

Overtreatment of Hypoglycaemia in Adults with Type 1 Diabetes Does Not Appear to Deteriorate Glycaemic Control during Closed-Loop Insulin Delivery

Y. Ruan¹, L. Bally^{3,9}, H. Thabit^{7,8}, J. K. Mader⁵, H. Kojzar⁵, S. Dellweg⁶, C. Benesch⁶, S. Hartnell², L. Leelarathna⁷, M. Tauschmann^{1,4}, M. E. Wilinska^{1,4}, M. L. Evans^{1,2}, S. Arnolds⁶, T. R. Pieber⁵ and R. Hovorka^{1,4}

¹Wellcome Trust–MRC Institute of Metabolic Science, University of Cambridge

²Department of Diabetes & Endocrinology, Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK

³Department of Diabetes, Endocrinology, Clinical Nutrition & Metabolism, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland

⁴Department of Paediatrics, University of Cambridge, Cambridge, UK

⁵Department of Internal Medicine, Division of Endocrinology & Diabetology, Medical University of Graz, Graz, Austria

⁶Profil Institut für Stoffwechselforschung GmbH, Neuss, Germany

⁷Central Manchester University Hospitals NHS Foundation, Manchester Academic Health Science Centre, Manchester, UK

⁸Division of Diabetes, Endocrinology and Gastroenterology, Faculty of Biology, Medicine and Health, University of Manchester, UK

⁹Department of General Internal Medicine, Inselspital, Bern University Hospital, University of Bern, Switzerland

Introduction It is currently unclear whether overtreatment of hypoglycaemia worsens glycaemic control in type 1 diabetes during closed-loop (CL) insulin delivery.

Methods We retrospectively assessed overtreatment of hypoglycaemia using continuous glucose monitoring (CGM) data collected in 60 adults with type 1 diabetes who underwent 4-week day-and-night CL and 4-week of sensor-augmented insulin pump therapy (SAP) in random order under free-living home settings. We defined overtreatment if at least one CGM value was above 10mmol/l within 60min of the onset of hypoglycaemia (CGM <3.5mmol/l for at least 10 min). For each participant, we calculated the frequency of hypoglycaemia, the frequency of overtreatment and the proportion of hypoglycaemic episodes with overtreatment. Correlation coefficients were used to assess the relationships between the frequency and the proportion of overtreatment of hypoglycaemia and participants' demographic characteristics and glycaemic outcomes.

Results Mean(SD) frequency of hypoglycaemia was 3.2(2.0) episodes per participant-week during CL, and was lower than 5.0(4.2) episodes during SAP (P<0.01). Overtreatment was infrequent and comparable between treatments (P>0.05) (CL: frequency 0.04[0, 0.05] episodes per participant-week, proportion 0.0[0, 2.1]% of all episodes; SAP: frequency 0.03[0, 0.05], proportion 0.0[0, 1.3]%; median [IQR]). No relationship was found between participants' baseline HbA1c levels and the frequency and proportion of overtreatment of hypoglycaemia (P>0.05).

Conclusion The frequency and the proportion of overtreatment of hypoglycaemia are low during closed-loop insulin delivery and sensor-augmented pump therapy. Infrequent overtreatment of hypoglycaemia does not seem to be associated with deteriorated glycaemic control in adults with type 1 diabetes.

Table 1. Metrics related to hypoglycaemic events (N = 60). Data are presented as mean(SD) or median[IQR].

Metrics	Closed-Loop	Open-Loop	P
Hypoglycaemic events (<3.5mmol/L) per week (#)	3.2 (2.0)	5.0 (4.2)	<0.001
Hypo overtreatment (proportion, %)	0.0 [0, 2.1]	0.0 [0, 1.3]	NS
Hypo overtreatment (# of events/week)	0.04 [0, 0.05]	0.03 [0, 0.05]	NS
Maximum sensor glucose within 60 min of hypo (mmol/L)	11.5 (1.6)	11.5 (1.1)	NS
Maximum sensor glucose within 90 min of hypo (mmol/L)	13.9 (2.1)	13.6 (2.1)	NS

Table 2. Demographic characteristics of the participants (N = 60).

