Curves to Complexity: Functional and Topological Insights into Glycemic Control in Type 1 Diabetes

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The source of the data is Jaeb Center for Health Research (2017). The datasets have been retrieved from http://https://public.jaeb.org/dataset/546. The analyses content and conclusions presented herein are solely the responsibility of the authors and have not been reviewed or approved by the Jaeb Center for Health Research.

Introduction

Can daily patterns of glycemic curves in patients with type 1 diabetes reveal functional or topological signatures that can discriminate different levels of glycemic control, overcoming the limitations of traditional indicators such as HbA1c?

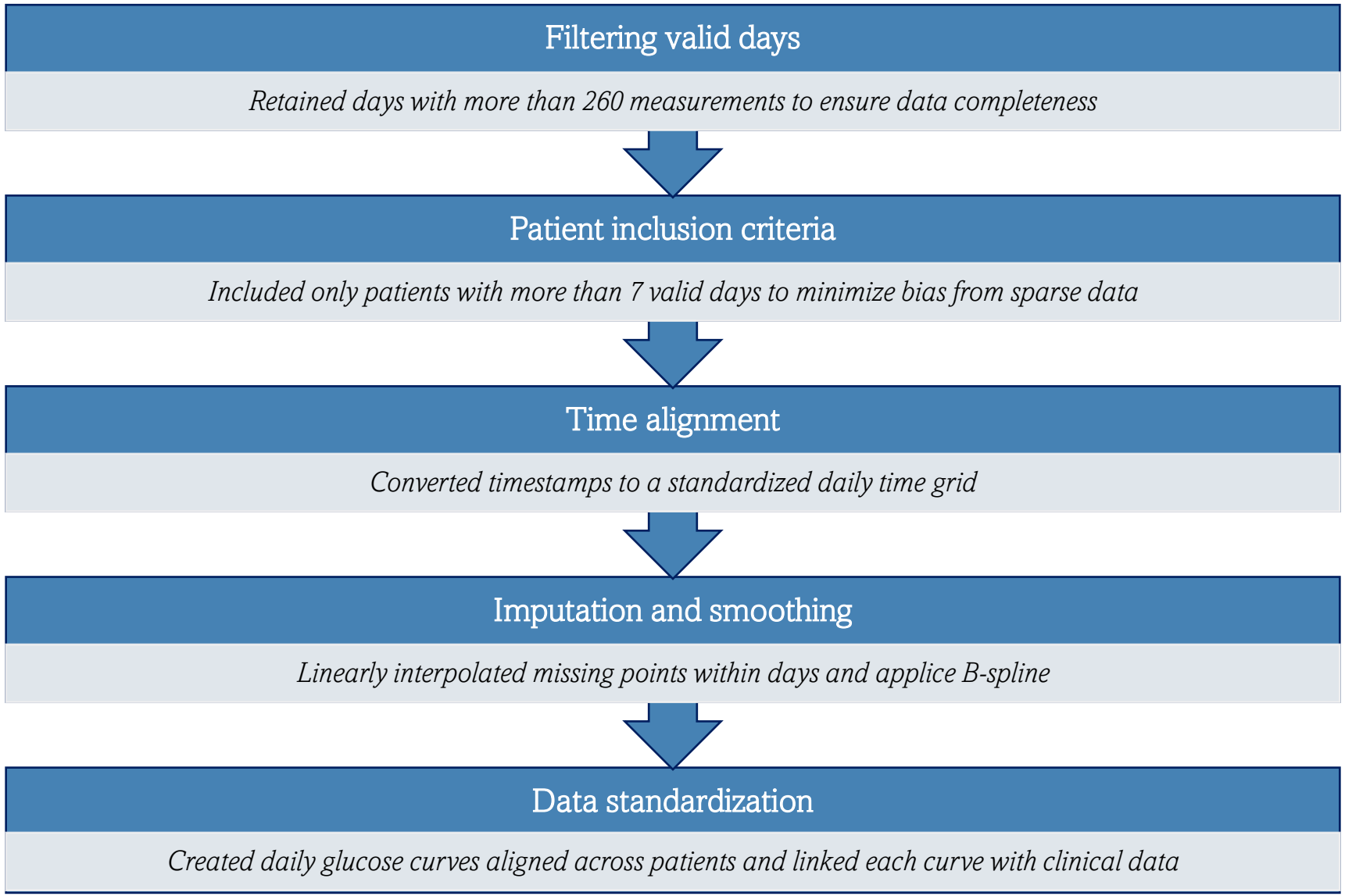
Context

- Continuous Glucose Monitoring (CGM) data enable high-resolution tracking of blood glucose fluctuations over 24-hour periods.
- Traditional summary metrics may overlook subtle yet clinically relevant glycemic patterns.
- Exploring the entire daily glucose curve using FDA and TDA may provide new insights into glycemic variability and control strategies.

