



The Probability of A1C Goal Attainment in Patients With Uncontrolled Type 2 Diabetes in a Large Integrated Delivery System: A Prediction Model

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OBJECTIVE

To assess patient characteristics and treatment factors associated with uncontrolled type 2 diabetes (T2D) and the probability of hemoglobin A_{1c} (A1C) goal attainment.

RESEARCH DESIGN AND METHODS

This was a retrospective cohort study using the electronic health record at Cleveland Clinic. Patients with uncontrolled T2D (A1C >9%) were identified on the index date of 31 December 2016 ($n = 6,973$) and grouped by attainment ($n = 1,653$ [23.7%]) or nonattainment ($n = 5,320$ [76.3%]) of A1C <8% by 31 December 2017, and subgroups were compared on a number of demographic and clinical variables. On the basis of these variables, a nomogram was created for predicting probability of A1C goal attainment.

RESULTS

For the entire population, median age at index date was 57.7 years (53.3% male), and the majority were white (67.2%). Median A1C was 10.2%. Obesity (50.6%), cardiovascular disease (46.9%), and psychiatric disease (61.1%) were the most common comorbidities. Metformin (62.7%) and sulfonylureas (38.7%) were the most common antidiabetes medications. Only 1,653 (23.7%) patients achieved an A1C <8%. Predictors of increased probability of A1C goal attainment were older age, white/non-Hispanic race/ethnicity, Medicare health insurance, lower baseline A1C, higher frequency of endocrinology/primary care visits, dipeptidyl peptidase 4 inhibitor use, thiazolidinedione use, metformin use, glucagon-like peptide 1 receptor agonist use, and fewer classes of antidiabetes drugs. Factors associated with lower probability included insulin use and longer time in the T2D database (both presumed as likely surrogates for duration of T2D).

CONCLUSIONS

A minority of patients with an A1C >9% achieved an A1C <8% at 1 year. While most identified predictive factors are nonmodifiable by the clinician, pursuit of frequent patient engagement and tailored drug regimens may help to improve A1C goal attainment.

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We previously reported a relatively high rate of clinical inertia in patients with uncontrolled type 2 diabetes (T2D) (hemoglobin A_{1c} [A1C] >7%, *N* = 7,389) despite a stable regimen of two oral antihyperglycemic drugs (OADs) for at least 6 months prior to the index A1C (1). In nearly two-thirds of patients, there was no evidence of pharmacologic intensification of diabetes therapy during the 6 months after the uncontrolled A1C. Most concerning was the observation that among patients in the highest index A1C category (A1C >9%, *N* = 1,448), therapy was not intensified in 44% of patients. While clinical inertia is one contributor to a reduced likelihood of A1C goal attainment, there are many other patient factors that may play a role, including socioeconomic circumstances. In addition, T2D is a progressive disease, and therefore, patients should inherently require more therapy over time to control glycemia. It has been demonstrated that persistent elevation in A1C above target (usually defined as A1C equal to or below 7%) confers an increased risk of diabetes-related complications, particularly those that are microvascular (2,3). Moreover, health care entities participating in accountable care organizations/shared savings programs monitor the percentage of patients with an A1C >9% (4). Thus, health care organizations are sharing risk with third-party payers related to these diabetes-related outcomes. There is minimal literature on the characteristics of an uncontrolled T2D population and the probability of reaching A1C goal attainment. The goal of this research was to identify a cohort of patients with uncontrolled T2D (A1C >9%) within the electronic health record (EHR) at Cleveland Clinic (CC) and to analyze the A1C goal attainment rate (A1C <8%) 1 year later. Using these data, a prediction model was developed in an attempt to identify variables that predict A1C goal attainment in this population. This model could serve as a means of identifying subgroups of patients who require additional resources or alternative approaches to T2D management in order to improve the rates of A1C goal attainment.

RESEARCH DESIGN AND METHODS

Study Cohort

The EHR system at CC was used to identify a cohort of adult patients (≥ 18 years) with a diagnosis of T2D and who were determined to have uncontrolled T2D as

reflected by an A1C >9% between 1 January 2015 and 31 December 2016 (based on A1C recorded closest to 31 December 2016). The CC health care system includes patients managed for diabetes by primary care providers or endocrinologists and covers care at academic institutions as well as community practices.

The first step in identifying the study cohort was to establish a T2D prevalence cohort within the CC EHR database as of 31 December 2016 (5). The Electronic Medical Records and Genomics (eMERGE) Network algorithm (6), modified to include ICD-10 codes in addition to ICD-9 codes as in the original algorithm, was used to calculate the earliest date when a patient record contained any of the following combinations: T2D code (ICD-9 codes 250.x0 or 250.x2; ICD-10 codes E11.xx) and T2D medication, T2D code and abnormal glucose, T2D code recorded twice and an outpatient insulin prescription, T2D medication and abnormal glucose, or insulin preceded by T2D medication. Patients with ICD-9 codes at any time specific for type 1 diabetes (250.x1, 250.x3) and/or ketoacidosis (250.10 and 250.12) or with ICD-10 codes E08 (diabetes mellitus due to underlying condition), E09 (drug or chemical induced diabetes mellitus), E10 (type 1 diabetes mellitus), or E13 (other specified diabetes mellitus) were excluded. Abnormal glucose was defined based on the American Diabetes Association criteria (fasting blood glucose [BG] ≥ 126 mg/dL, A1C ≥ 48 mmol/mol [$\geq 6.5\%$], or random BG ≥ 200 mg/dL). The earliest date that any of the five conditions was met was documented as the date on which the patient first met the criteria for T2D. Next, patients must have had a completed endocrinology or primary care visit during the period 2015–2016. Finally, to be included in the study, the most recent A1C between 1 January 2015 and 31 December 2016 must have been >9%. Patients without an A1C during this time window were not included.

