers, professional organizations, researchers, people with diabetes, and health care professionals (HCPs), needs to address to ensure that diabetes health technology can meet its full potential. These issues range from inadequate evidence on app accuracy and clinical validity to lack of training provision, poor interoperability and standardization, and insufficient security of data. We conclude with a series of recommended actions to resolve some of these shortcomings.

## Introduction

Coincident with the diabetes pandemic of the last three decades has been a revolution in digital and wireless technology.[1] These technological advances have been harnessed to support lifestyle and pharmacological interventions, as well as medical devices (blood glucose meters, continuous glucose monitoring (CGM) devices, insulin pumps, and smart pens).[2,3,4,5] At the forefront is the burgeoning field of digital health technology for people with or at risk for diabetes, which has proliferated and begun to permeate clinical care, research, and health product development.[6]

This position statement focuses on digital health apps. Digital health, also known as mobile health ("mHealth"), is defined by the World Health Organization (WHO) Global Observatory for eHealth (GOe) as "medical and public health practice supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants (PDAs), and other wireless or stationary devices."[7] Digital health apps can be generally broken down into three categories: those used for tracking wellness, those that function as standalone medical devices (e.g., for titrating insulin), and those that display, download, and/or use data from medical devices that diagnose, prevent, monitor, or treat a condition (e.g., blood glucose monitoring [BGM], continuous glucose monitoring [CGM], insulin pump, or closed loop control system [also known as Automated Insulin Delivery system]).[8] Among almost half a million health-related apps available for wireless devices (usually smartphones),[9,10] apps designed to help manage diabetes are among those most commonly available.[11] These are intended to improve health outcomes and quality of life by coaching people with diabetes, supporting healthy nutrition and weight control, encouraging glucose monitoring and remote monitoring, assisting with the interpretation of results, maintaining lifestyle modifications, guiding medication dosing and, ultimately, reducing complications.[12] Due to the vastness of the field of digital health apps, this position statement will go into discussion of only standalone apps that are not integral to a regulated medical device. Examples of what is out of scope of this position statement include insulin pumps and closed loop control systems.

Table 1 lists examples of digital health apps used for managing diabetes according to their intended purpose. It is important to note that many of the aforementioned apps have more than one feature, and not all are solely for managing diabetes. Earlier in 2019, Kebede and Pischke conducted a study that aimed to identify the most popular diabetes apps via a web-based survey among the diabetes social media community.[13]

**Table 1: Types of Digital Health Apps Used for Managing Diabetes**

| Category Name | Description/Definition | Examples |
|---|---|---|
| (i) Nutrition apps | • Offer databases where users can look up carbohydrate, fat, protein and calorie content;<br>• Support meal planning and insulin dose adjustment.[14] | Carbs and Cals<br>CarbControl<br>Foodily<br>Healthy<br>Low Carb Program |
| (ii) Physical activity apps | Allow users to track their activity, count calories, and set goals for exercise and weight management.[15] | My Fitness Pal<br>Nike + Running<br>Track 3 |
| (iii) Glucose monitoring apps | • Log glucose data, typically from an external device that measures glucose (e.g., BGM, CGM);<br>• Graphically display glucose levels to assist the patient and health care professionals (HCPs) with management of glucose control. | Dexcom Share<br>Diabetic<br>Diabetes Companion<br>Diabetes in Check<br>Glooko Mobile App<br>Tidepool Mobile |
| (iv) Insulin titration apps | An extension of (iii) that also integrate bolus calculators with traditional blood glucose meters to help people with diabetes calculate their basal, prandial, and correction insulin doses.[14] | FDA-cleared apps: WellDoc BlueStar,[16] Voluntis Insulia, Sanofi MyDose Coach, Glooko Mobile Insulin Dosing System, Amalgam iSage Rx,[17] and Hygieia d-Nav Insulin Guidance System[18] |
| (v) Insulin delivery apps | • For insulin pumps and smart pens to collect and display data; includes bolus calculators, data | Companion Medical InPen connects to its smartphone app via Bluetooth® to keep track of insulin data.[20] |

| | | |
|---|---|---|
| | downloaders, and firmware update apps.[19]<br>• Such apps also provide decision support. | Dexcom Clarity sends weekly summaries and pattern identification.[21]<br>Medtronic's Sugar IQ integrates BGM and insulin dosing analysis in close to real time.[22] |
| (vi) Closed loop control systems (also known as artificial pancreas systems, automated insulin delivery, or autonomous system for glycemic control) | Consists of a CGM, insulin infusion pump, and a computer-controlled algorithm (e.g., on a smartphone app) to allow communication between the CGM and insulin pump on the patient.[23] | Medtronic's MiniMed 670G/Guardian Sensor 3 is the first FDA-approved hybrid closed loop that automates basil insulin delivery (still requires meal boluses).<br>Medtronic's MiniMed 640G/Enlite Enhanced, which provides predictive low glucose management, is available in Europe.[24] |