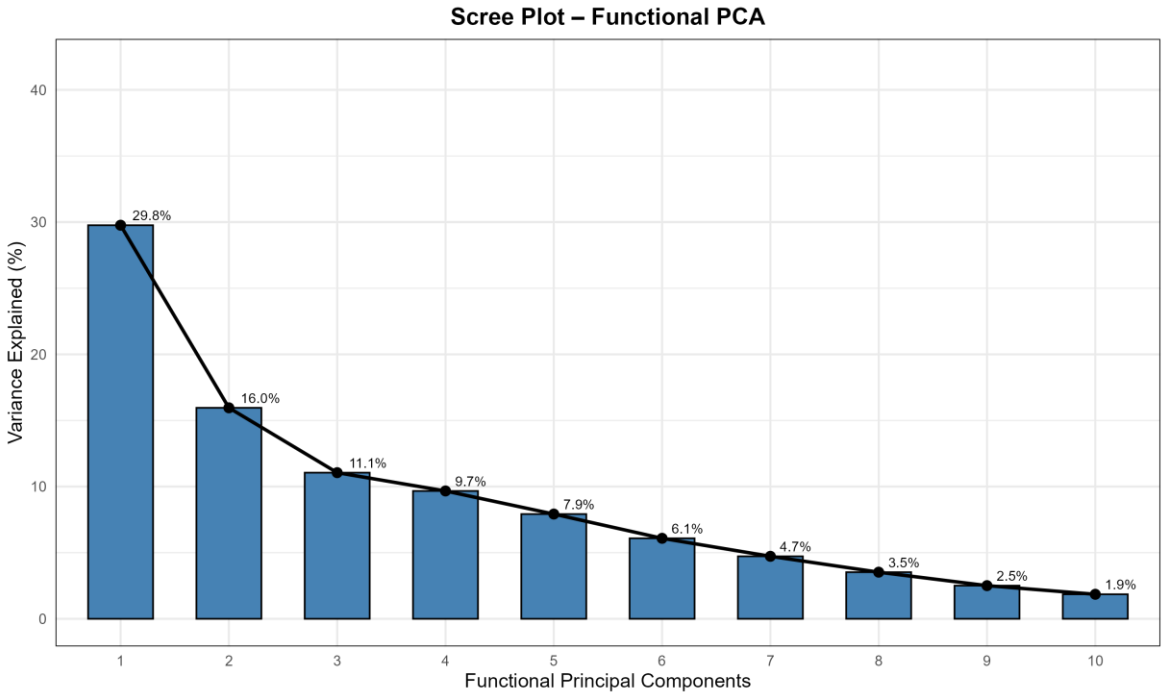
Data

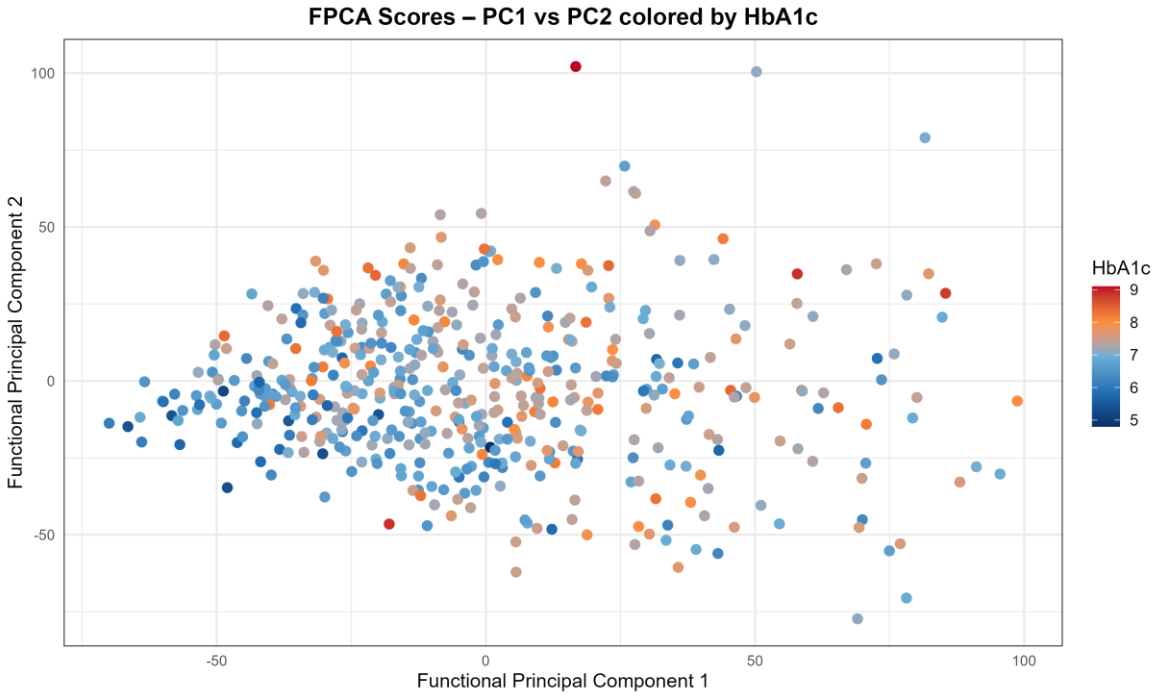
- **Sample:** 225 adults with type 1 diabetes.
- **Duration**: up to 6 months of CGM recordings per participant.
- **Measurements:** 288 glucose points per day (5-minute intervals).
- **Clinical variables**: HbA1c, frequency .of insulin boluses, fear of hypoglicemia

