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# Research: Treatment

# Improved glycaemic control and treatment satisfaction with a simple wearable 3-day insulin delivery device among people with Type 2 diabetes

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## Abstract

**Aim** To evaluate the PAQ® (CeQur SA, Horw, Switzerland), a wearable 3-day insulin delivery device that provides set basal rates and bolus insulin on demand, in people with Type 2 diabetes.

**Method** Adults with Type 2 diabetes with $HbA_{1c}$ concentrations ≥53 and ≤97 mmol/mol (7.0 and 11.0%) while treated with ≥2 insulin injections/day were enrolled in two single-arm studies comprising three periods: a baseline (insulin injections), a transition and a PAQ treatment period (12 weeks). Endpoints included $HbA_{1c}$, seven-point self-monitored blood glucose, total daily dose of insulin and body weight. Safety was assessed according to examination, hypoglycaemic episodes and adverse device effects.

**Results** A total of 28 adults were enrolled (age 63 ± 7 years, 86% men, BMI 32.3 ± 4.3kg/m$^2$, Type 2 diabetes duration 17 ± 8 years, $HbA_{1c}$ 70 ± 12 mmol/mol (8.6 ± 1.1%), total daily insulin dose 58.7 ± 20.7 U), of whom 24 completed the studies. When transitioned to PAQ, 75% of participants continued on the first basal rate selected. After 12 weeks of PAQ wear, significant improvements from baseline were seen [$HbA_{1c}$ –16 ± 9 mmol/mol (95% CI –20, –12) or –1.5 ± 0.9% (95% CI –1.8, –1.1) $P$<0.0001], and at all seven self-monitored blood glucose readings time points ($P$ ≤0.03). Total daily insulin dose increased by 12.1 ± 19.5 U (95% CI 3.9, 20.4; $P$=0.0058), the number of meal time boluses increased by 0.9 ± 1.5/day (95% CI 0.3, 1.5; $P$=0.0081) and body weight remained stable. Six participants had mild to moderate catheter site reactions and one mild skin irritation occurred. No participant experienced severe hypoglycaemia.

**Conclusions** Adults with Type 2 diabetes were safely transitioned from insulin injections to the PAQ and had significantly improved glycaemic control and treatment satisfaction with insulin therapy.

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## Introduction

Type 2 diabetes mellitus is a progressive disorder characterized by loss of insulin sensitivity and secretory capacity over time [1]. Six years after diagnosis, ~50% of people with Type 2 diabetes require insulin therapy [2].

Over time, many people with Type 2 diabetes require escalation to basal-bolus insulin therapy to reach glycaemic targets [3]; however, the majority of people on insulin in the USA do not achieve good control; in one report, 71% had an $HbA_{1c}$ concentration >53 mmol/mol (>7%) and 38% had an $HbA_{1c}$ concentration >64 mmol/mol (>8%) [4]. Adherence to and persistence with administering insulin therapy is often inadequate. Barriers to achieving adherence to insulin therapy include: the need for multiple daily injections (MDI); interference of MDI regimens with daily activities; injection pain and embarrassment; as well as just forgetting to administer injections [5].

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**What's new?**

- As Type 2 diabetes mellitus progresses, basal-bolus insulin is required to achieve glycaemic targets; however, because of barriers associated with multiple daily injections (MDI), many people with Type 2 diabetes do not reach their goal.
- Randomized controlled trials evaluating continuous subcutaneous insulin infusion (CSII) via pumps vs MDI in people with Type 2 diabetes have shown that CSII achieves better glycaemic control and treatment satisfaction scores than MDI, but use is limited because of cost and complexity.
- The PAQ, a simple wearable CSII device provides freedom from daily injections.
- Results suggest the PAQ device achieves improved glycaemic control and treatment satisfaction scores among people with Type 2 diabetes. The PAQ device may be a viable alternative to MDI.

Recent publications on randomized controlled trials (RCTs) evaluating continuous subcutaneous insulin infusion (CSII) vs MDI, including the OpT2imise trial, have provided evidence for its effectiveness in people with Type 2 diabetes, with insulin pumps achieving better glycaemic control and superiority in patient-reported outcome measures than MDI in selected groups of people with diabetes [6–9].

Insulin pumps, originally designed for people with Type 1 diabetes, are expensive and complicated to use. They were designed with features that arguably are not needed for most people with Type 2 diabetes, for example, multiple basal rate settings, different bolus types and meal-time bolus calculators. For Type 2 diabetes, one fixed basal rate per day seems adequate to fit basal insulin requirements for most people [10–12] and mealtime bolus calculators are not associated with greater reduction of $HbA_{1c}$ in people with Type 2 diabetes receiving CSII therapy [6].

In the present study, we evaluated the PAQ® (CeQur SA, Horw, Switzerland), a simple, discreet, wearable device. The PAQ has been designed to replace insulin injections, is worn on the abdomen for up to 3 days and delivers rapid-acting insulin (100 units/mL) via a Teflon cannula (no cassette tubing) to provide continuous basal delivery of 20, 24, 32, 40 or 50 U of insulin in one 24-h period (0.83 to 2.08 U/h) and on-demand bolus dosing in 2-U increments for up to 3 days (Fig. 1).

