



### INTRODUCTION

- Availability of digital technology helps to empower persons with type 2 diabetes mellitus (T2DM) in their efforts toward self-management and better glycemic control
- Digital technology allows for access to near-real-time patient data and presents an opportunity for care teams to deliver timely, tailored support with or without in-person contact.<sup>1,2</sup>
  - However, patients need more than theoretical knowledge about healthy eating, exercise, and self-management of blood glucose.<sup>3</sup>
  - Patients also need assistance and coaching for building awareness of their daily health-related behaviors.
  - This awareness building and engagement with pro-health behaviors seeds the implementation of a pro-health style.

### OBJECTIVE

This review aimed to evaluate the efficacy of digital interventions in reducing HbA1c in T2DM. Digital intervention in this context is understood as including, at the minimum, a blood glucose measuring device and a coaching component. Coaching is defined as direct interaction between the patient and a healthcare professional with the intention to provide advice, encouragement, and/or health information.

### METHODS

- A systematic literature review was conducted according to Cochrane guidelines, by searching MEDLINE®, Embase®, and the Cochrane Controlled Register of Trials (CENTRAL) from database inception to April 5, 2022
- Grey literature sources included:
  - Abstracts from relevant conferences held between 2018-2022 (via Embase or from hand searching)
  - United States clinical trials registry
  - Select company websites (e.g., Livongo, Vida, Omada, Dario, Onduo, OneDrop, WellDoc, Virta, and Lark).
- After exclusion of duplicates, two investigators reviewed all abstracts and proceedings identified through the searches and applied PICOS criteria to assess eligibility
  - Patients were adults (>18 years of age) with T2DM
  - Interventions were integrated solutions containing both human and digital components:
    - Digital component, including but not limited to patient data capture devices: Glucose meter (required), blood pressure cuff, digital scale, biofeedback sensors
    - Human component: Remote, or hybrid remote/in-person, coaching by healthcare professional
  - Comparators could be usual care or no intervention
  - Outcomes were assessed during full-text screening, and included HbA1c estimates, engagement rates (e.g., user engagement, retention, withdrawal), and safety (if any)
  - Study designs were randomized controlled trials, quasi-randomized trials with control group, observational studies using matching techniques, and observational studies with a control group

### RESULTS

#### Study selection

- In total, 6,288 records were identified from the SLR including 6,275 records via Embase®, MEDLINE®, and CENTRAL, and 13 additional records through conference proceedings and company websites
- After removal of duplicates and ineligible studies, 124 full-text articles were kept for full-text screening, of which a total of 28 studies<sup>4-31</sup> were included in the end

#### Study characteristics

- The studies were published between 2003-2021
- Distribution of the study types: 23 randomized controlled trials (RCTs), 2 comparative non-RCT, 1 cross-sectional, 1 prospective cohort, 1 observational cohort
- Studies were conducted in 9 different countries, but mostly in the United States (n=12 studies), followed by South Korea (n=6), United Kingdom (n=3), China (n=2), and one each in Belgium, Canada, France, India, and Malaysia
- Study populations ranged from 17 to 772 patients with mean of 202 and median of 143 patients
- Study follow-up ranged from 1 month to 24 months with mean of 7.9 months and median of 6 months

#### Patient characteristics

- All studies (n=28 studies) targeted adults with T2DM, but some studies used additional constraints on patient inclusion (Figure 1)
- Mean age of patients at enrollment ranged from 47.3 years of age to 64 years (mean = 55.8)
- Mean % of female participants ranged from 29% to 100% (mean = 51%)
- Ethnicities/races included: Korean, White, Chinese, and Black American
- All 28 studies reported mean HbA1c levels at baseline with minimum of 6.8%, maximum of 10.9% and median of 8.5% (Figure 2)
- 23 studies reported on using standard blood laboratory assays for HbA1c estimates. One study used Appraise Home HbA1C Kit. Four studies did not report this information.

