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Clinical Research Study

Comparing clinical outcomes between two continuous glucose monitors: similar diabetes-related events, all-cause hospitalizations and HbA1c reductions in type 1 and type 2 diabetes

Eden Miller[a], Gregory J. Roberts[b], Jennifer M. Joseph[c], Yelena Nabutovsky[c], Ignacio J. Reyes[b], Diana Souto[d], Naunihal Virdi[d,*], Irl B. Hirsch[e]

[a] Diabetes and Obesity Care, Bend, OR, USA
[b] Abbott, Sylmar, CA, USA
[c] Abbott, Santa Clara, CA, USA
[d] Abbott Diabetes Care, Alameda, CA, USA
[e] University of Washington School of Medicine, Seattle, WA, USA

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ABSTRACT

Objectives: We compared clinical outcomes after acquiring a FreeStyle Libre© Flash Continuous Glucose Monitoring System (FSL) or Dexcom (DEX) continuous glucose monitoring (CGM) device in individuals with type 1 diabetes (T1D) and type 2 diabetes (T2D) treated with intensive insulin therapy.

Design and Methods: This retrospective analysis of the IBM® MarketScan® Research Databases and IBM® Explorys® Electronic Health Records Database assessed differences in acute diabetes-related events (ADE), all-cause hospitalizations (ACH) and glycated hemoglobin (HbA1c) in T1D and T2D populations 6 months post CGM acquisition. Analyses were conducted in two study cohorts (Cohort 1, n = 7,494; Cohort 2, n = 678). Participants were T1D or T2D, age ≥ 18 years, treated with short or rapid-acting insulin and naïve to CGM, who acquired a CGM system. Users were propensity score matched on demographics and clinical factors.

Results: Cohort 1: Post-CGM ADE-free rates at 6 months ranged from 94.8 to 96.7% and ACH-free rates ranged from 90.4 to 95.4%, for both T1D and T2D groups, with no significant differences between CGM systems. Cohort 2: Significant HbA1c reductions were associated with use of the DEX and FSL devices in the T1D (-0.35% and -0.37%, respectively) and T2D (-0.73% and -0.79%, respectively) cohorts, both $p < 0.001$, with no significant differences in the magnitude of reduction between systems (T1D $p = 0.99$ and T2D $p = 0.84$).

Conclusions: Acquisition of the FSL and DEX systems was associated with similar rates of acute diabetes-related events and all-cause hospitalizations and similar HbA1c reductions in adults with T1D and T2D.

Introduction

Advances in glucose monitoring have led to the development of continuous glucose monitoring (CGM) devices that enable patients with diabetes to frequently check their current glucose levels, overall patterns and the direction and velocity of changing glucose. This information allows users to make more informed decisions about therapy adjustments and, importantly, to take immediate action to mitigate current or impending acute glycemic events.

There are currently two types of CGM systems: "flash" CGM, and traditional CGM. Both types of systems utilize sensors which measure glucose constantly. The Flash CGM system users in this analysis can see their data by scanning their sensor with a handheld reader or smartphone. Data for traditional CGMs is streamed directly onto a reader or smartphone where the data can be viewed.

The safety and efficacy of CGM systems in improving glycemic control and reducing healthcare resource utilization have been demonstrated in numerous large RCTs and real-world cohort studies involving T1D[1–7] and T2D populations treated with short- or rapid-acting insulin.[8–12] However, we are not aware of any real-world study that compares the relative efficacy of different CGM systems in reducing HbA1c levels, acute diabetes-related events (ADE) and all-cause hospitalizations (ACH) and improving overall glycemic control in individuals with T1D and T2DM.

In the current study, we report findings from a real-world study that utilized electronic health records and health insurance claims databases

* Corresponding author.
E-mail address: naunihal.virdi@abbott.com (N. Virdi).

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to assess the comparative effects of acquiring a CGM system on glycemic status, acute diabetes-related events and healthcare resource utilization in patients with T1D and T2D, managed with short or rapid-acting insulin.

Methods

Study design

This retrospective cohort study assessed the effects of acquiring a flash CGM vs. traditional CGM device within two large cohorts of T1D and T2D adults treated with short or rapid-acting insulin. In the first T1D/T2D cohort (Cohort 1), we evaluated event-free rates of acute diabetes-related events and all-cause hospitalizations. In the second T1D/T2D cohort (Cohort 2), we evaluated changes in glycated hemoglobin (HbA1c). Separate analyses were performed on T1D and T2D patients to compare the two CGM systems using propensity score matching to balance any differences in demographic and clinical characteristics.

Data sources

We used two IBM® databases for the analysis, MarketScan® Research Databases[13] (years 2017–2019) and Explorys® Electronic Health Records Database[14] (years 2017–2020). The MarketScan databases, used for the Cohort 1 analyses, contain individual-level, de-identified healthcare claims data for over 30 million privately insured (employer-sponsored employees and dependents) and Medicare Supplemental beneficiaries throughout the US. They contain detailed claims for paid outpatient services, inpatient admissions, and prescription drugs and supplies, including CGM devices, identified via National Drug Code (NDC) data. The Explorys Electronic Health Records Database, used for the Cohort 2 analyses, includes records for over 63 million people and draws from over 40 integrated delivery networks (IDNs), clinically integrated networks (CINs), and accountable care organizations (ACOs), with longitudinal data made available for an average of 3–4 years. Available data included demographic information, medical records, laboratory data, and pharmacy prescriptions. All data are de-identified by the vendor to protect patient privacy. Both databases contain information on diagnoses with International Classification of Diseases, 9th (ICD-9) and 10th (ICD-10) Revision codes, Systematized Nomenclature of Medicine – Clinical Terms (SNOMED-CT, US edition) (SNOMED) diagnosis codes in Explorys, and information on procedures with Current Procedural Terminology® (CPT) Fourth Edition codes, and Healthcare Common Procedure Coding System (HCPCS) codes. Basic demographic information is also provided, along with a person-level enrollment indicator, allowing for longitudinal patient follow-up. However, reasons for why a patient is no longer under observation, including switching employers, switching insurance, losing a job or death, are not provided in the databases.

Study population

Both cohorts included patients aged ≥ 18 years with a diagnosis of T1D or T2D treated with short- or rapid-acting insulin, who purchased (Cohort 1) or were prescribed (Cohort 2) a flash CGM system, FreeStyle Libre Flash Glucose Monitoring System and the FreeStyle Libre 14 day System (FSL) (Abbott Diabetes Care, Alameda, CA) or a traditional CGM system, Dexcom G5/G6 CGM system (DEX) (Dexcom, Inc., San Diego, CA) between October 2017 and September 2020. The index date for Cohort 1 was the date of CGM acquisition. The index date for Cohort 2 was the date of the patient's prescription for CGM.

Patients were excluded if they had less than 6 months of continuous health plan enrollment and prescription coverage prior to the index date, had a record of pre-index CGM acquisition prior to the study period or had gestational diabetes within 6 months prior to or on the index date. Additionally, for Cohort 2 inclusion, patients were required to have HbA1c data within 180 days prior to or including the index date and between 60–300 days after the index date, and a baseline HbA1c ≥ 7%.

