GLUCOSE VARIABILITY ALTERS THE RELATIONSHIP BETWEEN AVERAGE GLUCOSE AND TIME IN RANGE: IMPLICATIONS FOR CLINICAL PRACTICE

Yongjin Xu[1], Yashesvini Ram[1], Alan Cheng[1], Timothy C. Dunn[1], Ramzi Ajjan[2]
[1]Abbott Diabetes Care, Alameda, CA, US; [2]Leeds Institute of Cardiovascular and Metabolic Medicine, University of Leeds, Leeds, UK

PURPOSE

- Investigate the effects of glucose variability, measured as coefficient of variation (CV), on the relationship between average glucose (AG) and time in range (TIR). Determine the glucose distribution that best fits AG, TIR, and CV.

MATERIALS AND METHODS

- We collected real-world continuous glucose monitoring (CGM) sensor data among T1D and T2D users of flash glucose monitoring (FLASH, FreeStyle Libre, Abbott Diabetes Care). We required at least 5-day worth of glucose data for each sensor.
- For each sensor, we computed average glucose (AG), coefficient of variation (CV), and time in range (time below, within, and above 70-180 mg/dL: TB70, TIR, TA180). We then investigated the AG-TIR relationship in CV tertiles.
- In light of previously studied functions [1], nine real positive, asymmetrical distributions with two or fewer parameters were compared against the distribution of CGM data: Lognormal, Gamma, Inverse Gaussian, Inverse Gamma, Weibull, Normal, Pareto, Generalized t, and Exponential.
    - Best-fitted distribution models were identified using the fitDist function (R GAMLSS), and Akaike information criterion (AIC).
    - Using the glucose distribution models, each AG and CV pair calculated estimated TIR (eTIR). The highest linear correlation between eTIR and TIR identified the best distribution model.

REFERENCE

1. Rodbard, D. (2020). Glucose Time In Range, Time Above Range, and Time Below Range Depend on Mean or Median Glucose or HbA1c, Glucose Coefficient of Variation, and Shape of the Glucose Distribution. *Diabetes Technology & Therapeutics*, *44*(6), 1–9.

RESULTS

- CGM from 29,164 self-identified type 1 and type 2 diabetes users (739,037 sensors) were analyzed.
- AG-TIR relationship is affected by CV, with TIR varying up to 24% for the same AG.
- For AG of 120 mg/dl (6.7 mmol/l), median (IQR) TIRs were 95 (92-97), 82 (82-87), and 71 (64-75)% for CV tertiles of 24.7, 33.2, and 43% in average, respectively.
- For TIR of 70%, The mean (±SD) AGs were 160±9.8, 151±9.9, and 135±14.5 mg/dL for CV tertiles of 24.7, 33.2, and 43% on average, respectively.
- By AIC scores, Lognormal, Inverse Gaussian, and Gamma reflect the glucose distribution the best among the nine distribution functions investigated. Linear correlation analysis between eTIR and TIR showed the Gamma distribution (R^2=0.97) had a significantly better fit (p-value<0.0001) than Lognormal (R^2=0.85) and Inverse Gaussian (R^2=0.85) (Figure 1).

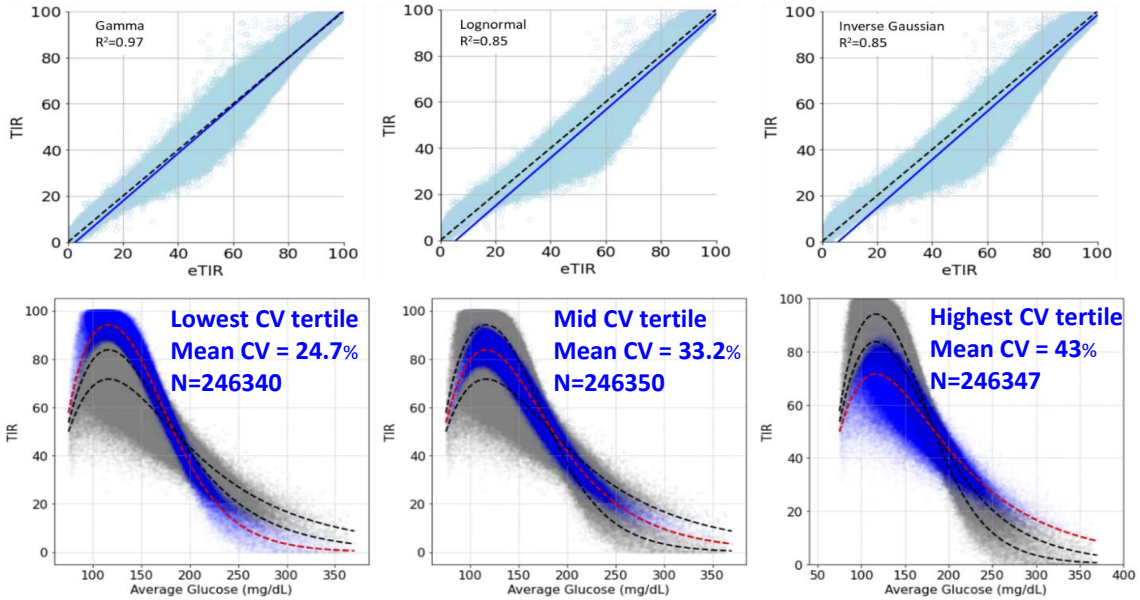


Figure 1. Top: Linear regression (blue line) of measured TIR compared to estimate (eTIR) values from average glucose and glucose standard deviation for Gamma, Lognormal, and Inverse Gaussian distributions. Dashed unity lines are presented as references. Bottom: distribution of average glucose and TIR in CV tertile. Blue dots are subjects in first (bottom left, CV mean 24.7%, range 8.2-29.5%), second (bottom middle, CV mean 33.2%, range 29.5-37%), and third (bottom right, CV mean 43%, range 37-84.6%) tertile groups, grey dots otherwise. Red curves are modeled TIR and AG curve for average group CV using Gamma distribution, black curves for other tertile groups.

CONCLUSIONS

- In clinical practice, TIR can be improved by reducing CV without altering AG, which has important clinical implications and offers one mechanism for the disconnect between TIR and glycated hemoglobin observed in some patients. The Gamma model is the best fit to connect AG, TIR, and CV.

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