Continuous Glucose Monitoring and Other Wearable Devices to Assess Hypoglycemia among Older Adult Outpatients with Diabetes Mellitus

Michael Weiner[1,2,3] Philip Adeoye[4] Margaret J. Boeh[5] Kunal Bodke[4] Jessica Broughton[5] Anietra R. Butler[4] Mackenzie L. Dafferner[4] Lindsay A. Dirlam[6] Denisha Ferguson[4] Amanda L. Keegan[4] NiCole R. Keith[4,7] Joy L. Lee[1,2] Corrina B. McCorkle[4] Daniel G. Pino[1,6] Mu Shan[8] Preethi Srinivas[4] Qing Tang[8] Evgenia Teal[9] Wanzhu Tu[4,8] April Savoy[2,3,10] Christopher M. Callahan[1,4,5] Daniel O. Clark[1,4]

[1] Department of Medicine, Indiana University, Indianapolis, Indiana
[2] Center for Health Services Research, Regenstrief Institute, Inc., Indianapolis, Indiana
[3] Center for Health Information and Communication, Department of Veterans Affairs, Veterans Health Administration, Health Services Research and Development Service CIN 13–416, Richard L. Roudebush VA Medical Center, Indianapolis, Indiana
[4] Center for Aging Research, Regenstrief Institute, Inc., Indianapolis, Indiana
[5] Senior Care, Eskenazi Health, Indianapolis, Indiana
[6] Lifestyle Health and Wellness, Eskenazi Health, Indianapolis, Indiana

Address for correspondence Michael Weiner, MD, MPH, Regenstrief Institute, Inc., 1101 West 10th Street, Indianapolis, IN 46202, United States (e-mail: mw@cogit.net).

[7] Department of Kinesiology, Indiana University, Indianapolis, Indiana
[8] Department of Biostatistics and Health Data Science, Indiana University, Indianapolis, Indiana
[9] Data Services, Regenstrief Institute, Inc., Indianapolis, Indiana
[10] Computer and Information Technology, Purdue School of Engineering and Technology, Indiana University-Purdue University Indianapolis, Indiana

Appl Clin Inform 2023;14:37–44.

Abstract

Background Hypoglycemia (HG) causes symptoms that can be fatal, and confers risk of dementia. Wearable devices can improve measurement and feedback to patients and clinicians about HG events and risk.

Objectives The aim of the study is to determine whether vulnerable older adults could use wearables, and explore HG frequency over 2 weeks.

Methods First, 10 participants with diabetes mellitus piloted a continuous glucometer, physical activity monitor, electronic medication bottles, and smartphones facilitating prompts about medications, behaviors, and symptoms. They reviewed graphs of glucose values, and were asked about the monitoring experience. Next, a larger sample ($N = 70$) wore glucometers and activity monitors, and used the smartphone and bottles, for 2 weeks. Participants provided feedback about the devices. Descriptive statistics summarized demographics, baseline experiences, behaviors, and HG.

Results In the initial pilot, 10 patients aged 50 to 85 participated. Problems addressed included failure of the glucometer adhesive. Patients sought understanding of graphs, often requiring some assistance with interpretation. Among 70 patients in subsequent testing, 67% were African-American, 59% were women. Nearly one-fourth (23%) indicated that they never check their blood sugars. Previous HG was reported by 67%. In 2 weeks of monitoring, 73% had HG (glucose $\leq$70 mg/dL), and 42% had serious,

Keywords
- wearable devices
- hypoglycemia
- diabetes mellitus
- glycemic control

received
May 8, 2022
accepted after revision
October 25, 2022
accepted manuscript online
November 9, 2022

Georg Thieme Verlag KG,
Rüdigerstraße 14,
70469 Stuttgart, Germany

DOI https://doi.org/10.1055/a-1975-4136.
ISSN 1869-0327.

clinically significant HG (glucose under 54 mg/dL). Eight patients with HG also had HG by home-based blood glucometry. Nearly a third of daytime prompts were unanswered. In 24% of participants, continuous glucometers became detached.

Conclusion Continuous glucometry occurred for 2 weeks in an older vulnerable population, but devices posed wearability challenges. Most patients experienced HG, often serious in magnitude. This suggests important opportunities to improve wearability and decrease HG frequency among this population.

