Optimization of the Health Economic Model of Type 2 Diabetes Based on Glycemic Variability Mechanism

[EE111]

Zhuoqi Gu, Kexin Zhan, Lei Chen, Xiaoyu Xi

The Research Center of National Drug Policy & Ecosystem, China Pharmaceutical University, Nanjing, Jiangsu, China

Background

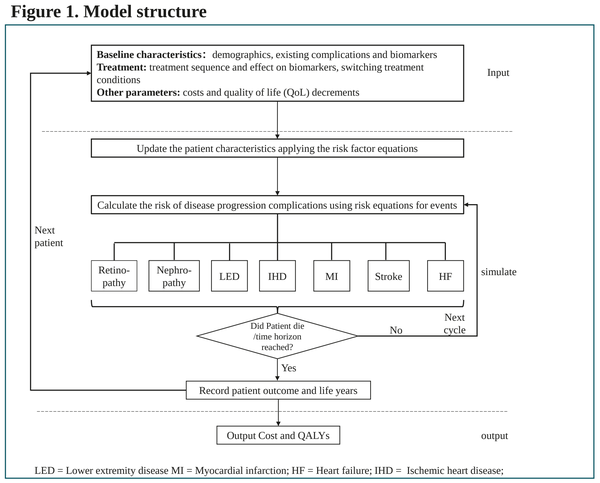
- As the global burden of type 2 diabetes(T2DM) increases, the economic evaluation of drugs becomes important. Many health economic models were used to estimate cost-effectiveness.
- HbA1c is widely used in health economics research as the gold-standard assay for assessing glycemic control measure, but it does not reflect short-term glycemic variability in patients. Limiting glycemic variability has gradually become an emerging therapeutic target in prevent associated complications, but their prognostic impact has been neglected in health economics research.
- Multiple studies have consistently demonstrated that innovative interventions exhibit efficacy advantages in reducing glycemic variability compared to placebo or conventional therapy. Neglecting this mechanism in health economic research will inevitably lead to an underestimation of the efficacy of these interventions.
- This study aims to optimize the health economic model based on the mechanism of glycemic variability so as to provide a suitable tool for evaluating novel interventions for T2DM.

Methods

Basic model structure

- The basic model is a micro-simulation cost-effectiveness model of the treatment of T2DM .Monte Carlo techniques are used to model disease progression.
- The UK Prospective Diabetes Study Outcomes Model 2 equations are used to supported the calculation of macrovascular and mortality event risks, while the microvascular event risks are sourced primarily from Bagust et al. (**Figure 1**)

Figure 1. Model structure



LED = Lower extremity disease MI = Myocardial infarction; HF = Heart failure; IHD = Ischemic heart disease;

Model validation

The face validity, verification(internal validity) and external validity of the basic model were assessed.

- **Face validity**
  - The face validity was evaluated by presenting the model structure, logic and relevant parameters to experts in the field of clinical and health economics through a colloquium.
- **Internal and external validation**
  - The internal validity was examined through verifying the individual equations and verifying their accurate implementation in code.
  - This study assessed the consistency of simulation results from two models that share the same underlying logic. Two models used the different programming approaches, modeling primarily by EXCEL formulas and VBA code. If the results exhibit consistency, it provides confirmation of strong internal validity.
  - External validation compared the model's results to event data reported in observational studies including UKPDS 33, Action to Control Cardio vascular Risk in Diabetes (ACCORD) , ADVANCE, UKPDS 80.
- A total of 42 the cumulative incidences for microvascular and macrovascular complications and mortality endpoints were simulated in this study in both internal and external validation.

Design of the glycemic variability mechanism module:

- Time in range (TIR) was used as the measure of glycemic variability, for which systematical clinical evidences were used for glycemic variability module.
- Risk adjustments for the probability of diabetes events are made dependent on glycemic variability in patients, and the formula was as follows:

$$R_{adjusted}=R_0 \times \beta_0 ^ ((TIR_{int}-TIR_{con})/10\%)$$

$R_{adjusted}$, adjusted risk of complications;R_0, risk of complications calculated in the base model;β_0, calibration coefficient from Published literatures;TIR_{int}, the TIR values for the intervention group;TIR_{con},the TIR values for conventional treatment group.

Glycemic variability module test

- To demonstrate the impact of glycemic variability module on the modeling results, the study performed pharmacoeconomic simulations with patients using T drug with improvement in glycemic variability to investigate the cumulative incidences of macrovascular, microvascular complications and death when the level of TIR was increased from 0% to 100%.

Results

Model validation

- **Face validity**
  - The model was assessed to have good face validity.
- **Verification**
  - For the set of results, the estimated intercept and slope coefficients of the regression line are (-0.012) and 0.996, respectively, which is close to the identity line. **(Figure 2)**
  - R^2 was 0.991，RMSE is 0.0134，SMAPE is 0.0649，indicating the good internal validity of the model.