## Research design and methods

Two prospective, open-label, non-controlled studies pilot studies using an identical design were consecutively conducted at the Medical University of Graz, Austria. A user inconvenience issue (non-safety-related) with the PAQ was identified after enrolment of eight participants into the study; therefore, enrolment was stopped and participants were followed to study completion. The PAQ was optimized for improved user convenience and a new study of identical design and population was started. Both studies were conducted in accordance with ISO-14155 and the Declaration of Helsinki [13,14]. The protocols were approved by the Ethics Committee and Austrian regulatory authority. Informed consent was obtained from each participant prior to study procedures being performed.

Participants were provided with PAQ devices according to estimated insulin requirements (see details below) and with insulin aspart (NovoRapid; NovoNordisk AS, Bagsvaerd, Denmark) with which to fill the PAQ.

Glucose meters (Life Scan One Touch Ultra; Life Scan, Milpitas, CA, USA), were provided to participants to self-monitor their blood glucose (BG) levels.

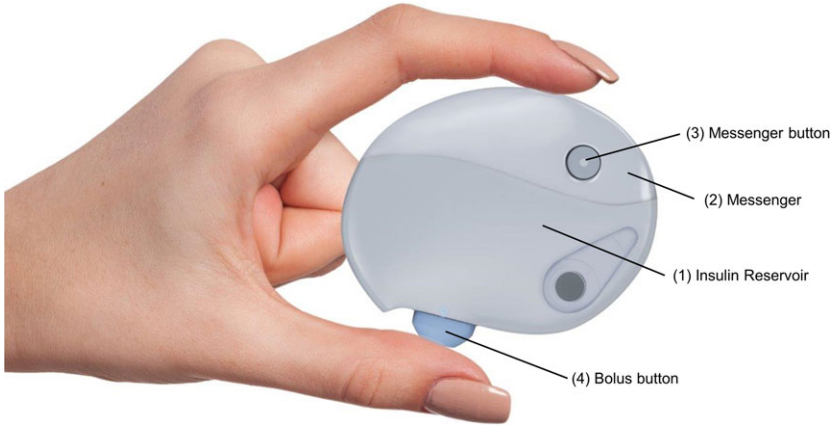


**FIGURE 1** Image of PAQ device. (1) Insulin reservoir: disposable component, replaced every 3 days; (2) Messenger: use up to 1 year; (3) Messenger button: when pressed elicits vibrations which notify user when to change the Reservoir or if there is an occlusion in the fluid path; (4) Bolus button: each push delivers 2 U of insulin.

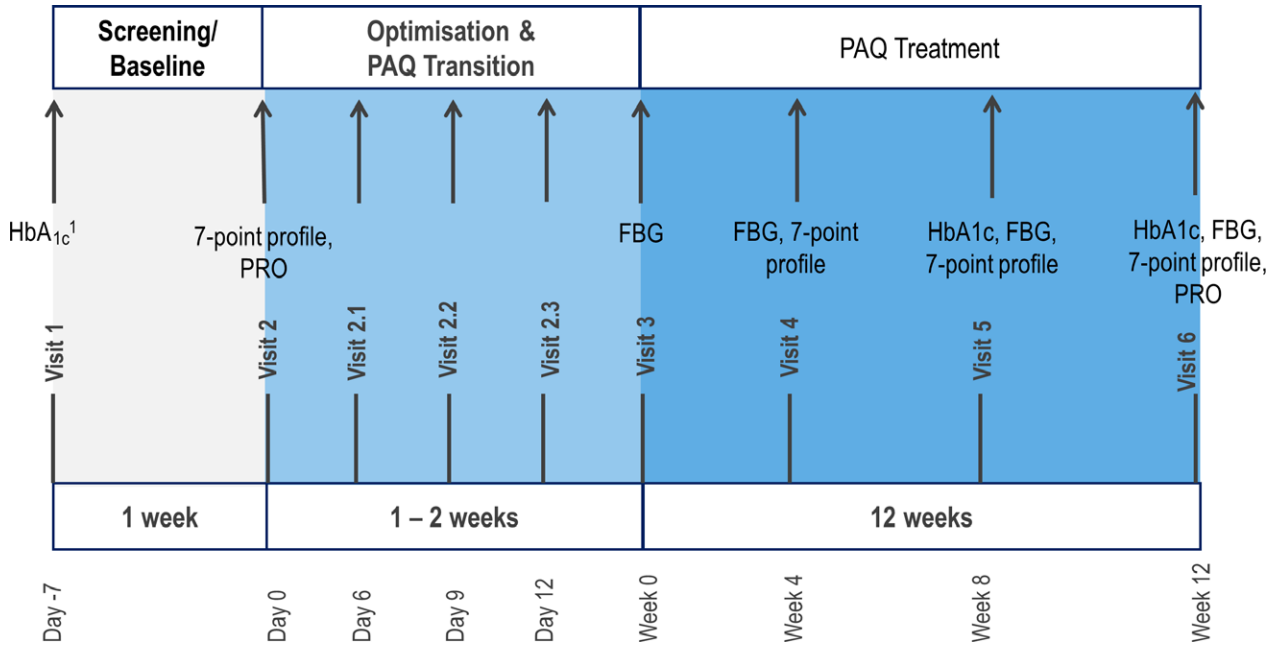


**FIGURE 2** Study visit schedule and primary and secondary efficacy endpoints. 1: $HbA_{1c}$ point of care for eligibility and blood draw for efficacy endpoints. Seven-point profiles collected on two non-consecutive days the week prior to their clinic visit. FBG, fasting blood glucose; PRO, patient-reported outcome.