Data Collection and Analysis

The following baseline characteristics and variables were recorded as identified in each patient's EHR within the 2-year period from 1 January 2015 through 31 December 2016, using the recorded value closest to 31 December 2016: age, race/ethnicity, sex, median household income, insurance status, time in T2D

data set (time from earliest date that patient met T2D criteria in the EHR per the modified Kho algorithm described above), A1C, completed endocrinology and primary care ambulatory encounters (all-cause), other encounters (phone, online messaging with health care provider using a patient portal, refills, and other [seen by nurse, review of test results, health education, immunization, home care, social work]), and antidiabetes medications. A diabetes medication class was identified as active if it remained in the current medication list in the EHR for at least 3 months after being initiated (first appearing on the medication list). A 3-month time frame was chosen to confirm that the medication was not only prescribed, but also that it was not discontinued early in the course of treatment for any reason. Income was defined according to 5-year estimates of 2011–2015 median household income at the block group level obtained from the American Community Survey (7) conducted by the U.S. Census Bureau.

The following comorbidities were recorded if they were present at any time in the patient's EHR dating back to 1998: obesity, cardiovascular disease, heart failure, hypoglycemia, psychiatric disease, cognitive impairment, chronic kidney disease (CKD), and alcohol or substance abuse. Charlson comorbidity index (CCI) score was determined based on all comorbidities identified through ICD-9 and ICD-10 codes in the patient's EHR (8,9). Please see Supplementary Table 1 for a complete list of ICD-9/-10 codes used to identify comorbidities. Figure 1 provides a schematic of the study data collection time frames.

On the basis of the most recent A1C value recorded between 1 January 2017 and 31 December 2017 (closest value to 31 December 2017) patients were grouped according to attainment of an A1C goal of <8% or nonattainment of that goal ($\geq 8\%$), and the two subgroups were compared. In recognition that A1C goals may vary by patient, a goal of <8% was chosen to allow for the capture of patients who were meeting individualized goals higher than 7%. Characteristics were reported using count with percentage for categorical variables and median with interquartile range (IQR; 25th, 75th percentile) for continuous variables. Categorical variables were evaluated for association using the χ^2 test, and continuous

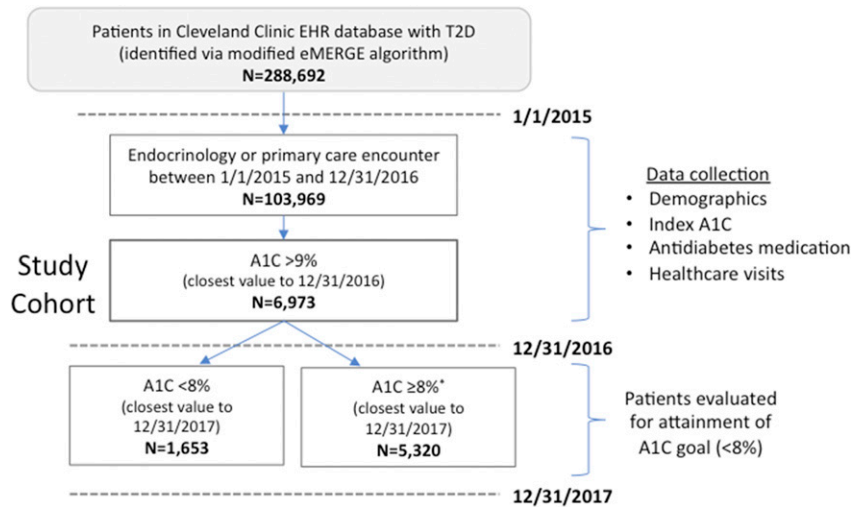


Figure 1—Study schematic: time frames for identifying relevant study data within each patient’s EHR. *Includes patients with missing A1C in 2017 ($n = 1,840$).

variables were tested using the Wilcoxon Mann-Whitney rank sum test. Patients with missing A1C data between 1 January 2017 and 31 December 2017 were included in the nongoal attainment subgroup (A1C $\geq 8\%$) because, in real-world practice, the absence of a documented A1C value to verify the patient’s control status results in the patient’s A1C arbitrarily being assigned/considered as uncontrolled by the Centers for Medicare & Medicaid Services.