Data Pre-processing



Functional Principal Component Analysis

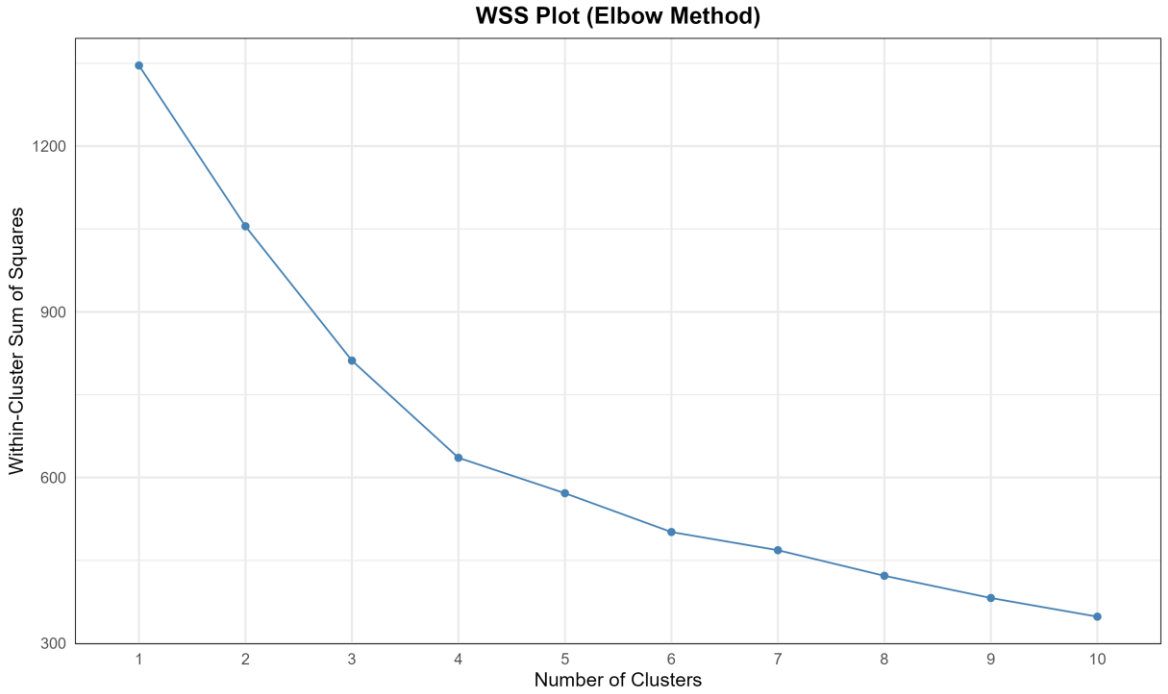


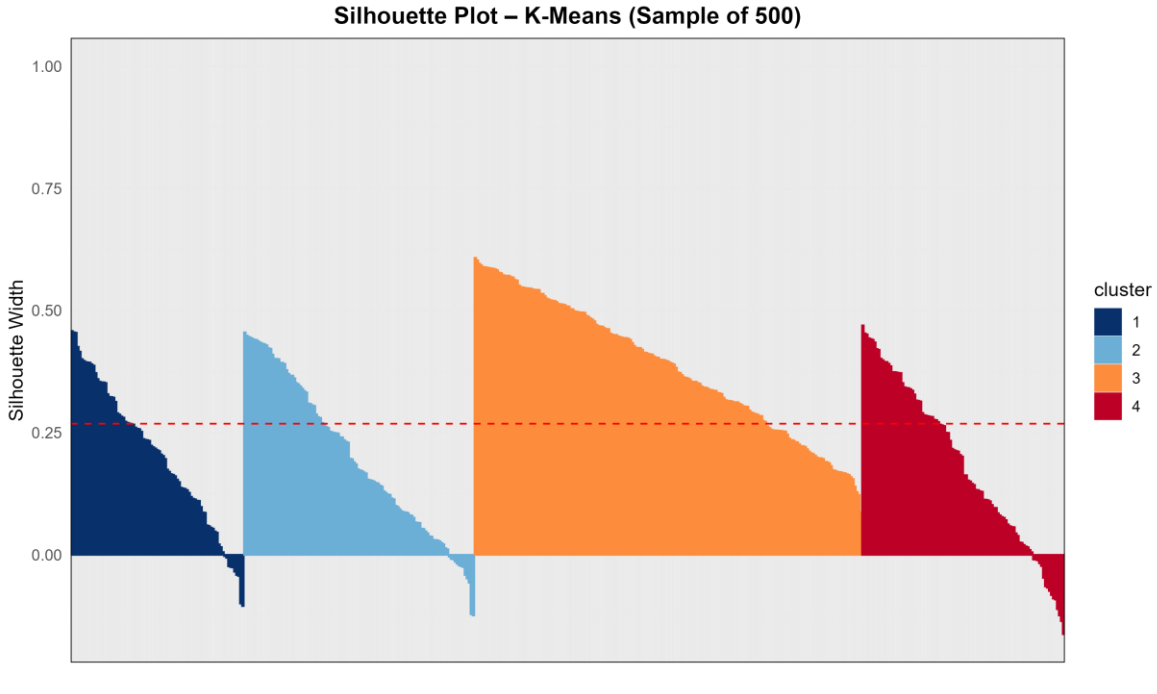


The first five harmonics (not shown here) further illustrate key patterns of variation:

- PC1 harmonic: contrasts morning vs. evening glycemic levels.
- PC2 and PC3 harmonics: capture midday peaks and instability.

