Type 2 Diabetes Hypoglycemia Prediction Using SMBG Data & Probabilistic Methods

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Objective

Hypoglycemia is a significant adverse outcome in patients with type 2 diabetes and has been associated with increased morbidity, mortality, and cost of care[1]. In addition, hypoglycemia is a major limiting factor for the optimization of insulin therapy. In patients with type 1 diabetes, continuous glucose monitoring (CGM) is commonly employed, but most patients with type 2 diabetes only check their glucose levels approximately one time per day. Our goal is to use self-monitored blood glucose (SMBG) values - from a sample size consistent with real-world testing frequencies - to accurately predict an individual's risk for hypoglycemia the following day. Results could then trigger interventions through an automated mobile health coaching technology.

Methods

A probabilistic model using machine learning algorithms [2] was trained with de-identified, self-monitoring blood glucose (SMBG) data from a randomized controlled trial [3]. For each patient, 10 SMBG data points were used from the week prior to a hypoglycemic event (< 70 mg/dL). Then, SMBG data, sans the hypoglycemia data point, was applied to test and validate the model. Next, using additional data sets, the model was iterated over three generations to optimize performance.

Figure 1: Machine Learning Methodology

- Data cleansing
- Identity influencers
- Prepare training and test data
- Train model
- Test model
- Optimize performance

Results

Gen 1: Performance Across Populations

Table 1: Comparison of performance (accuracy) of four first generation models across various population data sets.

Data Set (sample size)	Model 1	Model 2	Model 3	Model 4
Set 1* (1037)	91.00%	24.70%	93.30%	2.30%
Set 2* (6686)	95.20%	53.30%	96.00%	0.60%
Set 3* (1091)	94.00%	41.20%	97.00%	0.50%
Set 4* (2000)	97.00%	63.00%	97.50%	48.50%

Gen 2: Performance Over Time

Table 2: These models were optimized from the first generation Model 1. Note that optimizing the model for high sensitivity resulted in low specificity and vice versa.

	Segment of Week with Most BG's	Specificity	Sensitivity
Model 1.1	Beginning	0.12	0.86
	End	0.05	0.92
Model 1.2	Beginning	0.99	0.03
	End	1.00	0.06

Gen 3: Human vs. Machine

Figure 2: Process for comparing model's performance with that of human experts. The data provided to the model and human experts were blinded to occurrence of hypoglycemia on day eight. In this example the model correctly predicted hypoglycemia but the human expert did not.

10 SMBG Values in 7 Days

111 mg/dL	141 mg/dL	110 mg/dL	116 mg/dL	113 mg/dL	142 mg/dL	99 mg/dL	148 mg/dL	210 mg/dL	142 mg/dL
7 AM	12 PM	3 PM	6 AM	5 PM	1 PM	10 PM	8 PM	6 AM	12 PM

Day 8 Prediction	
Model	Hypoglycemia
Human Expert (Endocrinologists)	No Hypoglycemia