### Outcome measures

The primary endpoint was change in $HbA_{1c}$ from baseline after 12 weeks of using the PAQ. Secondary endpoints were evaluations of change from baseline for the following measurements at the timepoints indicated in Fig. 2: $HbA_{1c}$; fasting plasma glucose; seven-point self-monitored BG profile (before and 2 h after each meal and at bedtime); total daily dose of insulin; body weight; Barriers to Insulin Therapy questionnaire score [16]; and Diabetes Treatment Satisfaction Questionnaire (DTSQ) score. The status version of the DTSQ was used at baseline and week 12 [17,18]. The number of pre-set basal doses tried and number of days taken to identify the PAQ basal dose that achieved the desired fasting BG level were evaluated. Safety was evaluated through adverse event surveillance, insertion site examination, number of participants with hyperglycaemia (elevations in BG which required replacement of the PAQ), and hypoglycaemia, as defined by the American Diabetes Association working group on hypoglycaemia [19].

### Study participants

Adults aged >18 years with Type 2 diabetes who were not achieving glycaemic targets [$HbA_{1c} \geq 53$ and $\leq 97$ mmol/mol ($\geq 7.0$ and $\leq 11.0\%$)] on an established insulin therapy regimen (at least two injections per day) ± oral antidiabetic drugs were enrolled into the studies. Oral medications taken at baseline to manage BG levels (with the exception of those medications excluded) were continued throughout the study, without changing the dose unless medically required. Key exclusion criteria comprised sulfonylurea use within the last 2 months prior to study start, BMI >40 kg/m$^2$, history of recurrent severe hypoglycaemia (>2 episodes) requiring third-party assistance during the past 6 months, existing dermal irritation over the abdominal area and known hypersensitivity to skin adhesives.

### Study visit schedule

The outpatient studies comprised three periods (Fig. 2). During the 7-day screening/baseline period, the participants' glycaemic control was evaluated while they continued their current insulin therapy. PAQ transition was at least 6 days long (two 3-day PAQ wear periods), but could be extended to switch to the most suitable PAQ basal dose to achieve fasting BG target. The PAQ treatment period was 12 weeks in duration, and participants were seen every 4 weeks.

The investigator was instructed to select an initial PAQ basal dose that was closest to the participant's current daily basal dose. If the investigator believed a higher basal dose was needed to reach the fasting glucose target (3.9–7.2 mmol/l), he/she could select a higher basal dose. At the end of the first 48 h, if the participant's fasting self-monitored BG was at the desired target, the participant was to continue on the same PAQ basal dose for two PAQ 3-day wear periods before advancing to PAQ treatment. If the participant's fasting self-monitored BG was not at the desired target, they were instructed to return to the clinic to change the PAQ basal dose (Fig. 3). Initial bolus insulin doses using

