Trajectory of Glycated Hemoglobin Over Time Among Obese Type 2 Diabetes Patients on U-100 Basal-Bolus Insulin Regimen Using Real-World Data

CELEBRATING 100 YEARS OF INSULIN 1921-2021

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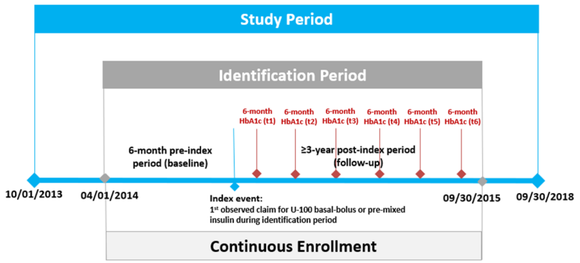
OBJECTIVES

Apply *an unsupervised* machine learning algorithm to identify patient clusters among obese type 2 diabetes mellitus (T2DM) patients on U-100 basal-bolus regimen based on HbA1c trajectory over 3 years

STUDY DESIGN

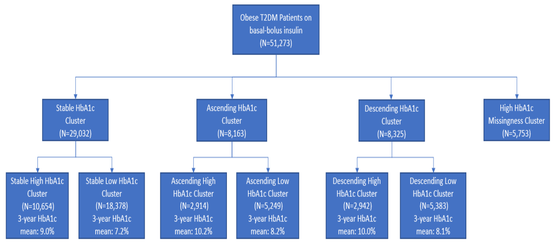
Figure 1. Study Design



- **Population:** Obese patients diagnosed with T2DM with ≥ 1 prescription claim for U-100 basal-bolus or pre-mixed insulin use during the identification period.

KEY RESULTS

Figure 2. HbA1c Clusters



A total of seven distinct patient clusters were identified based on the HbA1c trajectory, including High HbA1c Missingness cluster.

CONCLUSIONS

- **By applying an unsupervised machine learning algorithm to individuals' HbA1c trajectory over time, this study identified over 42% of 51,273 obese T2D patients on a basal-bolus regimen belonging to segments with poor HbA1c control during a three-year period, suggesting the significant existence of therapeutic inertia.**
- **Segmenting obese T2DM patients based on HbA1c trajectory over time could help formulate disease management strategies with tailored interventions for patients with therapeutic inertia.**

Background

- T2DM prevalence has consistently increased among patients with obesity; many require insulin treatment with a U-100 basal-bolus regimen.
- As endogenous insulin secretion dwindles and progressive increases in weight worsens IR, exogenous insulin doses can be quite high,[1] presenting unique disease management challenges to patients, treating physicians, and the health systems. These challenges could lead to therapeutic inertia and result in poor glycemic control (continuous increase or persistently high HbA1c).[2]
- Examining the HbA1c trajectory over a significant period could detect the existence and magnitude of therapeutic inertia.
- Past studies have not longitudinally examined HbA1c trajectory over time to identify subgroups of T2DM patients who experienced therapeutic inertia.[3]
- This study was conducted using the Veterans Health Administration (VHA) database.

Methods

- HbA1c data were captured longitudinally for a 3-year post-index period at each 6-month interval and structured prior to implementing clustering analysis. The HbA1c value closest to the middle point of each 6-month interval was recorded. If there were multiple HbA1c observations on the same date, the average value was recorded for that interval. If no HbA1c value was observed, it was recorded as missing. The analysis included patients with HbA1c records in at least 4 intervals.
- For patients with HbA1c records in fewer than 4 intervals they are grouped into High HbA1c Missingness cluster.
- For patients with HbA1c records in at least 4 intervals, a longitudinal unsupervised trajectory clustering method using R's *traj* package[4] was implemented. Twenty-four features of HbA1c trajectory were examined followed by feature reduction using factor analysis. It is followed by K-means clustering method to identify patient segments based on the trend of the HbA1c trajectory over a three-year period (Figure 2, second row). Then, the process was repeated to obtain the final distinct patient clusters by the level of HbA1c (Figure 2, third row).

Results

Patient Characteristics at Baseline

Across the seven identified clusters:

- Mean age for Ascending or Descending High HbA1c clusters were 61. Mean age for other clusters ranged from 64 to 66.
- Most patients were male (>90%) and white (>70%).
- Mean Quan-Charlson Comorbidity Index (CCI) Score ranged from 2.75 to 3.04 (moderate comorbidity = 2.0-4.9)[5].
- The percentage of patients with any new oral antihyperglycemic agent (AHA) use ranged between 48.44% - 62.63% but with only <=0.02% on SGLT-2 and <=1.22% on GLP-1.

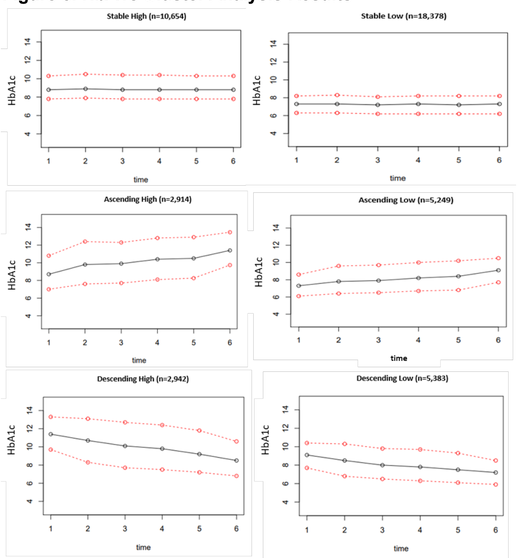
Patient Characteristics During Post-Index Period

Across the seven identified clusters:

- Mean BMI were similar (mean 37±5) with a small change over time.
- All clusters had 10-20% of patients with new AHA use over 3 years, except the High HbA1c cluster with descending trend (23%).
- Few patients used concentrated insulin with lowest percentage in High HbA1c Missingness cluster (0.45%) and highest percentage in Descending High HbA1c cluster (5.4%).
- Mean dispensed insulin TDD ranged from 108 (SD=60) units in the High HbA1c Missingness cluster to 133 (SD=68) units in the Stable High HbA1c cluster.

Results (2)

Figure 3. HbA1c Cluster Analysis Results



**Note: X-axis: Time; Y-axis: HbA1c values; Red lines: 10th and 90th percentile; Black line: Median.*

Limitations

- Patient records with missing age, sex, and race were excluded from the study. The VHA population is composed of nearly all male and predominantly white patients and is limited to enrollees without separate commercial coverage. Thus, these results may not be generalizable to broader populations.

References

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