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Research Article

Long-Term Safety and People Reported Outcomes of a Long-Duration Implantable CGM System in the US Post Approval Setting

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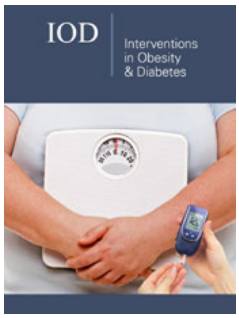
ISSN: 2578-0263



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Submission: October 24, 2024
Published: November 08, 2024

Volume 6 - Issue 5

How to cite this article: Katherine S Tweden*, Ben Romarowski, Mark Warren, Kashif Latif, Ralph Oiknine and Francine R Kaufman. Long-Term Safety and People Reported Outcomes of a Long-Duration Implantable CGM System in the US Post Approval Setting. Interventions Obes Diabetes. 6(5). IOD. 000648. 2024. DOI: 10.31031/IOD.2024.06.000648

Abstract

Background: The implantable Eversense CGM Systems have been shown to be safe and accurate over multiple sensor cycles. A post approval study was begun to assess safety and people-reported outcomes after repeated insertions in a US-based population.

Methods: Safety was evaluated over 2 years in adult study participants with either type 1 or type 2 diabetes. After baseline assessment (demographics, medical history, Diabetes Distress Scale (DDS) administration) and placement of the Eversense sensor, visits were made every 90 days to document Adverse Events (AEs). Sensors were replaced at 90 or 180 days according to the labeling. DDS and CGM Satisfaction Scale (CGM-SAT) were administered at 6 months and 1 and 2 years. The primary safety endpoint was the incidence of the composite of infection, secondary procedures to remove the sensor, and procedure-related AEs of at least moderate severity with a goal of <4%.

Results: Across 16 centers, 273 users were enrolled in the study (55% male, 80% reported having type 1 diabetes). A total of 1,528 Sensors were inserted during the study. The primary safety endpoint was met (p=0.005). The total and 4 subscale DDS scores were <2 after baseline and showed significant improvement from baseline. Users had stable high satisfaction (>95%), high benefits (>97%) and lack of hassles (>91%) with all CGM-SAT scores >4 by 360 days and beyond.

Conclusion: Repeated insertions/removals of the Eversense CGM Systems resulted in low levels of stress and high levels of satisfaction and demonstrated long-term safety.

Keywords: Continuous glucose monitoring; Implantable sensor; Eversense; Type 1 diabetes; Type 2 diabetes; Safety; People reported outcomes

Abbreviations: CGM: Continuous Glucose Monitoring; IFU: Instructions for Use; SMBG: Self-Monitoring of Blood Glucose; TIR: Time in Range; T1D: Type 1 Diabetes; T2D: Type 2 Diabetes; AE: Adverse Event; BG: Blood Glucose; SAEs: Serious Adverse Events; DDS: Diabetes Distress Scale; CGM-SAT: CGM Satisfaction Scale; FDA: Food and Drug Administration

Introduction

The use of Continuous Glucose Monitoring Systems (CGM) has been shown to improve diabetes management in randomized controlled trials [1-3], as well as real-world evidence studies [4-6]. To date, there have been two categories of CGM systems that measure glucose in the interstitial fluid: transcutaneous and fully implantable. Three transcutaneous CGM systems, inserted by the patient every 7-15 days, and one fully implantable CGM system, inserted by trained and certified health care providers, that has recently been approved to last up to 365 days are available for patients in the U.S.

