Prediction of hypoglycaemia frequency based on self-monitoring blood glucose data – an observational study

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BACKGROUND

Interpretation of self-monitoring of blood glucose (SMBG) data requires simple markers of overall control. Previously we found that the Hypoglycaemia Risk Parameter (HRP; based on mean and standard deviation of SMBG) predicts hypoglycaemia risk reasonably well in hospitalized patients.

AIMS

To evaluate the performance of the Hypoglycaemia Risk Parameter in outpatients and thus to predict the risk of hypoglycaemia

- based on clinical characteristics and
- based on SMBG values using HRP

STUDY DESIGN

- **Setting**: multicenter, prospective observational study
- **Participating centers**:
  - 1st Department of Medicine, Semmelweis University Faculty of Medicine, Budapest, Hungary,
  - 3rd Department of Medicine, Bajcsy-Zsilinszky Hospital, Budapest, Hungary,
  - Vanderlich Health Center, Veszprém, Hungary,
  - Endocrine and Diabetes Center, Csolnoky Ferenc Hospital, Veszprém, Hungary,
  - 77 Elektronika Ltd., Budapest, Hungary,
  - DRC Drug Research Center LLC, Balatonfüred, Hungary,
  - 3rd Department of Medicine, Semmelweis University Faculty of Medicine, Budapest, Hungary

PARTICIPANTS

- **Inclusion criteria**
  - diabetes type: type 1 or 2,
  - treatment: insulin (≥2 shots/day),
  - age: 18-75 years,
  - diabetes duration: 5-60 years.
- **Exclusion criteria**
  - acute decompensation,
  - severe hypoglycaemic events (≥1 event/month),
  - hypoglycaemia unawareness.

STUDY RELATED PROCEDURES

	V1 (baseline)	V2	V3	V4
Time (weeks)	0	4±1	8±1	12±1
Informed consent	√			
Physical examination	√			
Medical history	√			
Education on SMBG/e-Diary	√			
Download of SMBG		√	√	√
HbA1c		√	√	√
Collection of hypoglycaemia diary		√	√	√

VARIABLES COLLECTED

- **Outcomes**
  - monthly number of hypoglycaemic events (<4 mmol/l)
  - elevated hypoglycaemia risk (≥8 events/month)
- **Predictors**
  - age, sex, anthropometry, blood pressure, HbA1c
  - diabetes characteristics (type, duration, number of injections)
  - presence of diabetes complications
  - hypoglycaemia risk parameter (calculation requires ≥50 SMBG measurements/month with specified timing)

ANALYSIS

- **Number of hypoglycaemic events**
  generalized estimating equation (Poisson distribution, log link)
- **Elevated hypoglycaemia risk**
  - GEE (predictor – estimated number of events, binomial distribution, logit link)
  - discrimination – ROC analysis
  - calibration – Hosmer-Lemeshow test

BASELINE CHARACTERISTICS BY THE TYPE OF DIABETES

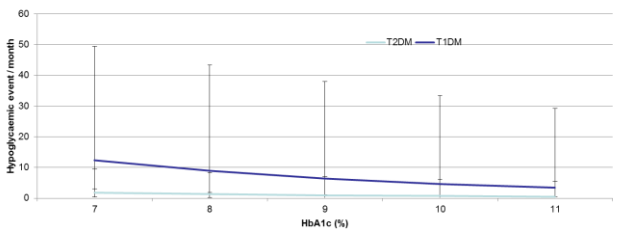
	Type 2 diabetes	Type 1 diabetes	p
N	44	55	
Age (yrs)	56±11	44±15	<0.0001
Diabetes duration (yrs)	13±9	19±12	0.003
Insulin dose (U/day)	59±30	58±32	0.85
Height (m)	1.67±9.3	1.71±10.0	0.03
BMI (kg/m²)	31.1±6.3	25.1±5.2	<0.0001
Blood pressure (mmHg)	133±16/78±8	126±14/76±9	0.08/0.37
Male, n(%)	20 (46.5)	23 (41.8)	0.69
Neuropathy, n(%)	17 (42.5)	15 (29.4)	0.27
Cardiovascular disease, n(%)	7 (18.4)	2 (3.8)	0.03
Number of injections, median[IQR]	4 [4;4]	4 [4;5]	<0.0001