Figure 1: Sub-populations of T2DM patients enrolled across included studies (n=28 studies)

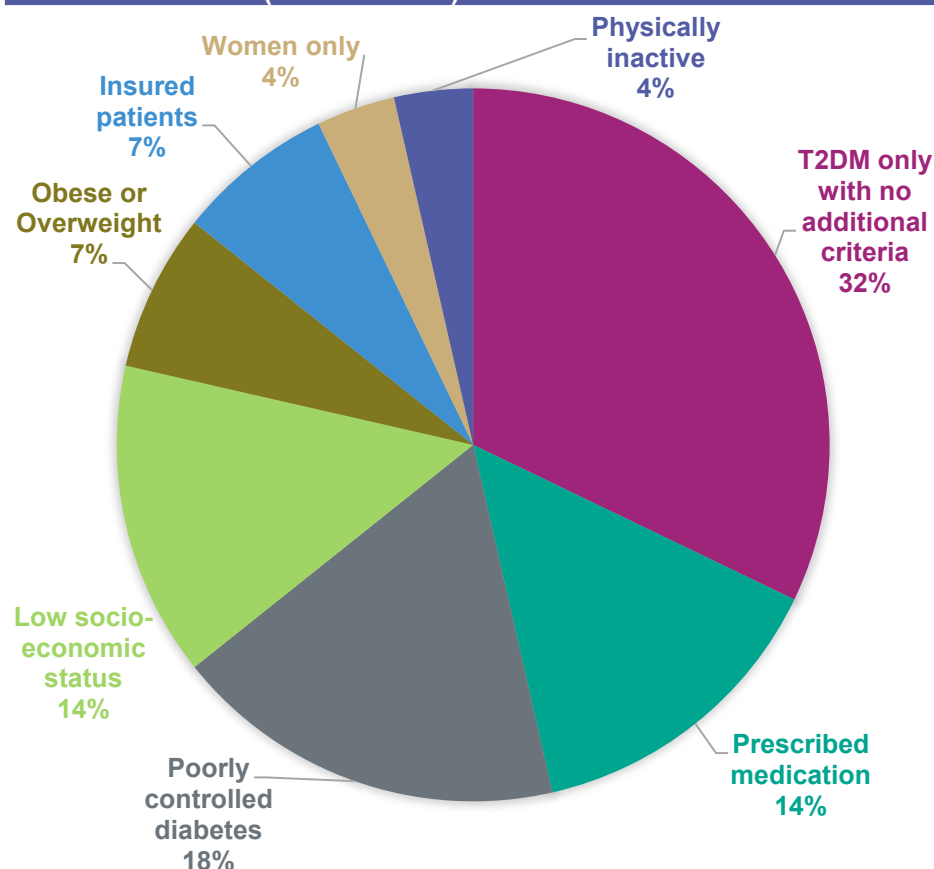
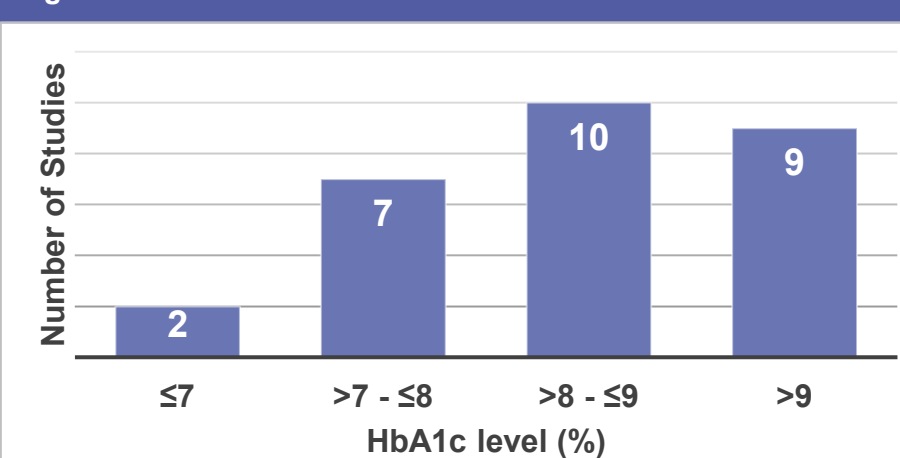