Four generations of fully implantable long-term sensors have been approved for commercialization in Europe and the US: the 90-day Eversense CGM System, the 180-day

Eversense XL CGM System (in Europe only), the 180-day Eversense E3 CGM System and the recently FDA approved Eversense 365 CGM System that lasts up to one year (Senseonics, Inc., Germantown, MD). The performance and safety results from multiple clinical trials [7-10] demonstrated good accuracy and safety. Specifically, the Eversense E3 CGM System demonstrated a Mean Absolute Relative Difference (MARD) of 8.7% against the Yellow Springs Instrument (YSI) including a Mean Absolute Difference (MAD) in the 40-60mg/dL range of 7.5mg/dL and a favorable safety profile with relatively few device- or procedure-related adverse events through 180 days [7,8,11]. The Eversense 365 CGM System has a MARD of 8.8% against the YSI and a MAD in the < 54mg/dL range of 7.7% [12].

After Food and Drug Administration (FDA) approval of the initial 90-day Eversense CGM System in the United States in 2018, a post marketing study was begun to assess the safety of multiple sensor insertions and removals over a 2-year time-period in a cohort of patients with type 1 and type 2 diabetes. The study transitioned to the 180-day Eversense E3 System after FDA approval in 2022. This report describes the safety results as well as two measures of person-reported outcomes in study participants with diabetes who used fully implanted sensors for at least two years.

Materials and Methods

Study design and participant enrollment

The study was a prospective, multi-center, two-year evaluation of the safety of the Eversense CGM System in U.S. adult patients with either type 1 or type 2 diabetes. The study was conducted between March 2019 to February 2024 across 16 sites in the United States. Patients were eligible for the study if they were 18 years of age or older and had a confirmed diagnosis of diabetes mellitus. Consistent with the device label, patients were not candidates for the system if they were critically ill or hospitalized, had a known contradiction to dexamethasone or dexamethasone acetate, or required intravenous mannitol or sorbitol solutions. Patients who were pregnant and wearing other CGM systems were also excluded. Centralized institutional review boards approved the study and all patients provided written and verbal informed consent. The study was performed in accordance with the Declaration of Helsinki and is on record on clinicaltrials.gov (NCT03908125).

Study device

Eversense CGM Systems consist of implantable, fluorescence-based, cylindrical glucose sensors (3.5x18.3mm); a smart transmitter; and an app that displays glucose information in real time and operates on a mobile device as described elsewhere [9]. Systems with 90-day longevity were used in the initial years of the study after which those with 180 day longevity were used subsequent to FDA approval of the Eversense E3 CGM System.

Study procedures

After baseline assessment, including demographics, medical history and administration of Diabetes Distress Scale (DDS), the Eversense sensor was inserted. Sensors were inserted into the upper arm by qualified health-care providers as described before [8]. In-clinic visits were made every 90 days to assess Adverse Events (AEs), including Serious Adverse Events (SAEs), at each visit and between visits during periodic phone calls. Sensors were replaced at either 90 days or 180 days through at least 2 years according to the labeling of the sensor resulting in up to 8 or more sensor cycles per participant over the study duration. Participants, including those with a combination of 90-day sensors and 180-day sensors, had a 2-year visit (720 days) for endpoint assessment.

Study outcomes

The primary safety objective was to demonstrate long-term safety of continuous use of the Eversense CGM System. The primary safety endpoint was the incidence of the composite of infection, secondary procedures to remove the sensor, or procedure-related AEs of at least moderate severity with a performance goal of <4%. In addition, a subset of study participants had some of their sensors placed into the same arm incision over the 2 years of the study after the expired sensor was removed. Primary endpoint related to AEs (infection, secondary procedures to remove sensors and procedure-related AEs of at least moderate severity) were reported for that subset to inform on the safety of this type of repeat insertion procedure. An additional safety objective was the incidence of all device and procedure-related AEs and all AEs regardless of relatedness. AEs were adjudicated by an independent clinical events committee for relatedness to the device or procedure. People-reported outcomes were assessed at baseline when applicable and periodically throughout the study using two validated measures, DDS [13] and the CGM Satisfaction Scale (CGM-SAT) [14]. Specifically, the CGM-SAT and DDS were administered at 6 months, 1 year and 2 years after sensor insertion including baseline administration of DDS.