Diabetes apps have enormous potential, given that more than 2.7 billion individuals in the world use smartphones[25] and about 0.5 billion people already use mobile apps for diet, physical activity, and chronic disease management.[26] Small-scale studies show promising results of digital programs targeting glucose control, medication adherence, weight loss, and quality of life.[27,28,29,30] However, longer-term clinical evidence is needed to more accurately assess the effectiveness of diabetes digital and health apps. Currently, many apps are "stand-alone"; however, there is an increasing trend towards integration and continued automation (both in data collection and algorithm-based response). As this trend gains momentum, the landscape of apps is likely to be transformed toward greater integration.

The market-driven explosion of health apps has been facilitated by current systems of regulation. However, not every app is useful or good. Our intent is not to slow growth, but rather to make a realistic assessment of what is safe and truly beneficial for people with diabetes. There are very few data on long-term benefits, and even high quality short-term data are limited.[31] While apps may benefit those with the technical, literacy, and numeracy skills to

interact with them, many people with diabetes (even in high-income countries) still lack access to health care and medications (including insulin) required to sustain life, which may represent more pressing problems to address.

The Diabetes Technology Working Group of the ADA and the EASD aims to complement already-published reviews, position statements, and guidelines on digital health applications[32,33,34,35] by reviewing their benefits and risks while providing approaches to handle the challenges they pose. In the following discussion of this article, we cover only standalone diabetes apps, as opposed to those that are integral to a regulated medical device (e.g., insulin pump, CGM system, Automated Insulin Delivery [AID] systems). Other topics not covered here that warrant future attention are: apps specific to gathering clinical evidence, and apps that support general electronic medical record (EMR) systems.

## The role of regulators

While most stakeholders in Europe and North America have a general understanding of the approval and regulatory processes governing pharmaceuticals and medical devices, our experience is that levels of awareness of these issues in relation to digital apps are lower. We believe it is important for people with diabetes, as well as health care professionals (HCPs), to understand aspects of diabetes app regulation.

*a) European Medicines Agency (EMA)*

The European Commission has recognized the growing digital health market. In 2012, it released guidance (updated in 2016) on the qualification and classification of standalone software used in the health care setting as a medical device.[36] Under this guidance, mobile apps are considered medical devices if they are used "specifically for diagnostic and/or therapeutic purposes," including the diagnosis, prevention, monitoring, treatment, or alleviation of disease.[36] In 2014, the Communication on Digital Transformation of Health and Care in the Digital Single Market was published, listing three priorities:

(i) Enable citizens to access their health data across the EU;

(ii) Allow researchers and other professionals to pool health data across the EU to advance research and personalized health; and

(iii) Use digital tools to empower people with diabetes to look after their health, prevent diseases, and enable feedback and interaction between users and HCPs.[37]

While the European authorities and Food and Drug Administration (FDA) share the broad principles of regulating both traditional health products and software, there are substantial differences in the organizational structure of medical product and software registration. The European Medicines Agency (EMA) and the FDA are each responsible for pharmaceutical regulation, but only the FDA regulates both pharmaceuticals and medical devices. In the European Union (EU), no single agency, but the European Commission, is responsible for regulation of medical devices; each individual country retains primary responsibility for organizing and delivering health services and medical care. As a result, EU member states maintain their own national pharmaceutical regulatory authorities, with the European Commission serving to complement national policies and ensure health protection according to EU policies (e.g. the new Medical Device Regulation [MDR]).[38] Instead, these responsibilities are retained by individual member states, which delegate to accredited notified bodies responsibilities for implementing these regulations. These entities are accredited by the EU to assess whether a product meets the standards set by the EU Medical Devices Directive (MDD), and their decision is valid across all member states. Assessments are based on evidence of safety and performance (in contrast, the FDA may also require clinical effectiveness data, especially for "high risk devices" (see classification of medical products)).[39] If these standards are met, then a manufacturer is authorized to market the product throughout the EU and label it with the Conformité Européenne (CE) Mark.[40]

In general, the process of obtaining a CE Mark in the EU in the past has been a lower hurdle than obtaining device approval or clearance by the FDA.[41] This difference in the US and EU is likely to narrow with the implementation of the European Union Medical Device Regulation (MDR), which repeals the existing directives on medical devices. The regulation was published on May 5, 2017 and allows a transition time of three years before coming into force on May 25, 2020. Currently approved medical devices will have time until May 26, 2020 to meet the new MDR requirements. Among the provisions in this set of regulations are the strengthening of post-market surveillance, establishment of a comprehensive EU database on medical devices, stricter control for high-risk devices before launch in the marketplace, and a new risk classification system for *in vitro* diagnostic medical devices in line with international guidance.[42]

The guidelines in individual countries align with those issued by the European Commission. For example, Sweden's Läkemedelsverket Medical Products Agency classifies medical software as a medical device if its stated purpose complies with the definition in Article 1 of Directive

93/42/EEC on medical devices ("used specifically for diagnostic and/or therapeutic purposes"), has a demonstrated benefit over risk, and is CE-marked.[43] In Germany, medical apps are classified as medical devices if they follow EU guidelines and the German Medical Devices Act and are CE-marked.[44] The situation in the UK was previously similar but is currently in flux as the UK is imminently set to leave the EU.