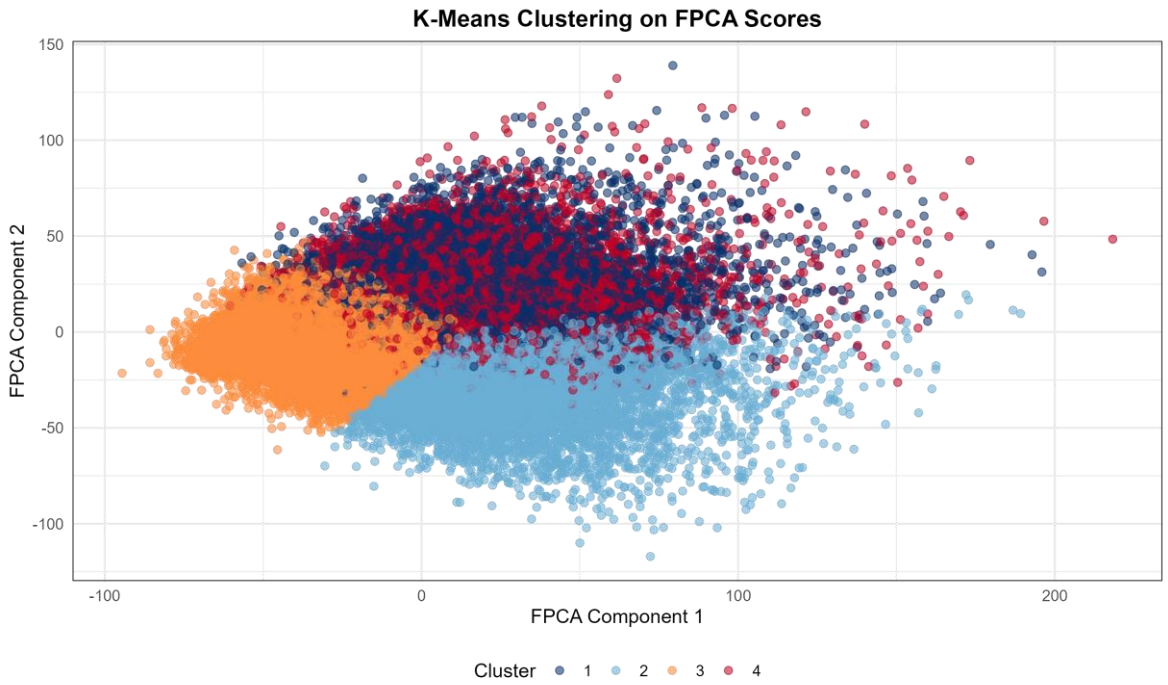
K-Means Clustering Diagnostics

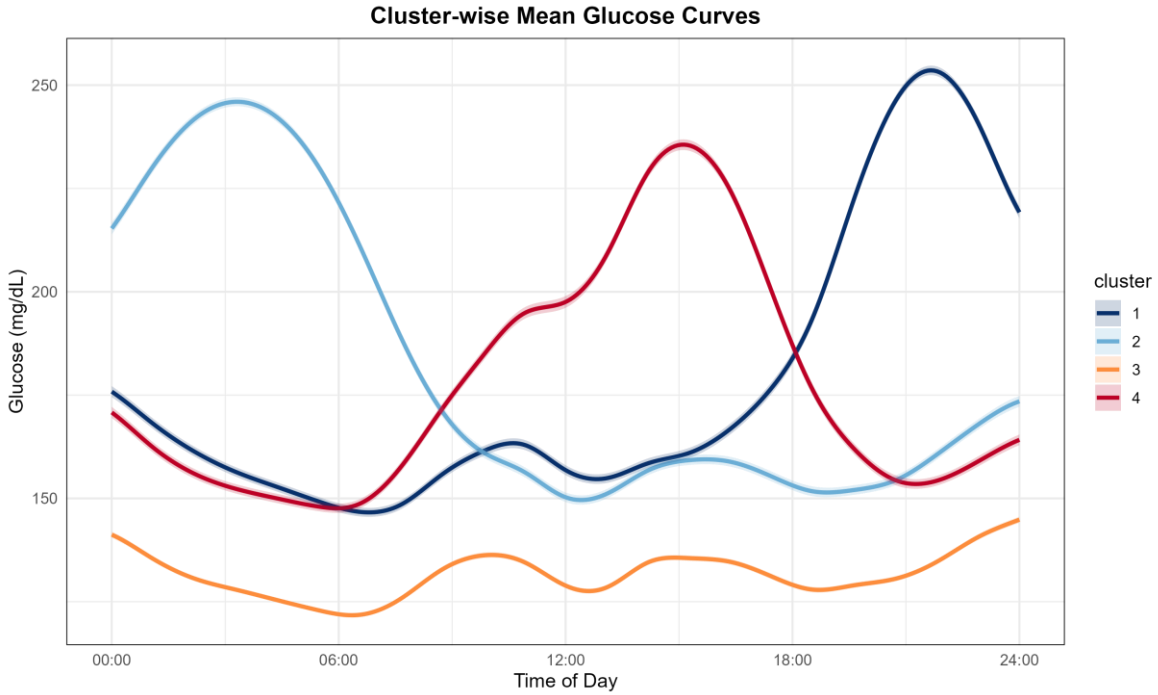




- The WSS (within-cluster sum of squares) curve shows a clear inflection at **k=4**.
  - Cluster 3: highest average silhouette (0.38) = most cohesive.
  - The overall average silhouette is <0.3 = overlap between clusters.