To identify T2D patients with intensive insulin therapy, we further limited the T2D cohort to those with pharmacy claims (Cohort 1) or prescription (Cohort 2) of short- or rapid-acting insulin (excluding pre-mix preparations) in the 6 months prior to CGM device acquisition. Use of short- or rapid-acting insulin was considered an indicator of intensive insulin therapy. Patients using pre-mix insulin preparations were excluded because this therapy often involves less intensive therapy (e.g., insulin administered at the largest meal of the day).

ICD-9 and ICD-10 codes (Cohort 1 and 2) and SNOMED-CT codes (Cohort 2) were used to identify patients diagnosed with T1D (ICD-9 250.x1, 250.x3; ICD-10 E10.xx) and T2D (ICD-9 250.x0, 250.x2; ICD-10 E11.xx), and the presence of comorbidities. In the rare case the closest claim to the index date had billing codes related to both T1D and T2D, the patient was not included. National Drug Code (NDC) data (Cohort 1 and 2) and prescription description fields (Cohort 2) were used to identify patients who acquired a FSL or DEX CGM system through pharmacy channels. Patients who acquired their CGM through durable medical equipment (DME) suppliers were not included in this study since CGMs ordered through DME are coded using HCPCS codes, which do not differentiate the CGM brand. NDC data were also used to identify the type of insulin (short- or rapid-acting) acquired by T2D patients within the 6 months prior to CGM acquisition.

Outcome measures

Cohort 1: IBM MarketScan Research Databases, 2017-2019

The primary outcome measures for Cohort 1 were all-cause hospitalizations (ACHs) and acute diabetes-related events (ADEs) during the 6 months following CGM device acquisition. ACHs were defined as hospitalizations for any reason. ADEs were defined as acute hyperglycemia or hypoglycemia events. These included inpatient events with the associated ICD-10 code as the primary diagnosis code or emergency outpatient events, such as emergency department services, urgent care, or ambulance services with the associated ICD-10 code in any position. Acute hyperglycemic complications included severe hyperglycemia requiring clinician intervention (E10–11.65, E13.65), diabetic ketoacidosis (DKA) (E10.1x, E13.1x), and hyperosmolarity (E11.00, E13.0x). Acute hypoglycemic complications included severe hypoglycemia requiring clinician intervention (E16.1, E16.2, E10–11.649, E13.649), and hypoglycemic coma (E10–11.641, E13.641). Patients were followed post-index until the earliest of the following events: occurrence of a study outcome, end of health plan enrollment, or end of study period (6 months post-index).

Cohort 2: IBM MarketScan Research Databases, 2017-2019

The primary outcome for Cohort 2 was the difference between a patient's baseline HbA1c and post-CGM HbA1c. Baseline HbA1c was defined as the value within 180 days pre-index closest to CGM prescription date including the CGM prescription date. The post-CGM HbA1c was defined as the value closest to 180 days post-prescription and within 60–300 days after CGM prescription. Secondary analyses included change in HbA1c among participants with ≥ 8.0% HbA1c at baseline and percentage of participants who achieved < 7.0% HbA1c post-CGM.

Propensity score matching

Cohort 1

Patients were propensity score matched for demographics, clinical characteristics, and diabetes treatment measured during the baseline period (6 months pre-index/CGM acquisition). Propensity score matching is used to minimize bias when estimating treatment effects and reduce confounding when assessing non-randomized, observational data.[15] Demographics included age, gender, and residence in a Metropolitan Statistical Area (MSA) at the time of CGM purchase. MSAs are areas de-

lineated by the US Office of Management and Budget (OMB) as having at least one urbanized area with a minimum population of 50,000. Clinical characteristics included baseline comorbidities and presence of ACH. Diabetes treatment factors included presence of an insulin pump, an endocrinologist visit, nutrition consult/therapy or diabetes education, presence of a hypoglycemia event, and presence of a hyperglycemia event. NDC along with HCPCS II codes were used to identify pre-CGM insulin pump use. CPT and HCPCS II codes were used to identify pre-CGM nutrition consult/therapy and diabetes education. Baseline characteristics between FSL and DEX patients were compared with t-tests or chi-squared tests for independence as appropriate. Propensity score matching was performed using a multivariable logistic regression model to estimate the probability of acquiring a DEX versus FSL. Exact matching was implemented for baseline ACH, hypoglycemia, hyperglycemia, and insulin pump use. All other covariates were included in the propensity score model. FSL and DEX patients were matched without replacement on propensity scores using a greedy nearest-neighbor matching algorithm with 1:2 matching ratio for the T1D population and 1:5 matching ratio for the T2D population. After matching, balance between covariates was evaluated with t-tests, chi-squared tests, and standardized mean difference, where less than 0.10 was considered as achieving balance.

Cohort 2

Demographic and clinical covariates included age, gender, race, insurance type, body mass index (BMI), baseline HbA1c, exact time from baseline HbA1c measurement to index date, exact time from index date to 6-month HbA1c measurement, and comorbidities. Propensity score matching of the entire cohort was performed using a multivariable logistic regression model with all covariates to estimate the probability of a DEX versus FSL prescription. FSL and DEX patients were matched without replacement using a greedy nearest-neighbor matching algorithm with 1:2 matching ratio for both the T1D and T2D cohorts. Propensity score matching was also used among patients with ≥ 8.0% HbA1c at baseline for the secondary analysis.

Statistical analysis

Cohort 1

Statistical analyses were conducted separately for T1D and T2D populations. To compare ACH and ADE between matched FSL and DEX patients, the Kaplan-Meier method with log-rank test was used to obtain event curves and 6-month event-free rates for each outcome. Cox proportional hazard regression models were run to provide covariate-adjusted event-free rates. All the factors used for matching were also used as covariates. Further analyses were conducted with acute hyperglycemia and acute hypoglycemia as two separate outcomes. Sub-analyses were conducted by age, gender, insulin pump use, and record of an endocrinologist visit to assess device differences in ADE within subgroups. For sub-analyses, patient groups were not re-matched; results were adjusted for covariates in the regression models. RStudio version 1.4.1103 (Boston, MA, USA) with R version 4.0.3 was used for statistical analysis.

Cohort 2

Statistical analyses were conducted separately for T1D and T2D cohorts. Changes between the pre- and post-index HbA1c values within each CGM device group were evaluated with paired t-tests. In the fully matched group, the effect of CGM device type on the primary outcome (difference in pre- and post-index HbA1c) was then evaluated with a multivariable linear regression model. All the factors used for matching were also used as covariates in the model. RStudio version 1.3.1073 (Boston, MA, USA) with R version 4.0.3 was used for statistical analysis.

Results

Study population characteristics

Cohort 1

T1D population. A total of 4636 T1D adults (DEX, n = 1275; FSL, n = 3361) who met inclusion criteria were identified. Baseline differences between DEX vs. FSL patients were observed. FSL patients were older, more likely to live in a non-metropolitan area, and had higher proportions of comorbidities, while DEX patients were more likely to have a baseline hypoglycemia event and were more likely to see an endocrinologist, see a dietician or receive diabetes education, and have an insulin pump. After propensity score matching, all baseline covariates were balanced between DEX and FSL patients with standardized mean differences less than 0.10. The matched cohort consisted of 3564 T1D adults (n = 1188 DEX; n = 2376 FSL). Baseline characteristics of the unmatched and matched T1D cohort are presented in Table 1.