More recently, the European Commission has made considerable efforts to introduce and implement the MDR as a new regulatory framework, which will provide clarity on what is (and what is not) a medical device software.[42]

*b) Food and Drug Administration (FDA)*

With a view to prioritizing its resources in the face of an explosive growth of digital health apps, the FDA has attempted to draw a line between those that do and do not require regulation. In 2015, it released a guidance document for mobile medical applications for apps that meet the definition of a device in section 201(h) of the Federal Food, Drug and Cosmetic Act (FDCA).[32] This definition covers apps intended to be used as accessories to regulated medical devices and those that are standalone software. However, the guidance expressed its intention to exercise "enforcement discretion" over those judged to pose a lower risk to users (e.g., apps that provide people with diabetes encouragement to meet their health goals or provide them with tools to track their health information). Thus, using this "risk-based" approach, mobile apps that calculate insulin doses are within the scope of regulation, while apps that simply organize and/or provide health or nutritional information are not. The FDA lists approved/cleared apps in its 510(k) and PMA databases and on its Registration & Listing Database.[45]

These guidelines were updated when the US Congress passed the 2016 21st Century Cures Act, which specifically excludes from the definition of "medical device" certain low-risk medical software. Examples of exclusions from regulation as a medical device include software that supports administrative functions, encourages a healthy lifestyle, serves as an electronic patient record, assists in displaying or storing data, or provides limited clinical data support.[46,47] By the end of 2019, the FDA will launch version 1.0 of the National Evaluation System for health Technology (NEST) initiative, which will be coordinated by the NEST Coordinating Center (NESTcc).[48] NEST will improve access to evidence across the total product lifecycle of medical devices by strategically and systematically leveraging real-world evidence generated by participating institutions and applying advanced analytics tailored to the unique data needs and

innovation cycles of medical devices.[49] Using a neural network data model that will represent nearly 500 million patient records from approximately 200 hospitals and 4000 outpatient clinics, this initiative seems promising for medical device stakeholders, especially if it will capture substantial data on people with diabetes.

An important distinction is the difference in the regulation of mobile health apps from the regulation of digital therapeutics (sometimes referred to as “digiceuticals”). Digital therapeutics are clinically-validated digital, usually online, health technologies intended to treat a medical or psychological condition.[50] These are governed by clinical data and regulatory approval as for drugs and medical devices. An example is Welldoc’s BlueStar Rx mobile app, which was cleared by the FDA as a prescription-only app to support the management of type 2 diabetes. An identical version without the bolus calculator was approved for direct sale without prescription (i.e., two versions are offered, allowing the company to offer the product through more channels). Both versions analyze diabetes data entered by the patient, comparing past data trends to form personalized guidance and creating a summary of curated data analytics to the health care team for clinical decision support, but the non-prescription version will not feature the insulin calculator that the full version does. As of October 2018, Welldoc is moving into Phase 2 for ongoing Quality Improvement research of BlueStar.[51] In essence, digital therapeutics like BlueStar Rx focus on delivering clinical outcomes and are regulated by the FDA. On the other hand, mobile health apps, especially those that do not provide clinical recommendations, are largely not.

Whether a mobile app has regulatory clearance/approval or not, we believe that all clinical performance claims made by “digital health technology” should be backed by clinical evidence and real-world performance/outcomes. Real-world data and real-world evidence have been increasingly recognized by regulatory bodies, including the FDA, to enhance clinical research and support regulatory decision making for drugs, biologics, and devices,[52,53] and thus the same should be done for mobile apps. The FDA has published a Digital Health Innovation Action Plan that outlines a reimagined approach to foster digital health innovation while continuing to protect and promote public health.[46] This effort includes three goals:

(i) Providing guidance to provide clarity on the medical software provisions of the 21st Century Cures legislation;

(ii) Launching an innovative pilot pre-certification program to develop a new approach to digital health technology oversight (FDA Pre-Cert for Software); and

(iii) Building expertise within the Agency (including recruitment of additional dedicated and specialized staff).