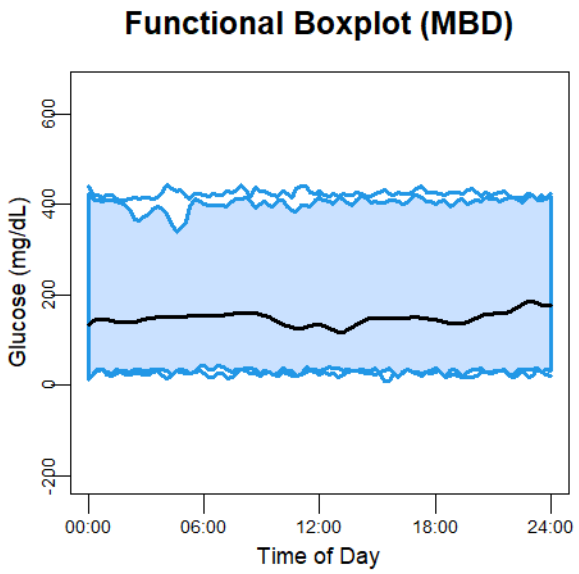
Cluster Visualization and Profiles

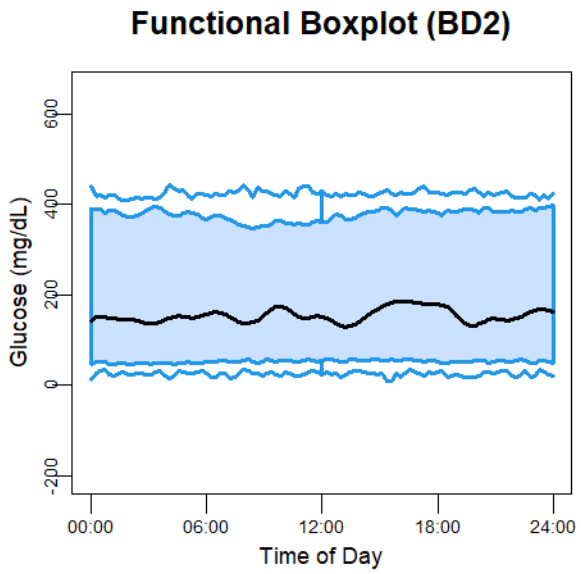


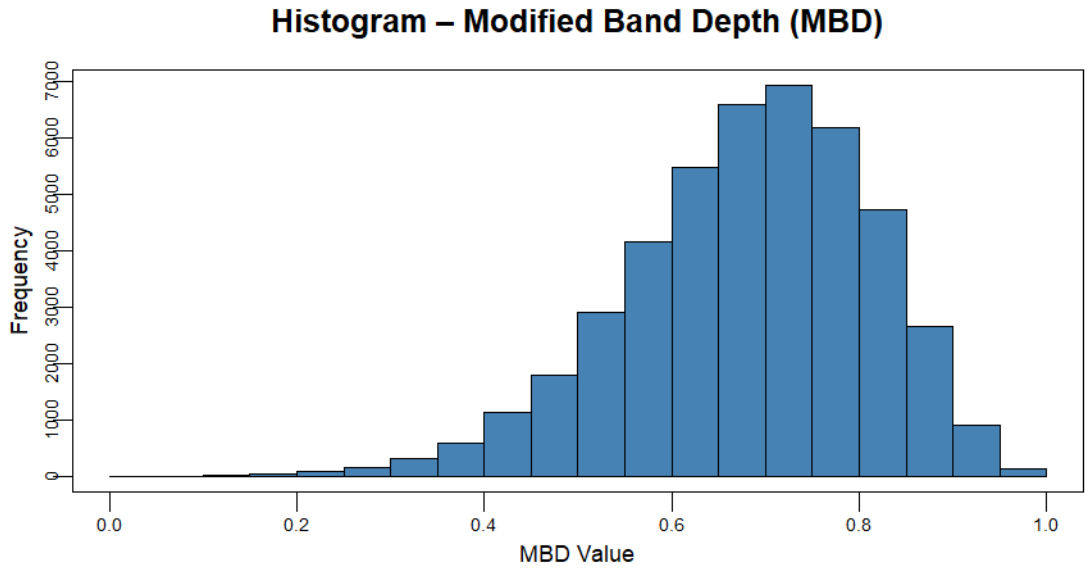


Cluster 3 appears more compact, consistent with higher silhouette scores. It has the most regular profile with well-defined meal-related peaks, associated with *lowest mean HbA1c (6.81)*