Prediction Model

The model was initiated with the 28 provided candidate variables and reduced to find the best fitting parsimonious model. Candidate variables included the following: age; sex; race; ethnicity; median income; insurance; A1C; time in the T2D data set; completed primary care and endocrinology office visits during 2015–2016; therapy with a dipeptidyl peptidase 4 inhibitor (DPP-4i), sodium–glucose cotransporter 2 inhibitor (SGLT-2i), sulfonylurea, thiazolidinedione (TZD), metformin, α -glucosidase inhibitor (AGI), glucagon-like peptide 1 receptor agonist (GLP-1RA), or insulin; total number of diabetes medications; obesity; history of cardiovascular disease, congestive heart failure, hypoglycemia, depression, other psychiatric diseases, cognitive impairment, CKD, or alcohol or substance abuse; and CCI score. Interaction terms between all therapies and the comorbidities listed above were also included in the initial model. The model reduction process was performed using Frank

Harrell’s “step-down” model approximation method (10), where all the risk factors are ranked by their impact on the full model’s R^2 from the least impact to the most impact and are removed from the model. At each removal, the model’s discrimination is calculated and stopped when the change in discrimination is less than a given threshold. The final prediction model was measured by the index of prediction accuracy (IPA) (11). The model was internally validated with 1,000 bootstrap samples to obtain bias-corrected discrimination using a concordance index (c-index). The c-index is a measure of the predictive accuracy (goodness of fit) for binary outcomes in a logistic regression model; values range from 0.5 (predictive accuracy of model no better than chance) to 1.0 (model predicts outcomes perfectly). The model was used to create a nomogram to predict the probability of goal attainment based on patient and treatment characteristics.

RESULTS

Study Cohort

The modified eMERGE algorithm initially identified 288,692 patients with T2D in the CC EHR database. Of these, 103,969 patients had a completed endocrinology or primary care encounter between 1 January 2015 and 31 December 2016, and 6,973 (6.7%) of these patients had an A1C $>9\%$ on their most recent visit prior to 31 December 2016; these patients comprised the study cohort (Table 1). For the entire population, the median

(IQR) age was 57.7 years (49.8, 66.2 years), 53.3% were male, and a majority of patients were white (67.2%). Median index A1C, reflective of the most recently recorded between 1 January 2015 and 31 December 2016, was 10.2% (9.6%, 11.4%). The median time between the recorded index A1C and 31 December 2016 was 96 days (IQR = 47, 183 days). Median length of time between the earliest date that a patient met the study’s criteria for T2D identification in the EHR and the index date of 31 December 2016 was 2.9 years (IQR = 1.7, 4.4 years). Obesity (50.6%), cardiovascular disease (46.9%), and psychiatric disease (61.1%) were the most common comorbidities. Overall, metformin (used by 62.7%) and sulfonylureas (used by 38.7%) were the most common antidiabetic therapies. In $\sim 13\%$ of patients, there were no recorded antidiabetic medications during the period 2015–2016.

Only 1,653 (23.7%) patients achieved a documented A1C $<8\%$ as of 31 December 2017. Median time between the recorded follow-up A1C and 31 December 2017 was 94 days (IQR = 48, 172 days). The baseline demographic (2015–2016) and comorbidity (1998–2016) characteristics of the patient subgroups stratified by A1C goal attainment status are presented in Table 1. The subgroup of patients who attained the A1C goal of $<8\%$ by 1 year versus those who did not (as of 31 December 2017) was observed to be older (median, 59.5 vs. 57.1 years; $P < 0.001$), a higher proportion were white (72.2% vs. 65.6%; $P < 0.001$) and non-Hispanic or Latino (92.0% vs. 89.8%; $P = 0.004$), had a higher median income (\$50,715 vs. \$49,057; $P = 0.006$), a higher proportion with Medicare insurance (35.2% vs. 29.9%; $P < 0.001$), lower median baseline A1C (9.9% vs. 10.3%; $P < 0.001$), and had a greater mean number of A1C measurements during 2015–2016 (3.13 vs. 3.01; $P = 0.044$). With regard to comorbidities, the baseline characteristics of the subgroup that attained goal included a lower prevalence of obesity (47.9% vs. 51.5%; $P = 0.011$) but a higher prevalence of CKD (16.3% vs. 14.0%; $P = 0.020$). Other comorbidities were similar between the subgroups. Mean CCI score was similar between the goal attainment subgroups, but with different score distributions (the subgroup that did not attain the goal had greater proportions of people with CCI scores of 2 and ≥ 3).

Table 1—Demographics and comorbidities of 6,973 patients with uncontrolled T2D (A1C >9%) in the CC EHR system as of 31 December 2016, stratified by A1C category as of 31 December 2017

