



ORIGINAL ARTICLE

Performance of an Automated Insulin Delivery System: Results of Early Phase Feasibility Studies

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Abstract

Background: Automated insulin delivery (AID) systems have demonstrated improvements in time-in-range (TIR, blood glucose 70–180 mg/dL) without increasing hypoglycemia. Testing a closed-loop system in an inpatient environment with supervised challenges allows for initial evaluation of performance and safety of the system.

Methods: Adults with type 1 diabetes (T1D) were enrolled into two similar studies ($n=10$ per study), with 3-day inpatient analysis periods. Participants tested a Lilly hybrid closed-loop (HCL) system comprising an investigational insulin pump, insulin lispro, a pump-embedded model predictive control algorithm, a continuous glucose monitor (CGM), and an external dedicated controller. Each protocol included meal-related and exercise challenges to simulate real-world diabetes self-management errors. Only study staff interacted with the HCL system. Performance was assessed using standard CGM metrics overall and within prespecified periods.

Results: Participants (25% male) had mean \pm standard deviation (SD) age 44.7 ± 14.2 years, T1D duration 30.2 ± 11.1 years, A1C $7.2\% \pm 0.8\%$, and insulin usage 0.53 ± 0.21 U/(kg·day). Percentage TIR 70–180 mg/dL (mean \pm SD) was 81.2 ± 8.4 overall, 85.2 ± 8.1 outside of challenge periods, 97.3 ± 5.3 during the nocturnal periods, and 74.5 ± 16.2 for the postprandial periods. During challenge periods, percentage TIR for the over-bolus challenge was 65.4 ± 29.2 and that for the delayed bolus challenge was 57.1 ± 25.1 . No adverse events (AEs), serious AEs, or unanticipated adverse device events occurred while participants were using the HCL system.

Conclusions: In participants with T1D, Lilly AID system demonstrated expected algorithm performance and safety with satisfactory glycemic outcomes overall and in response to simulated diabetes management challenges. Additional studies in less supervised conditions and with broader patient populations are warranted. ClinicalTrials.gov Registration number NCT03743285, NCT03849612.

Keywords: Automated insulin delivery, Hybrid closed loop, Early feasibility.

Introduction

AUTOMATED INSULIN DELIVERY (AID) systems have been demonstrated to improve glycemic control in people with type 1 diabetes (T1D).^{1,2} A closed-loop AID system consists of an insulin pump, a continuous glucose monitor (CGM), and a dosing algorithm that controls delivery of in-

ulin. A hybrid closed-loop (HCL) system additionally incorporates a bolus calculator to recommend boluses based on CGM sensor glucose values and manually entered meal carbohydrate (CHO) content.

Multiple AID systems, including several HCL systems, are in various stages of development and commercialization.^{3–7} These systems have been demonstrated to improve time-in-range

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(TIR) and reduce hypoglycemia and hyperglycemia in response to simulated and real-world challenges. HCL systems currently share many commonalities, but each also has differentiating characteristics and features that may better fit with certain clinical factors, user behaviors, and user preferences.⁸ The investigational HCL system consisted of an insulin pump that utilized acoustic volume sensing, a dedicated controller, and a control-to-target multimodel predictive control algorithm embedded on the pump.⁹ The algorithm calculates optimum basal doses based upon previous CGM glucose measurements and insulin doses as well as a prediction of future glucose levels derived from a control-relevant model of the user's glucoregulatory system.

HCL systems should initially be carefully evaluated in closely monitored settings to test the system in routine and challenge conditions before testing in a real-world outpatient environment. These two early feasibility studies evaluated the primary objective of establishing the performance and safety of an investigational HCL system in adults with T1D in a highly supervised inpatient environment. We incorporated intentional challenges mimicking common real-life diabetes management concerns to evaluate the robustness and responsiveness of the system during closely supervised use.

Methods

Participants and study design

Two early feasibility studies were conducted: STUDY 1 (NCT03743285) and STUDY 2 (NCT03849612). Participants were adults aged 18 to 65 years with T1D for at least 2 years, A1C $\geq 6\%$ to $\leq 9\%$, body mass index 18.5 to 37 kg/m², and who had been treated with insulin pump therapy with a rapid-acting insulin analogue for at least 6 months. Participants were excluded if they had an episode of severe hypoglycemia, >1 episode of diabetic ketoacidosis in the past 6 months, or other conditions that would increase their safety risk in the opinion of the investigator. All participants were required to give informed consent for participation in the study and before any study-specific procedures. The protocols were approved by local ethical review boards and were conducted according to International Conference on Harmonization Good Clinical Practice guidelines and the Declaration of Helsinki.

STUDY 1 and STUDY 2 both consisted of 10-day lead-in periods, inpatient challenges for a 47–52 h period, and phone follow-up (Fig. 1). Both studies had additional inpatient time and protocol elements (see Supplementary Data) that are not discussed here. Relevant differences between the protocols are included hereunder.

