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Glycaemic control after connected insulin pen initiation in people living with diabetes: Results from a real-world setting

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Abstract

Aims: This observational study investigated changes in glycaemic control in people living with diabetes after initiating a connected insulin pen to administer their bolus insulin in routine clinical practice.

Materials and methods: Data were collected from adults (≥18 years) with insulin-treated diabetes who were using a continuous glucose monitoring (CGM) device and started administering bolus insulin using a connected insulin pen. Key glycaemic outcomes were time in range (TIR; 3.9–10.0 mmol/L), time above range (TAR; >10.0 mmol/L), and time below range (TBR; <3.9 and <3.0 mmol/L) in the overall population and for subgroups by country and by baseline TIR for individuals with 3 months of baseline CGM data.

Results: Data were included from 86 133 individuals with a mean (standard deviation) age of 43.7 (15.7) years. There were small but statistically significant increases from baseline in TIR at month 3 (1.5%-points), month 6 (1.4%-points) and month 12 (1.1%-points), and statistically significant decreases from baseline in TAR and TBR (<3.9 and <3.0 mmol/L) at month 3, month 6 and month 12. Increases in TIR were largest for those with the lowest baseline TIR (3-month baseline average of <40% TIR). Increases in TIR were largest in Austria, with an increase in TIR of 4.7% at month 3.

Conclusions: These real-world data show that glycaemic outcomes improved after connected insulin pen initiation, especially in individuals with the highest unmet need (i.e., lowest baseline TIR). Combining a connected insulin pen with additional support, such as app-based training or education, may further improve glycaemic control.

KEYWORDS

bolus insulin, connected insulin pen, continuous glucose monitoring, diabetes, glycaemic control, real-world evidence

1 | INTRODUCTION

The challenges of managing multiple daily injections of basal and bolus insulin for people living with type 1 or type 2 diabetes may reduce treatment adherence, such as missing or forgetting an insulin injection or not taking one on time, potentially leading to suboptimal glycaemic control.[1,2] Non-adherence may be due to several factors; for example, daily activities, travelling, public

embarrassment around injecting, fear/dislike of injections, and burden of the disease.[1,3,4]

Some connected insulin pens provide information on the timing and dose of the previous injection, enabling users to identify a late, missed or incorrect dose. Moreover, connected insulin pens have a downloadable memory enabling subsequent analyses of such data. The use of connected insulin pens combined with continuous glucose monitoring (CGM) has made it possible to verify that a substantial proportion of people living with type 1 or type 2 diabetes use insulin therapy suboptimally, often with delayed injections, missed bolus doses or bolus doses that are too low.[5–8] Notably, in people living with diabetes, one missed basal or bolus dose in a 14-day period has been associated with significant reductions in the time spent in range (TIR),[9,10] as well as higher mean glycaemic levels and higher glucose management indicator values.[10] Conversely, a bolus dosing frequency of three or more doses per day (type 1 diabetes) and a missed bolus dose frequency of less than 20% (type 1 and type 2 diabetes) were associated with improved glycaemia.[11] When used with CGM, connected insulin pens could help individuals living with diabetes to manage their glucose levels and in concert with healthcare professionals (HCPs) to achieve better adherence, which has been associated with improved glycaemic control.[7,12]

The use of connected insulin pens has been associated with reduced daily glucose levels and glycated haemoglobin (HbA_{1c}) levels.[13] An individual's level of engagement with a connected insulin pen (in terms of frequency of data uploads) was also significantly associated with improved TIR.[9,14]

A Swedish study highlighted the potential benefit of initiating connected insulin pens on glycaemic control and dosing behaviour in people living with type 1 diabetes.[15] After pen initiation, individuals living with type 1 diabetes experienced an increase in TIR and a decrease in time above range (TAR) and time below range (TBR; <3.0 mmol/L). This study provided interesting insights on the potential impact of connected insulin pen use on diabetes management from a small cohort ($n = 94$) in a single country.

The aim of the current study was to use real-world data to investigate the potential impact of connected insulin pen initiation on glycaemic control using CGM in a large, multinational cohort of individuals living with diabetes.

2 | MATERIALS AND METHODS

2.1 | Study design, participants, and procedure

This was a retrospective, observational, real-world analysis of data from people living with type 1 or type 2 diabetes in Europe, Australia, Japan, and South Africa who initiated a connected insulin pen (NovoPen 6 or NovoPen Echo Plus) to administer their bolus insulin (fast-acting insulin aspart or insulin aspart) and were using CGM. Data were collected from all individuals (≥18 years of age) living with diabetes who were using a mobile app (Abbott, Glooko or Diasend) to view their pen injection and CGM data, and who had consented to sharing their data anonymously with Novo Nordisk for research purposes. Each participating healthcare centre introduced the connected insulin pen and conducted the follow-up based on their own clinical practice.