T2D population. A total of 6962 T2D adults (DEX, n = 707; FSL, n = 6255) who met inclusion criteria were identified. Similar baseline differences between DEX vs. FSL patients were also observed in the T2D cohort, including in demographics, hypoglycemia visits, comorbidities, specialist visits, and insulin pump use. After propensity score matching, all baseline covariates were balanced between DEX and FSL patients with standardized mean differences less than 0.10. The matched cohort consisted of 3930 T2D adults (DEX, n = 655; FSL, n = 3275). Baseline characteristics of the unmatched and matched T2D cohort are presented in Table 2.

Cohort 2

T1D population. A total of 896 T1D adults (DEX n = 116; FSL n = 780) who met inclusion criteria were identified. Baseline differences between DEX vs. FSL patients were observed, including in baseline HbA1c, demographics, and comorbidities. Patients prescribed FSL were more likely to be African American and to be insured through Medicaid and had increased comorbidities. After propensity score matching, all baseline covariates were balanced between DEX and FSL patients with all standardized mean differences less than 0.10. The matched cohort consisted of 348 T1D adults (DEX n = 116; FSL n = 232). Baseline characteristics of the unmatched and matched T1D population are presented in Table 3.

T2D population. A total of 3256 T2D adults (DEX n = 110; FSL n = 3146) who met inclusion criteria were identified. Baseline differences between DEX vs. FSL patients were observed, including in baseline HbA1c, demographics, and comorbidities. Similar differences noted in the T1D cohort were also observed in the T2D cohort. After propensity score matching, all baseline covariates were balanced between DEX and FSL patients with majority standardized mean differences less than 0.1 and all less than 0.2. The matched cohort consisted of 330 T2D (DEX n = 110; FSL n = 220). Baseline characteristics of the unmatched and matched T2D cohort are presented in Table 4.

Cohort 1: Post-CGM ACHs and ADEs

Matched T1D population

Both FSL and DEX patients experienced similar post-index event-free rates for all outcomes as illustrated in Fig. 1. The 6-month event-free rates for FSL vs DEX patients were 94.9% vs 95.4% for ACHs, respectively, (Fig. 1A) and 94.9% vs 94.8% for ADEs, respectively (Fig. 1B). The 6-month event-free rates for hyperglycemic events were 96.2% vs 96.1%, respectively, (Fig. 1C) and 98.4% vs. 98.5%, respectively, for hypoglycemic complications (Fig. 1D). Regression results showed no significant differences in any comparison, with all p-values >0.25.

The figure shows 6-month event-free rates of ACHs (A), ADEs (B), acute hyperglycemic events (C) and acute hypoglycemia events (D) after

Table 1
Cohort 1: T1D Population. IBM MarketScan Research Databases, 2017-2019.

	UNMATCHED			PROPENSITY SCORE MATCHED		
	DEX(N = 1275)	FSL(N = 3361)	P-value	DEX(N = 1188)	FSL(N = 2376)	P-value
Gender, n Male (%)	669 (52.5)	1829 (54.4)	0.248	631 (53.1)	1257 (52.9)	0.934
Age, yrs, mean (SD)	38.3 ± 13.4	41.7 ± 14.3	< 0.001	38.4 (13.5)	39.2 (13.7)	0.090
Outside MSA, n (%)	120 (9.4)	395 (11.8)	0.027	115 (9.7)	249 (10.5)	0.494
Hypoglycemia, n (%)	36 (2.8)	60 (1.8)	0.036	23 (1.9)	46 (1.9)	1.000
Hyperglycemia, n (%)	93 (7.3)	227 (6.8)	0.560	81 (6.8)	162 (6.8)	1.000
Presence of an ADE, n (%)	125 (9.8)	278 (8.3)	0.111	103 (8.7)	206 (8.7)	1.000
Presence of an ACH, n (%)	101 (7.9)	281 (8.4)	0.670	88 (7.4)	176 (7.4)	1.000
Comorbidities, n (%)						
Anemia	59 (4.6)	202 (6.0)	0.080	54 (4.5)	104 (4.4)	0.886
Coronary Artery Disease	36 (2.8)	162 (4.8)	0.003	36 (3.0)	71 (3.0)	1.000
Depression	102 (8.0)	285 (8.5)	0.640	90 (7.6)	199 (8.4)	0.448
Heart Failure	17 (1.3)	48 (1.4)	0.916	16 (1.3)	25 (1.1)	0.541
Hypertension	347 (27.2)	1081 (32.2)	0.001	321 (27.0)	665 (28.0)	0.569
Hypothyroid Disease	217 (17.0)	620 (18.4)	0.278	207 (17.4)	422 (17.8)	0.840
Lipid Disorder	415 (32.5)	1264 (37.6)	0.002	389 (32.7)	800 (33.7)	0.607
Liver Disease	20 (1.6)	75 (2.2)	0.191	18 (1.5)	40 (1.7)	0.815
Myocardial Infarction	9 (0.7)	34 (1.0)	0.425	9 (0.8)	15 (0.6)	0.828
Neuropathy	133 (10.4)	471 (14)	0.001	123 (10.4)	254 (10.7)	0.802
Obesity	134 (10.5)	419 (12.5)	0.074	121 (10.2)	258 (10.9)	0.577
Peripheral Vascular Disease	16 (1.3)	70 (2.1)	0.081	16 (1.3)	27 (1.1)	0.704
Pulmonary Disease	54 (4.2)	151 (4.5)	0.764	48 (4.0)	94 (4.0)	0.976
Renal Disease	42 (3.3)	140 (4.2)	0.201	39 (3.3)	70 (2.9)	0.655
Retinopathy	83 (6.5)	235 (7)	0.607	76 (6.4)	167 (7.0)	0.526
Endocrinologist, n (%)	794 (62.3)	1803 (53.6)	<0.001	742 (62.5)	1416 (59.6)	0.107
Dietician, nutrition therapy, diabetes education, n (%)	208 (16.3)	281 (8.4)	<0.001	131 (11.0)	262 (11.0)	1.000
Insulin Pump, n (%)	265 (20.8)	488 (14.5)	<0.001	232 (19.5)	464 (19.5)	1.000

Table 2
Cohort 1: T2D participants. IBM MarketScan Research Databases, 2017-2019.