Background and Significance

Hypoglycemia (HG) in people with diabetes mellitus (DM) is common and can lead to clinical signs and symptoms including dizziness, tremors, confusion, anxiety, diaphoresis, neurological changes, altered mood,[1] fear of recurrence,[2] coma,[3] and death.[4] Lower quality of life has also been reported.[5,6] Although symptoms are common when HG occurs, many people with DM remain unaware of the occurrence of HG,[7] which occurs in 20 to 60% of patients who receive oral medications for DM.[5,8,9] Other risk factors include shorter-acting insulin,[10,11] skipping meals,[12] intensive treatment for DM,[13,14] large fluctuations in blood glucose,[15] alcohol use, diabetic neuropathy, and infection.[16] Many social and psychosocial factors are associated with glycemic control or other diabetes-relevant behaviors or outcomes, such as self-care, blood pressure, lipid control, and quality of life. These factors include social support, stress, self-efficacy, depression, and food insecurity.[17,18] Access to diabetes education programs and endocrinologists also varies substantially by geography in the United States.[19] Some age groups face special challenges: although a guideline for older adults (65 or more years of age) has "liberalized" A1c targets to have a maximum of 8% rather than 7%,[20] Lee et al demonstrated that an educational intervention in support of the guideline still led to more severe HG episodes requiring emergency visits during early implementation.[21]

Both DM and HG are linked with dementia, one of the longer-term risks from these conditions: DM is associated with a roughly two-fold greater risk of dementia,[22,23] and the frequency of HG episodes appears to be an independent risk factor for dementia.[24] For example, in a cohort of 16,667 older adults followed for 27 years, a dose–response relationship between number of episodes of HG and dementia was demonstrated. Those with three or more HG episodes had a nearly two-fold greater adjusted risk of developing dementia.[24] This seminal report has been followed by two other cohort studies in older adults that confirm that HG is a risk factor for dementia[25] or cognitive decline.[26]

Although risk factors such as nutritional intake, medication adherence, and physical activity are modifiable, they are usually self-reported, if reported at all, in the outpatient setting. Among most people with DM, the typical lack of real-time glucose data decreases the chance that HG will be promptly identified and addressed. Wearable devices provide an opportunity to improve resolution of measurement and feedback to patients and their primary care teams about how to lower HG risk, such as by adjusting medications in response to other parameters. The Endocrine Society has suggested that intermittent use of continuous glucose monitoring (CGM) systems designed for short-term retrospective analysis may benefit adult outpatients with DM, for both detection of abnormalities, and management of changes to DM treatment regimens.[27] A randomized trial of CGM alone in older adults with type 1 DM showed that participants using CGM experienced a decrease in HG, from a mean of 73 minutes per day to 39 minutes per day after 6 months.[28] Whether older adults with DM and social risk factors can wear and use monitoring devices successfully represents an important knowledge gap.

Objectives

In a pilot feasibility trial, we sought to determine how successfully a combination of wearable devices and CGM could be used by older adults with DM in an urban safety-net medical institution, to explore HG events over two weeks. This report focuses on glucometry.

Methods

Setting

The setting was Eskenazi Health, a tax-supported safety-net institution of Marion County in central Indiana. Headquartered on an academic medical campus, Eskenazi Health has a 315-bed hospital, an emergency department, and a community-based network of 30 outpatient or residential sites. In 2018, Eskenazi had 15,653 adult admissions and 962,191 outpatient visits (34% in primary care), handled by 4,571 health professionals including 1,073 physicians. The payor mix was 27% Medicaid, 19% Medicare, 15% commercial, and 15% health advantage or self-pay.

Participants

The study had two phases, numbered 0 and 1. Phase 0 was a developmental phase targeting 10 patients to use CGM and wearable devices. It led to revisions and refinements of the approach. Phase 1 then targeted 70 patients to pilot the revised approach. At least one visit to an Eskenazi Health or Indiana University Health primary care clinic within the preceding 12 months was required.

Using printed flyers, clinic contact, telephone calls, and mailed letters following approval of primary care providers, we recruited patients aged 50 or older with a diagnosis of DM

who had active prescriptions for DM. English language and access to a telephone were required. We excluded patients with terminal illness, current or planned institutional residence within 6 months, evidence of cognitive impairment, dependence on others for personal needs, dialysis, ascorbic acid supplements, implanted medical devices, a bleeding disorder, preexisting arm skin lesions interfering with CGM usage, allergy to medical adhesives or isopropyl alcohol, and plans for imaging or high-frequency electrical heat (diathermy) treatment during the study period. These criteria applied to both phases. Phase 1 participants were required to pass a 15-minute "exposure test" that aimed to determine whether they had at least minimal ability to use the medication bottles, wrist-worn accelerometer, and smartphone. Participants were offered gift cards to participate: $25 for the completion of a baseline assessment, a total of $50 for the 2-week data collection, up to $10 for smartphone responses, and $25 for completing follow-up questions after the 2-week monitoring.