2.2 | Outcomes and statistical analysis

Data from participants who were using multiple apps were combined using the unique connected insulin pen serial number. Data were excluded if participants only had 1 day of injections or if they used a demonstration pen. For each participant, days with acceptable CGM data (i.e., ≥15% daily coverage) were included for outcome assessments in the period from 3 months before up to 12 months after connected insulin pen initiation. A sensitivity analysis including only those days with ≥70% CGM coverage was also completed. In the period after connected insulin pen initiation, days were only included in the analysis when participants were actively using the connectivity function of the pen. Specifically, days were included if participants had at least one upload of pen data to the app in the previous 14 days (or initiated the pen in the previous 14 days) (Figure S1). All days with acceptable CGM data were included for the analysis of the CGM endpoints, irrespective of bolus dose administration. All data available from the first date of launch of the connected insulin pens (9 March 2021) up to the date of analysis (11 June 2025) were included.

For each participant, the second day of bolus injections was considered to be the pen initiation day. Injections on the first day were typically demonstrations of pen use at a clinic and were therefore not considered to be therapeutic use of the connected insulin pen. Days that met the inclusion criteria of CGM coverage and upload activity were grouped into months following pen initiation, with a month being defined as 30.4 days, starting from day 1 (the pen initiation day). Month 1 was defined as days 1–30, month 2 as days 31–60, month 3 as days 61–91, and so forth. Month 0 was the first month before connected insulin pen initiation. For each participant, data from days on which the participant used CGM and actively used the connectivity of the pen were aggregated into a single monthly value. For instance, the aggregated percentage TIR represents the percentage TIR across all included days in a month.

Only months in which participants had days that met the inclusion criteria were included in the analysis, so a month may include a different number of days for different participants, depending on their device use. Furthermore, monthly data may be missing if the participant did not use CGM (<15% daily coverage) or did not fulfil the requirements to upload activity, or if the connected insulin pen initiation day was less than a year before the study analysis date. Mean estimates were obtained at 3, 6 and 12 months after initiation. The apps contained self-reported data on age, country of residence, and connected pen medications. Some apps additionally contained self-reported data on

diabetes type and sex. Connected insulin pens collected data on insulin dose and timing of injections. To assess glycaemic control after connected insulin pen initiation, the following CGM parameters were analysed: TIR (3.9–10.0 mmol/L [70–180 mg/dL]); time in tight range (TITR; 3.9–7.8 mmol/L [70–140 mg/dL]); TAR (>10.0 mmol/L [>180 mg/dL]); TBR (<3.9 mmol/L [<70 mg/dL] and <3.0 mmol/L [<54 mg/dL]); mean sensor glucose; and glycaemic variability (interday %CV). Additionally, the percentage of data obtained with CGM sensor use on each day was evaluated, as well as the number of upload days in each month. All CGM outcomes were compared with month 0 as baseline.

Connected insulin pen parameters that were included in the analysis were daily bolus dose (U), number of bolus injections per day, and number of missed bolus doses. Month 1 was used as the baseline for bolus insulin data instead of month 0, because these data were only available after connected insulin pen initiation, with change from baseline using months 3, 6 and 12 versus month 1 (Figure S1). A missed bolus dose was defined as a meal with no bolus injection within the window of 15 min before to 1 h after the start of a meal; meals were detected from CGM data using the clinically validated glucose rate increase detector (GRID) algorithm. The GRID algorithm searches for gradients in the CGM signal and identifies a meal when the signal level is above 7.2 mmol/L and when two gradients in a row are above 5.3 mmol/L/h or three gradients in a row are above 5.0 mmol/L/h.[16] The meal start is set to 45 min before the first detected time point. Air shot injections were detected by the iPrime algorithm based on size of dose and time to next dose. Priming injections were defined as an injection of 2 U or less followed ≤6 min afterwards by an injection of the same type of insulin and were excluded from the bolus summaries.

Other outcomes included the proportion of individuals meeting internationally recommended CGM targets (>70% TIR; <4% TBR <3.9 mmol/L [<70 mg/dL]; <1% TBR <3.0 mmol/L [<54 mg/dL]; >70% TIR; and <4% TBR <3.9 mmol/L [<70 mg/dL]).[17] Participants with good-quality CGM data (CGM coverage of ≥70%) throughout the 3 months prior to connected insulin pen initiation were included in a subgroup analysis based on baseline TIR (i.e., mean TIR during the 3 months before connected insulin pen initiation). Five baseline TIR subgroups were pre-specified (<40%, 40%–<50%, 50%–<60%, 60%–<70%, and ≥70% TIR). A subgroup analysis of change in TIR from baseline to month 3 was performed for each country with at least 1000 participants.

Monthly aggregated data were analysed with random effect models, with month as a fixed effect and participant as a random effect. The latter accounts for the correlation between the repeated results for each individual and handles the missing data, assuming these are missing at random. Three different types of models were used, depending on the endpoints. Endpoints that were reasonably well approximated by a normal distribution were analysed with a linear mixed model. Daily insulin dose (excluding air shots) was modelled by a log-normal mixed model. Binary endpoints were analysed by generalised estimating equations, based on a binomial distribution, and using an exchangeable model for the working correlation matrix.