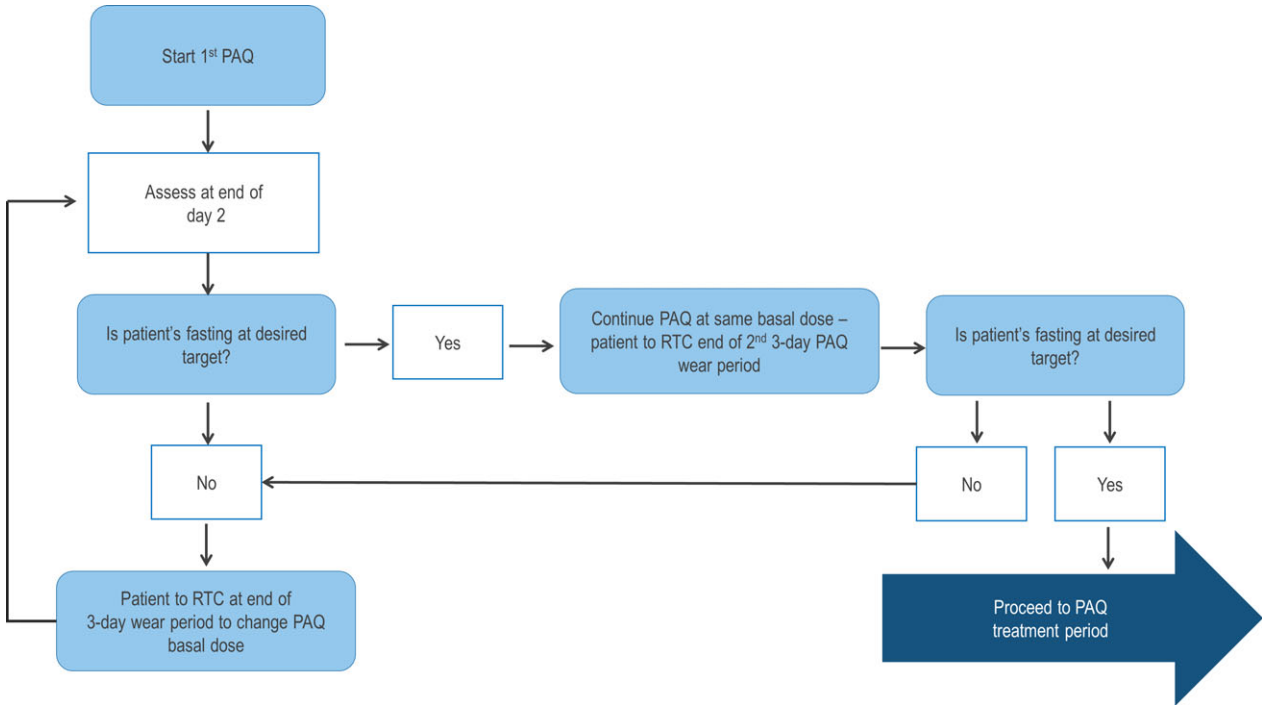


**FIGURE 3** Method for transitioning participants to the PAQ device. RTC, return to clinic.

the PAQ were to be similar to bolus doses administered at baseline; however, the bolus dose could be adjusted by the treating physician if deemed necessary.

### Statistical analysis

There were two analysis populations: an intention-to-treat (ITT) population, which consisted of all participants who received at least one insulin dose with the PAQ, and the per-protocol population, which consisted of all ITT participants who completed the study procedures up to week 12 without having previously defined major protocol deviations. Results from the efficacy analysis used the per-protocol dataset, while the ITT data were used for all PAQ transition period, patient-reported outcome and safety assessments. Results are presented as mean ± SD (95% CI), if not indicated otherwise. The change from baseline measurements at the end of the study were analysed using a two-sided paired *t*-test and a Wilcoxon signed-rank test for the continuous measurements, with a significance level of 0.05. Because the signed-rank *P* values did not differ to an extent that would change any inferences or conclusions based on the *t*-tests, only *P* values from the *t*-tests are reported.

The seven-point BG profiles were analysed using likelihood-based mixed-model repeated-measures analysis of variance. The model included the change from baseline as the dependent variable and time point and baseline as fixed effects. Participant and error were included as random effects. An unstructured covariance matrix was used to model the covariance within participants. Using SAS Proc Mixed, we obtained least-squares estimates of the changes from baseline and standard errors from the model to test the significance of the changes (based on a t distribution) at each of the seven time points. The raw *P* values from this analysis were then adjusted for multiplicity using Holm's step-down Bonferroni method [20].

## Results

A total of 34 adults were screened, 28 were enrolled, 27 completed the PAQ transition period and 24 completed the two studies from June 2014 to October 2015. Four participants did not complete the studies, one dropped out during the PAQ transition period and three during the PAQ treatment period. No participant completed early as a result of safety issues.

The baseline demographics for the ITT population are shown in Table 1. Pre-existing diabetes therapy included: pre-mixed insulins (14%); long-acting with rapid-acting insulins (64%); intermediate-acting with rapid-acting insulin (21%); biguanides (metformin, 54%); and dipeptidyl peptidase-4 inhibitors (29%).

In total, 898 devices were applied and used for a total of 2309 days. On average, participants wore 32 devices over a period of 82 days.

Significant reductions in $HbA_{1c}$ were seen from baseline at weeks 8 and 12: –15 ± 9 mmol/mol (95% CI –19, –11) or –1.4 ± 0.8% (95% CI –1.7, 1.0), $P$=0.0001, and –16 ± 9 mmol/mol (95% CI –20, –12) or –1.5 ± 0.8% (95% CI –1.8, –1.1; $P$<0.0001), respectively (Fig. 4).

**Table 1** Summary of demographic and baseline characteristics of the intention-to-treat population (*N* =28)

| Characteristic | |
|---|---|
| Age, years | |
| Mean (SD) | 62.8 (6.5) |
| Min, Max | 46.7, 73.0 |
| Gender, *n* (%) | |
| Female | 4 (14.3) |
| Male | 24 (85.7) |
| Race, *n* (%) | |
| White | 28 (100) |
| Weight, kg | |
| Mean (SD) | 99.6 (11.5) |
| Min, Max | 82.0, 120.0 |
| BMI, kg/m$^2$ | |
| Mean (SD) | 32.3 (4.3) |
| Min., Max. | 24.6, 41.3 |
| Diabetes duration, years | |
| Mean (SD) | 17.2 (7.8) |
| Min., Max. | 4.0, 35.0 |
| $HbA_{1c}$, mmol/mol | |
| Mean (SD) | 70 (12) |
| Min., Max. | 55, 97 |
| $HbA_{1c}$, % | |
| Mean (SD) | 8.6 (1.1) |
| Min., Max. | 7.2, 11.0 |
| Diabetes-related conditions, *n* (%) | |
| Peripheral neuropathy | 15 (53.6) |
| Retinopathy | 6 (21.4) |
| Nephropathy | 6 (21.4) |
| Mean (SD) daily insulin dose, Units | |
| Basal insulin | 28.9 (9.9) |
| Bolus insulin | 29.8 (16.6) |
| Total insulin | 58.7 (20.7) |
| Total injections per day | |
| Mean (SD) | 4.3 (1.5) |
| Min., Max.* | 1.0, 9.0 |

*The protocol enrolled participant who were on ≥2 insulin injections/day. During baseline period, one participant missed one of their two daily injections; hence total injections per day ranged from 1.0 to 9.0.