Activities and Measurements

An Abbott FreeStyle Libre Pro CGM was applied to participants' posterior arm, according to the manufacturer's instructions. This CGM, obtained from Abbott Diabetes Care (Alameda, California, United States), is an FDA-approved device whose monitor has an adhesive pad and small subcutaneous tube, adhering to the skin on the back of the arm for up to 2 weeks in each phase. It records the interstitial glucose level every 15 minutes. HG was defined as a glucose value of 70 mg/dL or less. Participants were blinded to CGM values during the monitoring period.

Phase 0

A Google Pixel smartphone was issued, as well as a wrist-worn Xiaomi Mi or Actigraph wGT3X-BT activity monitor with accelerometer. To record medication-taking, electronic Aardex MEMS bottles were issued for oral DM medications; participants were prompted about insulin self-administration via smartphone prompts eight times per day. Via apps or text messaging, the smartphone also prompted patients to provide information about dietary intake, behaviors, feelings, and any specific symptoms, such as dizziness, confusion, or sweating, since the previous response. Following data collection, participants were presented with a standardized color graph of CGM output from Abbott's FreeStyle software, depicting their glucose values and trends, and were interviewed regarding their experiences and any challenges they faced with the study procedures. Results were used to inform any adjustments needed for phase 1.

Phase 1

The Actigraph wGT3X-BT activity monitor was used. As in phase 0, the Google Pixel smartphone, MEMS bottles, and Abbott FreeStyle Libre Pro CGM were also used. For patients without a standard blood glucose meter, the Abbott Freestyle Freedom Lite blood glucose meter was provided, for recording and reporting of blood glucose. As in phase 0, participants were presented with a graph of their glucose values, and were interviewed regarding experiences and any challenges.

Data Management and Analysis

Measured data were compiled and analyzed, along with data about the patient's demographics, as reflected in the medical record. Descriptive statistics were used to summarize measurements. Denominators in individual questionnaire responses excluded cases with missing data. Research Electronic Data Capture (REDCap)[29,30] was used to manage data and study administration. We describe our experience with the monitoring devices, but the analysis focused on the use of continuous glucometry.

Results

Phase 0

We recruited 10 patients (seven African American, three White, six women, aged 50 to 85 years) to pilot the monitoring devices for 10 to 14 days. The CGM device exhibited a known problem with adhesive in adhesive-based continuous glucometers: the glucometers are sometimes dislodged from the skin prematurely, before the end of a full-monitoring period. Various "third-party" manufacturers have created reinforcing adhesive patches to address this issue. We tried these, as well as standard cloth medical tape to secure the CGM device, without much improvement in the function of adhesion. As a result, we changed our approach to use a simple nonprescription tubular elastic netting, obtained at CVS pharmacy and placed on the arm, covering the continuous glucometer. The netting's mesh grid is wide and nonobstructive. Skin-Tac, a tacky adhesive layer, was also applied to the skin before the continuous glucometer was placed.

As we showed participants the graphs of their glucose values, we found that they sought understanding of the graphs, and frequently considered links between the results and their earlier activities, as well as what changes they could make to their activities to improve their glucose values. Several participants did appear to have difficulty interpreting the graphs without instruction, but performance improved when a brief explanation was provided. The findings prompted the study team to pursue the use of both graphical and text-based summaries of glucose values for participants. Feedback from the participants as well as discussions with clinicians about priorities of recommendations led to the design of the reporting form.

Phase 1

Characteristics of participants who completed phase 1 ($N = 70$), whose age ranged from 50 to 85 years, are shown in ►Table 1. About two-thirds were Black or African-American. More than two-thirds had a hospital admission in the preceding 30 to 365 days. At baseline, nearly a quarter reported never checking their blood glucose, and about half reported having no daily routine for meals. Many (19%) had never used the Internet, but almost all (97%) had used a mobile phone at least twice in the previous week.

Table 1 Characteristics of participants in phase 1 ($N = 70$)

