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METHODS

Modified Klompas algorithm for classifying T1D and T2D

For the original Klompas algorithm¹, T1D was classified as:

1. > 50 % T1D ICD diagnostic codes AND no previous record of any prescription for oral hypoglycemic

medications (other than metformin), or

2. > 50% of all diabetes codes listed as T1D and prior use of glucagon, or

3. urine ketone strip use in year prior, or

4. negative C-peptide test ever (< 0.5 ng/mL), or

5. positive diabetes autoantibody test ever (\geq 50 unit/mL).

6. If conditions above were not met, then the patient was classified as T2D.

For T1D only, patients were required to have a prescription for insulin in year prior to the index date. In addition, no patients classified with T2D from the Klompas algorithm could have > 50% T1D ICD codes. In addition, patients were to have at least two diabetes diagnoses for the specific diabetes classification from outpatient records at least 30 days apart and before the index date. If not meeting the above conditions for T1D or T2D, they were classified as diabetes of unknown type and not included in the study.

Variable definitions

- Index date For CGM user, the first prescription release date for CGM glucose sensor. For nonCGM user, a randomly assigned date between 2015-2020.
- Age Age at index date and calculated from date of birth.
- **Gender** Gender reported as male or female.
- Ethnicity/race Patient self-identification as White/non-Hispanic, White/Hispanic, Black or African American, and Other (includes American Indian or Alaska Native, Native Hawaiian or Pacific Islander, and Asian).
- Region Region of United States identified by Veterans Integrated Services Network (VISN) associated with patient CGM sensor or glucose strip prescriptions. The four regions include: Northeast (VISNs 1, 2, 4), Midwest (VISNs 10, 12, 15, 23), South VISNs (5-9, 16, 17), and West (VISNs 19-22).
- Area deprivation index (ADI)² From the 2018 ADI national ranking based on the patient's 9-digit zip code recorded within one year prior to the index date.
 - ADI is based on the American Community Survey (ACS) Five Year Estimates.
- VHA usage
 - Active user of the VHA At least one in-person or telemedicine primary care, endocrinology, or diabetes clinic outpatient encounter within one year prior to the index date. This was based on clinic stop codes.
 - Baseline visit frequency Total count of outpatient encounters (PCP and endocrine/diabetes clinic). Only one visit per day was counted.
- **Baseline Body Mass Index (BMI)** BMI calculated from the formula = weight(kg) / [height (m)]² with the most recent recorded weight in the year prior to the index date and average height across all recorded values.
- HbA1c
 - Baseline HbA1c- HbA1c value closest to the index date and within 6 months prior to the index date
 - Postindex HbA1c
 - HbA1c value closest to the 6 month date after the index date, and within 3 months of the 6 month target.
 - HbA1c value closest to the 12 month date after the index date, and within 3 months of the 12 month target. Values identified by relevant LOINC codes from blood and extracted from outpatient settings.

- **Baseline blood pressure** The average systolic and diastolic blood pressure in the year prior to the index date. Extracted from vital sign measurements in outpatient settings.
- **Baseline lipids (HDL, LDL, Triglycerides, and Total Cholesterol)** For each lipid measurement, the closest value to the index date, and within one year prior to the index date. Values identified by relevant LOINC codes from blood/serum/plasma and extracted from outpatient settings.
- **Baseline creatinine** Serum creatinine value closest to the index date, and within one year prior to the index date. Values identified by relevant LOINC codes and extracted from outpatient settings.
- **Baseline estimated glomerular filtration rate (eGFR)** Calculated from the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation³, which incorporates baseline serum creatinine, age, gender, and ethnicity.
- Baseline comorbidities
 - **Diabetes Complications Severity Index (DCSI)**^{4,5} Modified version based on the definition using ICD diagnoses only. The weighted score was calculated from the presence of at least one outpatient ICD-9-CM or ICD-10-CM diagnostic code per category, and diagnosis within 2 years prior to the index date. There are seven categories (retinopathy, nephropathy, neuropathy, cardiovascular, cerebrovascular, peripheral vascular disease, and metabolic (hypo- and hyperglycemic related events)) with ranges of weights 0, 1, or 2 to indicate disease severity.
 - Elixhauser Comorbidity Index- Based on the published definitions^{6,7}, the score was calculated based on the presence of at least one outpatient ICD-9-CM or ICD-10-CM diagnostic code per category, within 2 years prior to the index date. There are 28 possible comorbid conditions. The final score included the sum of all comorbid conditions present for each person (excluding diagnosis of diabetes)
 - The revised score used in our propensity score models is comprised of categories not included in the DCSI (to avoid excessive overlap), this score includes: valvular disease, pulmonary circulation disorder, hypertension, chronic pulmonary disease, thyroid disease, liver disease, peptic ulcer disease, paralysis, arthritis, coagulopathy, obesity, weight loss, fluid electrolyte disorder, blood loss anemia, deficiency anemia, alcohol abuse, drug abuse, psychoses, depression, HIV/AIDS, lymphoma, metastatic cancer, and solid tumor (without metastasis).
- **Baseline insulin use** Users were identified through VA outpatient pharmacy filled prescription for either rapid/short, intermediate (NPH), long, or mixed insulin drug names. Baseline use included a filled prescription within one year prior to the index date.
- **Baseline non-insulin diabetes medication use** (oral and injectable)– Users were identified through VA outpatient pharmacy filled prescription for VA Drug Class 'oral hypoglycemic agents' and drug names for injectable glucagon-like peptide-1 receptor agonist (GLP1). Categories include Metformin, alpha glucosidase inhibitors, amylin analogs, dipeptidyl peptidase 4 inhibitors (DPP4), meglitinides, sulfonylureas, sodium-glucose co-transporter-2 inhibitors (SGLT2), and thiazolidinediones. Baseline use included a filled prescription within one year prior to the index date
- **Baseline insulin pump use** Pump users were identified through VA outpatient pharmacy filled prescriptions for the replaceable reservoir or cartridge used in insulin pumps. Baseline use included a filled prescription within one year prior to the index date.
- **Baseline blood glucose monitoring strips** Users were identified through VA outpatient pharmacy filled prescription for common blood glucose monitoring strips drug names. Baseline use included a filled prescription within one year prior to the index date.
- **Glucagon** Users were identified through VA outpatient pharmacy filled prescription for glucagon drug names. Baseline use included a filled prescription within one year prior to the index date.
- Lipid lowering medication Users were identified through VA outpatient pharmacy filled prescription for VA Drug Class 'Lipid-lowering' and limited to statins, fibrates, and ezetimibe. Baseline use included a filled prescription within one year prior to the index date.
- Antihypertensive medication Users were identified through VA outpatient pharmacy filled prescription for VA Drug Classes: 'Beta blockers/related', 'Alpha blockers/related' (limited to Doxazosin, Prazosin, and Terazosin), Calcium Channel Blockers, 'Antihypertensive combinations', 'Antihypertensives, other',