	UNMATCHED			PROPENSITY SCORE MATCHED		
	DEX(N = 707)	FSL(N = 6255)	P-value	DEX(N = 655)	FSL(N = 3275)	P-value
Gender, n Male (%)	348 (49.2)	3276 (52.4)	0.121	326 (49.8)	1648 (50.3)	0.831
Age, yrs, mean (SD)	51.7 ± 10.0	53.7 ± 9.7	<0.001	51.9 (9.7)	52.2 (10.0)	0.495
Outside MSA, n (%)	90 (12.7)	710 (11.4)	0.304	82 (12.5)	402 (12.3)	0.914
Hypoglycemia, n (%)	18 (2.5)	66 (1.1)	0.001	10 (1.5)	50 (1.5)	1.000
Hyperglycemia, n (%)	58 (8.2)	456 (7.3)	0.421	44 (6.7)	220 (6.7)	1.000
Presence of an ADE, n (%)	73 (10.3)	506 (8.1)	0.049	53 (8.1)	265 (8.1)	1.000
Presence of an ACH, n (%)	101 (14.3)	975 (15.6)	0.394	94 (14.4)	470 (14.4)	1.000
Comorbidities, n (%)						
Anemia	84 (11.9)	823 (13.2)	0.370	77 (11.8)	367 (11.2)	0.735
Coronary Artery Disease	104 (14.7)	961 (15.4)	0.687	96 (14.7)	487 (14.9)	0.936
Depression	89 (12.6)	789 (12.6)	1.000	81 (12.4)	418 (12.8)	0.830
Heart Failure	27 (3.8)	422 (6.7)	0.003	26 (4.0)	147 (4.5)	0.626
Hypertension	488 (69.0)	4565 (73.0)	0.028	453 (69.2)	2274 (69.4)	0.926
Hypothyroid Disease	134 (19.0)	991 (15.8)	0.038	119 (18.2)	579 (17.7)	0.808
Lipid Disorder	458 (64.8)	4146 (66.3)	0.448	423 (64.6)	2151 (65.7)	0.620
Liver Disease	60 (8.5)	497 (7.9)	0.668	57 (8.7)	278 (8.5)	0.919
Myocardial Infarction	19 (2.7)	206 (3.3)	0.452	17 (2.6)	82 (2.5)	1.000
Neuropathy	196 (27.7)	1956 (31.3)	0.058	180 (27.5)	944 (28.8)	0.517
Obesity	233 (33.0)	2295 (36.7)	0.055	212 (32.4)	1112 (34.0)	0.460
Peripheral Vascular Disease	41 (5.8)	424 (6.8)	0.363	39 (6.0)	201 (6.1)	0.929
Pulmonary Disease	66 (9.3)	693 (11.1)	0.178	62 (9.5)	313 (9.6)	1.000
Renal Disease	69 (9.8)	844 (13.5)	0.006	68 (10.4)	345 (10.5)	0.963
Retinopathy	51 (7.2)	401 (6.4)	0.459	43 (6.6)	225 (6.9)	0.843
Endocrinologist, n (%)	399 (56.4)	3211 (51.3)	0.011	368 (56.2)	1842 (56.2)	1.000
Dietician, nutrition therapy, diabetes education, n (%)	111 (15.7)	614 (9.8)	<0.001	104 (15.9)	481 (14.7)	0.471
Insulin pump, n (%)	105 (14.9)	307 (4.9)	<0.001	59 (9.0)	295 (9.0)	1.000

a DEX (dotted red line) or FSL (solid blue line) acquisition in the T1D cohort. ADE consists of acute hyperglycemic and acute hypoglycemic events. Hyperglycemic events consist of hyperglycemia, hyperosmolarity, and ketoacidosis. Hypoglycemic events consist of hypoglycemia and hypoglycemic coma. Both event types included ambulance, urgent care, emergency room visits, and inpatient hospitalizations. Survival rates were obtained using the Kaplan-Meier method with Cox proportional hazard regression models to adjust event-free rates for covariates listed in Table 1.

Matched T2D participants

Both FSL and DEX patients experienced similar post-index event-free rates for all outcomes as illustrated in Fig. 2. The 6-month event-free event rates for FSL vs DEX patients were 90.6% vs 90.4%, respectively, for ACHs (Fig. 2A) and 96.7% vs 96.4%, respectively, for ADEs (Fig. 2B). The 6-month event-free rates for hyperglycemic events were 97.2% vs 97.4%, respectively, (Fig. 2C) and 99.0% vs 99.4%, respectively, for hypoglycemic complications (Fig. 2D). Regression results showed no significant differences in any comparison, with all p-values >0.25.

Table 3
Cohort 2: T1D Population. IBM MarketScan Research Databases, 2017-2019.

	UNMATCHED			PROPENSITY SCORE MATCHED		
	DEX(N = 116)	FSL(N = 780)	P-value	DEX(N = 116)	FSL(N = 232)	P-value
HbA1c,%, mean (SD)	8.53 (1.33)	9.21 (1.75)	<0.001	8.53 (1.33)	8.59 (1.45)	0.668
Gender, n Male (%)	64 (55.2)	391 (50.1)	0.361	64 (55.2)	132 (56.9)	0.848
Age, yrs, mean (SD)	44.0 (15.9)	46.1 ± 16.5	0.201	44.0 (15.9)	43.4 (16.5)	0.741
BMI, kg/m^2, mean (SD)	28.3 (6.0)	28.7 (6.1)	0.564	28.3 (6.0)	28.2 (5.6)	0.925
Race, n (%)						
African American	<11	119 (15.3)	0.023	<11	16 (7.0)	1.000
Caucasian	102 (87.9)	639 (81.9)	0.143	102 (87.9)	206 (88.8)	0.953
Other	<11	22 (2.8)	0.284	<11	<11	0.928
Insurance Type, n (%)						
Medicaid	<11	73 (9.4)	0.010	<11	<11	1.000
Medicare	18 (15.5)	99 (12.7)	0.487	18 (15.5)	32 (13.8)	0.787
Private	57 (49.1)	360 (46.2)	0.616	57 (49.1)	109 (47.0)	0.791
Self Pay	<11	59 (7.6)	0.462	<11	11 (4.7)	1.000
Other	33 (28.4)	189 (24.2)	0.386	33 (28.4)	76 (32.8)	0.487
Comorbidities, n (%)						
Anemia	18 (15.5)	194 (24.9)	0.036	18 (15.5)	28 (12.1)	0.467
Coronary Artery Disease	13 (11.2)	142 (18.2)	0.084	13 (11.2)	25 (10.8)	1.000
Depression	39 (33.6)	277 (35.5)	0.769	39 (33.6)	74 (31.9)	0.84
Heart Failure	<11	79 (10.1)	0.353	<11	11 (4.7)	0.559
Hypertension	61 (52.6)	449 (57.6)	0.363	61 (52.6)	123 (53.0)	1.000
Hypothyroid Disease	37 (31.9)	259 (33.2)	0.862	37 (31.9)	75 (32.3)	1.000
Lipid Disorder	67 (57.8)	530 (67.9)	0.039	67 (57.8)	134 (57.8)	1.000
Liver Disease	<11	75 (9.6)	0.167	<11	12 (5.2)	1.000
Myocardial Infarction	<11	68 (8.7)	0.078	<11	<11	1.000
Neuropathy	44 (37.9)	357 (45.8)	0.138	44 (37.9)	82 (35.3)	0.723
Obesity	38 (32.8)	305 (39.1)	0.227	38 (32.9)	80 (34.5)	0.841
Peripheral Vascular Disease	<11	115 (14.7)	0.059	<11	17 (7.3)	1.000
Pulmonary Disease	24 (20.7)	219 (28.1)	0.119	24 (20.7)	51 (22.0)	0.89
Renal Disease	14 (12.1)	140 (17.9)	0.152	14 (12.1)	24 (10.3)	0.761
Retinopathy	29 (25.0)	239 (30.6)	0.259	29 (25.0)	62 (26.7)	0.829

Table 4
Cohort 2: T2D population. IBM MarketScan Research Databases, 2017-2019.