	Stratified by A1C as of 31 December 2017			P value
	All, N = 6,973	≥8%*, N = 5,320 (76.3%)	<8%, N = 1,653 (23.7%)	
Patient characteristics (2015–2016, value recorded closest to 31 December 2016)				
Age, median (IQR)	57.7 (49.8, 66.2)	57.1 (49.2, 65.7)	59.5 (51.2, 67.6)	<0.001
Sex, n (%)				0.113
Female	3,257 (46.7)	2,513 (47.2)	744 (45.0)	
Male	3,716 (53.3)	2,807 (52.8)	909 (55.0)	
Race, n (%)				<0.001
White	4,684 (67.2)	3,490 (65.6)	1,194 (72.2)	
Black	1,744 (25.0)	1,392 (26.2)	352 (21.3)	
Other	545 (7.8)	438 (8.2)	107 (6.5)	
Ethnicity, n (%)				0.004
Hispanic Americans	456 (6.5)	377 (7.1)	79 (4.8)	
Not Hispanic or Latino	6,299 (90.3)	4,779 (89.8)	1,520 (92.0)	
Unknown	218 (3.1)	164 (3.1)	54 (3.3)	
Median income, median (IQR) (missing, n = 96)	49,057 (37,958, 63,445)	49,057 (37,848, 61,892)	50,715 (37,958, 66,451)	0.006
Insurance type, n (%)				<0.001
Medicare	2,174 (31.2)	1,592 (29.9)	582 (35.2)	
Medicaid	982 (14.1)	807 (15.2)	175 (10.6)	
Private	3,035 (43.5)	2,290 (43.0)	745 (45.1)	
Other	782 (11.2)	631 (11.9)	151 (9.1)	
Current smoker	1,224 (17.6)	956 (18.0)	268 (16.2)	0.093
Years in T2D database, median (IQR)	2.93 (1.7, 4.4)	2.93 (1.76, 4.44)	2.93 (1.46, 4.51)	0.109
Years in T2D database, mean (SD)	3.77 (3.3)	3.79 (3.25)	3.71 (3.3)	
A1C, median (IQR)	10.2 (9.6, 11.4)	10.3 (9.6, 11.5)	9.9 (9.4, 11.0)	<0.001
Number of A1C measurements during 2015–2016, mean (SD)	3.04 (1.90)	3.01 (1.84)	3.13 (1.89)	0.044
Number of A1C measurements during 2015–2016, n (%)				0.022
0	0	0	0	
1	1,750 (25.1)	1,332 (25.0)	418 (25.3)	
2	1,564 (22.4)	1,233 (23.2)	331 (20.0)	
≥3	3,659 (52.5)	2,755 (51.8)	904 (54.7)	
Comorbidities (as recorded at any time in patient record, dating back to 1998), n (%)				
Obesity†	3,531 (50.6)	2,739 (51.5)	792 (47.9)	0.011
Cardiovascular disease	3,268 (46.9)	2,463 (46.3)	805 (48.7)	0.087
Congestive heart failure	848 (12.2)	657 (12.3)	191 (11.6)	0.388
Hypoglycemia	389 (5.6)	299 (5.6)	90 (5.4)	0.786
Depression	2,045 (29.3)	1,570 (29.5)	475 (28.7)	0.545
Psychiatric disease	4,259 (61.1)	3,223 (60.6)	1,036 (62.7)	0.128
Cognitive impairment	695 (10.0)	517 (9.7)	178 (10.8)	0.213
CKD	1,012 (14.5)	743 (14.0)	269 (16.3)	0.020
Alcohol or substance abuse	1,893 (27.1)	1,438 (27.0)	455 (27.5)	0.692
CCI score, mean (SD)	3.14 (2.3)	3.11 (2.24)	3.25 (2.41)	0.284
CCI by category, n (%)				<0.001
0	26 (0.4)	19 (0.4)	7 (0.4)	
1	1,759 (25.2)	1,320 (24.8)	439 (26.6)	
2	1,851 (26.5)	1,454 (27.3)	397 (24.0)	
≥3	3,337 (47.9)	2,527 (47.5)	810 (49.0)	

*Includes patients with missing A1C in 2017 (n = 1,840). †Obesity was determined by BMI (≥30 kg/m²); 30 patients had missing BMI data.

The cohort of 5,320 (76.3%) patients in the uncontrolled T2D group as of 31 December 2017 included 1,840 (34.6%) patients without any recorded A1C values in the EHR during 2017. Of these 1,840 patients with no recorded A1C during 2017:

1,233 (67.0%) had no recorded office visits; only 6.8% had one or more visit with an endocrinologist, and 29.5% had one or more visit with a primary care physician. However, all 1,840 patients with no recorded A1C value during 2017 had at least

one interaction of some type within the CC health care system during 2017, and 87% of them had >20 different interactions with the CC health care system during 2017 (an interaction could include contact other than office visits, such as phone