'Thiazides/Related diuretics', 'Antihypertensives, other', 'Ace inhibitors', 'Angiotensin II inhibitor', and 'Direct Renin inhibitor'. Baseline use included a filled prescription within one year prior to the index date.

- **Hypoglycemia** Hypoglycemia was based on published definitions^{8,9} and the presence of relevant ICD-9-CM and ICD-10-CM codes in any position from inpatient and emergency visits.
 - Baseline Presence of any event within one year prior to the index date.
 - Outcome
 - Presence of any event after and within one year after the index date.
 - Time to event days from the index date to the first event of hypoglycemia, death (competing risk), or follow-up (up to one year, i.e. censored outcome).
 - For the hypoglycemia definition that includes outpatient glucose lab values < 54 mg/dL, events were identified through ICD codes as mentioned above or presence of glucose laboratory values less than 54 mg/dL. Glucose values are limited to LOINC codes from blood/serum/plasma (no glucometer values) in the outpatient setting.
- **Hyperglycemia** Hyperglycemia was based on the presence of relevant ICD-9-CM and ICD-10-CM codes in any position from inpatient and emergency visits.
 - Baseline Presence of any event within one year prior to the index date.
 - Outcome
 - Presence of any event after and within one year after the index date.
 - Time to event days from the index date to the first event of hypoglycemia, death (competing risk), or follow-up (up to one year, i.e. censored outcome).
- Hospitalization
 - Baseline Count of distinct inpatient admissions within one year prior to the index date.
 - Outcome
 - Presence of any inpatient admission within one year after the index date.
 - Time to event days from the index date to the first event of hypoglycemia, death (competing risk), or follow-up (up to one year, censored outcome).
- **Baseline emergency service use** Count of distinct emergency room visits to VA hospitals within one year prior to the index date.
- **Hypoglycemic risk score** The 12-month risk of hypoglycemia-related utilization was calculated from the definition by *Karter et al* 2017⁹. The score was calculated from six data points: patient history of hypoglycemia-related utilization, insulin use, sulfonylurea use, emergency department use, chronic kidney disease, and age.
- **Insurance** –Indicator flags (binary variable indicating present or not present) for Medicare, Medicaid/Medi-Cal, and any type of private insurance in year prior to index date. Based on self-reported insurance by patient during any outpatient encounters.
- **Extended care** Indicator flag for any presence of long-term care from VA inpatient records or consults for nursing home, skilled nursing care, and any geriatric extended care for bowel and bladder, infusion therapy, home health aide, homemaker, respite care, or adult day care in the year prior to the index date.
- Hospice and palliative care Indicator flag for any consults for hospice or palliative care in the year prior to the index date.
- **Homelessness** Indicator flag for presence of any relevant ICD-9-CM and ICD-10-CM codes for homelessness or any outpatient clinic stop codes for homeless clinic locations in the year prior to the index date.
- **Death** Death was indicated from a completed date of death. Dates are recorded and gathered from available Social Security Administration (SSA), Medicare and Medicaid Services (CMS), VHA death benefits, VHA hospitals, and VA National Cemetery Association records.
- **Proportion of Days Covered (PDC)** To estimate medication adherence, the PDC was calculated from the total days covered by prescriptions divided by the total days in period from first fill to last run out date on the last prescription¹⁰. Good adherence is considered ≥ 80%.
- Upper respiratory infections Upper respiratory infections was based on the presence of relevant ICD-9-CM and ICD-10-CM codes in any position. Two separate variables were created for inpatient/ER setting and outpatient setting.

Musculoskeletal injuries and disorders – Based on all codes listed under 'Other joint disorders', 'Other dorsopathies', and 'Other soft tissue disorders' from ICD-10-CM diseases of the musculoskeletal system and connective tissue. ICD-9-CM codes were mapped from General Equivalence Mappings (GEMs) from CMS. Musculoskeletal injuries and disorders are based on the presence of relevant ICD-9-CM and ICD-10-CM codes in any position. Two separate variables were created for inpatient/ER setting and outpatient setting.

Imputation

Imputed variables included BMI, blood pressure, lab values (HbA1c, lipids, creatinine, eGFR), ADI, and ethnicity. There were no missing values for age or gender. For all other covariates there was either no missingness or missingness status was accepted as no actual event had occurred. T1D and T2D patient data was imputed separately.

Missingness in baseline values for individual variables prior to imputation ranged from approximately 1 to 17%. Baseline HbA1c within 6 months from the index date had the highest missingness rate (~17%) and blood pressure had the lowest (~1%). Imputation provided complete values for all individuals in both groups and supports data missing at random. All baseline variables included in the propensity score were used in the imputation process, except for highly correlated variables. All analyses were performed independently on each set of the five imputations and results were pooled. Imputation was performed by the R package "mice" and results were pooled using "MatchThem".

We imputed missing HbA1c values at baseline (i.e., 6 months prior to the index date). Imputed HbA1c values were only used for modeling PS for the acute event analyses. For the analyses of HbA1c changes, we used the mixed model approach that includes all available data to estimate model parameters, and appropriately utilizes partial missing data.

Propensity score

Covariates selection for inclusion in propensity score (PS) weighting among CGM users and nonCGM users were similar to those from *Karter et al* 2021¹¹.