	UNMATCHED			PROPENSITY SCORE MATCHED		
	DEX(N = 110)	FSL(N = 3146)	P-value	DEX(N = 110)	FSL(N = 220)	P-value
HbA1c,%, mean (SD)	8.95 (1.66)	9.35 (1.89)	0.026	8.95 (1.66)	9.11 (1.81)	0.441
Gender, n Male (%)	63 (57.3)	1484 (47.2)	0.047	63 (57.3)	111 (50.5)	0.293
Age, yrs, mean (SD)	59.8 (13.8)	60.3 (12.2)	0.696	59.8 (13.8)	59.5 (12.0)	0.837
BMI, kg/m^2, mean (SD)	33.7 (6.6)	35.1 (7.3)	0.061	33.7 (6.6)	34.0 (6.8)	0.729
Race, n (%)						
African American	16 (14.5)	832 (26.4)	0.007	16 (14.5)	38 (17.3)	0.636
Caucasian	90 (81.8)	2155 (68.5)	0.004	90 (81.8)	177 (80.5)	0.882
Other	<11	159 (5.1)	0.654	<11	<11	0.72
Insurance Type, n (%)						
Medicaid	<11	333 (10.6)	0.028	<11	<11	1.000
Medicare	32 (29.1)	824 (26.2)	0.57	32 (29.1)	57 (25.9)	0.63
Private	46 (41.8)	1111 (35.3)	0.194	46 (41.8)	97 (44.1)	0.783
Self Pay	<11	283 (9.0)	0.148	<11	12 (5.5)	0.93
Other	23 (20.9)	595 (18.9)	0.688	23 (20.9)	47 (21.4)	1.000
Comorbidities, n (%)						
Anemia	39 (35.5)	1328 (42.2)	0.189	39 (35.5)	75 (34.1)	0.902
Coronary Artery Disease	37 (33.6)	1254 (39.9)	0.225	37 (33.6)	66 (30.0)	0.585
Depression	37 (33.6)	1548 (49.2)	0.002	37 (33.6)	64 (29.1)	0.473
Heart Failure	17 (15.5)	777 (24.7)	0.035	17 (15.5)	32 (14.5)	0.956
Hypertension	99 (90.0)	2933 (93.2)	0.261	99 (90.0)	195 (88.6)	0.851
Hypothyroid Disease	30 (27.3)	958 (30.5)	0.544	30 (27.3)	73 (33.2)	0.334
Lipid Disorder	98 (89.1)	2959 (94.1)	0.053	98 (89.1)	192 (87.3)	0.766
Liver Disease	20 (18.2)	797 (25.3)	0.112	20 (18.2)	37 (16.8)	0.877
Myocardial Infarction	14 (12.7)	512 (16.3)	0.389	14 (12.7)	23 (10.5)	0.666
Neuropathy	59 (53.6)	2133 (67.8)	0.003	59 (53.6)	108 (49.1)	0.508
Obesity	72 (65.5)	2420 (76.9)	0.007	72 (65.5)	135 (61.4)	0.546
Peripheral Vascular Disease	22 (20.0)	973 (30.9)	0.019	22 (20.0)	38 (17.3)	0.65
Pulmonary Disease	39 (35.5)	1577 (50.1)	0.003	39 (35.5)	83 (37.7)	0.778
Renal Disease	38 (34.5)	1089 (34.6)	1.000	38 (34.5)	62 (28.2)	0.29
Retinopathy	30 (27.3)	1092 (34.7)	0.131	30 (27.3)	44 (20.0)	0.176

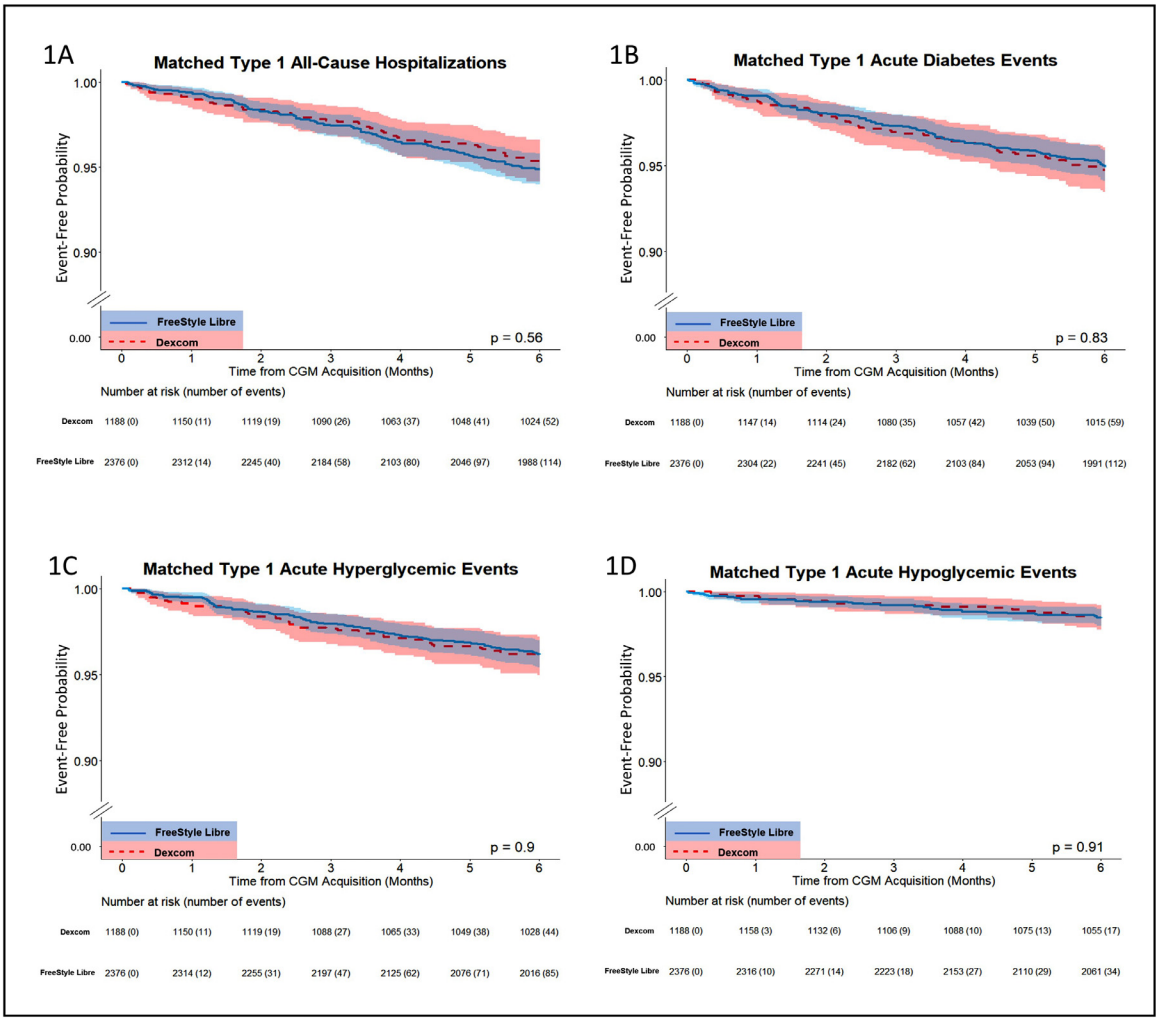

Fig. 1. Differences in post-index ACHs, ADEs, hyperglycemic events and hypoglycemic events: T1D.