Statistical methods

The study primary safety endpoint was that of a composite of incidence of infection, secondary procedures to remove sensors, and procedure-related AEs of at least moderate severity is <4% over the 2 years of device use. The primary safety composite endpoint was evaluated in the following hypothesis, against a performance goal of 4%:

H0: The rate of the composite of infection, secondary procedures to remove the sensor, or procedure-related adverse events of at least moderate severity (p) is greater than or equal to 4%. H0: p≥4%.

H1: The rate of the composite of infection, secondary procedures to remove the sensor, or procedure-related adverse events of at least moderate severity (p) is less than 4%. H1: p<4%.

The rate was tested against the performance goal of 4%, using an exact binomial test, with a one-sided p-value of 0.05 considered evidence of statistical significance. For the primary analysis, data was analyzed on a per cycle basis, with each cycle contributing an independent observation. A sample size of at least 1400 sensor cycles (one cycle defined as an insertion and removal of one sensor) was expected to provide greater than 95% power for the test of the performance goal of 4% based on rates of the endpoint

AEs observed in other investigational and European Post Market Clinical Follow-Up (PMCF) trials [4,8-10].

The subscales used for the CGM-SAT are a division of positively and negatively worded questions whereby answers are re-mapped to positively worded questions so that a higher score always means higher satisfaction. A participant's result in any given subscale is the average of the scores to each question. A mean score larger or equal to 3 indicates the patient's agreement or neutrality. The subscales used for the DDS are those identified in Polonsky et al. [13]. Individual results for each subscale are the average of the corresponding questions. An average score less or equal to 2 indicates the patient is experiencing slight or better than slight stress. The aggregate mean and Standard Deviation (SD) across study participants were reported for both questionnaires. To analyze the change in satisfaction or stress throughout the study, each patient's average score at baseline was compared with the end of the study score (day 720) for DDS whereas, by design, Day 180 was compared to Day 720 for CGM-SAT. Individual changes were aggregated, with mean change (SD) reported. A t-distribution with appropriate degrees of freedom was used to report confidence intervals for the mean. The results were tested against a null hypothesis of constant mean throughout the study (i.e. no change in the mean t, H_0:μΔ=0). The p-values of this test are reported using a paired t-test.

Results and Discussion

Two hundred seventy-three (273) study participants were consented and enrolled in the study and provided 1,517 total sensor cycles. Baseline demographics and medical characteristics are summarized in Table 1. The majority of the study population reported having type 1 diabetes (80%).

Table 1: Baseline demographics (n=273).

Demographics	N (%)
Age (Mean±SD, Median, Min – Max)	44.7±14.6, 47, 18-81
Gender	
Female	123 (45.1)
Male	150 (54.9)
Race	
Caucasian	235 (86.1)
Black or African American	23 (8.4)
Asian	7 (2.6)
Subject declined to answer	3 (1.1)
More than one race	3 (1.1)
American Indian or Alaska Native	1 (0.4)
Native Hawaiian or Other Pacific Islander	1 (0.4)
Ethnicity	
Not Hispanic or Latino	259 (94.9)
Hispanic or Latino	14 (5.1)
Diabetic Diagnosis	
Type 1	218 (79.9)
Type 2	55 (20.1)
Years since diabetes diagnosis (Mean±SD)	19±13
CGM Naïve	71 (26.0)
Diabetes Therapy Regimen	
non-insulin medications, basal insulin, lifestyle	10 (3.7)
Intensive insulin therapy	263 (96.3)