Baseline covariates in the propensity score for time-to-event analyses (hypoglycemia, hyperglycemia, and hospitalization) and HbA1c difference-in-differences included:

Age, gender, ethnicity, body mass index, US region, age at first diabetes diagnosis in the VHA, duration of time from first diabetes diagnosis in the VHA, area deprivation index (an evaluation of regional socioeconomic conditions), any endocrinology clinic visit, total counts of primary care and endocrinology visits, insurance type (private, Medicare, and/or Medicaid), hypoglycemic risk score, insulin type use (short/rapid-acting, long-acting, NPH, and mixed short- and long-acting), insulin pump use (for T1D only), glucagon use, non-insulin DM medications (metformin, sulphonylureas, SGLT-2, DPP-4, GLP-1, thiazolidinediones, glinides, alpha-glucosidase inhibitor, and amylin), lipid-lowering medication use, anti-hypertensive medication use, HbA1c, LDL, HDL, triglycerides, total cholesterol, serum creatinine, eGFR, systolic and diastolic blood pressure, comorbidities (each individual category and weight of the Diabetes Complication Severity Index (DCSI) and the summed score of remaining and non-overlapping conditions included in the Elixhauser comorbidity index), any inpatient or ER diagnoses of hypoglycemia, any inpatient or ER diagnoses of hypoglycemia, any extended medical care (long term inpatient stays, skilled nursing, and/or skilled home care), hospice or palliative care, or homelessness/housing insecurity in the year prior to index date.

For the propensity score among T1D, we only applied an indicator flag for general use of non-insulin medication and did not consider individual subtypes of non-insulin medications due to low frequency of their use. For T2D, we applied indicator flags for use of each individual subtype of non-insulin medications (metformin, sulfonylureas, SGLT-2, DPP-4, GLP-1, thiazolidinediones, glinides, alpha-glucosidase inhibitor, and amylin). In HbA1c difference-in-differences analyses, we included additional indicator flags (two binary variables) for missing HbA1c values at baseline or postindex. When HbA1c was examined as an outcome, baseline HbA1c values were not included in the propensity score models.

All PS models demonstrated excellent discrimination (C statistic ≥ 0.93 for each). Adding all pairwise interactions increased standardized mean differences (SMD) of covariates and did not improve model discrimination, so they were not subsequently used.

Sensitivity analyses

Additional exclusion criteria:

Additional criteria was applied to limit analyses to a healthier population included (at baseline): age less than 85 years, no more than 2 inpatient hospital stays and total length of any hospital stay less than 30 days, no homelessness/housing insecurity, no hospice or palliative care, and no excessive missingness among variables (for an individual, less than 40% missing among age, gender, BMI, lab values, ADI, and ethnicity).

Pre-COVID pandemic:

To account for possible disruptions in services or interaction with the VHA due to COVID concerns or protocols, analyses were restricted to people with index dates before or on February 29, 2020. As in previous publications, follow-up time and events were censored by at a certain date, in this case February 29, 2020¹².

Female only:

As the vast majority of the cohort was male (> 90 analyses were performed for HbA1c difference-in-differences using linear mixed models that included HbA1c at baseline and 6- and 12- months postindex in females only. Due to a significantly decreased sample size, overlap propensity score weighting was not feasible, and models were adjusted for key a priori selected covariates: age, BMI, hypoglycemic risk score, any endocrinologist visit, total number of primary care/endocrine visits, and insulin pump use (T1D only) or short insulin use (T2D only). Short acting insulin not adjusted for in T1D due to collinearity with insulin pump use. Other outcomes were too infrequent to examine in females.

Dose-response of CGM by Proportion of Days Covered (PDC):

To determine whether stepwise increases in PDC with CGM use was associated with "dose related" declines in HbA1c, CGM users were divided into four equal groups of potential PDC: (0-0.24), (0.25- 49), (0.50-0.74), and (0.75-1.0). The PDC was calculated based on all CGM sensor prescriptions within one year postindex date, accounting for death (calculated using death date if occurred). HbA1c difference-in-differences were calculated using linear mixed models that included HbA1c at baseline and 12-months postindex. Both interaction among each PDC compared to the lowest PDC group and the effect within each subgroup for HbA1c difference-indifferences was calculated. All models were adjusted for age, gender, ethnicity, region, hypoglycemic risk score, Elixhauser comorbidity score, number of primary care/endocrine visits, area deprivation index, index year, glucagon use, insulin type, and insulin pump use (T1D only) or short insulin use (T2D only). Short acting insulin not adjusted for in T1D due to collinearity with insulin pump use.

Mediation analyses

We examined the mediation effect of the number of post visits (count of primary care or endocrine) within one year on the relationship between CGM use and the difference in HbA1c from baseline to one year. We used linear regression for the difference in HbA1c outcome and Poisson regression for the number of post visits outcome. The final mediation analyses calculated the indirect effect of post visits on difference in HbA1c by incorporating models for the effect of CGM on post visits and the effect of post visits on the difference in HbA1c while controlling for CGM use. Overlap propensity score weights were used throughout the analyses. Mediation analyses were performed using the R package "mediation."¹³

RESULTS

Supplemental Table 1: Comparison of glucose control over 12 months among female T1D and T2D CGM users and non-CGM users

| Analyses | CGM user | CGM user | | | | Weighted difference-in-dif | ferences | |
|-------------------------------|------------------|----------------|------------|-----------------|----------------|----------------------------|-----------------------|---------|
| | Before baseline | After baseline | Difference | Before baseline | After baseline | Difference | Estimate (95% CI) | P-value |
| T1D (CGM, n = 426; Non | -CGM, n = 151) | | | | | | | |
| HbA1c at 6 mo (mean (SD)) | 8.74 (1.56) | 8.23 (1.33) | -0.51 | 8.58 (1.66) | 8.56 (1.69) | -0.02 | -0.54 (-0.78, -0.30) | <0.001 |
| HbA1c at 12 mo (mean (SD)) | 8.74 (1.56) | 8.36 (1.42) | -0.38 | 8.58 (1.66) | 8.62 (1.66) | +0.04 | -0.33 (-0.63, -0.04) | 0.04 |
| T2D (CGM, n = 926; Non | -CGM, n = 1,060) | | | | | | | |
| HbA1c at 6 mo (mean (SD)) | 9.01 (1.90) | 8.36 (1.64) | -0.66 | 8.43 (1.79) | 8.40 (1.91) | -0.03 | -0.57 (-0.72, -0.41)- | <0.001 |
| HbA1c at 12 mo (mean (SD)) | 9.01 (1.90) | 8.46 (1.74) | -0.55 | 8.43 (1.79) | 8.34 (1.82) | -0.09 | -0.42 (-0.60, -0.24) | <0.001 |

Abbreviations: CGM, continuous glucose monitoring; CI, confidence interval; HbA1c, hemoglobin A1c (%); n, sample size; mo, months; T1D, T1D diabetes; T2D, T2D diabetes.

