

Determining the Optimal Duration of a Clinical Trial Having Time-in-Ranges as Final Endpoints

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Objective:

Determining the optimal duration of CGM recordings to accurately assess time in different glucose ranges (TIRs) is crucial for the design of clinical trials evaluating overall glycemic control. Too short monitoring periods provide a poor estimation of TIRs, affected by weekly fluctuations, while extremely long trials result in excessive costs not justified by real benefits. In this work, we propose a mathematical approach to determine the minimum CGM duration warranting a desired level of accuracy for TIRs estimate.

Method:

Framing the problem as a random variable estimation problem, we derived a mathematical formula linking the number N of monitoring days with the uncertainty of TIRs estimate, expressed as standard deviation SD (Camerlingo et al., Sci. Rep., 2020). The formula was tested on CGM data of $N=148$ subjects with type 1 diabetes and was effective for predicting the uncertainty of time in range: 70-180 mg/dL (TIR), time below range: <70 mg/dL (TBR), and time above range: >180 mg/dL (TAR).

Result:

For a CGM system with 5-min sampling rate, $N=30$ days provide a SD of 6.31% for TIR, 12.1% for TAR, 27.2% for TBR, meaning that an estimated 60%, 35%, and 5% of TIR, TAR, and TBR, respectively, are associated with $\pm 3.78\%$, $\pm 4.24\%$, and $\pm 1.36\%$ confidence intervals. Furthermore, the formula suggests 56 days to reduce the SD of TBR at 20% and 48 days to reach a SD of 5% for TIR.

Conclusion:

We derived and validated a mathematical formula to estimate the uncertainty of TIRs already estimated from past clinical trials. This formula can also be used proactively to select the minimum CGM duration granting a desired level of accuracy, which is particularly significant in terms of clinical relevance and cost-effectiveness.