HEALTH AND MEDICINE

Understanding temporal changes and seasonal variations in glycemic trends using wearable data

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Seasonal variations in glycemic trends remain largely unstudied despite the growing prevalence of diabetes. To address this gap, our objective is to investigate temporal changes in glycemic trends by analyzing intensively sampled blood glucose data from 137 patients (ages 2 to 76, primarily type 1 diabetes) over the course of 9 months to 4.5 years. From over 91,000 days of continuous glucose monitor data, we found that glycemic control decreases significantly around the holidays, with the largest decline observed on New Year's Day among the patients with already poor glycemic control (i.e., <55% time in the target range). We also observed seasonal variations in glycemic trends, with patients having worse glycemic control in the months of November to February (i.e., mid-fall and winter, in the United States), and better control in the months of April to August (i.e., mid-spring and summer). These insights are critical to inform targeted interventions that can improve diabetes outcomes.



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INTRODUCTION

Diabetes is one of the most prevalent chronic conditions that affects 37.3 million people (\sim 11.3%) in the United States and more than 536 million people (\sim 10.5%) globally (1, 2). In addition, it is projected that the prevalence of diabetes will increase significantly in the coming decades (3). Yet, only a minority of people with diabetes achieve the recommended targets for glycemic control (4–6). According to a recent study, there will be alterations to the disease profile in various regions of the world due to increasing cases of diabetes and diabetes-related complications, such as neuropathy, retinopathy, kidney failure, and cardiovascular disease (7). Given the growing diabetes pandemic, there is an urgent need for greater understanding of the disease and variations in outcomes to develop tailored interventions that can change the status quo.

Recognizing the transforming role that wearable devices have played in various health domains makes a case for improving the use of such data in the diabetes domain (8-13). Clinical-grade wearable devices, like continuous glucose monitors (CGMs), provide a unique window into understanding how diabetes management varies in outpatient settings (14, 15). However, research shows that patient-generated data from CGMs is significantly underutilized (16, 17). For example, the clinical standard involves reviewing only about 2 weeks of prior CGM data to assess glycemic control (14, 15). In addition, only a minority of patients (<30%) revisit their CGM data regularly to learn from it and inform their treatment strategy (6, 18). Hence, there are still many unanswered questions about diabetes and glycemic trends despite advances in digital and wearable technology in this field. One important question that remains unknown relates to the influence of seasons, holidays, and changes in behavior during the days, weeks, months, and year, on glycemic trends.

On the basis of prior research, it is well known that there are seasonal variations in lifestyle behaviors and eating patterns that contribute to weight gain around the holiday seasons, for example (19–

23). However, seasonal variations in glycemic trends have not yet been studied, despite direct associations between food intake, lifestyle behaviors, and diabetes outcomes. To bridge this gap, our research leverages over 91,000 days of CGM data from 137 patients with diabetes, primarily type 1 diabetes, to investigate how glycemic trends vary across holidays, seasons, days/weeks, and subgroups of the population. We hope that insights from this study can be useful to develop targeted interventions that pinpoint the most vulnerable times for poor glycemic control to improve both short- and long-term diabetes outcomes.

RESULTS

Data overview

This study leverages retrospective and objective data from clinically validated CGMs used for daily management of diabetes to study glycemic trends and elicit seasonal variations in management. Figure 1 provides an overview of our dataset, which includes a total of 91,441 days of CGM [i.e., blood glucose (BG)] data from 137 subjects, primarily with type 1 diabetes. Subjects were recruited remotely from various geographical locations in the United States (fig. S1), and the dataset includes two independent cohorts that span various age groups, years with diabetes, and levels of glycemic control (see Fig. 1, B to D, and Table 1). Cohort 1 was recruited through an opt-in data sharing process under the Tidepool Big Data Donation Project (24). This cohort is composed of 100 subjects (ages 2 to 76, diabetes duration of 0 to 60 years) who use sensor-augmented insulin pump therapy for daily management (25). Meanwhile, cohort 2 was recruited through online sources under the SweetGoals project (26). This cohort is composed of 37 subjects (ages 19 to 29, diabetes duration of 2 to 27 years) who use varying forms of insulin therapy for daily management. All subjects had a minimum of 9 months of CGM data with at least 70% of readings present during the data collection period. Cohort 1 includes an average of 501 days (i.e., 1 year and 4 months) of CGM data per subject, while cohort 2 includes an average of 960 days (i.e., 2 years and 7 months) of CGM data per subject (Fig. 1E).