Safety outcome results

During the study, 1,528 sensors were inserted. The primary safety endpoint was met with p=0.005 as shown in Table 2. The composite rate was 42 events out of 1,528 sensor cycles (2.75%) with a 95% upper confidence limit of 3.54%. There were 47 study participants who elected to have their next sensor insertion into the same arm incision. Those study participants provided 102 insertions into the same arm. Comparing all insertions and same-arm insertions using a non-inferiority test showed no difference in endpoint related AEs between the two groups (p=0.66). There were 3 device-related SAEs due to hypoglycemia in 2 study participants and 1 procedure-related SAE in another study participant due to infection at the sensor site. All SAEs resolved. There were 360 AEs reported in total, of which 96 were adjudicated as related to the study device or insertion/removal procedures (Table 3). The most frequently reported related AEs as a percentage of sensors inserted were inability to remove the sensor on first attempt (1.6%, 24 events in 22 study participants), skin irritation to the adhesive

patch (0.9%, 13 events in 11 study participants), insertion site irritation (0.8%, 12 events in 9 study participants) and sensor insertion site pain (0.8%, 12 events in 10 study participants). All other events occurred in 6 or fewer cases. Hypoglycemia related to the device occurred at rates of only 0.3% (4 events in 3 study participants) of sensors inserted.

Table 2: Primary safety endpoint.

Primary Safety Endpoint	ITT Population (N=273)
Number of cycles	1528
Number of study participants	273
Event rate (%)	42/1528(2.75)
95% Upper confidence interval	3.54
One-sided p-value	0.0054
Infection, n/N (%)	5/1528(0.33)
Secondary procedure to remove sensor, n/N (%)	24/1528(1.57)
Procedure-related adverse event of at least moderate severity, n/N (%)	15/1528(0.98)

Table 3: Device-related and insertion/removal procedure-related adverse events.

Adverse Event (AE)	Number of Events	Percentage of Sensor Insertion Cycles	Number per 100 Patient Years
Total	96	6.3	22.0
Unable to remove Sensor on first attempt	24	1.6	5.5
Skin irritation, adhesive patch (erythema, pruritis, contact dermatitis, blister)	13	0.9	3.0
Sensor insertion site (erythema, swelling, pruritis, redness, rash)	12	0.8	2.7
Sensor insertions site - Pain	12	0.8	2.7
Skin discoloration	6	0.4	1.4
Sensor insertions site - Infection	5	0.3	1.1
Skin atrophy	5	0.3	1.1
Hypoglycemia	4	0.3	0.9
Scarring	4	0.3	0.9
Bleeding	3	0.2	0.7
Bruising	2	0.1	0.5
Cellulitis	2	0.1	0.5
Prolonged wound healing	2	0.1	0.5
Vasovagal episode/Cold sweat	2	0.1	0.5

Person-reported outcome results

For the DSS, the lower the numerical value indicates less distress on the measures, with a 5-point scale, for 17 questions grouped into 4 subscales. As seen in Table 4, there was a significant improvement from baseline to the 2-year time period for the overall score and for the 4 subscales that measured emotional burden (Emotional Burden Subscale), distress with physician interactions and expectations (Physician Distress Subscale), diabetes regimen distress (Regimen Distress Scale) and interpersonal distress (Interpersonal Distress Subscale). For all measures, the percentage of participants experiencing only slight stress increased from baseline compared to the other time points of measurement. With the CGM Satisfaction Scale, the higher the number on a scale from 1-5, the greater the satisfaction, for 44 questions grouped in two subscales (benefits and lack of hassles). The initial values at 180 days showed high satisfaction with a mean score of 4.0 that did not significantly change over time (Table 5). The percentage of participants who agreed or were neutral on the benefits and lack of hassle subscales was greater than 90 % across all measures which were maintained through two years.

Table 4: Diabetes Distress Scale (DDS)* changes over 2 years. *DDS is a 17 question, 6-point scale (1=not a problem, 6=a very serious problem); lower score depicts less distress with diabetes.