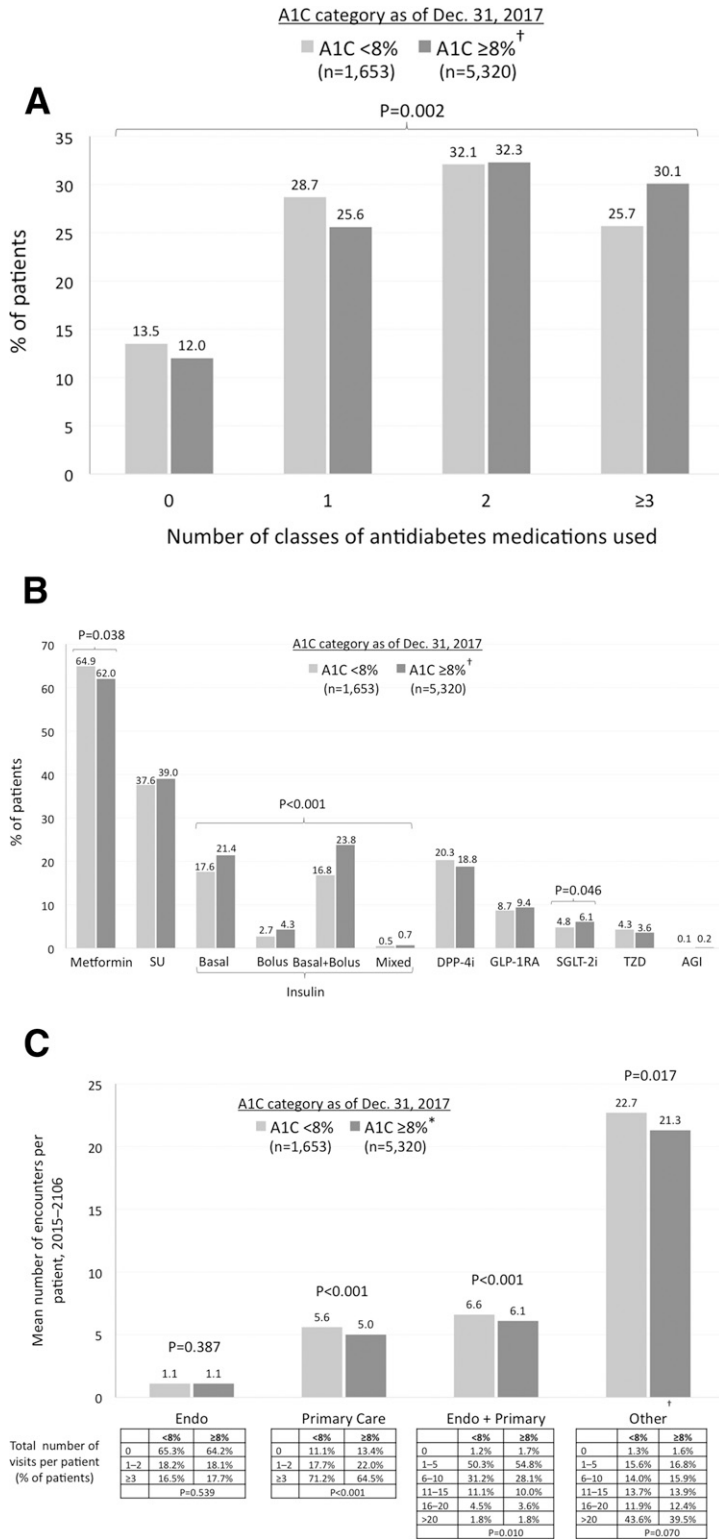


Figure 2—Baseline (2015–2016) diabetes treatment-related characteristics of patients with T2D and an A1C >9% as of 31 December 2016, stratified by A1C category (<8% or ≥8%) as of 31 December 2017. A: Number of different classes of antidiabetes medications used, 2015–2016. †Includes patients with missing A1C in 2017 (n = 1,840). B: Types of antidiabetes medications used, 2015–2016. The medications used between 1 January 2015 and 31 December 2016 include medications appearing on a patient’s current medication list in the EHR for at least 3 months after being initiated (first appearing on the medication list. †Includes patients with missing A1C in 2017 (n = 1,840). C: Number of physician encounters, 2015–2016. *Includes patients with missing A1C in 2017 (n = 1,840). †Includes phone/messaging via online patient portal/refill/other (seen by nurse, review of test results, health education, immunization, home care, or social work). Endo, endocrinology; SU, sulfonylurea.

encounters, online messaging with a health care provider through a patient portal, medication refills, and so on). Compared with patients who had a recorded A1C ≥8% during 2017, the no A1C subgroup had statistically significantly fewer endocrinology and/or primary care encounters and fewer A1C measurements during the 2015–2016 baseline period. In fact, almost half (41%) of the no A1C subgroup had only one recorded A1C during the 2-year baseline period. Supplementary Table 2 summarizes and compares the characteristics of patients in the uncontrolled T2D subgroup with a recorded A1C ≥8% as of 31 December 2017 against the characteristics of the subgroup with no recorded A1C during 2017.

T2D Treatment-Related Variables

Figure 2 presents diabetes treatment characteristics of the goal attainment (A1C <8%) and nongoal attainment (A1C ≥8%) subgroups during the baseline period (2015–2016). For the subgroup that attained the goal as of 31 December 2017, notable differences included a higher prevalence of patients using metformin (64.9% vs. 62.0%; P = 0.038) and lower proportions of patients using insulin (P < 0.001), as well as differences in the number of antidiabetes medications used per patient. The goal attainment subgroup had significantly higher mean numbers of primary care and other (nonphysician) encounters.

Prediction Model

The final prediction model included 17 variables found to be associated with the probability of A1C goal attainment. Older age, white and non-Hispanic ethnicity, Medicare or private health insurance, lower baseline A1C, higher number of completed endocrinology and primary care office visits, DPP-4i use, TZD use, metformin use, GLP-1RA use, and fewer classes of antidiabetes medications were identified to be predictors of an increased probability of A1C goal attainment. Factors included in the model that were associated with a lower probability of A1C goal attainment included insulin use and longer time in the T2D database (surrogate for duration of disease). The relationship between CCI score and probability of goal attainment was nonlinear. A CCI score of 2 was associated with lower probability than scores of 0, 1, or ≥3. The relationship between time since T2D was identified in the patient’s EHR (i.e., time

in T2D database) and the probability of goal attainment was also nonlinear, with 6 years being the duration associated with the lowest probability of goal attainment. The relationship between SGLT-2i use and probability of goal attainment was mixed. SGLT-2i use was associated with an increased probability of A1C goal attainment for patients with a history of obesity but no history of CKD. Otherwise SGLT-2i use was associated with a lower probability of A1C goal attainment.