P-values < 0.05 are bolded. Values presented before or after baseline as mean (SD).

Sample size is slightly reduced for HbA1c outcomes since those included must have either preindex HbA1c value, 6 mo postindex, or 12 mo postindex.

Difference-in-differences estimates reflect Linear Mixed Models with HbA1c status within 6 months before and 12 months after the index date and adjusted by baseline age, body mass index, hypoglycemic risk score, any endocrinologist visit, total number of primary care/endocrine visits, and insulin pump use (T1D only) or short insulin use (T2D only). Short insulin not adjusted for in T1D due to collinearity with insulin pump use. Reference group is non-CGM users.

To convert HbA1c from percentage to mmol/mol, use the formula: (HbA1c, mmol/mol) = [(HbA1c,%) - 2.152] \div 0.09148).

| 0 | |
|---|--|
| | |
| o | |

| | | T | ID | T2D | | | |
|---|-----------------------------------|----------------------|----------------------|------------------------------------|-----------------------------------|----------------------|----------------------|
| Outcomes | Additional exclusion criteria* | Pre-COVID-19** | Adjusted *** | Insulin pump users excluded**** | Additional exclusion criteria* | Pre-COVID-19** | Adjusted *** |
| n (CGM/Non-CGM) | 4,549/2,922 | 4,170/3,154 | 5,015/3,518 | 2,52111/3,321 | 13,824/25,799 | 8,763/25,959 | 15,706/29,912 |
| HbA1c (%), Difference-in-differe | nces (95% CI) | | | | | | |
| 6 months | -0.28 (-0.33, -0.23) | -0.24 (-0.29, -0.19) | -0.31 (-0.36, -0.25) | -0.28 (-0.35, -0.22) | -0.41 (-0.44, -0.38) | -0.31 (-0.35, -0.28) | -0.44 (-0.47, -0.41) |
| 12 months | -0.28 (-0.35, -0.20) | -0.25 (-0.33, -0.17) | -0.27 (-0.32, -0.21) | -0.30 (-0.39, -0.21) | -0.36 (-0.41, -0.32) | -0.29 (-0.35, -0.24) | -0.38 (-0.42, -0.35) |
| Events, HR (95% CI) | | | | | | | |
| Hypoglycemia events | 0.58 (0.38, 0.90) | 0.75 (0.50, 1.14) | 0.60 (0.44, 0.83) | 0.69 (0.47, 1.01) | 0.97 (0.74, 1.26) | 1.17 (0.86, 1.59) | 1.11 (0.91, 1.35) |
| Hypoglycemia events or glucose < 54 mg/dl | 0.72 (0.55, 0.94) | 0.73 (0.55, 0.95) | 0.68 (0.55, 0.83) | 0.71 (0.55, 0.92) | 0.93 (0.78, 1.11) | 1.08 (0.89, 1.33) | 1.06 (0.93, 1.21) |
| Hyperglycemia events | 0.81 (0.60, 1.09) | 0.83 (0.62, 1.10) | 0.78 (0.62, 0.97) | 0.80 (0.61, 1.04) | 0.83 (0.71, 0.96) | 0.92 (0.77, 1.11) | 0.98 (0.88, 1.10) |
| Hospitalization events | 0.73 (0.59, 0.89) | 0.75 (0.61, 0.92) | 0.66 (0.57, 0.78) | 0.72 (0.59, 0.88) | 0.87 (0.80, 0.96) | 0.93 (0.83, 1.04) | 0.90 (0.84, 0.97) |

Supplement Table 2. Sensitivity analyses for comparison of glycemic control, glycemic events and all-cause hospitalization for CGM users vs non-CGM users in the 12 months pre- and postindex dates

Abbreviations: CGM, continuous glucose monitoring; CI, confidence interval; HbA1c, hemoglobin A1c (%); n, sample size; HR, hazard ratio; ER, emergency room.

P-values < 0.05 are bolded. Data for beta estimates indicating % HbA1c differences at 6 and 12 months after CGM initiation using Linear Mixed Models. HR estimates reflect Cox proportional hazard model with time to event as the first occurrence of event within 12 months after the index date and adjusted by overlap weighting from propensity score model. Reference groups are non-CGM users.

*Additional exclusion criteria led to selection of people (at baseline) aged less than 85 years, with no more than 2 inpatient hospital stays and total length of any hospital stay less than 30 days, no homelessness/housing insecurity, no hospice or palliative care in the year preceding the index date, and those without high data missingness (no greater than 40% among the variables age, gender, BMI, blood pressure, lab values, ADI, and ethnicity).

** Pre-COVID-19 pandemic analyses are limited to people with index dates before March 1, 2020. For all events or 12-month follow-up, except for HbA1c, that occurred after March 1, 2020, time is censored on February 29, 2020.

*** Regression models were directly adjusted for age and four significant predictors (for T1D or T2D) of CGM (largest SMD between CMG users and non-CGM users) at baseline: insulin pump use (T1D only), short insulin use (T2D only), start year, endocrinology visit, and glucagon use. For T2D, endocrinology visits were adjusted through separate baseline hazard functions fit for presence or absence of the visit due to proportional hazard violation.

**** All people with insulin pump use at baseline were excluded from analyses.

Hypoglycemia and hyperglycemia events were identified by ICD-9/10 diagnostic codes in ER or inpatient setting. Hypoglycemia or glucose < 54 mg/dl included diagnoses or outpatient glucose lab values < 54 mg/dL. All-cause hospitalization events were identified by inpatient admissions.