Figure 2: Mean baseline HbA1c levels



#### Intervention characteristics

- The two main components present in all interventions were the technology (devices and software) and the human component (coaching)
- The technology component included a device for measuring blood glucose:
  - Self-monitoring glucose meter (SMBG) in 20 studies
  - Continuous glucose meter (CGM) in 6 studies
  - Both CGM and SMBG in 1 study (two intervention groups)
  - One study measuring glucose levels in clinic
- The coaching sessions varied significantly in terms of their frequency (how often the health care practitioners communicated with the patient), duration (both duration of the individual sessions and overall duration of coaching), mode of communication (in-person, video conferencing, phone calls, texting/short message system), and the content (personalized vs. generic).
- We grouped the interventions into three broad categories by considering the quality and intensity of the coaching component (n=number of studies, proportion out of all included studies):
  - **High intensity (n=8, 29%):** Patient data automatically uploaded to the cloud in regular intervals. The coaching includes personalized motivational and goal-setting components based the most recent data and delivered by dedicated staff. The communication can be either in-person or remote, however the communication happens regularly, at least once a week. Education includes specific modules explaining the disease, behavioral strategies, and psychological coping.
  - **Medium intensity (n=16, 57%):** Patient data are manually uploaded. Coaching includes personalized advice based on patient data but not a behavioral advice in terms of motivational and goal-setting component. The communication is ad-hoc, initiated by the health care practitioners. Education includes general information about the disease and technical information about the use of the device(s).
  - **Low intensity (4, 14%):** Limited data sharing. Generic feedback using pre-existing templates. The communication is asynchronous or delayed (e-mail or follow-up phone call). Limited or no education.

#### Primary outcomes (HbA1c)

- Most studies aimed the interventions at improving glycemic control using HbA1c levels as primary endpoint either directly or as a part of a multi-component outcome (Table 1)
- When separated into the three intervention categories, success of the intervention was proportional to the intensity of coaching:
  - **High intensity:** 7/8 (87.5%) of studies had significant results
  - **Medium intensity:** 12/16 (75%) of studies had significant results
  - **Low intensity:** 2/4 (50%) of studies had significant results

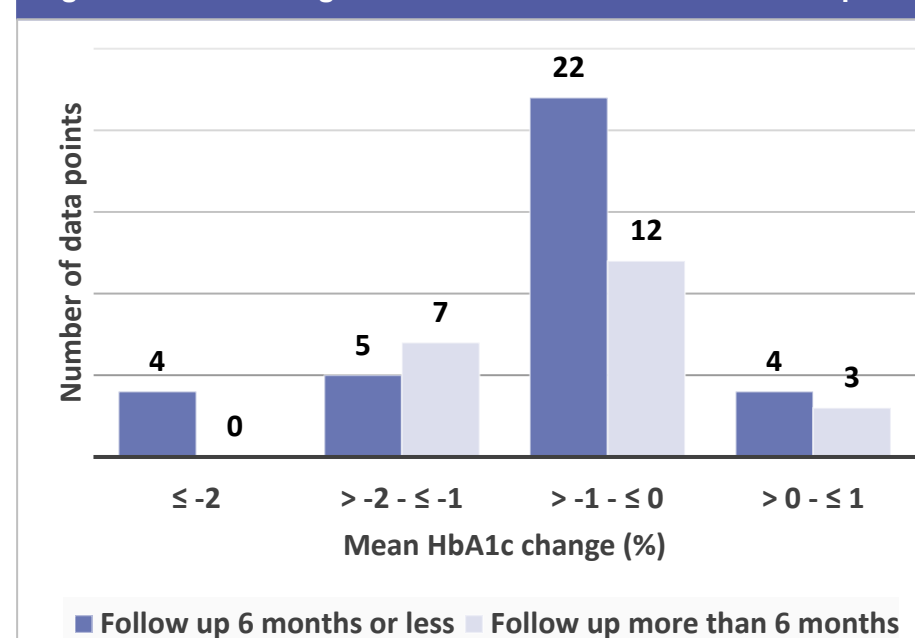
Table 1: Study endpoints and reported significant results

Reported primary endpoint	Number of studies	Number of significant results
Change in only HbA1c	19	14
Multiple endpoints including HbA1c*	4	4
HOMA2-IR**	1	1
Physical activity	1	0
Feasibility, acceptability, self-efficacy	3	2
<b>Total</b>	<b>28</b>	<b>21</b>

\* Multiple primary endpoints: HbA1c, glycemic control (HOMA2-IR, glycemic variability, fasting blood glucose, postprandial two-hour blood glucose, glycosylated hemoglobin), medication use, BMI, weight control, retention rate  
\*\* HOMA2-IR: Homeostatic Model Assessment of Insulin Resistance