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A

Continuous

В

0 to 18 years

19 to 34 years

C

Male

== Female

35 to 50 years

51 to 76 years

Fig. 1. Data overview. (A) Wearable medical device, CGM, used for daily management of diabetes. (B to E) Demographics of subjects (n = 137) and data summary per subject. (F) Example of glycemic trends and blood glucose (BG) variations over 1 week. (G) Distribution of clinically validated metrics for assessing CGM data.

Given that BG is affected by over 40 factors in daily living, such as food, medication, activity, sleep, stress, illness, and outside temperature, it is expected that glycemic trends can be highly variable for a person with diabetes (27-29). Figure 1F shows an example of BG variations for one subject during week 27 of year 2018 (i.e., 2 to 8 July). Note that, when the BG is greater than 180 mg/dl, that represents high BG or hyperglycemia, and when the BG is less than 70 mg/dl, that represents low BG or hypoglycemia (14, 15). The primary objective of a person with diabetes is to maintain BG levels in the target range of 70 to 180 mg/dl (14, 15). In this study, we quantified glycemic trends using clinically validated metrics for assessing diabetes management, including time in range (TIR), mean BG, and glycemic variability (GV) (14). Each metric is calculated daily (i.e., over a 24-hour period) for each

subject, and Fig. 1G shows the distribution of each metric (mean TIR = 59%, mean BG = 168 mg/dl, and mean GV = 31%) across all subjects. This figure also shows that subjects in cohort 2 had generally worse glycemic control with a low mean TIR per day of 48% [clinical target > 70% (14)] and high mean BG per day of 189 mg/dl. In contrast, more subjects in cohort 1 had better glycemic control with a mean TIR of 68% and mean BG of 153 mg/dl.

D

Glycemic control

Moderate (TIR: 55 to 70%)

Good (TIR: >70%)

Not reported

Effect of holidays on glycemic trends

Several studies in literature have observed changes in lifestyle and eating behaviors that contribute to weight gain during the holidays (19-23). However, the effect of holidays on glycemic trends and diabetes management outcomes is yet to be studied at scale (30). Building on the availability of objective data from clinically

Table 1. Overview of our dataset comprising two independent cohorts (n = 137 subjects) with a total of 91,441 days of CGM data. T1D and T2D means type 1 diabetes and type 2 diabetes, respectively, while NR means not reported.

	Cohort 1 Mean ± SD	Cohort 2 Mean ± SD	Total	
			Mean ± SD	Range
# Subjects	100	37	137	
Age	34 ± 21	23 ± 3	32 ± 19	2–76
Male/ female/NR	23/13/64	6/31/0	29/44/64	
T1D/ T2D/NR	41/0/59	37/0/0	78/0/59	
Years with diabetes	18 ± 17 (NR: 6)	12 ± 6 (NR: 2)	17 ± 16 (NR: 8)	0–60
Total CGM days	52,924	38,517	91,441	
CGM days/ subject	501 ± 172	960 ± 378	625 ± 319	296– 1,567
Total BG samples	14,416,242	7,181,253	21,597,495	
BG samples/ subject	144,162 ± 49,594	276,379 ± 108,843	179,871 ± 91,640	85,251- 451,236

validated CGMs used for daily management of diabetes, we set out to assess changes in glycemic trends across the year. Figure 2 presents the cumulative daily change in key glycemic metrics, particularly TIR and mean BG, extracted from two independent cohorts with diabetes (n = 137). CGM data from cohort 1 span the years of 2015 to 2019, while CGM data from cohort 2 span the years of 2015 to 2022. The TIR and mean BG was calculated for each subject and for each day of the year and then normalized by subtracting the subject's mean over the year and by dividing the mean over the year. The resulting change curve was averaged across all subjects and then smoothed with a 7-day running average.