In recent months, the FDA has further developed its digital health Software Precertification Pilot Program (Pre-Cert) with the goal of developing a more tailored pathway that enhances safety and effectiveness of such devices while supporting the innovation and availability of high-quality digital health tools. This program will allow the FDA to first look at the company, rather than primarily at the digital health software product being submitted, in order to expedite product reviews from vetted "excellent" companies.[54] The components of the Pre-Cert program are:

(i) Excellence appraisal and certification: Evaluating organizational excellence based on five criteria for quality and organizational excellence principles: 1) product quality, 2) patient safety, 3) clinical responsibility, 4) cybersecurity responsibility, and 5) proactive culture.

(ii) Review determination: A risk-based framework for pre-certified organizations is to be established to determine the premarket review pathways for their products. Incorporating principles from the International Medical Device Regulators Forum (IMDRF)'s Software as a Medical Device (SaMD) (discussed in the next section), the final framework for each Software as a Medical Device (SaMD) will be based on the state of the health care condition addressed, the significance of the information provided to support health care decisions, and descriptions of the core functionality and device.

(iii) Streamlined review: FDA review of the information received, which is made streamlined because (i) and (ii) provide information that does not need to be submitted again.

(iv) Real-world performance: Post-launch product monitoring efforts on product-specific real-world performance analytics (RWPA). RWPA will consist of real-world health analytics (RWHA: human factors and usability engineering, clinical safety, and health benefits), user experience analytics (UXA: user satisfaction, engagement, feedback channels, and issue resolution), and product performance analytics (PPA: cybersecurity and product performance; data to be collected by the respective company).[55]

The current pilot Pre-Cert program, which remains in a test plan phase, includes nine software companies (Apple, Fitbit, Johnson & Johnson, Pear Therapeutics, Phosphorus, Roche,

Samsung, Tidepool, and Verily), seven of whom have software relevant to diabetes. In 2019, FDA will test the effectiveness of the Pre-Cert program by reviewing a number of SaMD products under a traditional *de novo* pathway and, in parallel, a Pre-cert pathway to see if the Agency gets the same result.[48]

**Guidance from other bodies**

a) International Medical Device Regulators Forum (IMDRF)

The IMDRF, founded in 2011, is a group of international medical device regulators whose goals are to build on the work of the Global Harmonization Task Force on Medical Devices (GHTF) and accelerate medical device regulatory harmonization and convergence.[56] Members include officials from the FDA, European Commission, Australian Therapeutic Goods Administration, Chinese National Medical Product Association (NMPA), and Russian Federal Service for Surveillance in Healthcare (Roszdravnadzor).

The group has released several influential documents. Among them is "Software as a Medical Device (SaMD): Possible Framework for Risk Categorization and Corresponding Considerations," which was released in 2014 and introduces a foundational approach, harmonized vocabulary, and general and specific considerations for manufacturers, regulators, and consumers to consider in the context of SaMD.[57] In 2015, the group published "Software as a Medical Device (SaMD): Application of Quality Management System" to help manufacturers and regulators attain a common understanding and vocabulary for the application of medical device quality management system requirements to SaMD.[58] In 2017, IMDRF published "Software as a Medical Device: Clinical Evaluation" to provide guidance in gathering evidence for clinically meaningful SaMDs, elaborating on valid clinical association, analytical validation, and clinical validation.[59] These efforts on the global harmonization of medical device regulatory processes, including those governing digital health technology, provide guiding principles as a template for other regulatory agencies to incorporate into their respective frameworks.

b) World Health Organization (WHO)

In 2018, WHO published "Classification of digital health interventions v1.0" with similar aims of providing governments, technologists, clinicians, researchers, and other communities in digital health a shared and standardized language in assessing digital health interventions. The document organizes digital health technologies into interventions for clients, HCPs, health system or resource managers, and data services. It also presents health system challenges and

digital health interventions to address them. For example, the challenge of HCPs losing clients to follow-up can be addressed by sending alerts and reminders; this intervention is categorized under “client communication systems.”[60] WHO’s newly available resource provides several examples of current apps and their uses and, more importantly, a solid framework to underpin future developments in digital technology.

c) Nationwide Health Care Service

At least one nationwide health care service now provides a digital health apps certification program. The United Kingdom’s National Health Service (NHS) describes its process, which involves app providers to show evidence that their products pass tests in outcomes, clinical safety, data protection, security, usability and accessibility, interoperability, and technical stability.[61] The NHS has so far listed 13 apps that are "safe and secure" for the management of diabetes: Changing Health, GDm-Health, Liva UK, Low Carb Program, mapmydiabetes, Mumoactive, My Diabetes My Way, My Health Fabric, my mhealth: myDiabetes, nujjer, OurPath, Oviva, and Sugarmedown.[62] This is the only database dedicated solely to apps approved by a regulatory that we are aware of.

## Issues faced by the diabetes community

Although the rapid growth of digital health apps potentially brings great benefit, still-early development of the field also raises questions and challenges: for example, how physicians and other HCPs can maintain an adequate understanding of commonly used apps in order to provide guidance to people with diabetes, and how data can be kept confidential and secure. Below we outline nine major issues that need to be addressed by regulatory authorities, policymakers, professional organizations, researchers, product manufacturers, and HCPs.