From this model, we created a nomogram (Fig. 3) to predict the probability of goal attainment based on patient and treatment characteristics. The top line of the nomogram, labeled "Points," is used to calculate the points associated with each of the 17 variables. The subsequent 15 lines ("Age" through "CCI") are the risk factors (variables) used in the model. For a given patient, the value for each variable is plotted on these lines, and a vertical line is drawn up to the "Points" line to determine the points associated for that variable. The points for all variables are then added and the total points value is located on the "Total Points" line; from that spot on the "Total Points" line, a vertical line is drawn perpendicularly down to the "Probability of Goal Attainment" line. The probability of goal attainment is predicted according to the location at which the vertical line intersects the "Probability of Goal Attainment" line. The regression coefficients for the prediction model, including odds ratios and 95% CIs, can be found in Supplementary Table 3.

The calibration of the model was assessed with calibration curves (Supplementary Fig. 1), which measure the relationship between the outcomes predicted by the models and the observed outcomes in the cohort (10,12). The predictions made by the model were close to the actual outcomes. Probability of goal attainment was somewhat underestimated in the 50–60% range on the internal validation. The c-index was 0.648 (95% CI 0.633, 0.663), and the IPA was 5.0% (95% CI 3.9%, 6.0%).

Variance inflation factors were calculated to evaluate possible interrelationships of the model variables with one another. For all variables, the variance inflation factors ranged between 1 and 2, which suggests substantial multicollinearity is unlikely to be present (13).

A sensitivity analysis was conducted excluding the 1,840 patients who had no recorded A1C value during 2017. The regression coefficients for this analysis and calibration curves are presented in Supplementary Table 3 and Supplementary Fig. 2, respectively. Although the exact odds ratios were different between the two analyses, the effect of each predictor was similar, thereby supporting the decision to include the patients with no recorded A1C during 2017.

CONCLUSIONS

In this cohort of patients with uncontrolled T2D (A1C >9%), only a minority of patients (~25%) achieved an A1C <8% 1 year later. Unfortunately, most of the variables found to be predictive of A1C goal attainment are nonmodifiable from the standpoint of the clinician (e.g., age, race/ethnicity, type of insurance, and certain comorbidities). Perhaps patients with the noted characteristics predictive of poorer glycemic control (e.g., non-white race, younger age, Medicaid and other non-Medicare/private health insurance, very high A1C, and congestive heart failure) may warrant closer attention by clinicians. However, other variables identified as being predictive can be influenced by a provider, including medication choices and follow-up frequency. Patients who attained the defined A1C goal during the follow-up period were observed to have more frequent A1C assessments and used fewer different classes of antidiabetes medications than those who did not attain the defined A1C goal. The patients who attained the goal also had more completed encounters with primary care physicians and/or endocrinology specialists, and while this requires patient cooperation and diligence in following through with appointments, the clinician can nonetheless strive for a more aggressive follow-up schedule in those patients not meeting A1C goals.

The predictive contribution of SGLT-2i use was mixed and dependent on the concomitant presence or absence of obesity and CKD. SGLT-2i use was generally associated with a lower probability of A1C goal attainment, except for users who had obesity but not CKD; in the latter patient type, SGLT-2i use was a positive predictor of goal attainment. A negative predictive association with SGLT-2i agents in the nomogram was somewhat surprising, although the relatively small number of

patients using them makes it difficult to evaluate as a stand-alone variable. This class of drug would appear to be a good option for this cohort of patients with high cardiovascular risk, prevalent obesity, and markedly elevated A1C. It is possible that given their relatively recent introduction into the market and likely positioning as later-tiered therapy in many cases, patients using this class of drug may have been particularly difficult to manage. Certainly, data from recent cardiovascular and renal outcome studies with this class of drugs have clearly established many additional benefits in patients with T2D beyond improvements in glycemic control: cardiovascular risk reduction, a reduction in the risk of hospitalization for heart failure, and slowing the progression of CKD (14–18). Accordingly, SGLT-2i use in populations of patients at risk for these adverse outcomes would be expected to be beneficial, independent of the likely impact on probability of A1C goal attainment.

To our knowledge, the nomogram developed in this study is the first of its kind to integrate a wide variety of clinical and nonclinical patient-specific factors into a single predictive tool, rather than focusing on outcomes influenced by particular clinical interventions. The nomogram had a concordance index (global index for validating predictive ability) of 0.648, which is far from perfect predictability, yet higher than random chance (e.g., a coin flip = 0.5). Further, the IPA value was 5% (lack of any predictive value would be reflected by an IPA of 0). Data evaluating factors that are potentially predictive of A1C goal attainment in the U.S. are especially scarce. Al Mansari et al. (19) conducted an international (non-U.S.) study of adults with inadequately controlled T2D in 10 developing countries. This study identified many of the same variables contained in our nomogram as being predictive of glycemic goal attainment, including older age, Caucasian ethnicity, lower baseline A1C, shorter T2D duration (the surrogate variable in our study is "time in T2D database"), and insulin use (negative predictor and likely another surrogate for duration of T2D).