Figure 2A shows that glycemic control was significantly worse on and around major holidays, especially, New Year, Independence Day, Thanksgiving, and Christmas. In particular, TIR decreased by 7.88% on New Year (1 January) (P < 0.001); 7.96% on Independence Day (4 July) (P < 0.01); 5.09% on Thanksgiving (24 November) (P < 0.05); and 3.13, 5.56, and 7.02% on Christmas (25 December), 1 day after Christmas (26 December), and 2 days after Christmas (27 December) (P = 0.07, < 0.01, and < 0.01, respectively). Figure 2B shows that the observed decrease in TIR was due to an increase in mean BG on major holidays. In particular, mean BG increased by 4.52% on New Year (1 January) (P < 0.001); 2.55% on Independence Day (4 July) (P < 0.01); 2.34% on Thanksgiving (24 November) (*P* < 0.05); and 2.35, 3.58, and 5.59% on Christmas (25 December), 1 day after Christmas (26 December), and 2 days after Christmas (27 December) (P = 0.07, < 0.01, and < 0.001,respectively).

Seasonal variations in glycemic trends

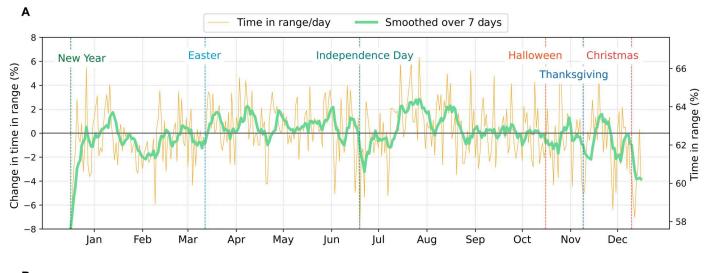
In addition to the effect of holidays, seasonal variations have been observed for health-relevant factors like physical activity, sleep,

mood, and cardiovascular risk factors (31-34). Most closely related to this work, seasonal variations have also been observed in hemoglobin A1C among patients with diabetes (35, 36). However, the effect of various seasons on glycemic trends is not well understood. To bridge this gap, we investigated the change in glycemic control across months of the year. Figure 3 (A and C) presents the cumulative percent change in key glycemic metrics (i.e., TIR and mean BG) across the population of 137 subjects with diabetes. From this figure, we observe worse glycemic control, evident from a notable decrease in TIR and increase in mean BG, in the last 2 months and first 2 months of the year (i.e., October to March). These months with worse glycemic control constitute mid-fall to end of the winter season in the United States. Conversely, we observe better glycemic control, evident from an increase in TIR and decrease in mean BG, during the months of April to September (with the exception of July). These months with better glycemic control constitute mid-spring to end of the summer season in the United States.

To further evaluate the monthly variations in glycemic control, we split the calendar year into two halves that are most aligned with the observed direction of change (i.e., increase or decrease). Figure 3 (B and D) shows the cumulative change in TIR and mean BG for 6month windows, April to September versus October to March. Our results show statistically significant differences, where the TIR increased by 0.56% between the months of April and September and decreased by 1.1% between the months of October and March (P < 0.001). In addition, mean BG decreased by 0.46% between the months of April and September and increased by 0.66% between the months of October and March (P < 0.001). These results show that glycemic trends do change across months of the year. More specifically, the observed changes in glycemic trends align with seasonal variations because months of April to September tend to be warmer months of the year, while months of October to March tend to be colder months of the year. The observed changes suggest that glycemic trends may be influenced by seasonal changes in physical activity, sun exposure, sleep, and mood (31-34).