Characteristic	Value
Nationality	British (27), Austrian (22), German (11)
Male/Female	31/29
Age (years)	40.0 (11.2)
BMI (kg/m ²)	25.2 (3.8)
Duration of diabetes (years)	22.1 (10.4)
Duration of pump use (years)	7.1 (5.2)
Total daily dose of insulin (U/kg)	0.57 (0.14)
Baseline HbA1c (%)	7.7 (0.9)

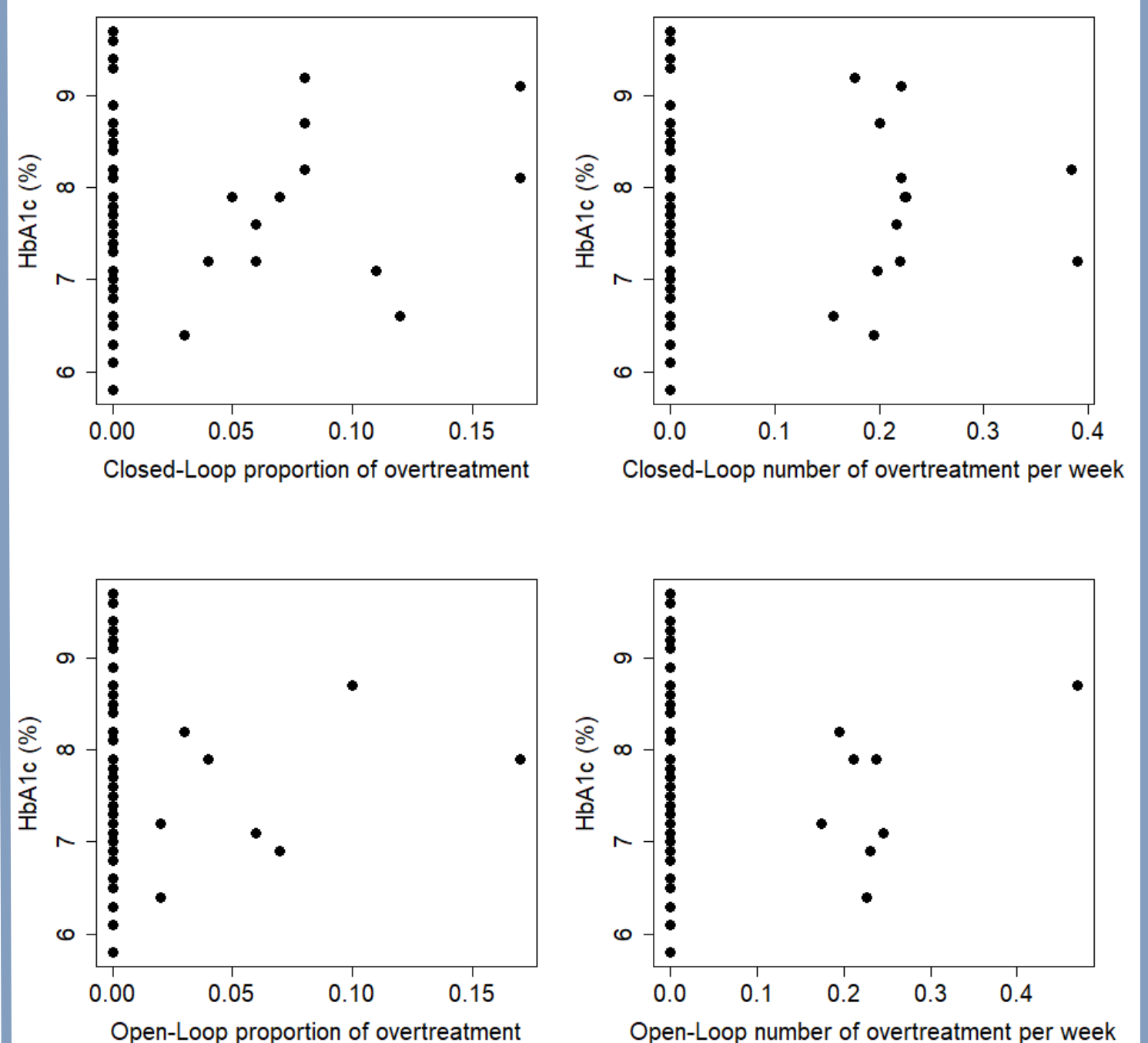


Figure 1. Scatter plots of baseline HbA1c versus the frequency and the proportion of overtreatment of hypoglycaemia (N = 60).