Characteristic	Value
Demographics	
Age, mean (SD) (years)	60 (7.4)
Gender, female (%)	59
Race (%)	
Black or African American	67
White	31
Other	1.4
Highest education level (%)	
Less than high school	5.7
High school	50
College	40
Graduate school	4.3
Medicaid (%)	16
Clinical features	
Body mass index, mean (SD) (kg/m^2)	36.2 (8.3)
Estimated glomerular filtration rate, mean (SD) (mL/min)	89 (32)
Medical conditions according to the medical record (%)	
Alcohol	4.3
Autonomic failure	24
Cancer	21
Coronary artery disease	7.1
Heart failure	13
Diabetic neuropathy	16
Hypoglycemia in preceding 12 mo	23
Infection in preceding 30 d	43
Hospital admission in preceding 30–365 d (%)	69
Medications for diabetes mellitus (%)	
Insulin	
Long acting	60
Other insulin	21
Sulfonylurea	36
Last A1c (%)	
≤6.5	27
>6.5, <7	7.1
≥7, <8	24
≥8, <9	14
≥9	27
Survey questions	
Do you ever check your blood glucose (yes, %)	77
Have you ever had a low blood glucose level (yes, %)	67
Do you have a daily routine for meals (yes, %)	49
Have you ever used the Internet (yes, %)	81
Do you have Internet service at home (yes, %)	79
Used a mobile phone more than once in the past week (%)	97
Worry or fear about low blood glucose (%)	
Baseline: "In the past month, has this been a problem?"	
Not at all	47
Very little	16
Some	30
A lot	7.1
After the monitoring period: "How has it changed in the past 2 weeks?"	
Worse	1.4
Same	79
Better	20

Worry or fear about low blood glucose in the past month was reported as "some" or "a lot" by 37%.

CGM indicated that HG occurred at least once in 51 (73%) of the participants within the 2-week monitoring period; 42% had serious, clinically significant HG (at least one glucose value less than 54 mg/dL). Eight patients with HG also had HG by standard home-based blood glucometry. After the monitoring period, worry or fear about low blood glucose was worse in 1.4%, unchanged in 79%, and better in 20%.

Unintended CGM sensor removals, such as a sensor falling off or being accidentally removed, occurred in 24% of participants; a new sensor was applied in such cases. One of the CGM sensors could not be activated and was deemed defective, so a new one was applied. One participant failed to complete phase 1, because the sensor fell off at the end of the monitoring period and could not be located. Sensor removals including the following observations: a visible ring or erythema marking the adhesive area ($N = 10$), presence of a small blood droplet ($N = 1$), and a small ecchymosis ($N = 1$).

Nearly a third of daytime smartphone prompts were unanswered. Upon visiting several homes to apply a CGM sensor, we found that many participants were not carrying the smartphones as instructed, and in some cases, others in the home were using the phones.

Discussion

Although CGM has been used in the study and clinical management of type 1 DM,[27,28,31,32] with improvements in A1c,[33,34] its periodic usage could be valuable in type 2 DM as well.[35] This pilot of CGM and wearable devices to monitor events relating to HG demonstrated feasibility of monitoring, engagement of older adults in a safety-net institution, and

potential for CGM. During the short monitoring period, the markedly high incidence of HG—73% of participants—and clinically significant HG values less than 54 mg/dL, indicate the likelihood that standard blood glucometry through self-monitoring misses many or most HG events, and indicates the urgency of more effective approaches to detecting, preventing, and managing HG. Complementing published reports about the benefits of CGM, this pilot demonstrated the limitations of "wearability" of CGM and other wearable devices among vulnerable older adults, and the need for improvements.

An intervention based on our findings could represent a step toward enabling patients and their health care professionals to see, share, and discuss the same information. Ratna et al demonstrated the value of using this CGM product as an educational tool in sharing data with the patient.[35] Additional strategies such as coordination with primary care clinicians and family members may be important for long-term success. Saleem et al have advocated for considering expanded uses of wearable devices, along with greater attention to incorporating the data into workflows and the electronic health record.[36] Karway et al noted heterogeneity in barriers to self-management, identifying a need for tailored targeting of treatment barriers in DM.[37,38] At a larger level, population-based dashboards might improve outcomes for communities. Unblinding the CGM readings, and enabling frequent real-time feedback of results, could lead to earlier detection of HG, and would enable patients to respond to glucose values more quickly. Some newer CGM devices do include Bluetooth connectivity for monitoring via smartphones. Richer educational strategies—perhaps incorporating CGM education into diabetes educational programs—and testing of patients' responses to events in simulated environments may also hold promise.[39] HG awareness training has been shown to help.[40] The use of secure messaging,[41] personalized goals and decision support,[42,43] web-based applications for sharing results,[44] and social networks[45] to inform and educate patients about managing DM may also be useful. Quinn et al found that the use of mobile telephones to provide educational and behavioral messaging in response to blood glucose values, medications, and behaviors decreased A1c without an apparent increase in HG,[46] but the intervention required manual data entry, a process that is probably not sustainable in practical terms. Easier and more automated approaches to detecting HG and managing and communicating DM data are needed. In addition, interventions to decrease coprescription of insulin with sulfonylureas or thiazolidinediones, and to assist with broader issues of polypharmacy, may be beneficial.