Daily and weekly variations in glycemic trends

Prior research has studied daily and weekly variations in many health-relevant factors like physical activity, mood, happiness, and body temperature (31, 34, 37, 38). Most closely related to the diabetes domain, prior work has also studied relationships between circadian clock and insulin resistance and nocturnal BG control (39-41). However, there are gaps in knowledge about how glycemic trends vary at a population-level across times of the day and days of the week. To bridge this gap, we sought to leverage rich CGM data from our study population (n = 137) to quantify daily and weekly variations in glycemic trends. In particular, the hourly TIR and mean BG were calculated for each subject and then averaged across all subjects in this study. Figure 4 presents variations in TIR and mean BG for every hour of the day and every day of the week. From this figure, we observe better glycemic control between the hours of around 9:00 a.m. to 5:00 p.m. and gradually worse glycemic control through the evening hours and nighttime hours. In addition, we observe comparatively worse glycemic control at nighttime (i.e., 12:00 a.m. to 6:00 a.m.) on Saturday, Sunday, and Monday and slightly better control during the same time between Tuesday and Friday. The best BG control is observed



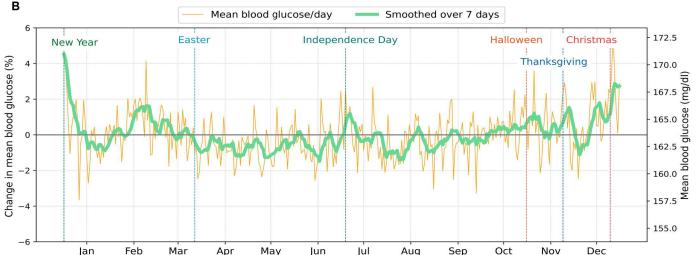


Fig. 2. The effect of holidays on glycemic trends in patients with diabetes (n = 137). (A) The cumulative change in TIR across days of the year, where U.S. holidays are marked with a vertical line. (B) The cumulative change in mean BG across days of the year, where U.S. holidays are marked with a vertical line.

between the hours of 11:00 a.m. and 1:00 p.m. on weekdays, and there is about a 2-hour delay in this window on Saturday.

Subgroup and individual-level differences in glycemic trends

Prior research also shows that glycemic trends vary across subgroups and across individuals (16, 17, 42). Hence, it is important to understand how glycemic trends vary across subgroups and individuals in this work. To achieve this, we used clinical targets as a basis for stratifying subjects into three subgroups based on glycemic control (4, 14). The good control subgroup is composed of subjects with mean TIR greater 70% across the full duration of their own CGM data (n = 50), the moderate control subgroup is composed of subjects with mean TIR between 55 and 70% across the full duration of their own CGM data (n = 38), while the poor control subgroup is composed of subjects with mean TIR less than 55% across the full duration of their own CGM data (n = 49). Figure 5A shows the daily change in TIR across subjects in each subgroup and smoothed over 7 days. From this figure, we observe that there is a

decline in glycemic trends around holidays for all three subgroups, independent of glycemic control. However, glycemic trends decreased more substantially during holidays for subjects in the moderate and poor glycemic control subgroups compared to subjects in the good glycemic control subgroup. In particular, TIR decreased by 2% or less in the good control subgroup on Independence Day, Thanksgiving, and Christmas. However, TIR decreased by around 5% on the same holidays in the poor control subgroups. In addition, the largest decline in glycemic trends was observed on New Year's Day for all subgroups, where TIR decreased by 2.56% for the good control subgroup, 7.17% for the moderate control subgroup, and 13.76% for the poor control subgroup.

Similar subgroup analysis was conducted for participants in four age groups, namely, 0 to 18 years (n = 28), 19 to 34 years (n = 60), 35 to 50 years (n = 23), and 51 to 76 years (n = 26). Figure 5B shows the daily change in TIR across subjects in each age group and smoothed over 7 days. From this figure, we observe different patterns of glycemic control in each age group, including around the holidays. Most notably, the subjects in the oldest age group (age 51 to 76)