The figure shows 6-month event-free rates of ACHs (A), ADEs (B), acute hyperglycemic events (C) and acute hypoglycemia events (D) after a DEX (dotted red line) or FSL (solid blue line) acquisition in the T2D cohort. ADE consists of acute hyperglycemic and acute hypoglycemic events. Hyperglycemic events consist of hyperglycemia, hyperosmolarity, and ketoacidosis. Hypoglycemic events consist of hypoglycemia and hypoglycemic coma. Both event types included ambulance, urgent care, emergency room visits, and inpatient hospitalizations. Survival rates were obtained using the Kaplan-Meier method with Cox proportional hazard regression models to adjust rates for covariates listed in Table 2.

Sub-analyses by age, gender, endocrinologist provider and insulin pump use showed no between-group differences in ADE-event free rates in either the matched T1D or T2D subgroups. (Table 5) No between-group differences were observed in events per patient per year in ACHs, ADEs, acute hyperglycemic events or hypoglycemic events. (**Supplementary Table 1**)

The table shows the event-free rates of acute diabetes-related events (ADE) 6 months after acquisition of a FSL or DEX in the T1D and T2D cohorts by gender, age, endocrinologist provider, and insulin pump use. Survival rates and p-values were obtained using the Kaplan-Meier method with Cox proportional hazard regression models to adjust for covariates listed in Tables 1 and 2.

Cohort 2: change in HbA1c

Matched T1D Population

Paired t-tests indicated significant reductions in HbA1c within both FSL (−0.37%, $p < 0.001$) and DEX (−0.35%, $p < 0.001$) groups (Fig. 3A). Multivariable regression results indicated there were no significant differences between FSL and DEX in the amount of reduction (−0.0001% [95% confidence interval −0.27, 0.27]; $p = 0.99$). Similar patterns were seen in the secondary analysis of patients with baseline HbA1c ≥8.0% (Fig. 3B), and the reductions were notably greater within both FSL (−0.66, $p < 0.001$) and DEX (−0.62, $p < 0.001$) groups. Multivariable regression results for the secondary analysis also indicated no significant differences in the amount of reduction (−0.013% [95% confidence interval −0.42, 0.39]; $p = 0.94$) between FSL and DEX patients. The percentages of DEX and FSL users with baseline HbA1c ≥ 7.0% who achieved < 7.0% at six months post-index were identical, 13.8% ($n = 16$) and 13.8% ($n = 32$), respectively, $p = 1.000$.

The figure shows the average reduction in HbA1c after a DEX or FSL prescription in the main T1D patient population (1A), and in patients with baseline HbA1c ≥ 8% (1B). Each of the reductions shown are an average of the per-patient reduction in HbA1c. The differences in HbA1c reduction between DEX and FSL are shown as the difference in difference (DID) estimates, 95% confidence intervals, and p-values from the multivariable linear regression models.

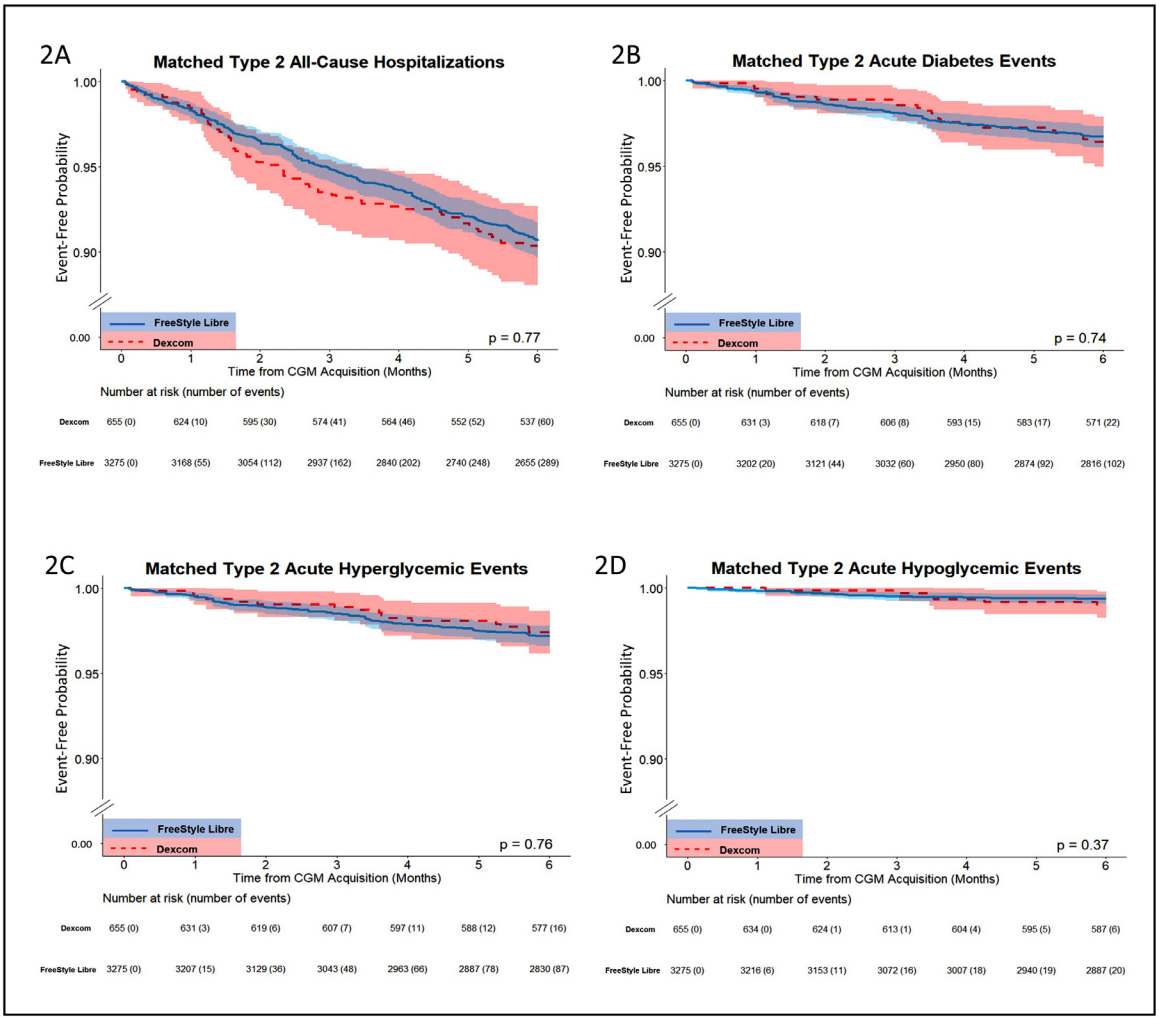

Fig. 2. Differences in post-index ACHs, ADEs, hyperglycemic events and hypoglycemic events: T2D.

