

## *In Silico* Simulation of Long-Term Type 1 Diabetes Glycemic Control Treatment Outcomes

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### Abstract

#### Objectives:

The goals of this study were to develop (1) a safe and effective protocol for the clinical control of type 1 diabetes using conventional self-monitoring blood glucose (SMBG) measurements and multiple daily injections with insulin analogues, and (2) an *in silico* simulation tool of type 1 diabetes to predict long-term glycemic control outcomes of clinical interventions.

#### Methods:

The virtual patient method was used to develop a simulation tool for type 1 diabetes using data from a type 1 diabetes patient cohort ( $n = 40$ ). The tool was used to test the adaptive protocol (AC) and a conventional intensive insulin therapy (CC) against results from a representative control cohort. Optimal and suboptimal basal insulin replacements were evaluated as a function of SMBG frequency in conjunction with the (AC and CC) prandial control protocols.

#### Results:

In long-term glycemic control, the AC protocol significantly decreased hemoglobin A1c in conditions of suboptimal basal insulin replacement for SMBG frequencies  $\geq 6$ /day, and reduced the occurrence of mild and severe hypoglycemia by 86–100% over controls, over all SMBG frequencies in conditions of optimal basal insulin.

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**Abbreviations:** (AACE) American Association of Clinical Endocrinologists, (AC) adaptive control, (ADA) American Diabetes Association, (CC) conventional control, (CGM) continuous glucose measurement, (CIR) carbohydrate-to-insulin ratio, (CSII) continuous subcutaneous insulin infusion, (DCCT) Diabetes Control and Complications Trial, (FPG) fasting plasma glucose, (IIT) intensive insulin therapy, (ISF) insulin sensitivity factor, (MBG) mean blood glucose concentration, (MDI) multiple daily injection, (MI) monomeric insulin, (SMBG) self-monitoring blood glucose

**Keywords:** blood glucose, compartmental models, decision support, diabetes, hyperglycemia, insulin, simulation, subcutaneous injection

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**Abstract cont.****Conclusions:**

A simulation tool to predict long-term glycemic control outcomes from clinical interventions has been developed to test a novel, adaptive control protocol for type 1 diabetes. The protocol is effective *and* safe compared to conventional intensive insulin therapy and controls. As fear of hypoglycemia is a large psychological barrier to glycemic control, the AC protocol may represent the next evolution of intensive insulin therapy to deliver increased glycemic control with increased safety. Further clinical or experimental validation is needed to fully prove the concept.

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