Functional Depth Analysis

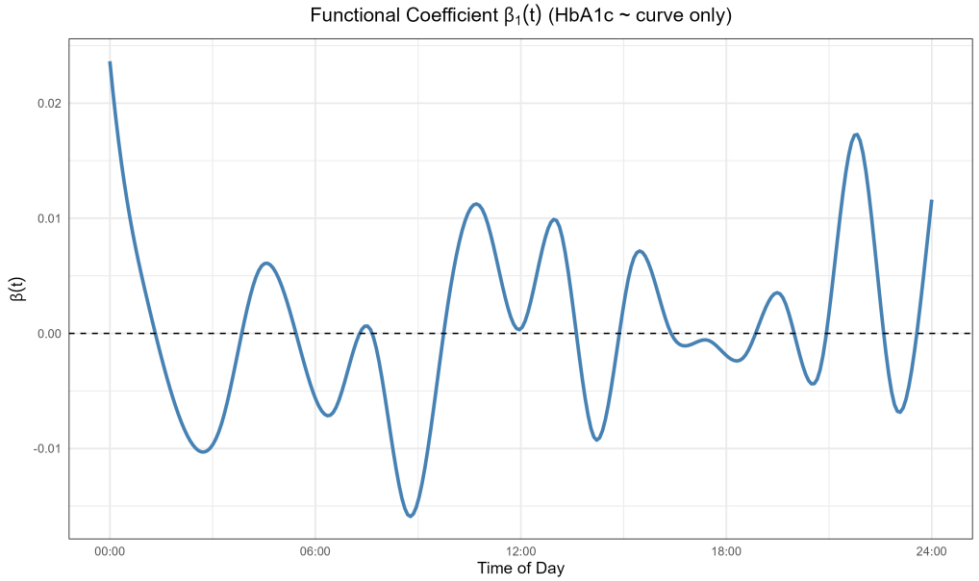


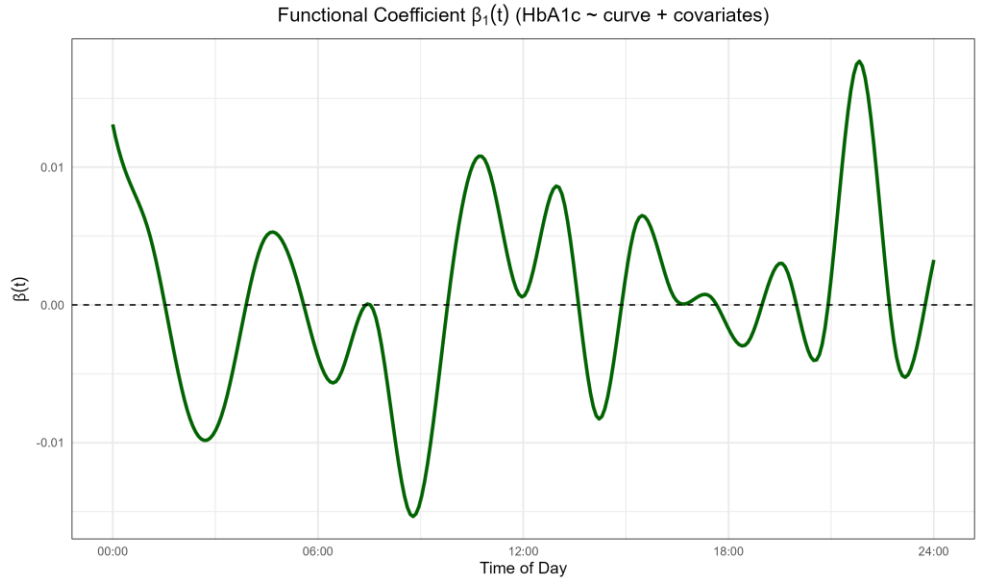


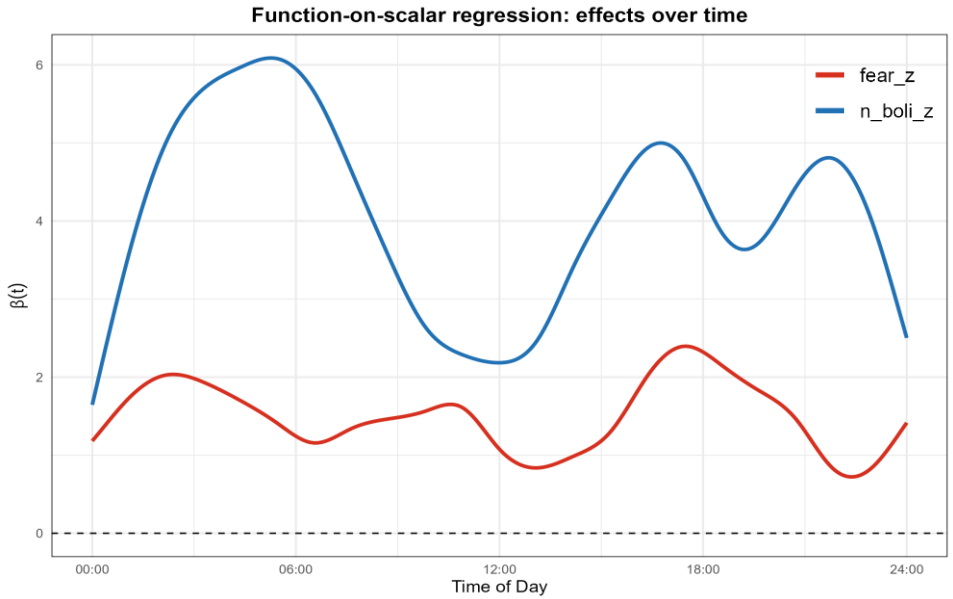


- MBD identifies overall centrality robustly, BD2 is more sensitive to local curve variations.
- Histogram confirms coexistence of a central core of stable curves and a set of more atypical profiles.
- For lower HbA1c the MBD shows more stable glycemic patterns.
- For higher HbA1c the MBD shows increased glycemic instability.