To convert HbA1c from percentage to mmol/mol, use the formula: (HbA1c, mmol/mol) = [(HbA1c,%) - 2.152] \div 0.09148).

| | T1D | T2D | | |
|--|---|---|--|--|
| (n=5,015 C | CGM users/3,815 non-users) | (n=15,706 CGM users/29,912 non-users) | | |
| ER dx or inpatient dx present on admission | ER dx only | ER dx or inpatient dx present on admission | ER dx only | |
| | | | | |
| 0.79 (0.52, 1.20) | 0.66 (0.34, 1.26) | 0.95 (0.74, 1.23) | 1.47 (0.91, 2.37) | |
| 0.75 (0.59, 0.96) | 0.69 (0.53, 0.89) | 0.98 (0.84, 1.15) | 1.03 (0.86, 1.22) | |
| 1.02 (0.72, 1.45) | 1.01 (0.69, 1.46) | 0.87 (0.71, 1.06) | 0.85 (0.69, 1.05) | |
| | ER dx or inpatient dx present on admission 0.79 (0.52, 1.20) 0.75 (0.59, 0.96) | (n=5,015 CGM users/3,815 non-users) ER dx or inpatient dx present on admission ER dx only 0.79 (0.52, 1.20) 0.66 (0.34, 1.26) 0.75 (0.59, 0.96) 0.69 (0.53, 0.89) | (n=5,015 CGM users/3,815 non-users) (n=15,706 C ER dx or inpatient dx present on admission ER dx only 0.79 (0.52, 1.20) 0.66 (0.34, 1.26) 0.95 (0.74, 1.23) 0.75 (0.59, 0.96) 0.69 (0.53, 0.89) 0.98 (0.84, 1.15) | |

Supplement Table 3: Sensitivity analyses using alternatively defined glycemic events for CGM users vs non-CGM users in the 12 months pre- and postindex dates

Abbreviations: CGM, continuous glucose monitoring; CI, confidence interval; dx, diagnoses; n, sample size; HR, Hazard Ratio; ER, emergency room.

P-values < 0.05 are bolded. HR estimates reflect Cox proportional hazard model with time to event as the first occurrence of event within 12 months after the index date and adjusted by overlap weighting from propensity score model. Reference group is non-CGM user. Hypoglycemia and hyperglycemia identified by ICD-9/10 diagnostic codes. Hypoglycemia or glucose < 54 mg/dl could also reflect an outpatient glucose lab values < 54 mg/dL.

For hypoglycemia, both ER and inpatient hypoglycemia diagnoses are in any position in the diagnostic list, but for inpatient diagnoses, hypoglycemia was also required to be present at the time of admission. * For hyperglycemia, an additional requirement was that the inpatient diagnoses must also be in principal position which reflects the diagnosis responsible for the length of stay. ER based only diagnoses used ICD codes just from ER admissions (i.e., ER dx).

Supplement Table 4: Negative controls for CGM users vs non-CGM users in the 12 months pre- and postindex dates in primary and sensitivity analyses

| | | T1D | | | T2D | |
|---|-------------------|-----------------------------------|-------------------|-------------------|-----------------------------------|-------------------|
| Outcomes | Primary analysis | Additional exclusion criteria* | Pre-COVID-19** | Primary analysis | Additional exclusion criteria* | Pre-COVID-19** |
| n (CGM/Non-CGM) | 5,015/3,518 | 4,549/2,922 | 4,170/3,154 | 15,706/29,912 | 13,824/25,799 | 8,763/25,959 |
| Negative control, HR (95% CI) | | | | | | |
| Musculoskeletal injuries and disorders, inpatient/ER only | 0.82 (0.65, 1.05) | 0.90 (0.69, 1.17) | 0.83 (0.62, 1.12) | 1.06 (0.96, 1.17) | 1.07 (0.96, 1.20) | 1.00 (0.87, 1.15) |
| Musculoskeletal injuries and disorders, outpatient only | 1.11 (1.0, 1.24) | 1.05 (0.95, 1.17) | 1.09 (0.96, 1.24) | 1.08 (1.04, 1.13) | 1.07 (1.02, 1.13) | 1.04 (0.98, 1.11) |
| Upper respiratory infections, inpatient/ER only | 1.08 (0.63, 1.86) | 0.95 (0.55, 1.64) | 0.94 (0.51, 1.71) | 1.15 (0.91, 1.46) | 1.17 (0.91, 1.51) | 1.24 (0.93, 1.66) |
| Upper respiratory infections, outpatient only | 0.84 (0.58, 1.21) | 0.89 (0.62, 1.28) | 0.81 (0.54, 1.21) | 1.12 (0.94, 1.34) | 1.16 (0.96, 1.40) | 1.06 (0.86, 1.31) |

Abbreviations: CGM, continuous glucose monitoring; CI, confidence interval; n, sample size; HR, Hazard Ratio; ER, emergency room.

Data for beta estimates indicating % HbA1c differences at 6 and 12 months, or at latest value in 3 to 12 months interval after CGM initiation. HR estimates reflect Cox proportional hazard model with time to event as the first occurrence of event within 12 months after the index date and adjusted by overlap weighting from propensity score model. Reference group is non-CGM user.

Negative controls identified by ICD-9/10 diagnostic codes for musculoskeletal related disorders and injuries (including back, joint, and soft tissue) or upper respiratory infections from either inpatient and ER setting or outpatient setting.

*Additional exclusion criteria analyses include people (at baseline) aged less than 85 years, with no more than 2 inpatient hospital stays and total length of any hospital stay less than 30 days, no homelessness/housing insecurity, no hospice or palliative care in the year preceding the index date, and those without high data missingness (no greater than 40% among the variables age, gender, BMI, blood pressure, lab values, ADI, and ethnicity).

**For pre-COVID-19 pandemic, analyses only include people with index dates before March 1, 2020. For all events or 12-month follow-up, except for HbA1c, that occurred after March 1, 2020, time is censored on February 29, 2020.