A supplementary analysis was conducted in participants that had monthly aggregated TIR values at both month 0 and month 3 as per the criteria above. The participants were grouped in three groups based on the calculated change in TIR: more than 5% change; a change between −5% and 5%; and a change of less than −5%. Baseline characteristics were compared across the groups to understand participants with the greatest change in TIR.

Analyses were conducted using R version 4.3.0 (21 April 2023) with libraries lme4 version 1.1-34 and geepack version 1.3.9.[18,19] A significance level of 0.05 was predefined for all statistical comparisons.

3 | RESULTS

3.1 | Demographics and baseline characteristics

Data were received from 118 909 accounts from users with CGM and a connected insulin pen who were sharing data. After removing duplicate accounts and including only adults who met the inclusion criteria, 86 133 individuals from 21 European countries, Australia, Japan and South Africa were included for analysis (Tables 1 and S1). The mean (standard deviation) age for all individuals was 43.7 (15.7) years. Some characteristics, such as diabetes type and sex, were not available for all participants based on the mobile app used and information provided by individuals.

The proportion of eligible participants decreased over time since connected insulin pen initiation (Figure S2). In Section 3, we focus on the data at baseline, month 3, month 6 and month 12.

CGM coverage increased from baseline (86.7%) to month 3 (90.0%), month 6 (90.3%) and month 12 (91.7%). The mean percentage of upload days (days with uploads as a percentage of all days included in the month) was 33.1% at month 1, 30.0% at month 3, 26.3% at month 6 and 24.2% at month 12 (i.e., on average, data were uploaded once every 3–4 days).

3.2 | Glycaemic outcomes

There was an immediate increase from baseline (month 0) in the percentage of TIR following connected insulin pen initiation. At month 3, the increase was +1.5%-points (95% confidence interval [CI] 1.4%-points, 1.6%-points); at month 6, the increase was +1.4%-points (95% CI 1.3%-points, 1.5%-points); and at month 12, the increase was +1.1%-points (95% CI 1.0%-points, 1.2%-points); see Table 2. There were statistically significant increases from baseline in TITR at month 3 (+1.1%-points [95% CI 1.0%-points, 1.2%-points]), month 6 (+1.0%-points [95% CI 0.8%-points, 1.1%-points]) and month 12 (+0.7%-points [95% CI 0.5%-points, 0.8%-points]); see Table 2. There were significant decreases from baseline in TAR, TBR (<3.9 mmol/L [<70 mg/dL]), and TBR (<3.0 mmol/L [<54 mg/dL]) at month 3, month

TABLE 1 Study population characteristics.

	Study population ($N = 86\,133$)
CGM days, *n* (*n*/individual)	15 251 801 (177.1)
Days with CGM and bolus injections, *n* (*n*/individual)	8 820 575 (102.4)
Age, mean (SD), years	43.7 (15.7)
Sex, *n* (%)	
Unknown	77 794 (90.3)
Male	4620 (5.4)
Female	3719 (4.3)
Diabetes type, *n* (%)	
Unknown	77 131 (89.5)
Type 1	8092 (9.4)
Type 2	503 (0.6)
LADA	241 (0.3)
Other[a]	166 (0.2)
Country, *n* (%)	
UK	28 038 (32.6)
Spain	17 716 (20.6)
France	10 909 (12.7)
Sweden	5305 (6.2)
Australia	3250 (3.8)
Denmark	3239 (3.8)
Austria	2837 (3.3)
Poland	2675 (3.1)
Japan	2216 (2.6)
Other[b]	9948 (11.5)
Mobile application, *n* (%)	
Abbott	74 394 (86.4)
Glooko	5438 (6.3)
Combined[c]	5361 (6.2)
Diasend	940 (1.1)
Connected insulin medication, *n* (%)	
Fast-acting insulin aspart	30 264 (35.1)
Insulin aspart	26 170 (30.4)
Insulin aspart, insulin degludec	9994 (11.6)
Fast-acting insulin aspart, insulin degludec	8832 (10.3)
Insulin detemir, insulin aspart	3241 (3.8)
Fast-acting insulin aspart, insulin aspart	2486 (2.9)
Fast-acting insulin aspart, insulin detemir	1494 (1.7)
Fast-acting insulin aspart, insulin aspart, insulin degludec	1104 (1.3)
Other[d]	2548 (3.0)

Abbreviations: CGM, continuous glucose monitoring; LADA, latent autoimmune diabetes of adults; SD, standard deviation.
[a]Including gestational diabetes, prediabetes and no diabetes.
[b]Other countries (all with <2% of participants) were Belgium, Croatia, Czech Republic, Finland, Germany, Greece, Ireland, Italy, Luxembourg, the Netherlands, Norway, Portugal, Slovenia, South Africa and Switzerland.
[c]Participants who used multiple mobile applications.
[d]Other insulin medications include human insulin and other combination regimens.