0.73

Feb

Mar

0.16

lan

0.5

-1.5

0.66

Oct-Mar

0.5

0.0

-0.5

-1.0

-0.46

Apr-Sep

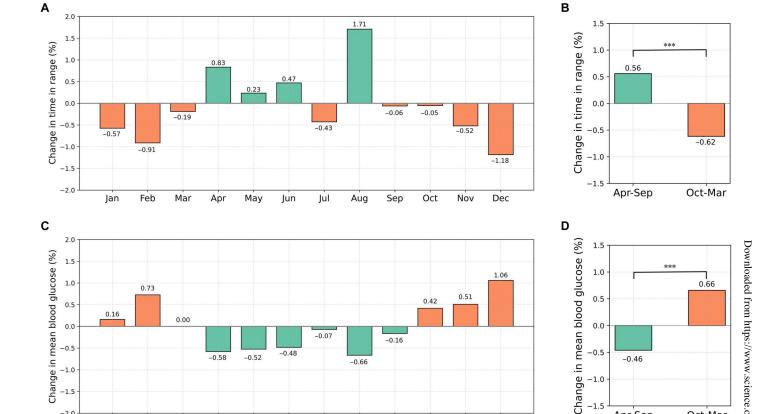


Fig. 3. Glycemic trends across months of the year. (A) The change in TIR for each month of the year (the zero mark represents the mean TIR over all the months of the year). (B) The change in TIR for two 6-month windows with distinct glycemic trends in the year. One-way analysis of variance (ANOVA) with a two-sided test was used for statistical analysis to evaluate differences in change in TIR in the months of April to September versus October to March. The differences were significant with P = 3.29 × 10⁻³⁰⁶ (i.e., P < 0.001). (C) The change in mean BG for each month on the year (the zero mark represents the mean BG over all the months of the year). (D) The change in mean BG for two 6-month windows with distinct glycemic trends in the year. One-way ANOVA with a two-sided test was used for statistical analysis to evaluate differences in change in mean BG in the months of April to September versus October to March. The differences were significant with P = 0 (i.e., P < 0.001).

-0.16

Sep

-0.07

Jul

-0.66

Aug

years) had the best glycemic control throughout the year with the least variability and lowest decreases around holidays. Meanwhile, subjects in the age groups of 19 to 34 years and 0 to 18 years had the lowest TIR per day when averaged across the days of the year, where the mean TIR per day was 54.7 and 61.3%, respectively. In addition, subjects in the age group of 19 to 34 years and the age group of 0 to 18 years showed the largest decrease in TIR on New Year's Day, where their TIR decreased by 11.6 and 7.3%, respectively. Last, fig. S2 shows the subgroup analysis across genders (male, female, and not reported). Given the large number of unreported genders (n = 64), insights from this figure are limited.

-0.58

Apr

-0.52

May

Jun

To complement the above analysis of glycemic trends at a population level and for different subgroups, we explored variations in glycemic trend at the individual level. Figure 6 shows the TIR and mean BG for each week of the year for all subjects in this study. From this figure, we observe that patterns of glycemic trends are highly variable throughout the year and highly variable across individuals. This critical observation further underscores the need for personalized interventions to improve diabetes outcomes.

DISCUSSION

0.51

Nov

Dec

0.42

Oct

This study is unique in its use of large-scale longitudinal data (over 91,000 days) from clinical-grade wearable devices to quantify variations in glycemic trends across different time horizons (i.e., times of the day/week, days/months of the year, seasons, and holidays). Although variations in other physiological metrics have been studied in prior literature, a number of studies rely on sparse data collected through manual logging methods that are often biased and erroneous or single point-in-time measurements that are irregularly sampled (19-21, 43). Meanwhile, there are other studies that use consumer-grade wearable devices to elucidate variations in physiological metrics (33). However, many of such studies are conducted with data from a healthy population (i.e., people without a diagnosed condition). Unlike prior work, routine use of clinical-grade wearable devices in the diabetes domain creates unmatched opportunities for understanding the dynamics of disease management in everyday settings (16, 17, 30, 44, 45). Retrospective analysis of routinely collected data can also reveal behaviors in the natural environment that are not altered by enrolling participants in a research study (46). Subsequently, insights from such analysis can inform the development of tailored interventions to improve the health outcomes of patients.