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  - **Low intensity:** 2/4 (50%) of studies had significant results
- 16 out of the 28 included studies reported the numerical values of mean HbA1c change at follow-up (rest of the studies reported absolute values of HbA1c at the beginning and at the follow up)
  - The results have been split into two categories: HbA1c change for follow up durations less or equal to 6 months and HbA1c change for follow-up longer than 6 months (Figure 3)

Figure 3: Mean change in HbA1c ≤6 or >6 months follow-up



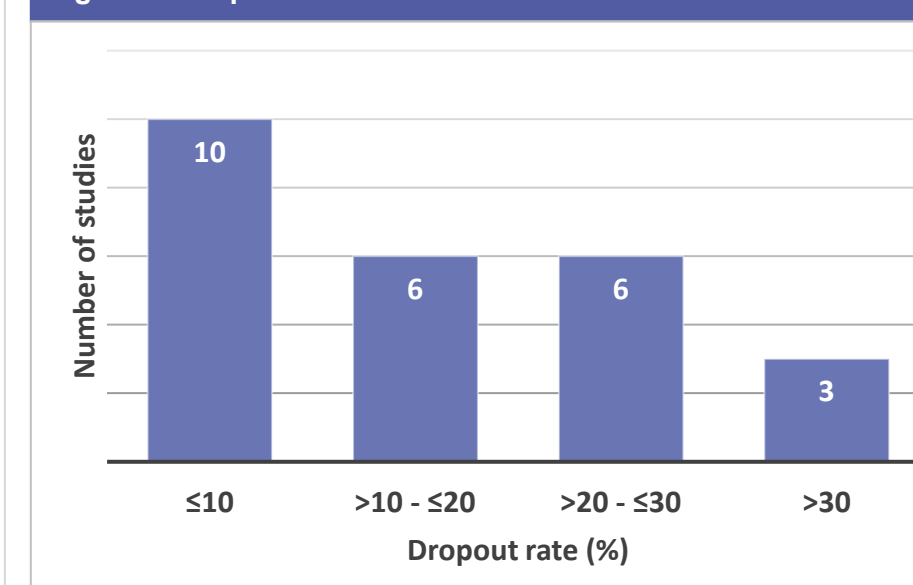
#### Patient engagement

- Patient engagement was reported in three different ways
  - Dropout rates (Figure 4) (reasons for dropouts were typically not reported)
  - Dedicated endpoint in clinical trials
  - Diabetes Treatment Satisfaction Questionnaire (DTSQ)
- Two out of the three studies investigating patient engagement as the primary endpoint found significant improvement in patient engagement with targeted interventions.
- DTSQ questionnaires showed improved scores in the intervention groups

#### Adverse events

- 11 of the 28 included studies reported on adverse events (AEs), with 7 of these studies reporting no intervention-related AEs
- Reported AEs seem unrelated to each other with no underlying pattern
- Authors themselves do not claim any relationship to the interventions

Figure 4: Dropout rates in the included studies\*



\* Dropout rate was defined as the % of patients lost to follow-up

### CONCLUSIONS

- **Most included studies reported success in reducing the HbA1c levels with digital interventions**
- However, the heterogeneous nature of the digital interventions targeting T2DM patients makes it difficult to identify relevant underlying patterns in the results
- When divided into three categories, the relative efficacy of the intervention was proportional to the intensity level of coaching component, i.e., higher intensity coaching resulted in a greater likelihood of better outcomes
  - The availability of health data provided by the technology is necessary but not sufficient for improved diabetes management
  - Coaching helps patients with interpretation of the data, with setting realistic goals, and with following-up on these goals
  - The more personalized and on-time coaching is the greater likelihood for better overall outcomes
- Overall adherence to the digital intervention, as measured by a variety of outcomes, was good, but it diminished over time. The satisfaction surveys show good results with the levels of satisfaction increasing as the patients experience the benefits of the interventions
- Only 11 studies reported adverse events, none of which established a link to the digital interventions. Adverse events in digital intervention studies are poorly reported.

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#### DISCLOSURES

Felix Lee, Edward Han-Burgess, and Adele Kennedy report employment and may hold stocks/shares in Sanofi. Boris Breznen and Mir-Masoud Pourrahmat report contract and employment, respectively, by Evidinno Outcomes Research Inc.

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