Although our package of devices enabled the generation and use of a large volume of data relating to DM and HG, we found the overall wearability of the devices to be rather poor and in need of improvement. The diverse array of commercial adhesive products marketed for CGM devices signals the need for a more durable product, in terms of physical application to the body. At the same time, the devices are sometimes uncomfortable to wear, and often lead to skin irritation or inflammation. The lack of requirement for a finger-stick calibration of the Abbott CGM device is a benefit. Since smartphones, which often require daily electrical charging, are not always carried, and measuring dietary intake with reliability and validity has proven elusive with many other approaches used by others, innovations in assessing diet are needed. Although smartphone cameras have been used to photograph and analyze meals for caloric intake, the process requires manual activation, and accuracy of automated analysis varies.[47] Even physical "bite counters" have been found to generate both false-negative and false-positive results.[48] The physical activity monitors that we tested were either too limited or too bulky for continuous usage over long periods. Smartwatches offer potential for improved convenience, wearability, and usability, but require a great deal of further study.[49] Body vests have been investigated and might actually address certain barriers, especially in disabled patients.[50] Currently, however, a collection of more usable devices is needed to enhance success in detecting, preventing, and treating HG.

Because CGM measures interstitial glucose, its underestimation of blood glucose is a known limitation.[51] Thus, in examining HG, false-positive events may be especially likely. Alitta et al found that, among 144 CGM values less than 70 mg/dL, 51% were associated with blood glucose values of 70 mg/dL or greater.[52] Gehlaut et al found that, among 108 patients with type 2 DM studied with CGM for 5 days, 49% had HG events, and 49% of these hypoglycemic patients experienced severe HG,[53] unlikely to be normoglycemic events masquerading as false positives. In our study, HG by CGM was uniformly confirmed when self-monitored blood glucose was measured. We maintain that, even considering CGM's modest margin of error, low CGM values warrant confirmation and investigation, since many of them represent clinically important HG. Newer real-time CGM may also provide a faster diagnosis with greater convenience. Tradeoffs of pricing, usability, accessibility of devices and data, and other factors will be important as patients and clinicians share decision-making about how to monitor.

Limitations

The study had limitations. The poor adhesiveness of CGM devices led to occasional interruptions in data collection. A small number of options were considered for monitoring dietary intake and physical activity. The monitoring period was short. Results might not reflect populations with substantially different demographics, geography, comorbidities, access to medical care, employment, or other characteristics. The analysis did not specifically summarize "time in range" for glucose. Although the study did not aim to separate type 1 from type 2 diabetes, most older adults with diabetes have type 2.

Conclusion

In summary, continuous measurement of glucose, physical activity, and food intake was achieved for up to 2 weeks in an

older vulnerable population with diabetes, but the wearable devices posed challenges relating to wearability, learnability, and usability. Most patients had documented HG within the short study period, and more than a third had serious, clinically important HG. We identified opportunities to decrease the frequency of HG, including shared monitoring results, tailored recommendations, and automated prompts based on triggers from continuous monitoring, but successful prompting will require more attention to engineering the workflow of activity to promote adherence and ease of reporting. Approaches to obviate the need for prompting would decrease the reporting burden for participants. Including the primary care team in the process may also be an important addition. Short of more robust and easier methods to capture data about physical activity, medication adherence, and dietary intake, a larger trial of CGM-based shared decision-making in primary care is a logical next step.

Clinical Relevance Statement

This study examines approaches to improving glycemic control and lowering the risk of hypoglycemia in older patients with diabetes mellitus. Older adults can use wearable devices but may benefit from better wearability of the devices. Integrating clinicians into workflow, assessment, and feedback appears important.

Multiple Choice Questions

During 2 weeks of monitoring vulnerable older adults with diabetes, what percentage developed HG as recorded via continuous glucometry?

a. 18%
b. 24%
c. 48%
d. 73%

Correct Answer: The correct option is d. HG is common, especially considering the multitude of risk factors and potential for unawareness of HG. Short-acting insulin, intensive treatment for diabetes, and skipping meals are three of the risk factors for HG, which occurs in 20 to 60% of patients who receive oral medications for DM.

What is an advantage of continuous glucometry over standard blood glucometry?

a. Continuous glucometry eliminates the need for insulin.
b. Continuous glucometry provides more timely measurement and feedback.
c. Per day, continuous glucometry is less costly than blood glucometry.
d. Continuous glucometry is more accurate.