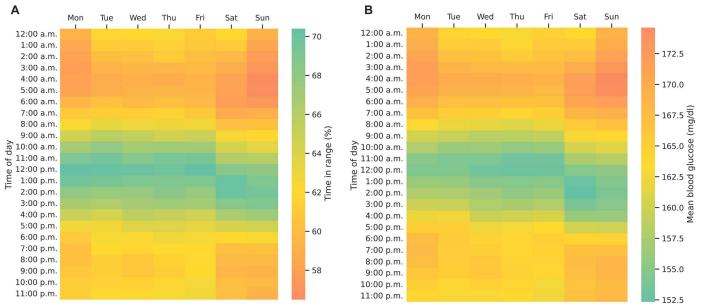


Fig. 4. Daily and weekly variations in glycemic trends across our study population (n = 137). (A) The average BG values in the target range (70 to 180 mg/dl) calculated for each subject per hour of the day and day of the week and then averaged across all subjects. (B) The mean BG calculated for each subject per hour of the day and day of the week and then averaged across all subjects.

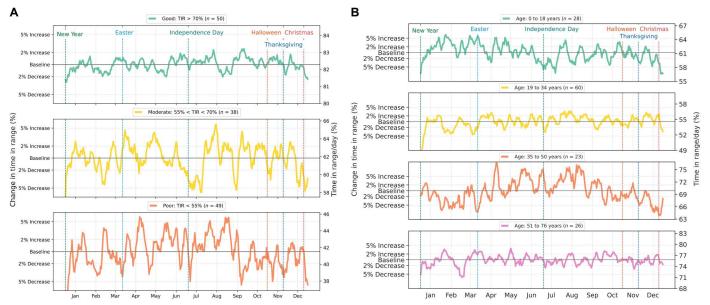


Fig. 5. Glycemic trends across the year for different subgroups. (**A**) Stratification by glycemic control, showing glycemic trends of subjects with good control (TIR > 70%), moderate control (55% < TIR < 70%), and poor control (TIR < 55%). (**B**) Stratification by age group, showing glycemic trends of subjects between the ages of 0 to 18 years, 19 to 34 years, 35 to 50 years, and 51 to 76 years.

In this work, the inclusion of subjects between 2 and 76 years of age, 0 to 60 years with diabetes, and with varying levels of glycemic control (i.e., good, moderate, and poor) enabled comparative analysis across subgroups of subjects to understand key differences that may exist. Some important findings from our subgroup analysis are that glycemic trends decreased more during the holidays (e.g., New Year) for subjects in the moderate and poor glycemic control subgroups compared to subjects in the good control subgroup. In

addition, we found that subjects in the oldest age group (ages 51 to 76) had the best glycemic control throughout the year with the least variability and lowest declines during the holidays. It is expected that the oldest subgroup also represents many people who have had diabetes for longer durations; thus, more experience with diabetes likely contributes to better management.

Another important finding from this study relates to seasonal variations in glycemic trends in which glycemic control was

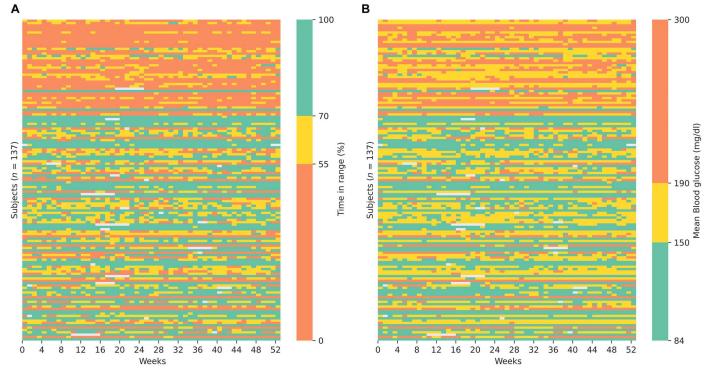


Fig. 6. Individual-level differences in glycemic control across our study population (n = 137). (A) Variations in TIR for all weeks of the year and for all subjects. (B) Variations in mean BG for all weeks of the year and for all subjects.

worse during the end of fall to winter months (i.e., November to February), and glycemic control was better during the end of spring to summer months (i.e., April to August, with the exception of July). This finding corroborates with results from prior work in the diabetes domain and beyond (35, 36, 47). For example, Quer et al. (33) found from smartwatch data that resting heart rate is lower in the summer months. In conjunction with the aforementioned study, it is consistent to infer that increased physical activity in the summer months may be a contributor to better glycemic control (i.e., higher TIR and lower mean BG). However, targeted research is needed to further understand the relationship between physical activity, months of the year, and glycemic trends.