Day 8 Actual	
65 mg/dL	Hypoglycemia

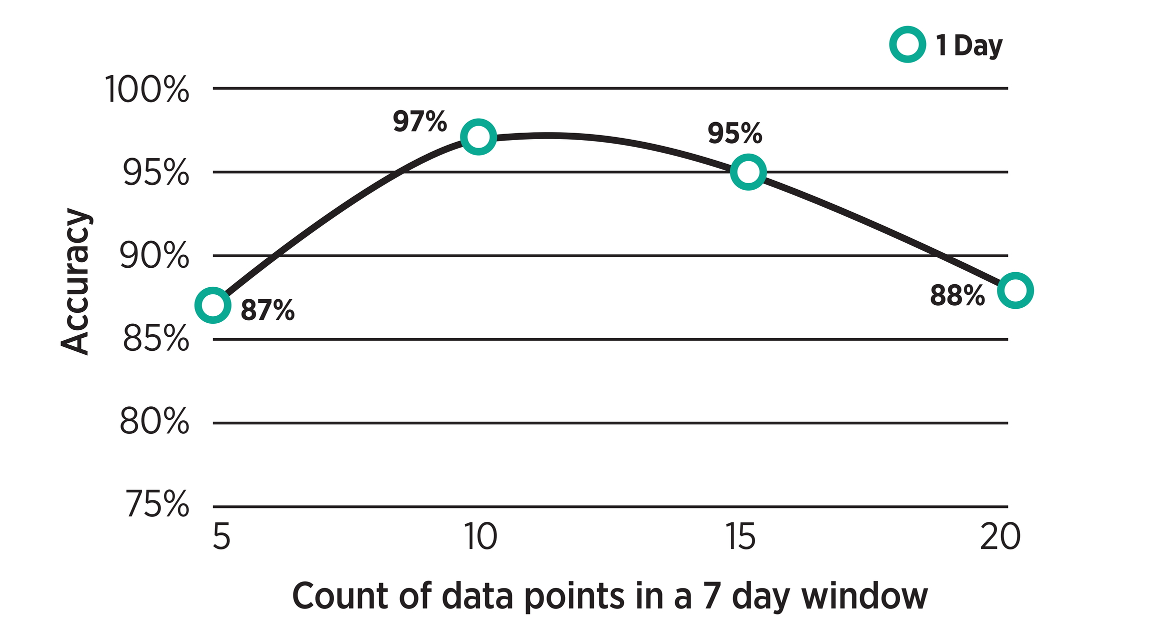
Gen 3: Human vs. Machine Cont'd

Table 3: Model 1.3 was optimized for sensitivity and specificity to minimize false negatives and false positives.

Predicted by	Specificity	Sensitivity
Model 1.3	69.50	91.67
Endocrinologist 1	73.20	75.00
Endocrinologist 2	81.80	41.62
Endocrinologist 3	84.49	41.66

Gen 1: Optimal Number of BG's Needed within 7 Days

Chart 1: Performance (accuracy) of model across sample sizes for next day prediction of hypoglycemia event



Conclusions

Real-world SMBG frequency (~1x/day) can provide adequate data to predict hypoglycemia in type 2 diabetes

- Prediction can be consistent across populations (Gen.1) and any day of the week (Gen.2)
- Optimization of specificity and sensitivity (Gen.3) may provide performance results sufficient to off-load hypoglycemia BG analysis from human experts
- Further study should test the models when used in real-time
- An automated mobile health coaching technology could use the model's predictions to provide interventions and education to manage or prevent hypoglycemia (Gen.3)

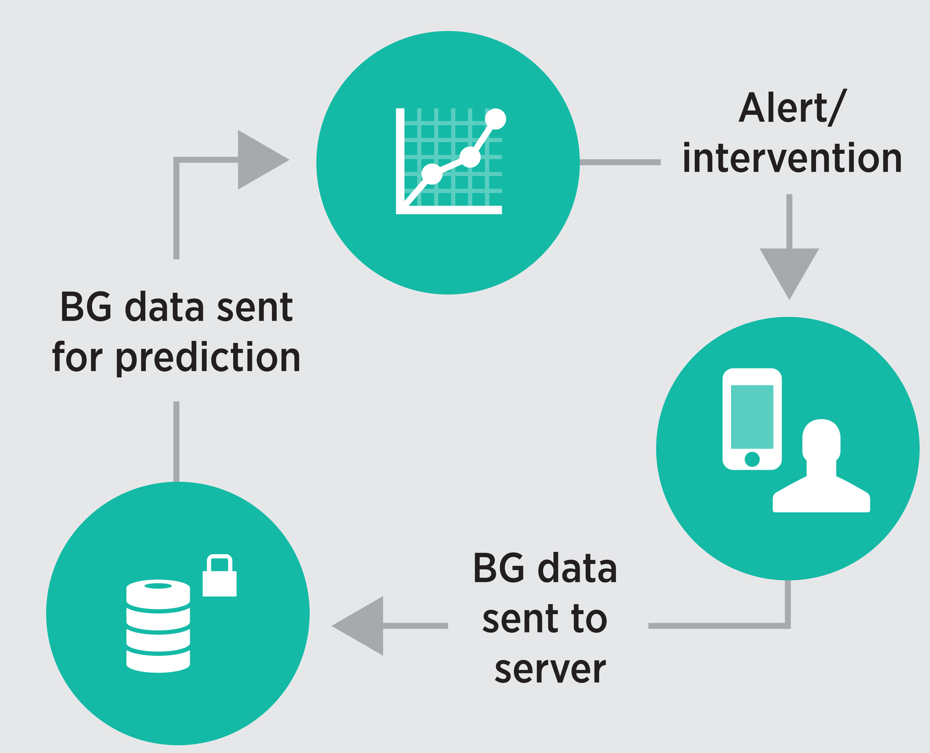


Figure 3: Real-time prediction and messaging on hypoglycemia delivered to patient's mobile device

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*Data on file, WellDoc Inc.