Correct Answer: The correct answer is b. Although blood glucometry can be done on demand, continuous glucometry measures glucose every few minutes. Today's systems can also provide users with an immediate understanding of the glucose levels. Although accuracy does not fully match that of blood glucometry, it is generally close.

Note

Aspects of this work were presented at Improving Primary Care through Industrial and Systems Engineering (i-PrACTISE), Boston, MA, June 3, 2019; and The Scottsdale Institute, February 27, 2020.

M.W. is Chief of Health Services Research and Development at the Richard L. Roudebush Veterans Affairs Medical Center in Indianapolis, Indiana. The views expressed in this article are those of the authors and do not necessarily represent the views of the Department of Veterans Affairs.

Funding

This study was supported by the Agency for Healthcare Research and Quality (grant no.: P30HS024384).

Conflict of Interest

M.W. reports stock ownership in AbbVie Inc., Amgen Inc., Boston Scientific Corporation, Bristol-Myers Squibb Company, IBM, Integer Hldgs Corp Com, Johnson & Johnson, Mallinckrodt PLC, Mead Johnson & Company, LLC, Medtronic, Mylan N.V., Novo Nordisk A/S, Perspecta Inc Com, Pfizer Inc., Roche Pharmaceuticals, Senseonics, Stryker Corp., Teva Pharmaceutical Industries Ltd., and Walgreens Boots Alliance, Inc.

Protection of Human Subjects

The study was performed in compliance with the World Medical Association Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects, and was reviewed by the Indiana University Institutional Review Board. All participants consented to the study, which was approved by the institutional review board of the university, with which the health system is affiliated. Declining participation had no consequences for employment or medical care.

References

1 Gonder-Frederick LA, Cox DJ, Bobbitt SA, Pennebaker JW. Mood changes associated with blood glucose fluctuations in insulin-dependent diabetes mellitus. Health Psychol 1989;8(01):45–59
2 Amiel SA, Dixon T, Mann R, Jameson K. Hypoglycaemia in type 2 diabetes. Diabet Med 2008;25(03):245–254
3 Ben-Ami H, Nagachandran P, Mendelson A, Edoute Y. Drug-induced hypoglycemic coma in 102 diabetic patients. Arch Intern Med 1999;159(03):281–284
4 Hsu P-F, Sung S-H, Cheng H-M, et al. Association of clinical symptomatic hypoglycemia with cardiovascular events and total mortality in type 2 diabetes: a nationwide population-based study. Diabetes Care 2013;36(04):894–900
5 Marrett E, Radican L, Davies MJ, Zhang Q. Assessment of severity and frequency of self-reported hypoglycemia on quality of life in patients with type 2 diabetes treated with oral antihyperglycemic agents: a survey study. BMC Res Notes 2011;4:251
6 Davis RE, Morrissey M, Peters JR, Wittrup-Jensen K, Kennedy-Martin T, Currie CJ. Impact of hypoglycaemia on quality of life and productivity in type 1 and type 2 diabetes. Curr Med Res Opin 2005;21(09):1477–1483
7 Clarke WL, Cox DJ, Gonder-Frederick LA, Julian D, Schlundt D, Polonsky W. Reduced awareness of hypoglycemia in adults with IDDM. A prospective study of hypoglycemic frequency and associated symptoms. Diabetes Care 1995;18(04):517–522

8 Chan S-P, Ji L-N, Nitiyanant W, Baik SH, Sheu WH-H. Hypoglycemic symptoms in patients with type 2 diabetes in Asia-Pacific-Real-life effectiveness and care patterns of diabetes management: the RECAP-DM study. Diabetes Res Clin Pract 2010;89(02): e30–e32

9 Alvarez Guisasola F, Tofé Povedano S, Krishnarajah G, Lyu R, Mavros P, Yin D. Hypoglycaemic symptoms, treatment satisfaction, adherence and their associations with glycaemic goal in patients with type 2 diabetes mellitus: findings from the Real-Life Effectiveness and Care Patterns of Diabetes Management (RECAP-DM) Study. Diabetes Obes Metab 2008;10(Suppl 1):25–32

10 Bullano MF, Al-Zakwani IS, Fisher MD, Menditto L, Willey VJ. Differences in hypoglycemia event rates and associated cost-consequence in patients initiated on long-acting and intermediate-acting insulin products. Curr Med Res Opin 2005;21(02): 291–298

11 Janka HU, Plewe G, Busch K. Combination of oral antidiabetic agents with basal insulin versus premixed insulin alone in randomized elderly patients with type 2 diabetes mellitus. J Am Geriatr Soc 2007;55(02):182–188

12 Briscoe VJ, Davis SN. Hypoglycemia in type 1 and type 2 diabetes: physiology, pathophysiology, and management. Clin Diabetes 2006;24(03):115–121