1. *Availability of evidence*

Although there are almost half a million mobile health apps available for download, there are far fewer randomized control trials (RCTs), case-control studies, and cohort studies that evaluate whether app-based interventions improve health-related behaviors. One of the reasons there are so few published RCTs of digital health is that a product is never “frozen” in time like a medication – an app usually is constantly learning and improving. Even a three-month RCT is likely to have at least a two-year timeline from conception to publication – a long period of time in a fast-developing space. What should also be kept in mind is that RCTs on digital health apps, are, by nature, never blinded, so a placebo effect cannot be ruled out. Another reason for

the relatively few RCTs is that the typically lower commercial value and shorter life cycles of these products does not support the high cost and time involved in conducting RTCs. As a result, developing apps to be used in medical studies may be a less attractive business model for mobile health app developers.

In 2016, Zhao and others searched for peer-reviewed articles in English published from January 2010 to June 2015 on app-based health interventions targeted at adult populations. While their initial search returned over 3300 articles, the exclusion of qualitative studies and those in which mobile apps were not the primary intervention tool resulted in a final 23 articles from which primary or secondary outcomes for analysis could be extracted.[63] This small number starkly contrasts with the number of mobile health apps available for download. Of these 23 articles, only 10 described studies relevant to diabetes management. Four of these ten provided interventions intended to improve lifestyle (e.g., physical activity, weight control, and diet control), and three aimed to improve medication management. However, only two actually measured changes during a lifestyle intervention, and only one was specifically targeted at diabetes management. Several of the apps assessed in this study improved short-term adherence and enhanced intervention effectiveness, but many others yielded no effect. Zhao and others concluded that their results provided a snapshot of the current evidence of effectiveness for health-related apps, but large sample, high-quality, adequately powered RCTs are required. Similarly in 2016, Drincic and others reviewed mobile medical apps that were commercially available to people with diabetes in the US or EU. They found only 14 apps with clinical outcomes data published in peer-reviewed literature or have been cleared by the US FDA or received a CE mark in Europe. Drincic and others found these apps to positively affect outcomes, such as HbA1c, hypoglycemia incidence, and diabetes self-care measures, in the short term. However, more data and long-term studies are needed.[31]

More recently, a 2018 comprehensive study for the US Agency for Healthcare Research and Quality found only 11 randomized clinical trials (RCTs) reporting health outcomes amongst the hundreds of commercially-available apps for diabetes self-management. Of these 11 RCTs, only five were associated with clinically significant but small improvements in HbA1c. None of the studies demonstrated improvements in quality of life, blood pressure, weight, or body mass index. Methodological issues included limited duration (2-12 months), potential confounding by other co-interventions, and inconsistency in the reporting of randomization, allocation, masking

of outcomes assessment, and method of analysis in relation to drop-outs. None of the studies were considered high quality.[64]

Thus, while the available studies of app-based interventions show promise for promoting healthy behavior and managing complex diseases, such as diabetes, they are extremely limited in both quantity and quality. The studies previously mentioned in this section all report their respectively assessed apps to improve or have promise in improving short-term outcomes. However, all of these studies also conclude that more rigorous, larger sample, and longer-term RCTs are required to distinguish the effect of these apps from possible concomitant effects. In principle, well-designed studies with larger sample sizes and longer durations are needed to gather and assess evidence of sustainable effectiveness over time.

2. *Adequate information and training*

Beyond the field of diabetes, evidence-based apps are available as clinical decision-making tools for HCPs, with a scope that includes disease diagnosis, medical calculators, literature search, and reference drug information.[65] With thousands of apps currently being developed and updated, issues arise. These issues include: how to keep HCPs up-to-date with the apps most appropriate to use, how to support people with diabetes to use these digital tools, and how to ensure that using them will result in benefit rather than harm. Although it is important for HCPs to stay up-to-date on the digital health app landscape, we acknowledge that it is unrealistic for HCPs to meet this expectation on top of their highly burdened workload. As a result, other stakeholders in the diabetes community should work with and alongside HCPs in addressing this issue.

