HbA1c Reduction with Digital Health Devices in Type 2 Diabetes: A Meta-Analysis of Randomized Controlled Trials

Felix Lee¹, Edward Han-Burgess², Adee Kennedy¹, Paul Serafini³, Mir-Masoud Pourrahmat¹, Boris Breznen³

¹Sanofi, General Medicines, Bridgewater, NJ, United States of America, ²Sanofi, General Medicines, Cambridge, MA, United States of America, ³Evidience Outcomes Research Inc., Evidence Synthesis, Vancouver, BC, Canada

INTRODUCTION

• Type 2 diabetes mellitus (T2DM) is a metabolic disorder characterized by chronic hyperglycemia due to impaired insulin secretion and action.
• As of 2021, 537 million adults are living with diabetes, and this number is expected to increase to 799 million by 2050.
• Many patients struggle to achieve glycemic control, putting them at risk for complications such as cardiovascular disease, nephropathy, retinopathy, and neuropathy.
• Glucose monitoring devices, such as self-measured blood glucose (SMBG) and continuous glucose monitoring (CGM), can help patients to achieve and maintain optimal control.
• In addition, evidence shows that patients need assistance and control, e.g., low blood glucose levels and awareness of adverse events.

OBJECTIVE

To compare the efficacy of digital T2DM interventions, defined as SMBG or CGM combined with an coaching component, in reducing HbA1c compared to usual care.

METHODS

Systematic Literature Review

A systematic review was conducted using standard methodologies from Cochrane. Details have been previously described, briefly:

1. MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials (CENTRAL) were searched from database inception to April 30, 2022. Searches were limited to the English language.
2. Relevant articles were considered for inclusion if they met the predefined eligibility criteria and if they demonstrated the effects of digital intervention on glycemic control in patients with T2DM at any stage of their disease.

Meta-Analysis

Randomized controlled trials (RCTs) were eligible for the meta-analysis (MA).

• If a study had more than one control or intervention arm, then the arm with the largest sample size was selected for the meta-analysis (MA).
• If a study treated participants for more than one year, then the results from the last timepoint were used.

Included articles were observational and clinical trials on adults (>18 years) old with T2DM who received a digital intervention (including both human coaching and digital glucose monitoring components) or usual care.

The primary outcome of interest was change in HbA1c.

RESULTS

Study Selection

• Of 5,389 records screened, 23 RCTs were included for the MA. (See Figure 1 for the PRISMA diagram and Table 1 for list of included studies).

Analysis

Across the included studies, the median age was 52.6 years (range: 22.6 to 71.6 years) and the median proportion of female participants was 67.0% (52.8% to 72.6%). At baseline, the median A1c was 7.4% (7.0% to 7.9%) and the median BMI was 31.0 kg/m² (24.0 to 40.0 kg/m²). The mean HbA1c was 6.2% (6.0% to 6.5%) at week 26.

• Three studies did not measure HbA1c in a lab, and so were excluded from the primary analysis but included in a sensitivity analysis. Gun (2001), Primson-Neto (2011), and Welch (2015) were included in the analysis.

• Two studies used CGM and were excluded in a sensitivity analysis: Allen (2011) and Lee (2019).

• Four studies were judged high risk of bias and were excluded in a sensitivity analysis: Allen (2011), Way (2015), and Sung (2007) because they did not employ double blinding (DB) and Ji (2018) and Jeong (2019) because it did not adequately report how HbA1c was collected.

Meta-Analysis

Primary Analysis

• The primary analysis estimated -0.31% (95% confidence interval [-0.45, -0.16], p < 0.001) lower A1c for those receiving an intervention compared to usual care (Figure 2; Table 1).

• A meta-regression analysis was conducted with A1c change as a categorical covariate, the following meta-regression equation was estimated:

  MD = b0 + b1(Intensity=low) + b2(Intensity=medium) + b3(Intensity=high)

  Where MD is the predicted mean difference (MD) of change in HbA1c, “Intensity=low” is the reference category, “Intensity=medium” is the intervention group in which the digital intervention was implemented in medium intensity and “Intensity=high” is the intervention group in which the digital intervention was implemented in high intensity.

  This predicts an MD of -0.43% (95% CI: -0.74, -0.12) of p < 0.001 for high intensity groups, MD = -0.32% (95% CI: -0.63, -0.01) of p = 0.030 for medium intensity and MD = 0.00% (95% CI: -0.30, 0.30) for low intensity.

  The beta (p < 0.04) and medium (p = 0.02) intensity coefficients were statistically significant.

  Heterogeneity was statistically significant (Q = 43.63; df = 19; p = 0.000305), with an estimated I² of 73.59% (95% CI: 51.7, 79.4) and F of 5.78 (95% CI: 4.32, 9.48).

Inclusion of Additional Studies

Two additional studies were not included in the meta-analysis due to limited baseline data.

Figure 1: PRISMA Diagram

RESULTS (Continued)

Sensitivity Analyses

• When included with all lab-measured HbA1c included, the final model was: MD = -0.37% (95% CI: -0.65, -0.09, p < 0.05). This model was more favorable to the digital intervention (MD: -0.40%, 95% CI: -0.56, -0.24, p = 0.42, 95% CI: -0.56, -0.24, p = 0.42).

• When CGM studies (MD: -0.31%, 95% CI: -0.47, -0.16, p = 0.16) and studies with high risk of bias were excluded (MD: -0.31%, 95% CI: -0.46, -0.15, p = 0.04), the point estimate was the same as the primary analysis, but the CI was wider.

CONCLUSIONS

This meta-analysis found significantly greater HbA1c reduction in T2DM patients on digital interventions compared to usual care. Studies with non-coachable measures of HbA1c Were included in a more favorable result for the digital intervention – Excluding CGM studies or those with high risk of bias led to similar results as compared with the primary analysis. This association between digital intervention intensity and HbA1c reduction was not statistically significant and further research is warranted to understand optimal intensity for digital interventions.

REFERENCES

• Pimazoni et al., Diabet Med. 2021. (in press)

DISCLOSURES

• The study was funded by Sanofi. Medical writing and post-grant preparation support was provided by St. John’s Healthcare, Evidence Outcomes Research Inc., and Health Economics Research, Sanofi.

FUNDING

This study was sponsored by Sanofi. Medical writing and post-grant preparation support was provided by St. John’s Healthcare, Evidence Outcomes Research Inc., and Health Economics Research, Sanofi.