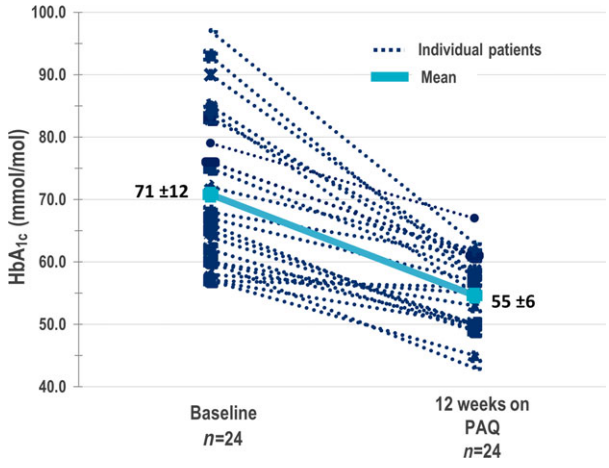


**FIGURE 4** Change from baseline in $HbA_{1c}$ values after 12 weeks of continuous subcutaneous insulin infusion with the PAQ. Per protocol population.

Mean fasting plasma glucose decreased significantly from baseline at weeks 4, 8 and 12: –1.7 ± 2.2 (95% CI –2.6, –0.7; *P*=0.0011), –2.4 ± 2.9 (95% CI –3.6, –1.2; *P*=0.0003) and –1.9 ± 3.5 (95% CI –3.5, –0.5; *P*=0.012), respectively.

Concomitantly at week 12, significant reductions were seen across all time points in the seven-point self-monitored BG profile compared with baseline: fasting –1.8 ± 3.1 (95% CI –3.1, -0.5; *P*=0.023), post-breakfast –3.0 ± 3.2 (95% CI –4.4, –1.6; *P*=0.001), pre-lunch –1.6 ± 2.8 (95% CI –2.8, –0.4; *P*=0.023), post-lunch –1.9 ± 2.7 (95% CI –3.1, –0.7; *P*=0.012), pre-dinner –1.9 ± 3.0 (95% CI –3.2, –0.7; *P*=0.018), post-dinner –2.7 ± 4.1 (95% CI –4.6, –0.9; *P*=0.012), bedtime –1.9 ± 3.5 mmol/l [95% CI –3.5, –0.4; *P*= 0.023 (Fig. 5)].

Most participants (21/28 [75%]) received the correct PAQ basal dose to achieve the targeted fasting BG at the first PAQ transition visit. Five participants (18%) required one change in their basal dose (one being a decrease) and two other participants (7%) required two increases in their basal dose. The mean number of days taken during PAQ transition was 8.7 ± 4.8 (95% CI 6.8, 10.6).

The daily basal insulin dose significantly increased from baseline at the end of the PAQ transition period [6.6 ± 8.4 U (95% CI 3.1, 10.2); *P*=0.0008] and then remained constant for the rest of the study.

Daily bolus insulin at week 12 did not increase significantly from baseline: 29.8 ± 16.6 U (95% CI 23.4, 36.3) vs 35.9 ± 24.9 U (95% CI 25.4, 46.4; *P*=0.1269). The mean number of meal time bolus doses administered per day increased from baseline to week 12: 3.0 ± 0.7 (95% CI 2.7, 3.3) vs 3.9 ± 1.2 (95% CI 3.4, 4.5), an increase of 0.9 ± 1.5 (95% CI 0.3, 1.5; *P*=0.0081). The combined basal and bolus dose resulted in a significant increase in total daily insulin dose from baseline to week 12: 58.7 ± 20.7 U (95% CI 50.7, 66.7) vs 70.9 ± 31.3 U (95% CI 57.7, 84.1), an increase of 12.1 ± 19.5 U (95% CI 3.9, 20.4; *P*=0.0058).

Body weight remained stable from baseline at week 12: +1.2 ± 3.4 kg (95% CI –0.2, 2.6; *P*=0.087).