3. *Accuracy, clinical validity, and quality*

Because the majority of mobile health apps are not subject to regulation, data for assessment of accuracy, hereby defined as the ability to correctly differentiate patient and healthy cases (the sum of true positive and true negative cases over the sum of all cases),[66] often may not be available. Patient involvement and self-management are the key to diabetes care, but there is a fine line between empowerment and unregulated harm. For example, potentially questionable data and/or medical opinion from a mobile health app can place a burden on a consultation if the information provided does not align with clinical guidelines in disease management.[67]

A number of studies have evaluated the accuracy of mobile medical and health apps, though there are few studies that focus on diabetes health apps. Chavez and others analyzed the 89 most popular free English-language diabetes apps by each app's level of engagement, functionality, aesthetics, information, and number of diabetes-specific management tasks met. Using the Mobile App Rating Scale (MARS), they found that while this subset of mobile health apps ranked "acceptable-good" in engagement, functionality, and aesthetics, they ranked "poor-acceptable" in information, app quality score, and app subjective score.[68] Bierbrier and others evaluated the accuracy of 14 smartphone medical calculation apps aimed at internists, including those that calculated the severity or likelihood of liver disease or of having a pulmonary embolism. Of 1240 calculations run on these apps, 98.6% were accurate, with six of the 14 functions assessed as 100% accurate. Although errors were overall few, some were clinically significant. The authors point out that in the absence of regulation, the responsibility for any adverse consequences of using these apps falls on the individual clinician.[69]

Additionally, a 2018 study by Lum and others pointed out the need for quality assurance mechanisms for diabetes apps to support people with diabetes. Of the approximately 370 diabetes apps that met the researchers' criteria for blood glucose self-management (blood glucose level recording; goal setting for blood glucose levels and HbA1c; reminders, alerts, and action prompts; and patient education on hypoglycemia and hyperglycemia management), the majority did not provide real-time decision support or situation-specific education on blood glucose self-management. All of these apps recorded blood glucose levels. However, only about a third had goal setting and reminders to measure blood glucose and record HbA1c. Approximately a third of apps alerted users to hypoglycemia or hyperglycemia, and only ten percent of apps educated users on blood glucose management.[70]

Thus, greater scrutiny is needed to oversee the accuracy, clinical validity, and quality of mobile health apps to protect patient safety. Apps that can be used by adolescents of parents for their children, as well as during pregnancy or old age, have to ensure that the advice given is suitable for this age-group. In addition, apps should clearly define the user group.

Another factor that should be considered is the standardization of language and presentation (e.g., blood sugar, time in range, standard deviation, body mass index, etc.). Setting standards for how information is presented would lead to fewer errors in translation and interpretation from app to HCP to patient.

4. *Technological issues*

Technological issues apply to diabetes digital health apps. These include the maintenance of mobile apps so that they are up-to-date with the latest technological platforms and operating systems and free of bugs that degrade app performance. App developers need to consider carefully battery usage, input/output ports (e.g., USB port, headphone jack, lightning port), and the impact of inconsistent illumination, mobile device cases, and inconsistent resolution with smartphone cameras.[19] Additionally, the speed at which mobile app versions are released or new features are rolled out, as well as the tolerance level of acceptable error within a release, is far greater than those of medical technologies. From the user perspective, this provides greater medical choice in medical apps, but makes it more challenging to find and ensure acceptable performance among many apps of varying quality.

5. *Interoperability and Standardization*

Consumers use a variety of mobile technological platforms, including Android and Apple iOS. Android and Apple iOS are the dominant platforms in the US market, with a keyword search for "diabetes" performed in the Apple and Google Play stores in 2017 identifying 246 available apps for Android and 100 for Apple iOS.[71] As of 2012, more than 75% of physicians in the US use Apple iOS devices.[72] However, where these apps are available for less popular platforms, app developers should ensure they operate consistently to the same standard.

It is also important that data recorded in health apps be easily transmitted from smartphones to other platforms, such as electronic health records for sharing with HCPs. An example Is Apple Health, which is a health informatics mobile app that functions as a central repository for health information. Apple's Healthkit can be integrated into multiple mobile health and fitness apps on Apple products, and record and share health data.[73] An example of an app integrated with Apple Health is Tidepool Mobile, which can connect to Apple Health and show data from users' insulin pumps, CGM, and sources outside of Dexcom devices.[74] Google Fit is an approximate equivalent to Apple Health for the Android platform.[75] Advances in integration and automation of data collection have come far, and we anticipate these advances to continue and improve.

6. *Differences among populations*

In 2017, an estimated 12 million people ≥65 years of age and 193,000 people <20 years of age had diabetes in the US.[76] The differences in these two populations are important because

younger populations (usually with type 1 diabetes) are typically more proficient at using smartphones than older populations. Consequently, apps targeted for older people with diabetes must be designed with their expected level of technology proficiency kept in mind. In addition, currently available diabetes management apps may not be available in languages other than English or accessible to people with certain physical or mental disabilities (e.g., color blindness, blindness, hearing impairment, etc.). Furthermore, those from remote regions and areas of extreme socioeconomic deprivation may not have access to smartphone technology. The cost of obtaining and activating a smartphone, not to mention the cost of apps that are not free of charge to download, may be a significant barrier on top of the premium prices paid for most branded diabetes drugs.[72]