Diabetes Distress Scale	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD) [95% CI] p value
Visit	Screening	Day 180	Day 360	Day 720	Change from Screening
Total Score	1.9 (0.8)	1.7 (0.7)	1.7 (0.7)	1.7 (0.7)	-0.2 (0.7) [-0.3, -0.04]

Emotional Burden Subscale	2.1 (1.0)	1.9 (0.9)	1.8 (0.8)	1.8 (0.8)	-0.2 (0.8) [-0.3, -0.03]
Physician Distress Subscale	1.5 (0.6)	1.4 (0.5)	1.3 (0.4)	1.3 (0.4)	-0.1 (0.5) [-0.2, -0.04]
Regimen Distress Subscale	2.1 (1.0)	1.9 (0.9)	1.8 (0.9)	1.9 (0.9)	-0.2 (0.9) [-0.3, -0.01]
Interpersonal Distress Subscale	1.7 (1.0)	1.6 (0.9)	1.5 (0.9)	1.5 (0.7)	-0.2 (0.9) [-0.3, 0.001]

Table 5: CGM satisfaction scale* over two years. *CGM-Sat is a 44 question, 5-point scale (1=strongly agree, 5=strongly disagree); higher scores reflect more satisfaction with CGM.

CGM Satisfaction Scale	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD) [95% CI] p value
Visit	Day 180	Day 360	Day 720	Change from Day 180
Total Score	4.0 (0.5)	4.1 (0.5)	4.1 (0.5)	-0.1 (0.5) [-0.1, 0.03] p=0.2
Agree or Neutral (%)	95	98	96	
Benefits of CGM Subscale	4.1 (0.6)	4.2 (0.5)	4.2 (0.6)	-0.05 (0.5) [-0.1, 0.04] p=0.3
Agree or Neutral (%)	97	97	98	
Lack of Hassles of CGM Subscale	4.0 (0.7)	4.1 (0.6)	4.1 (0.6)	-0.08 (0.5) [-0.2, 0.02] p=0.1
Agree or Neutral (%)	92	94	95	

Discussion

The primary safety endpoint of this large, prospective post market study evaluating the long-term safety of the 90-day and 180-day Eversense CGM Systems in people with either type 1 or type 2 diabetes was met demonstrating that the incidence of infection, secondary procedures to remove the Eversense implanted sensor and any procedure-related AE at least moderate in severity was <4%, (in fact the mean was only 2.75%), over a 2 year period involving at least 8 sensor insertion cycles per study participant. Infection, arguably the most consequential AE, occurred at a low rate of 0.3% (1.1 per 100 patient years). There were only 3 related SAEs (2 due to hypoglycemia and 1 due to infection) that were all resolved without long-term sequelae. In addition, two other AEs of interest occurred at low rates, specifically the inability to remove the sensor on the first attempt (1.6%, 5.5 per 100 patient years) and skin irritation (0.9%, 3.0 per 100 patient years). As seen in the Instruction for Use (IFU) manuals for the three transcutaneous sensors commercialized in the US, all have risk of infection at the insertion site, skin irritation, and issues with insertion and removal and premature dislodgement of the sensor [15-17]. As indicated in their respective IFUs, only 80% of 10-day CGM systems last 10 days [15] and only 68% of 15-day CGM systems last 15 days [16] compared to 90% survival for 180 days with the fully implantable Eversense E3 CGM System [7,11].

The findings of this post marketing safety study are similar to what has previously been reported during a Post-Market Clinical Follow-up (PMCF) registry with the 90-day and 180-day XL Eversense CGM systems in Europe and South Africa from June 2016 to August 2018 [4]. During that PMCF registry, 969 study participants used an Eversense CGM system for at least 6 months and 173 study participants used the system for at least 1 year during which time the most frequently reported related AEs were sensor site infection (0.96%; 2.46 events per 100 Patient-Years [PYs]), inability to remove the sensor upon first attempt (0.76%; 1.90 events per 100 PYs), and adhesive patch location site irritation (0.66%; 1.59 events per 100 PYs). Additionally, a real-world analysis from the Deidentified Sensor Glucose (SG) data from August 1, 2018 to May 11, 2019 from the Eversense Data Management System (DMS) were analyzed in the first 205 study participants who reached a 90-day wear period on the Eversense CGM system in the US [5]. In this report, 2% of study participants reported mild skin infection at the insertion site, 2% had failure to remove the sensor on the first attempt, and 2.5% of study participants reported skin irritation of the adhesive patch. These multiple real-world data support the low adverse event rates for the fully implantable Eversense CGM Systems.