Figure 2.Verification

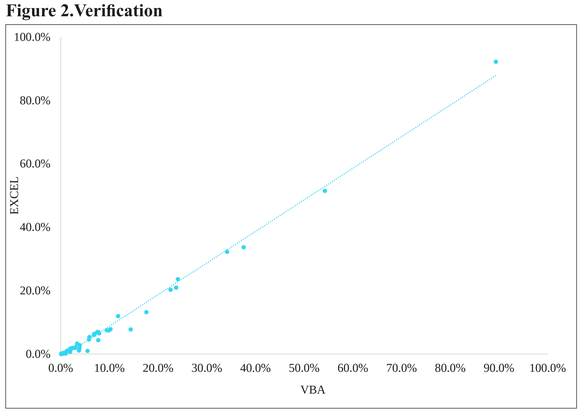
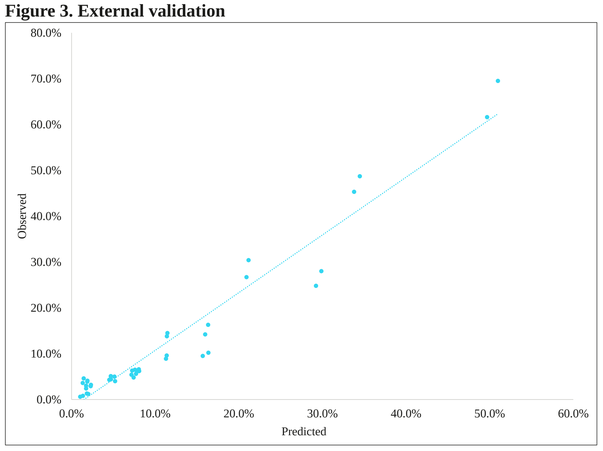


Figure 3. External validation



- **External validity**
  - For the set of results, the estimated intercept and slope coefficients of the regression line are (-0.091) and 1.258, respectively, which is close to the identity line. **(Figure 3)**
  - R^2 is 0.942，RMSE is 0.0379，SMAPE is 0.1211，indicating the good external validity of the model.

Glycemic variability module test

- In the first 10 years, patients in the T1 to T5 groups differed in the cumulative incidence of retinopathy, massive proteinuria and death, and the cumulative incidence of complications declined progressively as the level of control of glycemic variability improved.
- However, for amputation events, early improvement in glycemic variability had little effect on the adverse clinical outcomes due to the low baseline patient prevalence.(**Figure 4**)
- In the long term, the impact of the glycemic variability gap on clinical events diminished.(**Figure 5**)

Figure 4. 10-year cumulative incidence of each clinical event

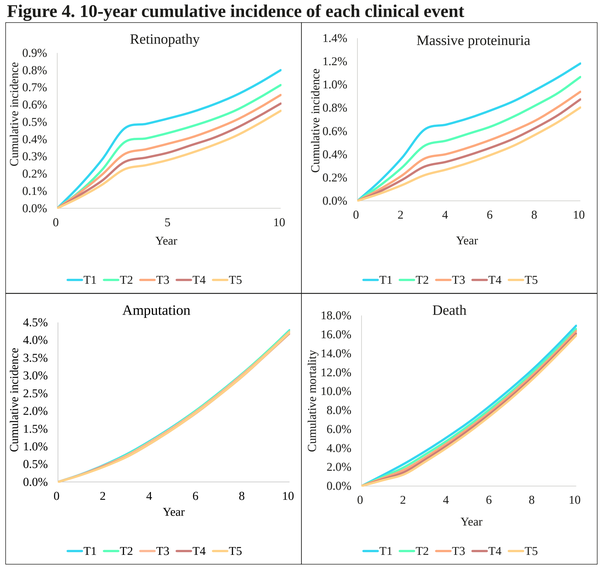
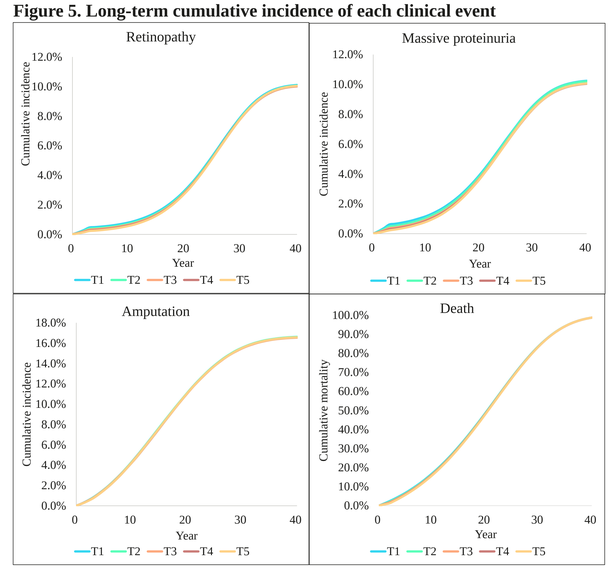


Figure 5. Long-term cumulative incidence of each clinical event



Conclusions

- This study is the first to quantify the mechanism of glycemic variability and optimize a health economic model for T2DM.
- Three types of model validation were conducted to assess the credibility and performance of the basic model.
- Glycemic variability module test results showed that the inclusion of the glycemic variability mechanism had a significant impact on patients' lifelong health outcomes, consistent with the results of the clinical observational researches, demonstrating the rationality of the module's design.

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Email: [gzq18373207656@163.com]