So far, app developers have made strides in increasing the durability of benefits by utilizing "gamification" to encourage long-term behavior changes and adherence to diabetes management principles. An example is a patient engagement program, in which "points" can be earned for time spent in range for blood glucose measurements and redeemed for pharmacy rebates, HCP visits, or other benefits. This approach can also be used to encourage health outcomes;[77] examples exist within mySugr and Medtronic Inner Circle.[78,79] Additionally, United Healthcare launched its Motion program, offering up to $4 per day for beneficiaries who meet activity goals.[80] While gamification can certainly incentivize consumers to monitor their health better, it is not a one-size-fits-all solution. Such programs may have the drawback of leaving behind those who are in the most need of help, such as those experiencing socio-economic deprivation. Additionally, clear proof that gamification improves outcomes and results in long-term changes in health is missing.[81]

Another potential way to engage consumers, particularly those of older populations, is to involve Centers for Medicare & Medicaid Services (CMS) reimbursement. Reimbursement policies in the US could include, for example, sharing of health data in place of an office visit or sharing of CGM data.

7. *Appropriate role of health care professionals (HCPs)*

HCPs play an important role in advancing the use of diabetes mobile health apps. While a mobile health app cannot (and should not) replace a HCP, mobile health apps can certainly supplement and bolster medical practice.

As previously discussed, HCPs need to be supported to stay up-to-date on the diabetes digital app landscape. The ability to communicate regularly with people with diabetes and monitor their glycemic data gives health care professionals an unprecedented opportunity to monitor and improve quality of care and health outcomes (see Recommendations below).

8. *Role of professional organizations*

Professional organizations like ADA and EASD play an important role in shaping the future of health care. In addition to the above-mentioned efforts of the WHO and IMDRF to classify digital health technology, issues remain that professional organizations need to address. We believe the American Medical Association, the International Diabetes Federation, and many others can make a greater positive impact on patient populations worldwide in collaboration with WHO and IMDRF (see Recommendations below).

9. *Data security and privacy*

Data security is a key aspect in a digital world, especially for medical data. Although diabetes apps primarily permit people with diabetes to monitor their own data and discuss their data with health professionals, safety regarding data security and privacy remains a risk and cybersecurity has to be ensured.

Users may believe that their health data stored in apps are private, but that is often not the case. A 2014 study of diabetes apps for Android smartphones demonstrated that diabetes apps routinely shared information with third parties.[82] Because of the potential adverse impact of sharing sensitive health data, app developers should implement and fully disclose their privacy policies to users. App developers should also allow users to have full control over what data they are willing to share with third parties. Such cybersecurity measures must be implemented to protect privacy and enhance data security so that people with diabetes have adequate privacy protection and are not judged or discriminated based on their blood glucose levels, adherence to their care, or just their diabetes diagnosis.

People with diabetes have a high need for secure information when viewing their glucose levels and insulin doses on wireless diabetes devices, such as blood glucose monitors, continuous glucose monitors, and insulin pumps. Medical devices are prone to security breaching attacks; for example, incidents have been reported when data from insulin pumps were accessed remotely and their function controlled without knowledge of the user. Although there have been

no publicly reported incidents of users being harmed from hacking attacks, such situations have the potential to be life-threatening.[83] Data stored in health data apps should be sufficiently encrypted to prevent serious and malicious attacks.

An example that the cybersecurity regulation of diabetes mobile health apps could follow is the Diabetes Technology Society's guidance on the "Standard for Wireless Diabetes Device Security (DTSec)." DTSec establishes a high level of assurance that electronic products deliver the security protections claimed by their developers and required by their users. A DTSec-certified product must pass evaluation by a DTSec-approved lab and the DTSec Working Group (DWG) before it can be listed under a publicly disclosed DTSec evaluated products list.[84]

## Conclusions and Outlook

Digital health technology, especially digital health apps, for people with or at risk for diabetes has developed at a rapid pace and become an increasingly common aspect of diabetes care and self-management in certain populations. However, several barriers remain that prevent digital health technology from reaching its full potential to improve diabetes therapies and the lives of people affected by diabetes.

Insufficient evidence (at least from a conventional way of looking at evidence) of clinical validity, effectiveness, accuracy, and safety are some of the largest issues that limit the effectiveness of diabetes digital health technology. Furthermore, poor usability due to technological issues, interoperability issues, and differences among populations is another barrier. This web of interconnected issues cannot be solved by one party alone; rather, commitment from regulators, industry, clinical experts, and funding and patient organizations is needed for the necessary clinical evidence to be gathered.

We outline a list of considerations for regulatory agencies, manufacturing companies, international and national professional societies, funding bodies, researchers, HCPs, and people with diabetes to take into careful consideration. These can be categorized into the following themes:

- More systematic and structured guidelines for digital health app development and assessment [1a-c, 3d-e],
- Improved consistency and accessibility of safety reports and app documentation [2a-b, 2d],

- Greater investment in gathering of clinical data to provide evidence on digital health interventions [4a-b, 5a-b],
- Increased accessibility for all consumer populations to use diabetes mobile apps confidentially and securely [2c, 2g, 3c], and
- Increased communication and cooperation across stakeholder groups [1d-g, 2e-f, 3a-b, 3f, 6a-c, 7a-c].