13 UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet 1998;352(9131):837–853

14 Nathan DM, Genuth S, Lachin J, et al; Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med 1993;329(14):977–986

15 Torimoto K, Okada Y, Hajime M, Tanaka K, Tanaka Y. Risk factors of hypoglycemia in patients with type 2 diabetes mellitus: a study based on continuous glucose monitoring. Diabetes Technol Ther 2018;20(09):603–612

16 Li X, Yu S, Zhang Z, et al. Predictive modeling of hypoglycemia for clinical decision support in evaluating outpatients with diabetes mellitus. Curr Med Res Opin 2019;35(11):1885–1891. Doi: 10.1080/03007995.2019.1636016

17 Walker RJ, Strom Williams J, Egede LE. Influence of Race, Ethnicity and Social Determinants of Health on Diabetes Outcomes. Am J Med Sci 2016;351(04):366–373

18 Walker RJ, Smalls BL, Campbell JA, Strom Williams JL, Egede LE. Impact of social determinants of health on outcomes for type 2 diabetes: a systematic review. Endocrine 2014;47(01):29–48

19 Hill-Briggs F, Adler NE, Berkowitz SA, et al. Social determinants of health and diabetes: a scientific review. Diabetes Care 2020;44 (01):258–279

20 Moreno G, Mangione CM, Kimbro L, Vaisberg EAmerican Geriatrics Society Expert Panel on Care of Older Adults with Diabetes Mellitus. Guidelines abstracted from the American Geriatrics Society Guidelines for improving the care of older adults with diabetes mellitus: 2013 update. J Am Geriatr Soc 2013;61(11): 2020–2026

21 Lee SJ, Boscardin WJ, Stijacic Cenzer I, Huang ES, Rice-Trumble K, Eng C. The risks and benefits of implementing glycemic control guidelines in frail older adults with diabetes mellitus. J Am Geriatr Soc 2011;59(04):666–672

22 Strachan MWJ, Reynolds RM, Marioni RE, Price JF. Cognitive function, dementia and type 2 diabetes mellitus in the elderly. Nat Rev Endocrinol 2011;7(02):108–114

23 Ninomiya T. Diabetes mellitus and dementia. Curr Diab Rep 2014; 14(05):487

24 Whitmer RA, Karter AJ, Yaffe K, Quesenberry CP Jr., Selby JV. Hypoglycemic episodes and risk of dementia in older patients with type 2 diabetes mellitus. JAMA 2009;301(15):1565–1572

25 Yaffe K, Falvey CM, Hamilton N, et al; Health ABC Study. Association between hypoglycemia and dementia in a biracial cohort of older adults with diabetes mellitus. JAMA Intern Med 2013;173 (14):1300–1306

26 Feinkohl I, Aung PP, Keller M, et al; Edinburgh Type 2 Diabetes Study (ET2DS) Investigators. Severe hypoglycemia and cognitive decline in older people with type 2 diabetes: the Edinburgh type 2 diabetes study. Diabetes Care 2014;37(02):507–515

27 Klonoff DC, Buckingham B, Christiansen JS, et al; Endocrine Society. Continuous glucose monitoring: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 2011;96(10): 2968–2979

28 Pratley RE, Kanapka LG, Rickels MR, et al; Wireless Innovation for Seniors With Diabetes Mellitus (WISDM) Study Group. Effect of continuous glucose monitoring on hypoglycemia in older adults with type 1 diabetes: a randomized clinical trial. JAMA 2020;323 (23):2397–2406

29 Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap) – a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009;42(02): 377–381

30 Harris PA, Taylor R, Minor BL, et al; REDCap Consortium. The REDCap consortium: building an international community of software platform partners. J Biomed Inform 2019;95:103208

31 Massa GG, Gys I, Op 't Eyndt A, et al. Evaluation of the FreeStyle® Libre flash glucose monitoring system in children and adolescents with type 1 diabetes. Horm Res Paediatr 2018;89(03):189–199

32 Beck RW, Riddlesworth T, Ruedy K, et al; DIAMOND Study Group. Effect of continuous glucose monitoring on glycemic control in adults with type 1 diabetes using insulin injections: the DIAMOND randomized clinical trial. JAMA 2017;317(04):371–378

33 Lind M, Polonsky W, Hirsch IB, et al. Continuous glucose monitoring vs conventional therapy for glycemic control in adults with type 1 diabetes treated with multiple daily insulin injections: the GOLD randomized clinical trial. JAMA 2017;317(04):379–387