Despite the unique contributions of this work, there are some limitations that must be acknowledged and addressed in future work. First, this study does not include analysis of factors that affect glycemic trends such as food, insulin use, and physical activity (28). Given that majority of our study population includes persons with type 1 diabetes (i.e., insulin-dependent diabetes), variations in insulin use (for example) will directly influence variations in glycemic trends; hence, such factors should also be studied. A second limitation is that demographic data from this study did not include gender for a notable portion of our study population; thus, we were unable to fully analyze potential differences across genders. A third limitation is that there was unequal representation of subjects across age groups. More specifically, 44% (i.e., 60 of 137) of participants are between ages of 19 and 34 years, while the other age groups have fewer participants ranging from 17 to 20% of the study population. Last, our study leverages wearable data from subjects with type 1 diabetes who have high adherence (i.e., \geq 70%) to CGMs for daily management of their diabetes. Given this unique

population, our findings may not generalize to a population with type 2 diabetes and/or persons who do not use or have access to CGMs for diabetes management.

Building on these limitations, future work should consider analysis of glycemic trends in conjunction with factors that affect these trends to further inform interventions. In addition, prior work suggests that there are gender-related differences in glycemic control (48); however, more research is needed to understand temporal and seasonal variations across genders. Last, more research is needed to understand how findings from studies with advanced diabetes technology relate or translate to the larger population of persons with diabetes who do not have access to advanced technologies like CGMs, such as persons from lower-income backgrounds and/or racial minorities (49–51).

MATERIALS AND METHODS

Data description

This study leverages a total of 91,441 days of CGM data from 137 subjects with diabetes, primarily type 1 diabetes (ages 2 to 76, years with diabetes of 0 to 60). As shown in Table 1, our dataset includes representation from two independent cohorts recruited through online sources, one from the Tidepool Big Data Donation Project (24) and the other from SweetGoals study (26). Cohort 1 comprises 100 subjects (mean \pm SD age, 34 \pm 21 years) with an average of 501 days (i.e., 1 year and 4 months) of CGM data per subject; meanwhile, cohort 2 comprises 37 subjects (mean \pm SD age, 23 \pm 3 years) with an average of 960 days (i.e., 2 years and 7 months) of CGM data per subject. Given the remote recruiting format, subjects in this study come from various states within the United States. The

geographical location of subjects in cohort 1 is unavailable, while fig. S1 shows the geographical location of subjects in cohort 2. In addition, data on the specific CGM type are unavailable for cohort 1, while majority of subjects (>80%) in cohort 2 used a Dexcom CGM (52). However, because CGMs are wearable devices, missing data are not uncommon (45), so we instated an inclusion criteria of >70% of data present (i.e., <30% missing data) for all subjects in this study to facilitate analysis of temporal changes in glycemic trends. Overall, our combined dataset includes a total of 21,597,495 BG samples from 137 subjects with diabetes and an average of 179,871 BG samples per subject (range, 85,251 to 451,236).

It is important to note that, because the SweetGoals study (26) is a randomized control trial, only retrospective baseline data collected during the initial screening are used for cohort 2 (i.e., this dataset does not include sensor data from the intervention period of that study). In addition, our use of the aforementioned dataset in this study was approved by the Committee for Protection of Human Subjects at Dartmouth College, and all subjects provided informed consent for use of their diabetes device data for research.

Data analysis

In this study, we use clinically validated metrics, specifically, TIR and mean BG for assessing temporal changes and seasonal variations in glycemic trends (14, 15). TIR is identified as one of the most useful CGM metrics in clinical practice, and it refers to the percentage of BG readings within the target range of 70 to 180 mg/dl (14). Conversely, mean BG refers to the mean glucose value within a given period. Both metrics were calculated to assess daily, weekly, and monthly variations in glycemic trends. Last, in Fig. 1G, we evaluated GV, which refers to BG oscillations (or fluctuations) that occur throughout the day, and we used the preferred coefficient of variation as the metric for quantifying GV (53). Thus, GV is defined as the SD over the mean BG, calculated daily, and expressed as a percentage.