It is possible that there will be a population of patients with uncontrolled T2D unlikely to get to the goal, regardless of the methods used. However, identifying management practices and patient characteristics that are likely to be associated with a higher probability of A1C goal attainment may allow for a more

Points per Variable

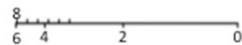
Age



A1C



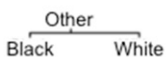
Time (years) in T2D database



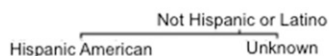
Number of completed office visits



Race



Ethnicity



Insurance



DPP-4i



TZD



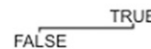
Metformin



SGLT-2i (Obesity=NO; CKD=NO)



SGLT-2i (Obesity=YES; CKD=NO)



SGLT-2i (Obesity=NO; CKD=YES)



SGLT-2i (Obesity=YES; CKD=YES)



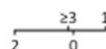
Insulin



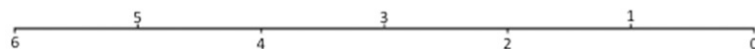
GLP-1RA



CCI



Classes of Diabetes Medication



Total Points



Probability of goal attainment

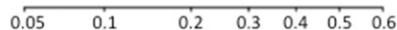


Figure 3—Prediction model nomogram. For each variable, the patient’s status/numerical value is plotted on the unique scale for that variable and a vertical line is drawn from that location up to the points line to determine a points value for that variable. The points for all variables are then added for a total points score. From the location of the total value on the total points line on the bottom, a vertical line is drawn perpendicularly from that location down to the probability of goal attainment line. The probability of goal attainment for the patient is predicted according to the value at which the vertical line intersects the probability of goal attainment line. An online calculator application version of the nomogram is available at <http://riskcalc.org:3838/Type2DiabetesA1CGoalAttainment/>. The model was initiated with 28 candidate variables, including the 17 variables represented in the final prediction nomogram plus the following 11 variables that were not retained in the final model: sex, median income, therapy with an AGI, sulfonylurea, history of cardiovascular disease, history of congestive heart failure, history of hypoglycemia, history of depression, history of other psychiatric disease, history of cognitive impairment, and history of alcohol or substance abuse.

appropriate allocation of resources and interventions to aid with A1C goal attainment. Those patients with low predicted probabilities of A1C goal attainment could be enrolled in more focused types of programs/interventions, rather than continue to flounder in the current usual-care approach. Alternative approaches could include assistance from a chronic care coordinator with regular contact with the patient or pharmacist for medication review and assistance. What is clear is that alternative approaches to T2D management must be developed, as the current approach to care has only helped to attain the protocol-defined A1C goal (<8%) in ~50% of patients (20).

The finding that Medicare insurance was a predictor of the probability of A1C goal attainment paralleled that of older age also being a positive predictor, as reported previously in large U.S. data sets (20–22). Yet, there are specific challenges with Medicare insurance not seen with commercial insurance plans that might have been expected to somewhat offset this expectation. For example, the so-called “donut-hole” gap in coverage with Medicare plans can potentially hinder medication adherence (23,24), and therefore, a lower A1C goal attainment might have been expected in this group.

The number of primary care and endocrinology office encounters was observed to be a predictor of A1C goal attainment in the model. All of the patients with no recorded A1C in 2017 were noted to have had some type of interaction with the CC health care system, but two-thirds of them had no office visits during that time. Further investigation of this observation is required. This finding would seem to suggest that more frequent face-to-face encounters can be an important factor in the likelihood of A1C goal attainment and seems to be an intuitive finding. More frequent face-to-face encounters may be speculated to improve patient (and provider) engagement, as recommended by the 2018 American Diabetes Association/European Association for the Study of Diabetes consensus statement, which emphasized that a patient-centered approach with self-management and engagement be a part of the T2D management approach (25). However, increasing the number of office encounters in the current health care environment has numerous challenges. We

speculate that patients with an A1C >9%, particularly those on complex regimens, may not only benefit from more frequent office-based encounters but also, perhaps, from other nontraditional forms of contact and communication. For example, virtual visits, and/or shared medical appointments may be used to improve access to care. These issues will need to be topics of further study, as the volume of these types of alternative encounters between patient and health care provider increases in number.

Mental illness is common in patients with chronic diseases like diabetes (26–28). The prevalence of depression was close to 30% in this study cohort, similar to that reported elsewhere for populations with T2D (29–31). Depression has been shown to have a negative impact on diabetes self-care behaviors in general (32–34), although not all analyses have found this (29). In our study, neither the prevalence of depression nor other psychiatric disease were different between the A1C attainment cohorts. The current study was not able to differentiate between depression and diabetes distress, which are often handled as unique diagnoses in studies looking specifically at the impact of these factors on T2D behaviors and outcomes. For example, one study found that diabetes distress was associated with poor A1C outcomes, while depression without diabetes distress was not (35). Our entire cohort consisted of patients who were selected for having uncontrolled diabetes; therefore, it is not surprising that certain characteristics, such as depression and other mental illness, were equally high in both groups. Similarly, the rate of alcohol or substance abuse was 27% in our study population, which is very consistent with other reports of alcohol abuse in patients with diabetes (36,37). Epidemiologic data on substance abuse in T2D are scarce. The rate of smoking in our cohort (17.6%) was within the range of other reported data (38).