People reported outcomes have become increasingly important, particularly in the assessment of diabetes technology, because of the emotional toll and physical burden of diabetes self-management. Rates of diabetes distress are high, with estimates between 20-40% [18], which can negatively impact time in range, HbA1c, and adherence to the diabetes regimen [19,20]. As a result, the American Diabetes Association recommends assessing diabetes distress in their clinical guidelines [21]. In addition, validated measures of the impact of diabetes devices, such as CGM systems, are critical to understand what matters to the patient and if they perceive that their needs are being met. While there is no doubt that diabetes technologies have improved patient outcomes and quality of life, due to issues with usability and reliability, it is not a given that patients will report benefit with any particular device when used in the real world.

The results of person reported outcomes from this large U.S. cohort using Eversense CGM over a 2-year time period showed improvement in measures of diabetes distress, as assessed with the Diabetes Distress Scale. The improvement was present by the 180-day time period and was sustained for the two years of the study. At baseline approximately two-thirds of study participants

had slight distress across all the domains, and this increased to three-quarters of the study participants over the two years of evaluation suggesting the repeated sensor insertion and removal procedures did not increase diabetes distress. The CGM Satisfaction Scale showed high levels of satisfaction with the Eversense systems, again sustained over the two-year time period. By the end of the study, all measures were >4 out of a 5 (on a 5-point scale), with >90% of study participants agreeing or neutral on the benefits and lack of hassles of Eversense, again suggesting the reliability, usability and functionality of the Eversense system was valued by the participants, and that the insertion and removal procedures did not distract from satisfaction with the system on the whole.

A previous assessment of person reported outcomes with the fully implantable 180-day Eversense XL System was reported in 2018 by Barnard et al. [22]. Fifty-one participants took part in this evaluation in the United Kingdom and Germany, with self-reported measures taken at the 90-day time period. Similar to the present study, study participants reported improvements in all domains on the Diabetes Distress Scale, with individual item results as low as 1.14 and the highest being 2.24. In addition, 72% judged the fully implantable CGM to be very helpful in managing their diabetes more easily, 92% indicated they did not experience pain or discomfort, 84% reported they would choose to be inserted again, and 93% of first time CGM users and 86% of previous CGM users stated they had reduced burden of diabetes with Eversense CGM.

While this study evaluated both the first and third generation Eversense systems, at the present time, only Eversense E3 is available in Europe and Eversense 365 is available only in the U.S. Eversense 365 has a one-year duration and an improved calibration scheme of 1 calibration per day through day 13 and then 1 calibration per week for the remainder of the year-long system wear [12]. There are many unique attributes to the Eversense E3 and 365 CGM Systems. Beyond the long duration of wear up to 1 year (Eversense 365 CGM System only), there is an excellent accuracy profile, the MAD is 7.7% for glucose values <54mg/dL and 7.8% for glucose values 54-69mg/dL [12]. Because Eversense measures glucose in the interstitial fluid through fluorescent technology, it is not susceptible to vitamin C or acetaminophen inaccuracies. The removable and rechargeable transmitter is waterproof and held in place by a mild silicone adhesive, allowing for the low rates of skin irritation. The transmitter elicits vibratory alerts directly on the arm for high and low glucose values, including for the predictive high and low glucose alarms, as well as the threshold and rate of change alarms.