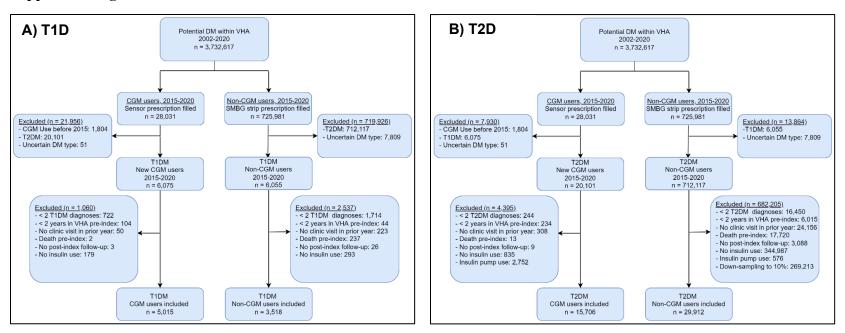
| | Supplemental Table 5: Comparison of glycemic control pre- and 12 months post- initiation of CGM within T1D and T2D |
|---|--|
| (| CGM users by proportion of days covered (PDC). |
| | |

| Analyses | | T1D $(n = 4,930)$ |) | | T2D (n =15,292) | | | | | |
|------------------|-------|-------------------------------------|---------|-------------------------------------|-----------------|----------------------|---------|-------------------------|--|--|
| | Η | HbA1c (%), Difference-in-difference | ces | HbA1c (%),Difference-in-differences | | | | | | |
| PDC (proportion) | n | Estimate (95% CI) | P-value | Interaction P-value | n | Estimate (95% CI) | P-value | Interaction P- value | | |
| (0-0.25) | 548 | 0.00 (-0.10, 0.11) | 0.94 | | 1,446 | -0.29 (-0.40, -0.18) | < 0.001 | | | |
| [0.25-0.50) | 594 | -0.08 (-0.18, 0.01) | 0.09 | 0.20 | 1,238 | -0.34 (-0.46, -0.22) | < 0.001 | 0.43 | | |
| [0.50-0.75) | 1,269 | -0.29 (-0.35, -0.22) | <0.001 | < 0.001 | 3,150 | -0.48 (-0.55, -0.41) | < 0.001 | < 0.001 | | |
| [0.75-1.0] | 2,519 | -0.41 (-0.45, -0.36) | < 0.001 | < 0.001 | 9,458 | -0.52 (-0.55, -0.49) | < 0.001 | < 0.001 | | |

Abbreviations: CGM, continuous glucose monitoring; CI, confidence interval; HbA1c, hemoglobin A1c (%); n, sample size; PDC, Proportion of Days Covered; T1D, T1D diabetes, T2D, T2D diabetes.

P-values < 0.05 are bolded. Difference-in-differences estimates reflect Linear Mixed Models with HbA1c status within 6 months before and within 12 months after the index date. Those included must have either preindex HbA1c value, 6 month postindex, or 12 month postindex. All models are adjusted for age, gender, ethnicity, region, hypoglycemic risk score, Elixhauser comorbidity score, number of primary care/endocrine visits, area deprivation index, index year, glucagon use, insulin type, and insulin pump use (T1D only) or short insulin use (T2D only). Short insulin not adjusted for in T1D due to collinearity with insulin pump use. For interaction analyses, reference group is PDC (0, 0.25), i.e., proportion of days covered with prescriptions for sensors are between 0 and 25% of the total year.

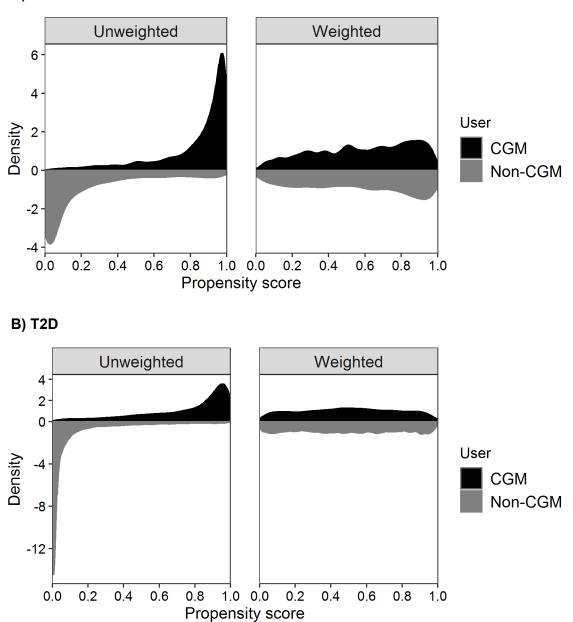
To convert HbA1c from percentage to mmol/mol, use the formula: (HbA1c, mmol/mol) = [(HbA1c,%) - 2.152] \div 0.09148).



Supplement Figure 1: T1D and T2D cohort selection and exclusion

Abbreviations: CGM, continuous glucose monitoring; DM, diabetes mellitus; n, sample size; SMBG, self-monitoring blood glucose; T1D, T1D diabetes; T2D, T2D diabetes; VHA, Veteran Health Administration. Exclusion criteria and the number of excluded participants are shown within boxes in each panel.

Supplement Figure 2: Mirrored density plot of propensity scores before and after overlap weighting among T1D and T2D CGM users and non-CGM users



A) T1D

Abbreviations: CGM, continuous glucose monitoring; T1D, T1D diabetes; T2D, T2D diabetes. Propensity score averaged over all five imputations.