GLYCAEMIC MEASURES AT V2

	Type 2 diabetes	Type 1 diabetes	p
N	44	55	
HbA1c (%)	7.3±1.3	7.5±1.3	0.43
Mean SMBG glucose (mmol/l)	8.7±2.2	8.8±1.7	0.69
SD of SMBG (mmol/l)	2.5±0.8	3.7±1.0	<0.0001
HRP	0.59±0.20	0.81±0.25	<0.0001
Hypoglycaemia frequency (/month)	3.7±6.1	14.0±11.2	<0.0001
SMBG measurements (/month)	120±39	151±61	<0.0001

CLINICAL PREDICTORS OF HYPOGLYCAEMIA FREQUENCY

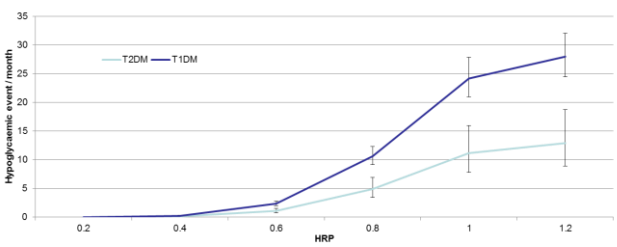
	OR	95% CI	p
Type of diabetes			<0.0001
type 1	1	Ref.	
type 2	0.149	0.082-0.269	
HbA1c	0.723	0.612-0.583	<0.0001



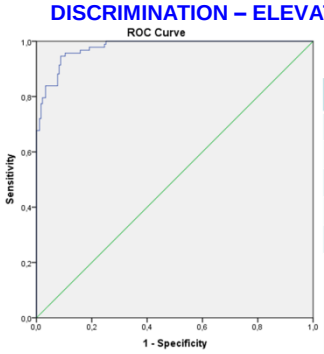
HRP AS A PREDICTOR OF HYPOGLYCAEMIA FREQUENCY

	B	SE	p
Type of diabetes			<0.0001
type 1	0	Ref.	
type 2	-0.773	0.203	
HRP	19.298	1.716	<0.0001
HRP*HRP	-8.440	0.894	<0.0001

Overall variance explained r^2=0.638, p<0.0001



DISCRIMINATION – ELEVATED HYPOGLYCAEMIA RISK

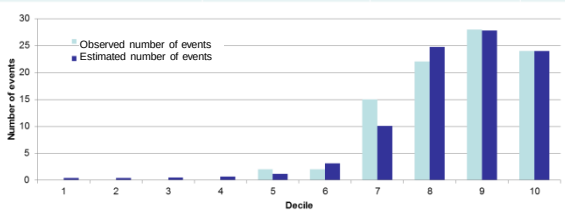


AUC 0.978; 95% CI 0.965-0.991, p<0.0001

Estimated number of events	Sensitivity	Specificity
2.7	100%	75%
5.7	95%	91%
6.0	**90%**	**92%**
6.7	85%	92%
9.1	80%	92%

CALIBRATION – ELEVATED HYPOGLYCAEMIA RISK

	OR	95% CI	p
Estimated number of events (/event)	1.710	1.489-1.964	<0.0001



Hosmer-Lemeshow test: χ^2=9.731 df=8 p=0.28 ; r^2=0.822

SUMMARY AND CONCLUSIONS

- Our results suggest that
  - the estimation of the frequency of hypoglycaemic events based on clinical characteristics has very imprecise, while
  - the frequency and an increased risk of hypoglycemic events can be predicted reasonably well using type of diabetes and HRP
- Based on our findings, predicted hypoglycaemia risk will be reported in Dcont® glucometers.

Clinical trial ethical approval and registration number: No 076816/2015/OTIG)