Nine device-related AEs were reported in nine participants (32%). Six participants (21%) experienced mild to moderate cannula site reactions (e.g. irritation from a dislodged cannula rubbing the skin, redness and one mild infection effectively treated with oral antibiotics), one patient had mild application site irritation and three participants experienced mild hyperglycaemia, which resolved with replacement of the device. No participant experienced severe hypoglycaemia requiring third-party assistance. Twenty-two participants (79%) experienced self-monitored BG ≤3.9 mmol/l, mean value 3.5 mmol/l, 13 participants (46%) had symptomatic and 19 participants (68%) had asymptomatic episodes, all resolving without sequalae. The rate of hypoglycaemic (≤ 3.9 mmol/l) episodes per 30 days for the entire study in the ITT

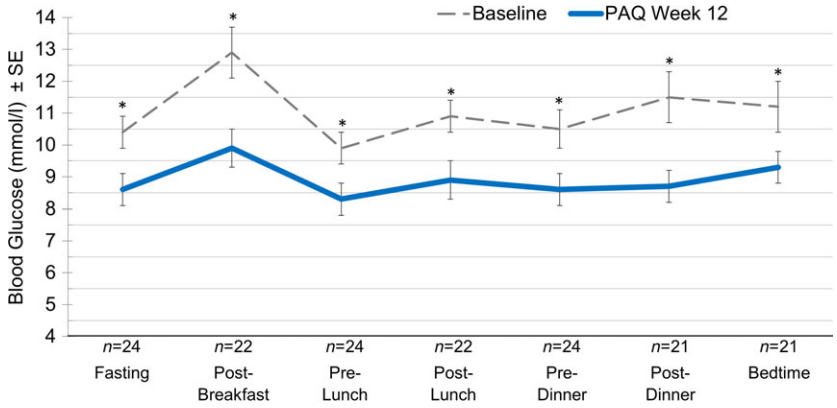


**FIGURE 5** Mean seven-point self-monitored blood glucose values at baseline and after 12 weeks of continuous subcutaneous insulin infusion with the PAQ. Per protocol population. *$P < 0.05$.

**Table 2** Summary of hypoglycaemic rates in the intention-to-treat populiation

| | Hypoglycaemic rate (episodes per 30 days) statistics | | | | | | |
|---|---|---|---|---|---|---|---|
| Visit | *N* | Mean | Median | SD | SE | Min. | Max. |
| Baseline | 28 | 1.1 | 0.0 | 3.00 | 0.57 | 0 | 13 |
| Transition | 27 | 3.2 | 0.0 | 6.12 | 1.18 | 0 | 26 |
| PAQ week 4 | 25 | 2.0 | 1.0 | 3.37 | 0.67 | 0 | 16 |
| Week 8 | 24 | 1.9 | 1.0 | 3.01 | 0.61 | 0 | 14 |
| Week 12 | 28 | 2.2 | 0.5 | 4.31 | 0.81 | 0 | 22 |
| PAQ total | 28 | 2.1 | 0.9 | 3.57 | 0.68 | 0 | 19 |

Hypoglycaemia defined as blood glucose ≤ 3.9 mmol/l.

**Table 3** Summary of Diabetes Treatment Satisfaction Questionnaire score change from baseline after 12 weeks of wearing the PAQ (intention-to-treat population)

| DTSQ variable | N | Baseline, mean | Mean score after 12 weeks on PAQ | Change, mean | Lower CL change | Upper CL change | Student's *t*-test | *P* |
|---|---|---|---|---|---|---|---|---|
| Hypoglycaemia score | 27 | 1.61 | 1.19 | –0.48 | –1.35 | 0.39 | –1.142 | 0.2638 |
| Hyperglycaemia score | 27 | 3.75 | 1.74 | –2.11 | –3.12 | –1.10 | –4.307 | 0.0002 |
| DTSQ total score | 27 | 29.18 | 33.30 | 4.04 | 1.33 | 6.75 | 3.061 | 0.0051 |

CL, confidence limit; DTSQ, Diabetes Treatment Satisfaction Questionnaire.

population increased from 1.1 during the 1-week baseline period to 2.1 during the PAQ 12-week treatment period (Table 2).

Patient-reported outcome measurements indicated that participants favoured the PAQ device over insulin injections. The total DTSQ score significantly improved at the end of the PAQ treatment period as compared with baseline [+4.0 ± 6.9 (95% CI 1.3, 6.8); $P$=0.005]. The PAQ was seen as more flexible and convenient than baseline therapy and participants were more satisfied to continue treatment. The hyperglycaemia score significantly decreased at week 12 as compared with baseline [–2.11 ±2.5 (95% CI –3.12, –1.10); $P$=0.0002 (Table 3)].

The total overall Barriers to Insulin Therapy score did not change over time, but a trend toward a reduction in participants' feelings of 'stigmatization by insulin injections' was seen [–1.9 ± 5.4 (95% CI –4.0, 0.3); $P$=0.0890].

## Discussion

The switch from injectable insulin therapy to, and optimization with, the PAQ was associated with a significant reduction in $HbA_{1c}$ concentrations. It is recognized the two studies had limitations, for example, the participants were not randomly allocated to PAQ therapy and the sample size was small; however, the substantial mean decrease in $HbA_{1c}$ (–16 mmol/mol) seen after 12 weeks of wearing the PAQ

device was much larger than the decrease in $HbA_{1c}$ of ~4 mmol/mol typically seen for participants in the MDI arm of RCTs [6,21–23]. Additional RCTs, of longer duration and with MDI as the active control, are needed to determine the efficacy of the PAQ device.