6 and month 12. The proportion of individuals who met the clinical target of >70% TIR increased from 23% at baseline to 25% at month 3, month 6 and month 12 (Table 2). A similar increase was seen in the proportion of participants achieving the target of >70% TIR and <4% TBR (<3.9 mmol/L [<70 mg/dL]; Table 2). There was a small decrease in %CV from baseline (−0.3%-points) to month 3, month 6 (−0.3%-points) and month 12 (−0.4%-points); see Table 2. Mean glucose levels were 10.3 mmol/L (186.1 mg/dL) at baseline, 10.2 mmol/L (183.4 mg/dL) at month 3, 10.2 mmol/L (183.7 mg/dL) at month 6 and 10.2mmol/L (184.2 mg/dL) at month 12 (Table 2). Results from a sensitivity analysis including only days with ≥70% CGM coverage showed similar results (Table S2).

When the data were analysed by individuals' change in TIR, participants with a ≥5% change in TIR at month 3 had a lower mean baseline TIR than those individuals with a −5% to +5% change in TIR or ≤−5% (Table S3). Of the individuals with a ≥5% change in TIR, only 11% had a baseline TIR >70%, compared with 31% and 29% in the −5% to +5% and ≤−5% groups, respectively.

3.3 | Bolus dose

The mean total daily bolus dose increased slightly from 21.6 U at month 1 to 21.8 U at month 3, 21.7 U at month 6 and 21.9 U at month 12 (Table 2). A slight but statistically significant reduction was seen in the number of bolus doses from month 1 to month 3, month 6 and month 12. No major changes from baseline were observed for the number of missed bolus doses at month 3, month 6 and month 12 (Table 2).

3.4 | Change in TIR by baseline TIR

Based on stratification of the CGM data by baseline TIR, the largest changes in TIR were observed in individuals with baseline TIR less than 40% or at least 70% (Table 3). The subgroup with the lowest TIR at baseline (<40%) showed the greatest statistically significant improvement in TIR from baseline to month 3 (+3.8%-points [95% CI 3.5%-points, 4.1%-points]), from baseline to month 6 (+4.5%-points [95% CI 4.2%-points, 4.9%-points]) and from baseline to month 12 (+4.6%-points [95% CI 4.2%-points, 5.1%-points]). In individuals with the highest baseline TIR (≥70%), TIR decreased from baseline to month 3 (−1.5%-points [95% CI −1.7%-points, −1.3%-points]), from baseline to month 6 (−2.3%-points [95% CI −2.5%-points, −2.1%-points]) and from baseline to month 12 (−3.2%-points [95% CI −3.5%-points, −3.0%-points]).

3.5 | Change in TIR by country

Estimated change in TIR from baseline to month 3 was greatest in Austria, with an increase of 4.7%-points (Table 4). The proportion of participants in Austria achieving >70% TIR increased from 34.9% at baseline to 43.0% at month 3. Participants from Austria and Japan

TABLE 2 CGM parameters, glycaemic outcomes, bolus dosing information and proportions of individuals achieving clinically meaningful targets ($N = 86\,133$).