Today's world of products and services, including digital health apps, is moving towards a market of integration. Apps are converging towards a data-capturing and auto-analyzed future with algorithm-based recommendations for users affecting their behavior and decisions. We envision an ongoing role of EASD, ADA, and other professional medical associations in supporting and expanding the field of diabetes digital health technology in the march to integration and continued automation. We call upon regulatory agencies and manufacturing companies to work urgently and collaboratively with health professionals, researchers, and people with diabetes to create an environment in which diabetes can be managed safely and effectively, bringing benefits to all stakeholders and the entire diabetes community.

**Consensus Report Recommendations**

1. **Regulatory agencies should:**
    a. establish and update standards to be met by digital health technology developers at premarketing and postmarketing stages, such as elements of clinically validated information (not necessarily from RCTs), service systems to support users, effectiveness parameters to enhance outcomes, and functions to transmit data to other devices, while also supporting the innovation of the market
    b. provide a regulatory paradigm, such as that outlined by IMDRF, which is tailored specifically to software, taking the short product life cycle and rapid turnover of updates into account
    c. provide guidance for obtaining and promoting evidence of safety, effectiveness, and other performance measures
    d. find ways to evaluate digital health apps' security, accuracy, and reliability (e.g., by recognizing and following the DTSec model), including supporting companies (often small) to generate real world data when they have a product that has achieved a certain standard
    e. provide, publicize, and maintain a single publicly accessible international database of available digital health apps and their utility/quality, including harmonizing on the parameters that would measure utility/quality and how these parameters would be assessed[85]
    f. publish an annual summary of regulatory activities
    g. work to harmonize their activities
2. **Manufacturing companies should:**
    a. comply with regulations, industry standards, and best practices established for digital health app development and marketing, such as providing a regularly updated flow chart that describes the decision-making process for releasing app updates; a broader plan for software maintenance and testing; and plans for obsolescence in a specific mobile device model or operating system for which the app has been validated is ceased[16]

b. include sufficient documentation, training modules, and help-desk resources to ensure optimal use
c. provide interfaces that are user-friendly across all demographic groups and can be personalized with real-time insights and suggestions for individual users (taking their socioeconomic status into account, especially around health literacy)
d. report all safety-related data promptly and transparently to the regulatory authorities
e. cooperate with academic and health care professionals to provide balanced and adequate information for people with diabetes and package the output data in standardized formats for ease of access in electronic health records
f. enable users to opt to submit their data anonymously to track outcomes and demographics following a crowd-sourcing model
g. incorporate high degrees of data security and patient confidentiality (e.g., by adhering to the DTSec model)

**3. International and national professional societies should:**

a. bring people with diabetes, health care professionals, manufacturing companies, and regulatory authorities together to facilitate digital health technology interventions
b. encourage academia and medical associations to advance research in digital health app effectiveness, safety, and outcomes
c. help set expectations for HCPs and consumers of the strengths and limitations of digital technology
d. provide evidence-based guidelines on the effectiveness of digital health interventions
e. recommend appropriate forms of structured education required for HCP to support people with diabetes to benefit from the best digital health (HCPs cannot be trained in the use of each app; however, they can be supported in maintaining a basic understanding of what apps can do and how they are used)

f. maintain a list of endorsed apps that have passed a threshold of accuracy, dependability, and ease of use for both people with diabetes and HCPs

4. **International and national research funding bodies should:**
    a. provide or facilitate funding for well-designed independent clinical evidence that measure safety, effectiveness, outcomes, and use in real-world settings
    b. provide or facilitate significant financial support for long-term data collection
5. **Researchers/academics should:**
    a. openly report and share the patient-level results of all clinical evidence
    b. develop and validate specific and appropriate patient-related outcome measures
6. **Health care professionals should:**
    a. be knowledgeable of digital health apps and their strengths and weaknesses
    b. support and inform people with diabetes on the use of digital health apps to augment diabetes management and lifestyle modification
    c. utilize health data to improve quality of care and health outcomes
7. **Consumers of digital health apps–people with diabetes, family members, caregivers–should:**
    a. consider digital health apps as a valuable addition or supplement to disease management or prevention
    b. discuss with their health care professionals available and appropriate digital health app options, as well as advice or counseling received from the app that affects behavior or care decisions
    c. submit app reviews, which would include information on digital health app efficacy, success, errors, and malfunctions, as well as report apps that appear to be unsafe or illegally marketed, to the manufacturers and appropriate regulatory agencies and care organizations (e.g., ADA)

734 **References**


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