The reduction seen in $HbA_{1c}$ concentrations can be attributed to both a reduction in the patients' fasting as well as pre- and postprandial BG levels. It is hard to determine whether improvement in fasting plasma glucose is attributable to the constant and slow infusion of basal insulin via the PAQ or to optimization of the participants' insulin therapy. To explore this, we evaluated the 16 evaluable participants on a long- and short-acting insulin regimen at baseline. We evaluated the change from their baseline basal dose to the PAQ basal dose at the end of the optimization/transition period. Five participants (31%) had no change to their basal dose, six (38%) rounded up to the closest PAQ dose (average increase 5.3 U/day), two (13%) rounded down (average decrease 3.5) and three (19%) had an increase in their basal dose [average 18.9 U (Fig. 6)]. Given that 13 out of 16 participants (81%) in this group either matched, slightly increased or decreased their basal dose to accommodate the set PAQ basal dose and achieved their fasting target, it may be an indication of better basal insulin delivery with the PAQ. The better pre- and postprandial glucose values may be attributable to better insulin kinetics or better adherence to meal-time bolus administration. The increase in number of meal-time bolus doses administered may be attributable to the ease and discretion with which participants can administer bolus doses with the PAQ. Both explanations for improved $HbA_{1c}$ concentrations achieved with the PAQ device need to be investigated in future studies.

The reduction seen in $HbA_{1c}$ concentrations was clinically relevant. While none of the participants had $HbA_{1c}$ values <53 mmol/mol at baseline, 50% of the participants achieved this American Diabetes Association-defined target [24] at the end of the study and 75% achieved a concentration <58 mmol/mol (baseline 17%). There was no severe hypoglycaemia. While RCTs have yet to demonstrate a relationship between time in range and decreased glycaemic variability with regard to cardiovascular mortality, Steineck *et al.* [25] reported lower cardiovascular mortality in people with Type 1 diabetes using insulin pump therapy as compared with MDI. They hypothesized that not only reduction in $HbA_{1c}$ but also less severe hypoglycaemia and hyperglycaemia might be causative for their findings [25].

In four previously reported RCTs in people with Type 2 diabetes who were taking at least 1–2 insulin injections per day (±oral antidiabetic drugs) and were randomized to either CSII or MDI, no difference was seen in total daily insulin dose at the end of the study between the two groups [21–23,26]. In the OpT2mise trial, a reduction in total daily insulin dose was seen in the CSII group. These participants had been optimised over 2 months on basal-bolus therapy prior to randomization