		Month 0	Month 3[a]	Change (95% CI)	Month 6[a]	Change (95% CI)	Month 12[a]	Change (95% CI)
TIR	%	52.4 (52.3, 52.6)	53.9 (53.7, 54.0)	1.5 (1.4, 1.6)	53.8 (53.6, 54.0)	1.4 (1.3, 1.5)	53.5 (53.3, 53.7)	1.1 (1.0, 1.2)
	Time	12 h 35 m	12 h 56 m	21.3 m (19.7 m, 22.8 m)	12 h 55 m	20.1 m (18.3 m, 21.8 m)	12 h 51 m	15.9 m (13.9 m, 18.0 m)
TITR	%	32.3 (32.1, 32.4)	33.4 (33.2, 33.5)	1.1 (1.0, 1.2)	33.2 (33.1, 33.3)	1.0 (0.8, 1.1)	32.9 (32.8, 33.1)	0.7 (0.5, 0.8)
	Time	7 h 44 m	8 h 0 m	16.0 m (14.6 m, 17.4 m)	7 h 58 m	13.7 m (12.2 m, 15.2 m)	7 h 54 m	9.5 m (7.7 m, 11.3 m)
TBR (<3.9 mmol/L [<70 mg/dL])	%	3.32 (3.29, 3.35)	3.19 (3.16, 3.22)	−0.13 (−0.16, −0.11)	3.21 (3.18, 3.24)	−0.11 (−0.14, −0.08)	3.17 (3.13, 3.21)	−0.15 (−0.19, −0.11)
	Time	48 m	46 m	−1.9 m (−2.3 m, −1.5 m)	46 m	−1.6 m (−2.0 m, −1.2 m)	46 m	−2.2 m (−2.7 m, −1.6 m)
TBR (<3.0 mmol/L [<54 mg/dL])	%	0.50 (0.49, 0.51)	0.47 (0.46, 0.48)	−0.03 (−0.04, −0.02)	0.47 (0.46, 0.48)	−0.03 (−0.04, −0.01)	0.47 (0.45, 0.48)	−0.03 (−0.05, −0.02)
	Time	7 m	7 m	−0.4 m (−0.6 m, −0.3 m)	7 m	−0.4 m (−0.5 m, −0.2 m)	7 m	−0.5 m (−0.7 m, −0.3 m)
TAR	%	44.3 (44.1, 44.4)	42.9 (42.8, 43.1)	−1.3 (−1.5, −1.2)	43.0 (42.8, 43.2)	−1.3 (−1.4, −1.2)	43.3 (43.1, 43.5)	−1.0 (−1.1, −0.8)
	Time	10 h 37 m	10 h 18 m	−19.4 m (−21.0 m, −17.7 m)	10 h 19 m	−18.5 m (−20.4 m, −16.7 m)	10 h 24 m	−13.9 m (−16.0 m, −11.7 m)
Mean glucose	mmol/L	10.3 (10.3, 10.3)	10.2 (10.2, 10.2)	−0.1 (−0.2, −0.1)	10.2 (10.2, 10.2)	−0.1 (−0.1, −0.1)	10.2 (10.2, 10.2)	−0.1 (−0.1, −0.1)
CV	%	35.9 (35.8, 35.9)	35.6 (35.6, 35.7)	−0.3 (−0.3, −0.2)	35.6 (35.5, 35.6)	−0.3 (−0.4, −0.3)	35.5 (35.4, 35.6)	−0.4 (−0.5, −0.3)
CGM coverage	%	86.7 (86.6, 86.8)	90.0 (89.9, 90.1)	3.3 (3.2, 3.4)	90.3 (90.2, 90.4)	3.6 (3.5, 3.7)	91.7 (91.6, 91.8)	5.0 (4.9, 5.1)
Bolus dosage[b]	U/day	21.6 (21.5, 21.7)	21.8 (21.7, 21.9)	0.01 (0.01, 0.01)	21.7 (21.6, 21.9)	0.01 (0.00, 0.01)	21.9 (21.7, 22.0)	0.01 (0.01, 0.02)
Injections[b]	*n*/day	3.94 (3.92, 3.95)	3.90 (3.89, 3.91)	−0.04 (−0.05, −0.03)	3.87 (3.86, 3.89)	−0.06 (−0.07, −0.05)	3.88 (3.86, 3.89)	−0.06 (−0.07, −0.04)
Missed bolus dosages[b]	*n*/day	0.64 (0.64, 0.64)	0.63 (0.63, 0.63)	−0.01 (−0.01, −0.01)	0.63 (0.62, 0.63)	−0.01 (−0.01, −0.01)	0.64 (0.64, 0.65)	0.00 (−0.00, 0.00)

Proportions of individuals achieving clinically meaningful targets in the overall population (percentage and relative change in odds of achieving target[b])

	Month 0	Month 3	Change (95% CI)[c]	Month 6	Change (95% CI)[c]	Month 12	Change (95% CI)[c]
>70% TIR	23%	25%	0.14 (0.12, 0.15)	25%	0.13 (0.11, 0.16)	25%	0.12 (0.10, 0.15)
<4% TBR (<3.9 mmol/L [<70 mg/dL])	71%	72%	0.07 (0.05, 0.09)	72%	0.06 (0.04, 0.09)	72%	0.09 (0.06, 0.11)
<1% TBR (<3.0 mmol/L [<54 mg/dL])	86%	87%	0.09 (0.06, 0.11)	87%	0.05 (0.02, 0.09)	87%	0.09 (0.06, 0.13)
<25% TAR (>10.0 mmol/L [>180 mg/dL])	23%	25%	0.11 (0.09, 0.12)	25%	0.10 (0.08, 0.12)	24%	0.09 (0.07, 0.12)

(Continues)

TABLE 2 (Continued)

Proportions of individuals achieving clinically meaningful targets in the overall population (percentage and relative change in odds of achieving target[b])							
	Month 0	Month 3	Change (95% CI)[c]	Month 6	Change (95% CI)[c]	Month 12	Change (95% CI)[c]
<5% TAR (>13.9 mmol/L [>250 mg/dL])	27%	29%	0.11 (0.10, 0.13)	29%	0.12 (0.10, 0.14)	29%	0.11 (0.09, 0.14)
Mean < 8.6 mmol/L (<154 mg/dL), <1% TBR (<3.0 mmol/L [<54 mg/dL])	23%	25%	0.13 (0.11, 0.15)	25%	0.12 (0.09, 0.14)	24%	0.08 (0.06, 0.11)
>70% TIR, <4% TBR (<3.9 mmol/L [<70 mg/dL])	16%	18%	0.17 (0.14, 0.19)	17%	0.14 (0.11, 0.17)	17%	0.12 (0.09, 0.15)
>70% TIR, <1% TBR (<3.0 mmol/L [<54 mg/dL])	21%	23%	0.14 (0.12, 0.16)	23%	0.13 (0.11, 0.16)	23%	0.12 (0.09, 0.15)

Note: Data are mean (95% CI).