Studies have shown race and ethnicity to be factors affecting glycemic control (39–41), and these emerged as predictive variables in the nomogram, with black and Hispanic american characteristics each associated with lower probability of goal attainment relative to white and non-Hispanic/Latino characteristics. The reasons for this are likely complex and worthy of additional analyses to tease out contributing factors. Prior studies have noted lower A1C testing rates in African Americans and Latinos compared

with whites (42). Perceived discrimination in general (43) and education discrimination (44) have been identified as barriers to glucose control. Clearly, these are complex issues that EHR data are not designed to capture and/or evaluate. Yet, the development of nomograms for unique racial/ethnic groups would be an extremely interesting topic for future research.

One possible limitation of the nomogram is that it was developed based on a single institutional data set and may not be generalizable to other T2D populations. Also, despite use of the eMERGE algorithm to identify patients with T2D, it is possible that some patients with T1D or latent autoimmune diabetes of adulthood may have been included as a result of misdiagnosis or miscoding. Certain variables that might be expected to influence goal attainment were not factored into the model, such as hypercholesterolemia, treatment intensification or lack of such, and patient adherence to medication usage and medical appointments. Poor treatment adherence is a well-known barrier to glycemic goal attainment (45), and one that we could not capture within the EHR data; future studies linking clinical EHR data and claims data (for adherence evaluation) would be valuable. One important variable that could not be identified with complete accuracy in our analysis was duration of T2D. We could only determine duration “in the T2D database,” which reflected the known duration of T2D while the patient was a member of the CC health care system, and this was used as a surrogate variable for total duration of disease. Further, we recognize the potential for confounding between variables in our analysis. For example, we suspect that the negative predictive influence of insulin therapy is largely a consequence of its use in patients with other negative predictors such as longer duration of disease, comorbidity burden, and worse A1c status, for example. We also recognize that insulin use likely correlates with longer duration of T2D, given the progressive nature of the disease and decline in β -cell function over time. A large national study in Italy found that patients with T2D placed on insulin therapy had higher overall risk profiles and longer duration of disease than those who were not (46). We also did not factor in specifics of insulin therapy such as duration of use or type of insulin (e.g., basal, bolus). The number of classes of

medication may also be a confounding factor with duration of T2D. These and other potential confounders will be important to address in future research. It is important to keep in mind that the nomogram was designed to assess the collective influence of multiple factors, and no individual variable should be interpreted out of the context of the nomogram as a whole.

It should be noted that fully one-third of patients in the study cohort had no A1C measurement during 2017 and, per protocol, were included in the subgroup that did not attain the goal ($A1C \geq 8\%$). While this could be considered a limitation of the study findings, it also highlights a limitation of real-world clinical practice. Patients with a lack of A1C documentation are considered uncontrolled by the Centers for Medicare & Medicaid Services. Diligent A1C follow-up and documentation in patients with T2D is an area that should be monitored by organizations to ensure maximum credit and reimbursement from Medicare, particularly institutions that are participating as Accountable Care Organizations, on risk-based contracts, or shared savings contracts. Further, American Diabetes Association guidelines recommend A1C testing at a minimum of twice yearly in patients with well-controlled T2D, and more frequently in patients with uncontrolled disease (47). In addition, about two-thirds of the patients lacking A1C data in 2017 had no recorded office visits. Although it is possible that some either left the CC health care system or died at some point during 2017, all of these patients had at least one nonoffice visit interaction (e.g., phone encounters, online messaging with a health care provider through a patient portal, medication refills) with the CC health care system during that year, and a substantial majority (87%) had more than 20 interactions. A comparison of the no A1C patients to those with a recorded A1C $\geq 8\%$ during 2017 found that the no A1C subgroup had fewer A1C measurements and provider visits during the baseline time period of 2015–2016, also. In fact, almost half (41%) of the no A1C subgroup had only one recorded A1C during the 2-year baseline period. It is possible that many patients in this subgroup were simply less diligent or regular with follow-up medical care. Finally, the current study was not designed to compare characteristics of this group of

uncontrolled T2D patients with those of the overall T2D population in the CC EHR system, although summary characteristics of the overall T2D population as of 2013 have been published previously (48). The proportion of patients in the current study with an index $A1C > 9\%$ (6.7%) was similar to that reported for the entire CC T2D population in 2013 (7.0%) (48).

An online calculator based on this risk prediction nomogram is available at <http://riskcalc.org:3838/Type2DiabetesA1CGoalAttainment/>. It is important to keep in mind that this nomogram was based on and should be considered specific to patients on the worst end of the glycemic control spectrum, many of whom were likely noncompliant/nonadherent patients. Future analyses of this type and resulting nomograms could be developed using different A1C baseline values and targets, and it would be interesting to see if the predictive factors vary based on modifying the characteristics defining the cohort of study. Yet, the nomogram presented here could serve as a valuable tool at the point of care for uncontrolled patients, ideally integrated into the EHR with automated score computation, or perhaps as an app-based tool. It could help to identify the high-risk patients with an $A1C > 9\%$ that would potentially benefit from more frequent encounters, or from alternative intervention strategies, in an attempt to increase the likelihood of A1C goal attainment. In addition, the nomogram could also be applied on a larger scale to an enterprise's EHR data to identify high-risk patients, allowing for the subsequent implementation of a variety of intervention strategies. Ongoing research in such areas may help drive the continued evolution of purposeful risk reduction strategies for patients with T2D.

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