Our approach for analyzing the effect of holidays on glycemic trend was informed by prior work on fluctuations in weight gain over the holidays (21). Per Eq. 1, we assessed the daily change in TIR (ΔTIR_{day i}) for all subjects by calculating TIR for each subject for each day of the year, then normalized by subtracting each subject's mean TIR across the year, and divided by the subject's mean TIR for the year. It should be noted that, for the metrics TIR_{year}, the TIR was first calculated for each day of the year for a given subject and then averaged across the year for that subject. The daily change in TIR for each subject was summarized across all subjects by taking the mean for each day of the year, and, then, the resulting change curve was smoothed with a 7-day running average as shown in Fig. 2A. Similarly, the change in mean BG (ΔmBG_{day i}) was calculated for each subject for each day of the year as shown in Eq. 2. This daily change was then summarized by taking the mean for each day of the year across all subjects. The resulting change curve was then smoothed with a 7-day running average as shown in Fig. 2B

$$\forall \text{sub} \in \{0, 1, \dots, 137\}, \Delta \text{TIR}_{\text{day } i}(\%)$$

$$= \left(\frac{\text{TIR}_{\text{day } i} - \text{TIR}_{\text{year}}}{\text{TIR}_{\text{year}}}\right) * 100 \tag{1}$$

$$\forall \text{sub} \in \{0, 1, \dots, 137\}, \Delta \text{mBG}_{\text{day } i}(\%)$$

$$= \left(\frac{\text{mBG}_{\text{day } i} - \text{mBG}_{\text{year}}}{\text{mBG}_{\text{year}}}\right) * 100 \tag{2}$$

Following this, we assessed seasonal variations in glycemic trends by evaluating the change in TIR and mean BG for each month of the year. As shown in Eqs. 3 and 4, we calculated the average TIR and mean BG for each month of the year for each subject, then normalized this by subtracting the subject's respective mean metric for the year, and divided by the subject's mean metric for the year. The monthly change was summarized by taking the average across all subjects for each month of the year. The results of this analysis is shown in Fig. 3 (A and B)

$$\forall \text{sub} \in \{0, 1, ... 137\}, \Delta \text{TIR}_{\text{month } i}$$

$$= \left(\frac{\text{TIR}_{\text{month } i} - \text{TIR}_{\text{year}}}{\text{TIR}_{\text{year}}}\right) * 100$$
(3)

$$\forall \text{sub} \in \{0, 1, ... 137\}, \Delta \text{mBG}_{\text{month } i}$$

$$= \left(\frac{\text{mBG}_{\text{month } i} - \text{mBG}_{\text{year}}}{\text{mBG}_{\text{year}}}\right) * 100 \tag{4}$$

In addition, we assessed the daily and weekly variations in glycemic trends of the full population by calculating the TIR and mean BG for each subject for every hour of the day and day of the week and then averaging the corresponding values across all subjects. The results of this analysis are shown in Fig. 4. Following this, we assessed the variation in glycemic trends across subgroups based on glycemic control (good control, TIR > 70%; moderate control, 55% < TIR < 70%; and poor control, TIR < 55%) and based on age (0 to 18 years, 19 to 34 years, 35 to 50 years, and 51 to 76 years). For each subgroup, the change in TIR was assessed per Eq. 1, and the results are shown in Fig. 5. Last, to assess individual-level variations in glycemic trends, the average TIR and mean BG for each subject for each week of the year are presented in Fig. 6.

Statistical analysis

In this study, we use one-way analysis of variance (ANOVA) with a two-sided test for statistical analysis (54, 55). More specifically, ANOVA was used to evaluate differences in the change in TIR and mean BG on (i) holidays versus non-holidays and (ii) seasonal variations (i.e., glycemic changes in the months of April to September versus October to March). Significance levels of P < 0.05, 0.01, and 0.001 were used to assess the strength of evidence against the null hypothesis.

Supplementary Materials

This PDF file includes: Figs. S1 and S2

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