Abbreviations: CGM, continuous glucose monitoring; CI, confidence interval; h, hours; m, minutes; TAR, time above range; TBR, time below range; TIR, time in range (3.9–10.0 mmol/L [70–180 mg/dL]); TITR, time in tight range (3.9–7.8 mmol/L [70–140 mg/dL]).

[a]Periods with ≥1 upload per 14 days.

[b]Baseline for bolus insulin data is month 1 instead of month 0, and change from baseline is month 3 versus month 1, month 6 versus month 1 and month 12 versus month 1.

[c]Relative change in odds of achieving target.

had the largest number of upload days in month 3, with uploads on 38.2% and 37.9% of days included in this month, respectively (i.e., uploads on >1 in every 3 days).

4 | DISCUSSION

This analysis of data from a large, real-world cohort from Europe, Australia, Japan, and South Africa demonstrated an increase in TIR and a decrease in TAR and TBR from baseline to months 3, 6 and 12 following connected insulin pen initiation to administer bolus insulin in individuals living with diabetes. In clinical practice, an improvement in TIR of ≥5% for an individual is regarded as clinically meaningful. Here we observed mean improvements at the population level of 1.5%, 1.4% and 1.1 % at 3, 6 and 12 months, respectively. In itself, these are not clinically important improvements, but they indicate the potential of connected devices as the first step in providing better patient support, and our data point to groups that in particular may benefit from this technology.

The internationally recognised consensus statement recommends spending >70% of the day in TIR, <4% in TBR (<3.9 mmol/L [<70 mg/dL]) and <1% in TBR (<3.0 mmol/L [<54 mg/dL]).[20] This study showed a 2% increase from baseline to month 3 and month 6 in the proportion of individuals who achieved the clinical target of >70% TIR with <4% TBR (<3.9 mmol/L [<70 mg/dL]), corresponding to 1723 individuals in total achieving this target.

The findings from this large, multinational, real-world study, whilst of a smaller magnitude, are broadly in line with findings from previous small, national, real-world cohort studies and clinical trials of connected insulin pens. Connected insulin pen initiation has been associated with increases in TIR (ranging from 5.2% to 8.5%-points),[15,21,22] decreases in TAR (ranging from 5.5% to 12.5%-points),[15,21,22] and decreases in TBR (ranging from 0.6% to 1.5%-points for TBR [<3.0 mmol/L])[12,15] in both type 1 and type 2 diabetes. The improvements in TIR are relevant because they help to inform the overall impact of connected insulin pen initiation on glycaemic control (including glycaemic variability) beyond that provided by HbA_{1c} alone.[23]

Our data suggest that individuals with lower TIR generally benefit the most from a connected bolus pen. This is seen both when stratifying individuals based on baseline TIR, where participants with baseline TIR <40% increased the most, and in the supplementary analysis where baseline characteristics were compared across participants grouped by their 3-month change in TIR. An increase in mean TIR of 3.8%, 4.5% and 4.6% at months 3, 6 and 12, respectively, for individuals with baseline TIR <40% was found. Whilst this does not meet the threshold of 5% for clinically meaningful improvements, it is noteworthy given the fact that the change occurred without any specific intervention or training beyond introducing a connected insulin pen. Notice that we also observed a small decrease in TIR for individuals with high baseline TIR ≥70%, indicating that the findings of the baseline-stratified analysis will to some extent be explained by regression towards the mean, with the highest and lowest baseline

TABLE 3 Change of TIR and TBR by baseline TIR.

Subgroup	*n*	Month 0	Month 3[a]	Change (95% CI)	Month 6	Change (95% CI)	Month 12	Change (95% CI)
TIR (%)								
Any baseline TIR	40 770	54.4	55.0	0.6 (0.5, 0.8)	55.1	0.7 (0.6, 0.8)	54.8	0.4 (0.2, 0.6)
Baseline TIR <40%	9578	28.5	32.3	3.8 (3.5, 4.1)	33.0	4.5 (4.2, 4.9)	33.1	4.6 (4.2, 5.1)
Baseline TIR 40%–50%	7079	45.6	46.6	0.9 (0.6, 1.3)	47.0	1.4 (1.0, 1.7)	47.1	1.5 (1.1, 1.9)
Baseline TIR 50%–60%	8058	55.4	55.6	0.2 (−0.1, 0.5)	55.9	0.5 (0.2, 0.8)	55.6	0.3 (−0.1, 0.6)
Baseline TIR 60%–70%	7216	64.9	64.2	−0.6 (−0.9, −0.4)	64.1	−0.7 (−1.0, −0.4)	63.9	−0.9 (−1.3, −0.6)
Baseline TIR >70%	8839	80.1	78.6	−1.5 (−1.7, −1.3)	77.8	−2.3 (−2.5, −2.1)	76.9	−3.2 (−3.5, −3.0)
TBR (%)								
Any baseline TIR	40 770	3.4	3.3	−0.11 (−0.14, −0.08)	3.3	−0.08 (−0.11, −0.04)	3.3	−0.13 (−0.17, −0.09)
Baseline TIR <40%	9578	1.7	1.8	0.15 (0.10, 0.20)	1.9	0.20 (0.15, 0.26)	1.9	0.21 (0.14, 0.28)
Baseline TIR 40%–50%	7079	3.3	3.2	−0.10 (−0.18, −0.03)	3.3	−0.06 (−0.14, −0.03)	3.2	−0.13 (−0.23, −0.03)
Baseline TIR 50%–60%	8058	4.1	3.8	−0.24 (−0.31, −0.16)	3.9	−0.15 (−0.23, −0.07)	3.7	−0.32 (−0.42, −0.22)
Baseline TIR 60%–70%	7216	4.5	4.2	−0.31 (−0.39, −0.22)	4.2	−0.35 (−0.44, −0.26)	4.2	−0.33 (−0.43, −0.22)
Baseline TIR >70%	8839	3.8	3.6	−0.13 (−0.20, −0.06)	3.7	−0.10 (−0.18, −0.03)	3.6	−0.14 (−0.23, −0.05)