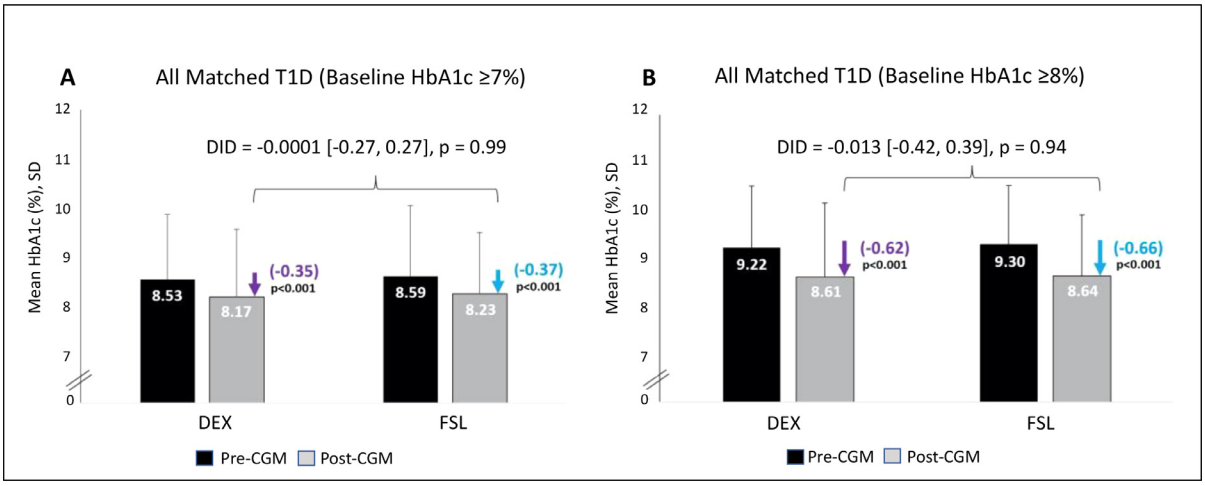

Fig. 3. Change in HbA1c in all matched T1D and by Baseline ≥ 8.0%.

Table 5
6-Month ADE-free within the matched T1D and T2D Populations.

	FSL		DEX		
	N (%)	6-month ADE-Free	N (%)	6-month ADE-Free	p-value
T1D	*N* = 2376		*N* = 1188		
Gender					
Male	1257 (53)	96.1%	631 (53)	95.5%	0.53
Female	1119 (47)	93.6%	557 (47)	94.0%	0.81
Age					
18–39	1282 (54)	93.5%	662 (56)	93.5%	0.92
40+	1094 (46)	96.5%	526 (44)	96.4%	0.90
Endocrinologist					
Has endocrinologist	1416 (60)	94.6%	742 (62)	94.1%	0.65
No endocrinologist	960 (40)	95.3%	446 (38)	95.8%	0.75
Insulin Pump					
Has insulin pump	464 (20)	95.1%	232 (20)	97.3%	0.21
No insulin pump	1912 (80)	94.9%	956 (80)	94.2%	0.43
T2D	*N* = 3275		*N* = 655		
Gender					
Male	1648 (50)	97.2%	326 (50)	96.3%	0.46
Female	1627 (50)	96.2%	329 (50)	96.4%	0.83
Age					
18–49	1249 (38)	95.5%	250 (38)	96.6%	0.42
50+	2026 (62)	97.5%	405 (62)	96.3%	0.21
Endocrinologist					
Has endocrinologist	1842 (56)	96.8%	368 (56)	96.6%	0.85
No endocrinologist	1433 (44)	96.6%	287 (44)	96.2%	0.77
Insulin Pump					
Has insulin pump	295 (9)	96.1%	59 (9)	96.4%	0.90
No insulin pump	2980 (91)	96.8%	596 (91)	96.4%	0.69

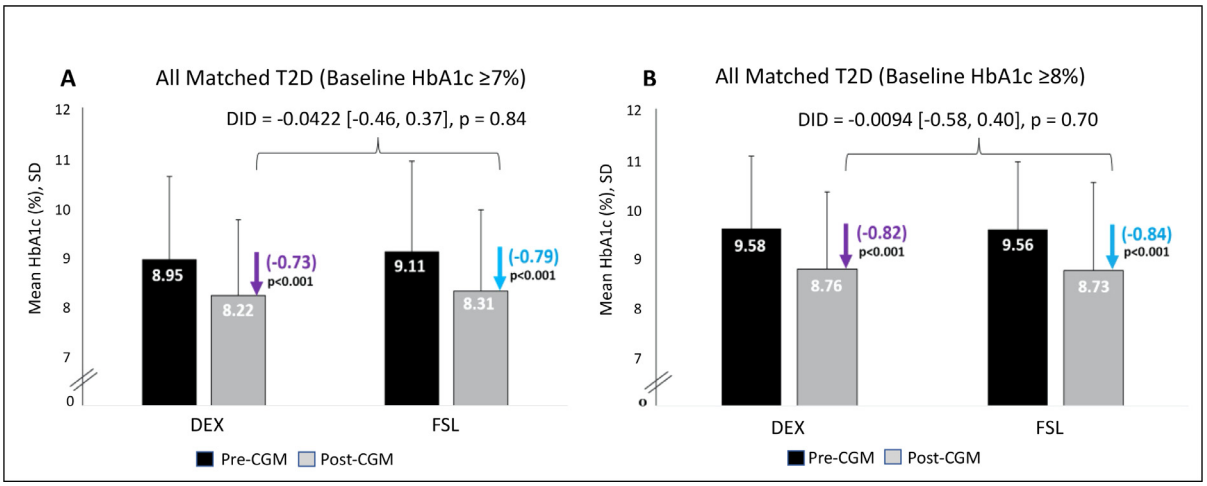

Fig. 4. Change in HbA1c in all matched T2D and by baseline ≥ 8.0%. .

Matched T2D Population

Paired t-tests indicated significant reductions in HbA1c within both FSL (−0.79%, $p < 0.001$) and DEX (−0.73%, $p < 0.001$) user groups (Fig. 4A). Multivariable regression results indicated there were no significant differences between FSL and DEX in the amount of reduction (−0.0422% [95% confidence interval −0.46, 0.37]; $p = 0.84$). Similar patterns were seen in the secondary analysis of patients with baseline HbA1c ≥8.0% (Fig. 4B), and the reductions were greater within both FSL (−0.84%, $p < 0.001$) and DEX (−0.82%, $p < 0.001$) users. Multivariable regression results for the secondary analysis also indicated no significant differences in the amount of reduction (−0.094% [95% confidence interval −0.58, 0.40]; $p = 0.70$) between FSL and DEX patients. The percentages of DEX and FSL users with baseline HbA1c ≥ 7.0% who achieved <7.0% at six months post-index were similar, 18.2% ($n = 20$) and 18.6% ($n = 41$), respectively, $p = 1.000$.