Supplement Figure 3: Glycemic control and adverse events in the 12 months pre- and post- initiation of CGM within key subsets, based on baseline characteristics and adherence to CGM, of T1D and T2D CGM users

A) T1D, HbA1c outcomes

| | | | Sample | Estimate | Interaction | |
|----------|----------|----------------|--------|-----------------------|-------------|--|
| Outcome | | Subgroup | Size | (95% CI) | P-value | |
| HbA1c at | - | Age < 65 | 3153 | -0.4 (-0.44, -0.36)* | <0.001 | |
| 6 months | - | Age ≥ 65 | 1862 | -0.19 (-0.23, -0.15)* | | |
| - | • | HbA1c < Median | 2462 | 0.08 (0.04, 0.11)* | <0.001 | |
| | - | HbA1c ≥ Median | 2553 | -0.71 (-0.76, -0.66)* | | |
| | • | Low Hypo Risk | 3824 | -0.31 (-0.34, -0.27)* | 0.067 | |
| | | High Hypo Risk | 1191 | -0.37 (-0.44, -0.3)* | | |
| - | - | PDC < 0.80 | 2936 | -0.23 (-0.27, -0.19)* | <0.001 | |
| | - | PDC ≥ 0.80 | 2079 | -0.45 (-0.49, -0.4)* | | |
| | 1 -0.5 0 | | | | | |

B) T1D, event outcomes

| | | | | # Events | Odds ratio | Interaction |
|-----------------|---|----------|----------------|------------|--------------------|-------------|
| Outcome | | | Subgroup | Pre / Post | (95% CI) | P-value |
| Hypoglycemia | | _ | Age < 65 | 104 / 81 | 0.78 (0.56, 1.07) | 0.521 |
| | | | Age ≥ 65 | 75 / 50 | 0.66 (0.44, 0.97)* | |
| | | | HbA1c < Median | 66 / 44 | 0.65 (0.43, 1)* | 0.551 |
| | | - | HbA1c ≥ Median | 113 / 87 | 0.77 (0.57, 1.05) | |
| | | • | Low Hypo Risk | 35 / 40 | 1.19 (0.75, 1.88) | 0.017 |
| | | | High Hypo Risk | 144 / 91 | 0.61 (0.46, 0.81)* | |
| | | | PDC < 0.80 | 94 / 86 | 0.94 (0.69, 1.3) | 0.017 |
| | | | PDC ≥ 0.80 | 85 / 45 | 0.49 (0.32, 0.74)* | |
| Hypoglycemia | | | Age < 65 | 292 / 203 | 0.66 (0.54, 0.81)* | 0.934 |
| orglucose | | | Age ≥ 65 | 181 / 122 | 0.66 (0.51, 0.85)* | |
| < 54 mg/dl | | | HbA1c < Median | 218 / 127 | 0.54 (0.42, 0.7)* | 0.039 |
| < 54 mg/ui | | | HbA1c ≥ Median | 255 / 198 | 0.77 (0.63, 0.95)* | |
| | | | Low Hypo Risk | 212 / 161 | 0.76 (0.62, 0.95)* | 0.077 |
| | | | High Hypo Risk | 261 / 164 | 0.57 (0.46, 0.72)* | |
| | | | PDC < 0.80 | 276 / 211 | 0.76 (0.62, 0.92)* | 0.053 |
| | | | PDC ≥ 0.80 | 197 / 114 | 0.54 (0.41, 0.69)* | |
| Hyperglycemia | | | Age < 65 | 259 / 202 | 0.76 (0.62, 0.94)* | 0.004 |
| JF - 0 J | _ | | Age ≥ 65 | 104 / 122 | 1.28 (0.96, 1.71) | |
| | | | HbA1c < Median | 108 / 106 | 1.01 (0.75, 1.36) | 0.42 |
| | | - | HbA1c ≥ Median | 255 / 218 | 0.86 (0.7, 1.07) | |
| | | | Low Hypo Risk | 109 / 129 | 1.23 (0.95, 1.6) | 0.004 |
| | | | High Hypo Risk | 254 / 195 | 0.73 (0.58, 0.92)* | |
| | | | PDC < 0.80 | 213 / 213 | 1.04 (0.84, 1.29) | 0.048 |
| | | | PDC ≥ 0.80 | 150 / 111 | 0.73 (0.55, 0.97)* | |
| All-cause | | | Age < 65 | 450 / 342 | 0.7 (0.59, 0.83)* | 0.009 |
| hospitalization | | <u> </u> | Age ≥ 65 | 233 / 229 | 1.01 (0.83, 1.25) | |
| noopitalization | | | HbA1c < Median | 273 / 221 | 0.78 (0.62, 0.97)* | 0.678 |
| | | | HbA1c ≥ Median | 410 / 350 | 0.83 (0.7, 1)* | |
| | | | Low Hypo Risk | 269 / 270 | 1.03 (0.86, 1.23) | <0.001 |
| | | | High Hypo Risk | 414 / 301 | 0.62 (0.51, 0.75)* | |
| | | | PDC < 0.80 | 407 / 345 | 0.82 (0.7, 0.97)* | 0.809 |
| | | | PDC ≥ 0.80 | 276 / 226 | 0.79 (0.64, 0.98)* | 0.000 |

C)T2D, HbA1c outcomes

| | | | | Sample | Estimate | Interaction | |
|----------|---------|---|----------------|--------|-----------------------|-------------|--|
| Outcome | | | Subgroup | Size | (95% CI) | P-value | |
| HbA1c at | + | | Age < 65 | 5620 | -0.72 (-0.77, -0.68)* | <0.001 | |
| 6 months | - | | Age ≥ 65 | 10086 | -0.39 (-0.42, -0.36)* | | |
| | | • | HbA1c < Median | 7472 | 0.19 (0.17, 0.22)* | <0.001 | |
| | + | | HbA1c ≥ Median | 8234 | -1.15 (-1.19, -1.11)* | | |
| | • | | Low Hypo Risk | 10322 | -0.54 (-0.57, -0.52)* | <0.001 | |
| | + | | High Hypo Risk | 5384 | -0.44 (-0.49, -0.4)* | | |
| | + | | PDC < 0.80 | 7540 | -0.45 (-0.49, -0.41)* | <0.001 | |
| | | | PDC ≥ 0.80 | 8166 | -0.56 (-0.59, -0.53)* | | |
| | -1 -0.5 | 0 | | | | | |