Abbreviations: CGM, continuous glucose monitoring; CI, confidence interval; TBR, time below range (<3.9 mmol/L [<70 mg/dL]); TIR, time in range (3.9–10.0 mmol/L [70–180 mg/dL]).
[a]40 770 individuals with 3 months of CGM data prior to bolus pen initiation and periods with ≥1 upload per 14 days included.

TABLE 4 Change in TIR and change in proportion achieving >70% TIR by country.

		TIR, %			Proportion achieving >70% TIR, %				
Country[a]	*n*	Month 0	Month 3	Change (95% CI)	Month 0	Month 3	Change[b] (95% CI)	Mean age, years (SD)	Upload days,[c] %
Australia	3250	50.4	51.8	1.4 (0.8, 2.0)	19.7	22.0	0.15 (0.05, 0.26)	48.5 (16.7)	30.9
Austria	2837	58.7	63.5	4.7 (4.0, 5.5)	34.9	43.0	0.41 (0.28, 0.55)	50.4 (16.5)	38.2
Belgium	1194	52.9	53.0	0.1 (−0.8, 1.0)	21.3	22.1	0.04 (−0.10, 0.21)	44.0 (16.7)	27.1
Czechia	1642	61.1	62.6	1.5 (0.7, 2.2)	39.2	41.2	0.09 (−0.02, 0.21)	42.0 (16.1)	31.1
Denmark	3239	52.9	54.2	1.3 (0.7, 1.8)	22.5	24.5	0.12 (0.03, 0.22)	47.0 (16.6)	28.3
Finland	1250	51.9	51.8	−0.07 (−0.91, 0.77)	21.3	22.7	0.08 (−0.05, 0.24)	43.1 (16.1)	27.3
France	10 909	52.6	54.7	2.15 (1.82, 2.48)	21.7	26.0	0.27 (0.21, 0.33)	43.3 (16.9)	31.3
Japan	2216	60.9	62.0	1.16 (0.51, 1.81)	34.7	36.5	0.08 (−0.01, 0.18)	48.4 (15.1)	37.9
Poland	2675	63.8	65.1	1.26 (0.73, 1.79)	41.9	44.4	0.11 (0.03, 0.19)	41.6 (15.1)	35.0
Portugal	1449	48.8	50.8	1.95 (1.19, 2.71)	16.8	21.0	0.32 (0.16, 0.50)	41.0 (15.3)	29.0
Spain	17 716	56.0	56.7	0.7 (0.5, 0.9)	25.0	25.9	0.05 (0.02, 0.09)	41.8 (14.4)	29.2
Sweden	5305	56.8	58.6	1.79 (1.29, 2.29)	30.9	34.2	0.16 (0.08, 0.24)	42.7 (16.3)	17.7
UK	28 038	45.8	47.4	1.59 (1.39, 1.79)	15.8	17.6	0.14 (0.10, 0.17)	43.6 (15.3)	30.9

Abbreviation: TIR, time in range (3.9–10.0 mmol/L [70–180 mg/dL]).
[a]Countries with >1000 individuals included in the study.
[b]Relative change in odds of achieving target.
[c]Days with uploads in month 3 as a percentage of all days included in this month.

subgroups showing the largest changes towards the mean overall baseline TIR.

Looking at the differences in TIR improvements between countries, participants from Austria had the highest mean change in TIR of 4.7% from baseline to month 3. Individuals from Austria also had the highest percentage of upload days of all countries in this study. Based on these data and those of a previous study,[14] there may be an association between the number of upload days (indicative of an individual's engagement with the connected insulin pen and the data generated) and improvements in TIR. Based on the association between connected insulin pen engagement and improved glycaemic control, training programmes provided by HCPs for individuals who start using a connected insulin pen could increase engagement; therefore, further improving glycaemic control.