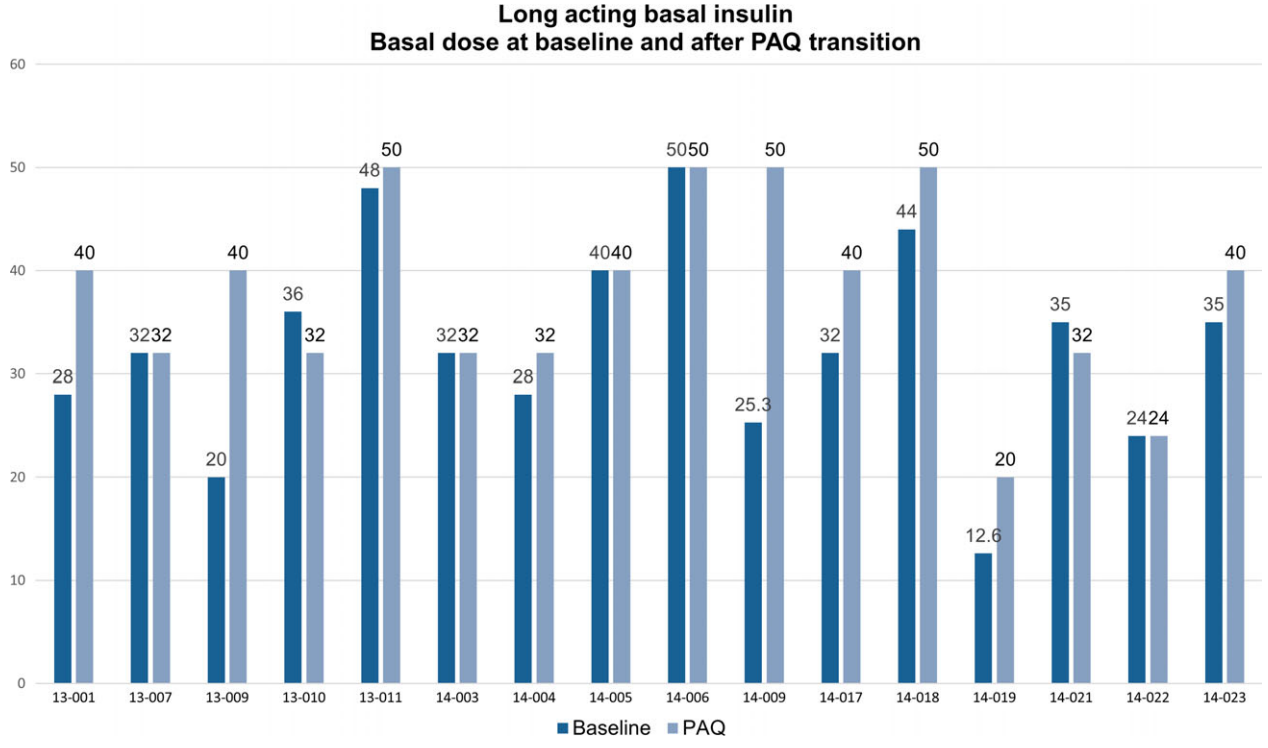


**FIGURE 6** Sixteen evaluable participants received long- and short-acting basal insulin at baseline. Basal dose at baseline and then at the end of the PAQ transition period is presented. Five participants: no change in dose; six participants: rounded up to closest PAQ dose (average increase 5.3 U/day); two participants: rounded down to closest PAQ dose (average decrease 3.5 U/day); three participants: had increase in their basal dose (average increase 18.9 U/day).

and entry into the study, with a mean total daily insulin dose of 1.1 U/kg [6]. In the present study, a reduction in total daily insulin dose compared with baseline (at least two injections per day) was not seen, possibly because participants started at a lower mean total daily insulin dose (0.6 U/kg) and optimization of the participants' insulin therapy occurred after baseline total daily insulin dose values were obtained.

No significant change in body weight was seen in the present study, which is consistent with the meta-analysis of the five RCTs comparing CSII with MDI in people with Type 2 diabetes performed by Pickup *et al.* [9].

Intensification of insulin therapy can often result in an increase in hypoglycaemia [3]. Given the reduction in $HbA_{1c}$ observed in the present study, one might have expected clinically significant hypoglycaemia but this was not seen. It is difficult to compare the results in the present study with those of other studies on CSII in participants with Type 2 diabetes because the methods used to measure and report hypoglycaemia differ and reporting has been incomplete.

Given the small sample size in these combined studies and high baseline scores seen for the participants' injectable insulin therapy, the DTSQ results were notable. Use of the DTSQ change version would have overcome the ceiling effects seen in this study and would probably have shown a more marked improvement in the results. The significant change in the questionnaire's perceived frequency of hyperglycaemia (indicating participants had less concern about high BG values), correlated with the reduction seen in $HbA_{1c}$. One application every 3 days eliminates the daily injection burden, potentially leading to the improved scores in convenience, flexibility and satisfaction. The significant change in the total score reflected the participants' satisfaction with the PAQ. This increased satisfaction may have contributed to the participants taking more mealtime insulin administrations than at baseline, which could also have been a factor in better $HbA_{1c}$ control. The observation of increased mealtime bolus administration with the PAQ was also seen in the first PAQ proof-of-concept study [27].

In conclusion, the concept behind the PAQ insulin delivery device is to provide an alternative mode of insulin delivery (in place of MDI) that is easy to use (non-programmable, fixed basal rates and no meal time calculator), safe and effective. The data from the present study suggest that the PAQ's overall performance might be able to achieve this goal. The transition from the participants' previous injectable insulin therapy to PAQ was easy; most of the participants could switch and continue on the first basal dose selected after two 3-day wear periods. Improved glycaemic control was achieved without the occurrence of severe hypoglycaemia. The adverse device events were predominantly mild and consistent with other body-worn CSII devices. Clinically meaningful reductions in $HbA_{1c}$ values were seen after 12 weeks of PAQ use, and fasting plasma glucose and seven-point profile values were significantly improved. In addition, the wearable device improved treatment satisfaction. All performance measurements showed that the PAQ can safely deliver both a constant basal and bolus insulin on demand. Future studies are needed to elucidate the durability of the $HbA_{1c}$ reduction seen with the device and to assess how PAQ compares to injectable insulin therapy.

#### Funding sources

CeQur SA sponsored the study, designed and drafted the protocol with Drs Mader and Pieber, monitored the study, maintained and cleaned the data in the database, performed the statistical analysis and interpreted the results with Drs Mader and Pieber.

#### Competing interests

J.K.M. is a member in the advisory board of Becton-Dickinson, Boehringer Ingelheim, Eli Lilly, Medtronic and Sanofi, and has received speaker honoraria from Abbott Diabetes Care, Astra Zeneca, Eli Lilly, Nintamed, Novo Nordisk, Roche Diabetes Care, Sanofi, Servier and Takeda. L.L. was an employee and is now a consultant for CeQur. F.A. and T.P. have no conflict of interest to report. D.J. is a statistical consultant for CeQur. M.T. is a paid consultant for CeQur and other Clinical Research Organizations and pharmaceutical companies developing diabetes medications including Prosciento, Kinexum, Hanmi, Servier, Merck MSD. He is a shareholder of Eli Lilly. J.L.W. is an employee of CeQur. T.R.P. is an advisory board member of Novo Nordisk A/S, a consultant for Roche Diabetes Care, Novo Nordisk A/S, Eli Lilly & Co, Infineon, Carnegie Bank, and has served on speaker's bureau of Novo Nordisk A/S and Astra Zeneca.

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