The figure shows the average reduction in HbA1c after a DEX or FSL prescription in the main T2D patient population (2A), and in patients with baseline HbA1c ≥ 8% (2B). Each of the reductions shown are an average of the per-patient reduction in HbA1c. The differences in HbA1c reduction between DEX and FSL are shown as the difference in difference (DID) estimates, 95% confidence intervals, and p-values from the multivariable linear regression models.

Discussion

To our knowledge, this is the first study to compare the relative efficacy of flash CGM vs. traditional CGM acquisition on diabetes-related events, all-cause hospitalizations and HbA1c in two large US populations of individuals with T1D and T2D treated with intensive insulin therapy. Results from our analyses showed similar event-free rates (ADE

and ACH) for both FreeStyle Libre and Dexcom systems following acquisition. Reductions in HbA1c were also similar between systems.

Previous prospective, observational cohort studies have demonstrated clinical benefit of both flash CGM and traditional CGM devices. In a recent study of 1913 T1D adults who used the FSL device, hospital admissions for severe hypoglycemia and/or DKA decreased 33.3%, from 3.2% to 2.2%, $p = 0.031$, with significantly fewer participants who reported severe hypoglycemic events (from 14.6% to 7.8%, $p < 0.0001$) or hypoglycemic coma (from 2.7% to 1.1%, $p = 0.001$) at 12 months.[6] More recently, Bergenstal et al. reported significant reductions in other important clinical outcomes, such as rates of acute diabetes-related events (ADEs) and all-cause hospitalizations in the six months following acquisition of an FSL device.[16]

Additionally, similar HbA1c reductions were observed in a cohort of 1365 individuals with diabetes (77% T1D, 16% T2D, 7% other) with baseline HbA1c ≥8.5% who used the FSL device.[10] Given the importance of lower HbA1c for long-term diabetes complication reduction, our findings show a clear clinical benefit of CGM use in individuals with T1D and T2D treated with intensive insulin regimens. While prior studies demonstrated improvements in clinical outcomes within flash CGM and traditional CGM patient cohorts, evidence on the association between CGM type and clinical outcomes is lacking, although relevant for clinical decision-making.

One interesting aspect of our findings was the difference in the baseline demographic characteristics in the unmatched Cohort 1 (Tables 1 and 2) regarding where patients were receiving their care and their utilization of other healthcare services. In general, FSL users were older, had more comorbidities, and received less specialty care. This was particularly notable in the unmatched T1D cohorts in which a significantly larger proportion of the DEX vs. FSL cohorts was under an endocrinologist's care (62.3% vs. 53.6%, $p < 0.001$, respectively) and had received nutritional counseling and/or diabetes education (16.3% vs. 8.4%, $p < 0.001$, respectively). Likewise, in both T1D and T2D cohorts, fewer FSL users utilized an insulin pump. The driving factors behind these differences and specific reasons for selecting one CGM over another cannot be construed from the data. Given the equally low acute diabetes events and all-cause hospitalizations experienced by patients using both systems, our findings suggest clinicians should consider placing more emphasis on helping patients select the CGM device that best meets their individual needs and preferences including affordability, interoperability with insulin pumps, ease of use, and system features.

Differences within the unmatched Cohort 2 (Tables 3 and 4) were also notable. Compared with DEX, FSL T2D patients were more likely to be female, African American, on Medicaid, and have comorbidities such as depression, heart failure, neuropathy, or pulmonary disease. Baseline HbA1c and age also tended to be higher in those prescribed FSL. The FSL T1D patient population was also more likely to be African American, on Medicaid, have elevated HbA1c, anemia, and lipid disorder compared to DEX patients. These characteristics suggest that patients using FSL in general were more diverse racially and socioeconomically and included those with more comorbidities compared with DEX users.

This study has several strengths, including the use of large and recent population-based data sources with wide geographical coverage across the U.S. These data allowed us to identify the specific type of CGM patients acquired and compare clinical outcomes over time. To our knowledge, this is the first study to conduct such a comparison with real-world data. Another strength is use of a propensity score matched study design to account for relevant confounders. Propensity score matching is a widely accepted and utilized method in observational studies for building treatment and control groups with exchangeability, or similar characteristics.

This study also has limitations that should be considered. Data limitations for Cohort 1 included lack of certain demographic and clinical information, such as race/ethnicity, direct socioeconomic status, education, and glycemic status (e.g. baseline HbA1c). Due to data limitations, only patients who acquired a FSL or DEX CGM system through pharmacy channels were included in the study. Patients who acquired their CGM through DME suppliers were not included since CGMs ordered through DME are coded using HCPCS codes, which do not differentiate the CGM brand. Moreover, the datasets provided no information about the frequency and severity of severe hypoglycemia and hyperglycemia. Nor do we know the status of glycemic control (e.g., percentage of time in range [%TIR], glycemic variability) within Cohort 1. However, the low rates for ACH and ADE may be associated with improvements in HbA1c observed in Cohort 2. Additionally, we could not discern whether medications (insulin or noninsulin treatment) were optimized. Additional studies are needed to determine generalizability to the Medicaid and broader Medicare population. Because Cohort 1 did not include Medicaid beneficiaries, our findings are not generalizable to Medicaid beneficiaries, a population that often has a higher rate of severe complications and often limited access to CGM and other diabetes management technologies.[20] Our study used propensity score matching to balance the cohorts; however, there may be factors that cannot be captured in insurance claims or electronic health records that could be important to match upon; these could include specific reasons for choosing one device over another. Although MarketScan claims are fully paid and adjudicated, miscoding (either intentional or unintentional (e.g. documenting the wrong diagnosis)) could have occurred in some instances.

Conclusions

This study found that at a population level, T1D and T2D patients experienced similar rates of acute diabetes events, all-cause hospitalizations, and HbA1c reductions after obtaining either a flash CGM (FreeStyle Libre) or a traditional CGM (Dexcom). These results may provide valuable guidance to clinicians when collaborating with patients to develop personalized treatment regimens. Given comparable outcomes between both devices, patient affordability, ease of use, and system features should be considered when selecting which CGM is most appropriate.

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Disclosures

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Eden Miller: Writing – original draft, Writing – review & editing. **Gregory J. Roberts:** Data curation, Formal analysis, Validation, Writing – review & editing. **Jennifer M. Joseph:** Data curation, Formal analysis, Validation, Writing – original draft, Writing – review & editing. **Yelena Nabutovsky:** Data curation, Formal analysis, Validation, Writing – original draft, Writing – review & editing. **Ignacio J. Reyes:** Data curation, Formal analysis, Validation, Writing – review & editing. **Diana Souto:**

Writing – original draft, Writing – review & editing. **Naunihal Virdi:** Writing – original draft, Writing – review & editing. **Irl B. Hirsch:** Writing – original draft, Writing – review & editing.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ajmo.2022.100008.

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