This study confirms previous findings from a real-world pilot study in Sweden, which showed that connected insulin pen initiation was associated with an increase in TIR and decreases in both TAR and TBR <3.9 mmol/L (<70 mg/dL) in individuals living with type 1 diabetes who had low baseline TIR.[12] Further research to understand the more qualitative aspects of connected insulin pen use both for individuals living with diabetes and for HCPs would be beneficial in helping to investigate how injection data availability could be leveraged to the highest potential. However, by providing automatic recording of insulin dose information and missed dose alerts, connected insulin pens may help empower individuals to take control of their condition and achieve greater glycaemic control.[24]

The strength of this study was the large population available from a multinational cohort including 24 countries, counting Australia and Japan, and long follow-up. This was an observational study reflecting real-world life with diabetes, outside of carefully controlled clinical trial settings; it included data from a large range of individuals living with diabetes at various levels of glycaemic control, spanning the full range of baseline control from those with low baseline TIR (<40%) and those with high baseline TIR (≥70%). The large range of individuals included allowed for relevant subgroup analysis to be performed.

However, there are several limitations that should be considered when interpreting the data. There may have been some selection bias because only individuals who had consented to share their data for research purposes were included in the analysis. This group may differ from the population as a whole in both their baseline glucose control and the association between connected insulin pen use and glucose control. These may differ further between countries. Although device initiation is generally associated with an educational programme, no information was available on how connected insulin pens were initiated and whether any guidance or training was provided by HCPs to treating physicians or individuals initiating a connected insulin pen, and differences in usage and engagement may be related to country-specific or clinic-specific guidance. Owing to the data collected from the source systems, there are limited additional clinical data available; for example, limited or no information was available for diabetes type, clinical characteristics, history and duration of diabetes, concomitant treatments (including information on basal insulin injections), and the glycaemic targets recommended by HCPs. Furthermore, no information was available on how data were used by the participants or HCPs, or on how frequently clinical visits occurred. Therefore, the time points of 3, 6 and 12 months may not reflect standard clinical practice. Finally, only months in which participants had days that met the inclusion criteria were included in the analysis, and monthly data may be missing if participants did not use CGM or did not fulfil the requirements to upload activity, or if the connected insulin pen initiation day was less than a year before the study analysis date. Potential future applications that may include information from connected insulin pens and CGM devices could provide additional data for further analysis.

Overall, connected insulin pen initiation was associated with improvements in TIR, TAR and TBR at month 3, month 6 and month 12 following connected insulin pen initiation in a real-world setting, aligning with previous findings. When stratifying individuals based on baseline TIR, the greatest improvements were seen in those with the greatest need (TIR <40% at baseline). These findings further highlight the benefit of connected insulin pen use on glycaemic control, especially in individuals with low TIR.

The data presented in this manuscript suggest that connected pen initiation may play a supporting role in improving glycaemic outcomes in the management of diabetes.

AUTHOR CONTRIBUTIONS

All authors provided substantial contributions to the conception and design of the study or the interpretation of data. All authors contributed to the review and revision of the manuscript and approved the final version. All authors are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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CONFLICT OF INTEREST STATEMENT

PA has received research support or consultant fees, or has served on advisory panels for Abbot, Dexcom, Eli Lilly, Insulet, Medtronic, Novo Nordisk, Roche, Sanofi, and Tandem in the past 24 months. BG has received fees for the activities of speaking, scientific advising or clinical research from A. Menarini Diagnostics, Abbott, Asten Santé, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Dexcom, Dinno Santé, Eli Lilly, Elivie, Gilead, GlaxoSmithKline, Homeperf, Insulet, Intarcia, Intercept Pharmaceuticals, ISIS Diabète, Janssen, Johnson & Johnson, LifeScan, Linde Homecare France, Medtronic, Merck Sharp & Dohme, MetaCure, Nestlé, Novartis, Novo Nordisk, ORKYN', Pfizer, Roche, Sanofi and VitalAire. NVH, AK, and NNK are employees of Novo Nordisk A/S and hold stock options. JKM is a member of the advisory boards for Abbott Diabetes Care, Becton Dickinson/Embecta, Biomea Fusion, Eli Lilly, Medtronic, Novo Nordisk, Pharmasens, Roche Diabetes Care, Sanofi and Viatris; has received speaker honoraria from A. Menarini Diagnostics, Abbott

Diabetes Care, Becton Dickinson/Embecta, Eli Lilly, MedTrust, Novo Nordisk, Roche Diabetes Care, Sanofi and Ypsomed; and is a shareholder of decide Clinical Software GmbH and elyte diagnostics.

PEER REVIEW

The peer review history for this article is available at https://www.webofscience.com/api/gateway/wos/peer-review/10.1111/dom.70051.

DATA AVAILABILITY STATEMENT

Restrictions apply to the availability of individual participant level data analysed during this study to ensure adherence to the Novo Nordisk data sharing agreement. Moreover, because participant data is continuously updated (either by the addition of data from new data uploads or the removal of data because participants withdraw consent to sharing their data), it is not possible to perform a repeat analysis using the exact dataset (accessed June 11, 2025) that was used to perform the analysis presented in this manuscript.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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