34 Laffel LM, Kanapka LG, Beck RW, et al; CGM Intervention in Teens and Young Adults with T1D (CITY) Study Group CDE10. Effect of continuous glucose monitoring on glycemic control in adolescents and young adults with type 1 diabetes: a randomized clinical trial. JAMA 2020;323(23):2388–2396

35 Ratna S, Subashini R, Unnikrishnan R, Mohan V. Use of freestyle libre ProTM flash glucose monitoring system in different clinical situations at a diabetes centre. J Assoc Physicians India 2017;65 (08):18–23

36 Saleem JJ, Wilck NR, Murphy JJ, Herout J. Veteran and staff experience from a pilot program of health care system-distributed wearable devices and data sharing. Appl Clin Inform 2022;13 (03):532–540

37 Karway G, Grando MA, Grimm K, Groat D, Cook C, Thompson B. Self-management behaviors of patients with type 1 diabetes: comparing two sources of patient-generated data. Appl Clin Inform 2020;11(01):70–78

38 Groat D, Soni H, Grando MA, Thompson B, Kaufman D, Cook CB. Design and testing of a smartphone application for real-time self-tracking diabetes self-management behaviors. Appl Clin Inform 2018;9(02):440–449

39 Watson AJ, Grant RW, Bello H, Hoch DB. Brave new worlds: how virtual environments can augment traditional care in the management of diabetes. J Diabetes Sci Technol 2008;2(04):697–702

40 Cox DJ, Kovatchev B, Koev D, et al. Hypoglycemia anticipation, awareness and treatment training (HAATT) reduces occurrence of severe hypoglycemia among adults with type 1 diabetes mellitus. Int J Behav Med 2004;11(04):212–218

41 Kuo A, Dang S. Secure messaging in electronic health records and its impact on diabetes clinical outcomes: a systematic review. Telemed J E Health 2016;22(09):769–777

42 Huang ES, Nathan AG, Cooper JM, et al. Impact and feasibility of personalized decision support for older patients with diabetes: a pilot randomized trial. Med Decis Making 2017;37(05): 611–617
43 Montori VM, Fernández-Balsells M. Glycemic control in type 2 diabetes: time for an evidence-based about-face? Ann Intern Med 2009;150(11):803–808
44 Watson AJ, Kvedar JC, Rahman B, Pelletier AC, Salber G, Grant RW. Diabetes connected health: a pilot study of a patient- and provider-shared glucose monitoring web application. J Diabetes Sci Technol 2009;3(02):345–352
45 Kim H-S, Jeong YJ, Baik SJ, et al. Social networking services-based communicative care for patients with diabetes mellitus in Korea. Appl Clin Inform 2016;7(03):899–911
46 Quinn CC, Shardell MD, Terrin ML, Barr EA, Ballew SH, Gruber-Baldini AL. Cluster-randomized trial of a mobile phone personalized behavioral intervention for blood glucose control. Diabetes Care 2011;34(09):1934–1942
47 Rollo ME, Ash S, Lyons-Wall P, Russell A. Trial of a mobile phone method for recording dietary intake in adults with type 2 diabetes: evaluation and implications for future applications. J Telemed Telecare 2011;17(06):318–323
48 Desendorf J, Bassett DR Jr, Raynor HA, Coe DP. Validity of the Bite Counter device in a controlled laboratory setting. Eat Behav 2014; 15(03):502–504
49 Lu T-C, Fu C-M, Ma MH-M, Fang C-C, Turner AM. Healthcare applications of smart watches. a systematic review. Appl Clin Inform 2016;7(03):850–869
50 Baig MM, GholamHosseini H, Gutierrez J, Ullah E, Lindén M. Early detection of prediabetes and T2DM using wearable sensors and internet-of-things-based monitoring applications. Appl Clin Inform 2021;12(01):1–9
51 U.S. Food & Drug Administration. Summary of safety and effectiveness data: Freestyle Libre Pro Flash Glucose Monitoring System. Published 2016. Accessed September 14, 2020 at: https://www.accessdata.fda.gov/cdrh_docs/pdf15/P150021B.pdf
52 Alitta Q, Grino M, Adjemout L, Langar A, Retornaz F, Oliver C. Overestimation of hypoglycemia diagnosis by FreeStyle Libre continuous glucose monitoring in long-term care home residents with diabetes. J Diabetes Sci Technol 2018;12(03):727–728
53 Gehlaut RR, Dogbey GY, Schwartz FL, Marling CR, Shubrook JH. Hypoglycemia in type 2 diabetes–more common than you think: a continuous glucose monitoring study. J Diabetes Sci Technol 2015;9(05):999–1005