The use of CGM with relevance to the patient's needs in diabetes management may assess the effects of CGM systems on the anti-aging gene Sirutin 1. Sirutin 1 is critical for the prevention of diabetes and multiple organ disease syndrome. The long-term use of CGM may be associated with therapeutic Sirtuin 1 levels and with relevance to insulin levels. Sirtuin 1 activator consumption may be important to the use of CGM systems [23-25]. The limitations of this study include two generations of Eversense sensors were used, the 90-day and the 180-day systems, perhaps masking what might have been even greater benefit with the longer duration sensor that requires half the number of procedures. The advantages of this study are that it was long-term, involved a large cohort of study participants at over 15 sites across the US undergoing at least 8 total sensor insertion and removals procedures.

Conclusion

These data demonstrate the safety and acceptability of the fully implantable Eversense CGM systems over long term use. The composite safety endpoint evaluating serial Eversense insertions and removal procedures over a 2-year period was met. The very low rates of adverse events resulting from the insertion and removal procedures and from the long-term wear of the sensors themselves and the improvements in patients' diabetes distress and reported satisfaction demonstrates that Eversense CGM meets patient expectations and needs in their diabetes management journey.

Acknowledgement

The authors wish to thank all of the post approval clinical sites and their teams for the conduct of the study and all of the study participants for their contribution to the study. Specifically, the following sites participated in this study: AM Diabetes & Endocrinology, Bartlett, TN, USA (Dr K Latif); Diabetes and Endocrinology Specialists, Inc, Chesterfield, MO, USA (Dr R Oiknine); Physicians East, PA, Greenville, NC, USA (Dr M Warren);Texas Diabetes & Endocrinology, Austin, TX, USA (Dr K Ozer and Dr Hien Tran); The Center for Diabetes and Endocrine Care, Fort Lauderdale, FL, USA (Dr S Lerman); Denver Endocrinology, Diabetes & Thyroid Center, Englewood, CO, USA (Dr L Gerard); MODEL Clinical Research, Baltimore, MD, USA (Dr P Levin); Metro Detroit Endocrinology Center, Dearborn, MI, USA (Dr A Elkadry); Hoag Memorial Hospital, Newport Beach, CA, USA (Dr D Ahn); Diabetes and Glandular Disease Clinic, San Antonio, TX, USA (Dr M Kipnes); Clinical Research Solutions, Cypress TX, USA (Dr R Patel); Albany Medical College, Albany, NY, USA (Dr R Busch); PMG Research of Wilmington, LLC, Wilmington, NC, USA (Dr M Favorito); Consano Clinical Research, Shavano Park, TX, USA (Dr M Welch); Diabetes and Endocrinology Consultants of PA, Feasterville, PA, USA (Dr A Schorr); and Atlanta Diabetes Associates, Atlanta, GA, USA (Dr B Bode).

References

1. Lind M, Polonsky W, Hirsch IB, Heise T, Bolinder J, et al. (2017) 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 317(4): 379-387.

2. Beck RW, Riddlesworth T, Ruedy K, Ahmann A, Bergenstal R, et al. (2017) Effect of continuous glucose monitoring on glycemic control in adults with type 1 diabetes using insulin injections: The DIAMOND randomized clinical trial. JAMA 317(4): 371-378.

3. Battelino T, Conget I, Olsen B, Fuhrmann IS, Hommel E, et al. (2012) The use and efficacy of continuous glucose monitoring in type 1 diabetes treated with insulin pump therapy: A randomized controlled trial. Diabetologia 55(12): 3155-3162.

4. Deiss D, Irace C, Carlson G, Tweden KS, Kaufman FR (2020) Real-world safety of an implantable continuous glucose sensor over multiple cycles

of use: A post-market registry study. Diabetes Technol Ther 22(1): 48-52.