Functional Regression Models

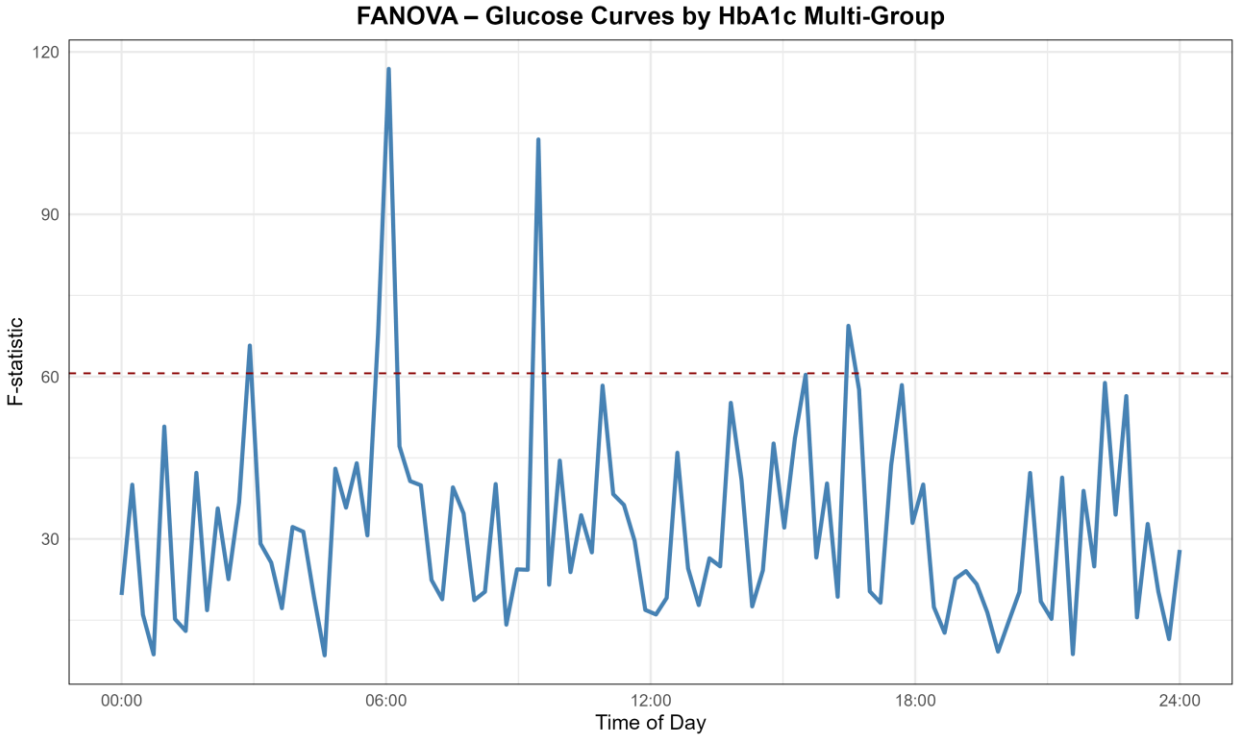


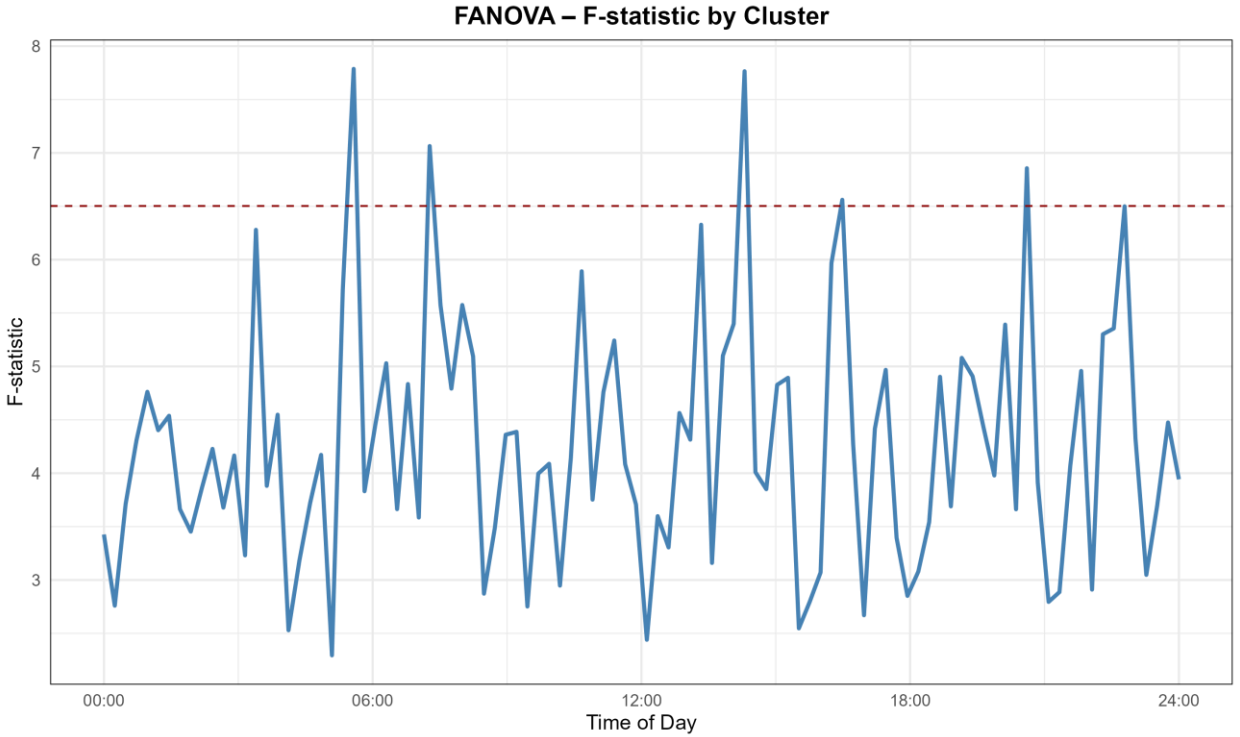




HbA1c:
has significant relationship with PC1.
Insulin boluses:
peaks match typical meal and insulin times.
Fear:
smaller, but non-negligible effects in specific periods.

Functional ANOVA Results



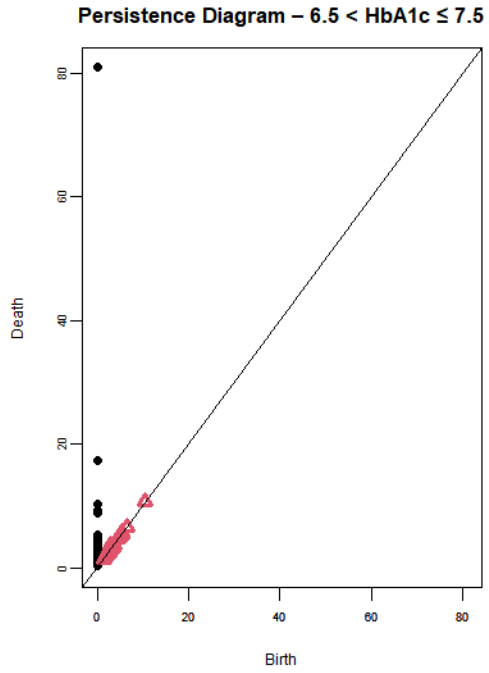


- Differences between clusters show mostly F-statistics below the significance threshold;
- No systematic differences in glycemic curves across clusters, with only occasional peaks in postprandial or night periods.

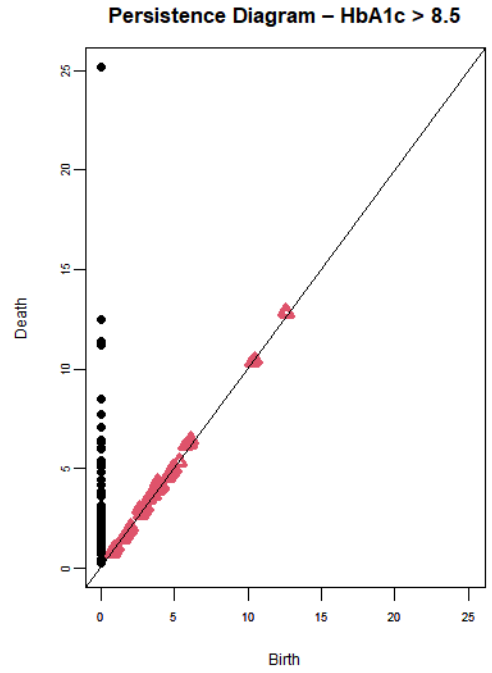
- Differences between HbA1c groups display scattered significant peaks, especially in early morning and afternoon;
- Time-specific variability related to glycemic control, but no consistent pattern across the day.

Topological Data Analysis

Persistence Diagram – HbA1c ≤ 6.5
No topological features



Persistence Diagram – 7.5 < HbA1c ≤ 8.5
No topological features



- Persistence diagrams show simple topological structures in most HbA1c groups, with little or no persistent features in well-controlled patients (HbA1c ≤ 6.5 and 7.5–8.5 groups).
- Increased topological complexity emerges in poorly controlled groups (6.5< HbA1c ≤ 7.5 and HbA1c > 8.5), reflected in more persistent connected components away from the diagonal.
- Bottleneck distance (~40.49) between intermediate and poorly controlled groups highlights significant topological differences, suggesting greater variability and fragmented glycemic patterns in patients with worse glycemic control.

Conclusions

Functional analysis showed distinct glucose patterns:
HbA1c was the main predictor, though clusters overlapped partially.

- Lower HbA1c linked to stable, central curves;
- Higher HbA1c to greater variability and instability.

- TDA revealed *simple structures* in well-controlled patients;
- but *more complex*, fragmented patterns in poorly controlled ones.

Combined FDA and TDA approaches provide quantitative tools for deeper understanding of glycemic control dynamics, with potential applications in personalized diabetes management.