D) T2D, event outcomes

| | | | # Events | Odds ratio | Interaction |
|-----------------|---|----------------|-------------|--------------------|-------------|
| Outcome | | Subgroup | Pre / Post | (95% CI) | P-value |
| Hypoglycemia | | Age < 65 | 196 / 155 | 0.81 (0.64, 1.01) | 0.512 |
| | | Age ≥ 65 | 292 / 237 | 0.88 (0.74, 1.06) | |
| | | HbA1c < Median | 206 / 167 | 0.86 (0.69, 1.08) | 0.828 |
| | | HbA1c ≥ Median | 282 / 225 | 0.84 (0.7, 1.02) | |
| | | Low Hypo Risk | 61 / 109 | 1.89 (1.38, 2.59)* | < 0.001 |
| | | High Hypo Risk | 427 / 283 | 0.7 (0.59, 0.82)* | |
| | | PDC < 0.80 | 273 / 266 | 1.06 (0.89, 1.27) | <0.001 |
| | | PDC ≥ 0.80 | 215 / 126 | 0.6 (0.48, 0.76)* | |
| Hypoglycemia | | Age < 65 | 412 / 296 | 0.7 (0.6, 0.83)* | 0.821 |
| or glucose | | Age ≥ 65 | 724 / 481 | 0.69 (0.61, 0.78)* | |
| < 54 mg/dl | | HbA1c < Median | 566 / 359 | 0.64 (0.56, 0.74)* | 0.129 |
| < 54 mg/ui | | HbA1c ≥ Median | 570 / 418 | 0.75 (0.65, 0.86)* | |
| | | Low Hypo Risk | 377 / 311 | 0.85 (0.73, 1)* | 0.001 |
| | - | High Hypo Risk | 759 / 466 | 0.62 (0.54, 0.7)* | |
| | | PDC < 0.80 | 618 / 490 | 0.76 (0.67, 0.86)* | < 0.001 |
| | | PDC ≥ 0.80 | 518 / 287 | 0.52 (0.44, 0.6)* | |
| Hyperglycemia | - | Age < 65 | 722 / 446 | 0.56 (0.49, 0.64)* | < 0.001 |
| JI - 0 J | | Age ≥ 65 | 830 / 628 | 0.79 (0.71, 0.89)* | |
| | | HbA1c < Median | 488 / 336 | 0.7 (0.6, 0.82)* | 0.586 |
| | + | HbA1c ≥ Median | 1064 / 738 | 0.67 (0.6, 0.75)* | |
| | | Low Hypo Risk | 387 / 352 | 0.95 (0.82, 1.1) | < 0.001 |
| | + | High Hypo Risk | 1165 / 722 | 0.57 (0.51, 0.64)* | |
| | | PDC < 0.80 | 866 / 681 | 0.79 (0.71, 0.89)* | < 0.001 |
| | - | PDC ≥ 0.80 | 686 / 393 | 0.55 (0.48, 0.63)* | |
| All-cause | - | Age < 65 | 1189 / 911 | 0.69 (0.62, 0.77)* | < 0.001 |
| hospitalization | | Age ≥ 65 | 1796 / 1577 | 0.9 (0.83, 0.98)* | |
| nospitalization | | HbA1c < Median | 1336 / 1087 | 0.8 (0.72, 0.88)* | 0.517 |
| | - | HbA1c ≥ Median | 1649 / 1401 | 0.84 (0.76, 0.91)* | |
| | | Low Hypo Risk | 925 / 964 | 1.09 (0.99, 1.2) | < 0.001 |
| | + | High Hypo Risk | 2060 / 1524 | 0.65 (0.59, 0.7)* | 0.001 |
| | | PDC < 0.80 | 1585 / 1438 | 0.92 (0.84, 1) | <0.001 |
| | _ | PDC ≥ 0.80 | 1400 / 1050 | 0.72 (0.65, 0.79)* | 0.001 |

Abbreviations: CGM, continuous glucose monitoring; CI, confidence interval; HbA1c, hemoglobin A1c (%); PDC, proportion of days covered; T1D, type 1 diabetes, T2D, type 2 diabetes.

For HbA1c outcome, difference-in-differences estimates using Linear Mixed Models indicate % HbA1c difference at 6 months after CGM initiation. The sample size shown in panels A and C reflect the eligible participants, and are the correct denominator for those who may develop outcome events (panels B and D). However, for the HbA1c outcome, participants must have at least one pre- or postindex HbA1c, and therefore, the correct sample size for HbA1c outcomes is slightly reduced compared to number in figure. OR, odds ratios for adverse events in 12 month "post-CGM" vs. "pre-CGM" period using Generalized Estimating Equations. *p < 0.05 for interaction. All models were adjusted for age, gender, ethnicity, region, pre-CGM HbA1c and hypoglycemic risk score, Elixhauser comorbidity score, number of primary care/endocrine visits, area deprivation index, index year, glucagon use and insulin type, except when variable is the stratification category.

Median baseline HbA1c % (mmol/mol) for T1D and T2D is 8.2% (66 mmol/mol) and 8.4% (68 mmol/mol), respectively. People with 'low' Hypoglycemic Risk Score are categorized as 'Low Hypo Risk' and those with 'intermediate' or 'high' Hypoglycemic Risk Score are categorized as 'High Hypo Risk'. Hypoglycemia and hyperglycemia identified by ICD-9/10 diagnostic codes in ER or inpatient setting. Hypoglycemia or glucose < 54 mg/dl include diagnoses or an outpatient glucose lab values < 54 mg/dL. Hospitalization identified by inpatient admissions. To convert HbA1c from percentage to mmol/mol, use the formula: (HbA1c, mmol/mol) = [(HbA1c,%) - 2.152] \div 0.09148).

Mediation analyses

For T1D, the effect of CGM use on the difference in HbA1c is not significantly mediated via the number of post visits. The total effect of CGM use on the HbA1c difference is -0.27 (p < 0.001, 95% CI [-0.34, -0.21]), but the indirect effect (average causal mediation effect) mediated through the number of post visits is quite small at -0.009 (95% CI [-0.026, 0.01]), which is not significant (p = 0.26).

For T2D, the effect of CGM use on the difference in HbA1c is not significantly mediated via the number of post visits. The total effect of CGM use on the difference is -0.29 (p < 0.001, 95% CI [-0.33, -0.25]), but the indirect effect (average causal mediation effect) mediated through the number of post visits is quite small at -0.008 (95% CI [-0.018, 0.002]), which is not significant (p = 0.07).

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