5. Sanchez P, Dastidar SG, Tweden KS, Kaufman FR (2019) Real-world data from the first U.S. commercial users of an implantable continuous glucose sensor. Diabetes Technol Ther 21(12): 677-681.
6. Olofsson KE, Svensson AM, Franzen S, Ismail HA, Törnblom M, et al. (2023) Real-world study of flash glucose monitoring among adults with type 2 diabetes within the Swedish national diabetes register. Diabetes & Vascular Disease Research 20(1): 1-9.
7. Garg SK, Liljenquist D, Bode B, Christiansen MP, Bailey TS, et al. (2022) Evaluation of accuracy and safety of the next-generation up to 180-day long-term implantable eversense continuous glucose monitoring system: The PROMISE study. Diabetes Technol Ther 24(2): 84-92.
8. Kropff J, Choudhary P, Neupane S, Barnard K, Bain SC, et al. (2017) Accuracy and longevity of an implantable continuous glucose sensor in the precise study: A 180-day, prospective, multicenter, pivotal trial. Diabetes Care 40(1): 63-68.
9. Christiansen MP, Klaff LJ, Brazg R, Chang AR, Levy KJ, et al. (2018) A prospective multicenter evaluation of the accuracy of a novel implanted continuous glucose sensor: PRECISE II. Diabetes Technol Ther 20(3): 197-206.
10. Christiansen MP, Klaff LJ, Bailey TS, Brazg R, Carlson G, et al. (2019) A prospective multicenter evaluation of the accuracy and safety of an implanted continuous glucose sensor: The PRECISION study. Diabetes Technol Ther 21(5): 231-237.
11. Eversense E3 CGM user guide.
12. Bailey TS, Denham D, Brazg RL, Iaocara S, Masciotti J, et al. (2024) Evaluation of accuracy and safety of the next-generation 365-day implantable eversense CGM system: The ENHANCE study. Submitted for Publication.
13. Polonsky WH, Fisher L, Earles J, Dudl RJ, Lees J, et al. (2005) Assessing psychological distress in diabetes: Development of the diabetes distress scale. Diabetes Care 28(3): 626-631.
14. Juvenile diabetes research foundation continuous glucose monitoring study group (2010) Validation of measures of satisfaction with and impact of continuous and conventional glucose monitoring. Diabetes Tech Ther 12(9): 679-684.
15. Dexcom G7 continuous glucose monitoring system user guide.
16. FreeStyle Libre 3 Continuous Glucose Monitoring System User's Manual.
17. Guardian connect system user guide.
18. Skinner TC, Joensen L, Parkin T (2020) Twenty-five years of diabetes distress research. Diabet Med 37(3): 393-400.
19. Poole L, Hackett RA (2024) Diabetes distress: The psychological burden of living with diabetes. Lancet Diabetes Endocrinology 12(7): 439-441.
20. Hessler DM, Fisher L, Polonsky WH, Masharani U, Strycker LA, et al. (2017) Diabetes distress is linked with worsening diabetes management over time in adults with type 1 diabetes. Diabet Med 34(9): 1228-1234.
21. American Diabetes Association professional practice committee (2024) Facilitating positive health behaviors and well-being to improve health outcomes: Standards of care in diabetes. Diabetes Care 47(Suppl 1): S77-S110.
22. Barnard K, Kropff J, Choudhary P, Neupane S, Bain SC, et al. (2018) Acceptability of implantable continuous glucose monitoring sensor. J Diabetes Sci Technol 12(3): 634-638.
23. Martins IJ (2016) Anti-aging genes improve appetite regulation and reverse cell senescence and apoptosis in global populations. Advances in Aging Research 5(1): 9-26.
24. Martins IJ (2019) Insulin therapy and autoimmune disease with relevance to non-alcoholic fatty liver disease. Nonalcoholic Fatty Liver Disease-An Update, pp. 1-14.
25. Martins IJ (2018) Sirutin 1, A diagnostic protein marker and its relevance to chronic disease and therapeutic drug intervention. EC Pharmacology and Toxicology 6(4): 209-215.