Study devices

During the lead-in period, participants continued using their commercially available insulin pump and used a masked Dexcom G5 CGM (San Diego, CA) and a Contour Next (Ascensia Diabetes Care, Parsippany, NJ) glucose meter for calibrations. During the inpatient period, participants continued using the Dexcom G5 and the Contour Next meter for all calibrations and blood glucose (BG) monitoring. They wore an investigational insulin pump (DEKA Industries, Manchester, New Hampshire), with lispro insulin (Humalog[®]), and an embedded HCL MPC algorithm, controlled through a user interface available on a dedicated controller (Android phone platform). No changes were made to the HCL algorithm while these studies were ongoing.

Procedures

Lead-in period. At the start of the lead-in period, participants continued using their personal insulin pump and any personal CGM in addition to the use of a masked Dexcom G5 CGM. Participants were instructed to consume one or more test meals to assess CHO counting and CHO ratios during this period. Participants returned to the research site to allow research personnel to review participant CGM data, pump settings, and study diary entries to assess baseline glucose control, and to facilitate adjustment of the pump settings if needed.

Inpatient period. Participants began the inpatient period within 2 days of completion of the lead-in period. Upon admission, participants were transitioned to the investigational AID system with insertion of a new infusion set, pairing of the CGM transmitter with the AID controller, and beginning the warm-up period. The system was initiated with the insulin dosing parameters (CHO ratios, insulin sensitivity factors, and basal rates) from the participant's personal pump as well as the participant's average total daily insulin dose (TDD)

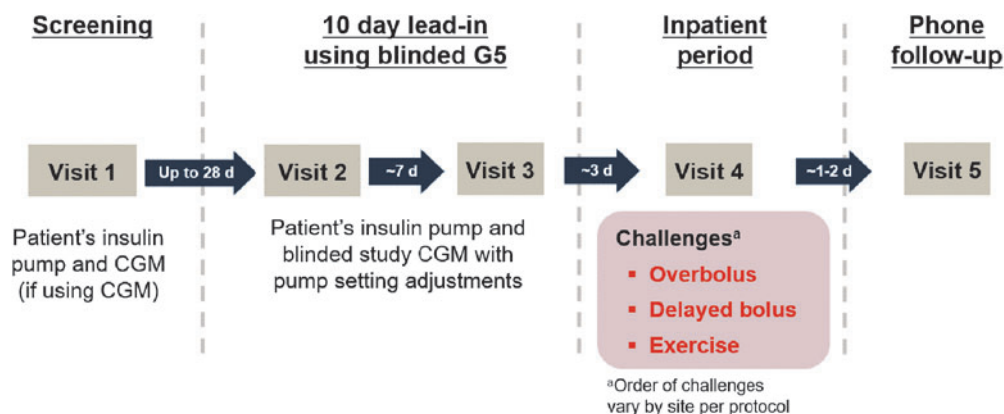


FIG. 1. Study design. CGM, continuous glucose monitoring; G5, Dexcom G5 CGM device.

calculated by the investigator using the average TDD across the last 3 days. Before lunch on the first inpatient day, the system was started in HCL mode.

During each day of the inpatient period, site personnel performed routine CGM calibrations twice a day per the manufacturer's recommendations, and also when the CGM was reading $\pm 30\%$ off of the BG on two consecutive readings. The system bolus calculator used the current CGM value and estimated CHO content for meals to calculate prandial boluses. Additional BG monitoring was conducted during the inpatient period with additional CGM calibrations done when indicated.

Challenges. Three challenges were conducted as a part of both protocols:

- An overbolus challenge to simulate excess insulin delivered as a prandial bolus when CHOs are overestimated.
- A delayed insulin bolus to simulate when insulin is unintentionally delayed and the bolus calculator is used.
- Unannounced exercise.

Research personnel conducted the overbolus challenge as follows: (1) measured BG value ~ 15 min before start of breakfast; if ≥ 100 mg/dL, proceeded with challenge; if < 100 mg/dL, gave up to 30 g of fast-acting CHOs before start of meal and delayed start of challenge by 30 min; (2) calculated breakfast insulin bolus through the system bolus calculator, using the CGM glucose value and estimated CHO amount ~ 15 min before start of meal; (3) added $\sim 30\%$ to the total system bolus calculator dose recommendation before the start of the meal and administered the bolus; the amount could be adjusted for safety-related reasons.

Research personnel conducted the delayed bolus challenge as follows: (1) recorded BG and ketone values ~ 15 min before start of the meal, (2) provided meal, and (3) delivered an insulin bolus determined by the AID system bolus calculator using CHO content consumed and the current CGM BG value at 60 min after completion of meal. Participants underwent the delayed bolus challenge at dinner in STUDY 1 and at breakfast in STUDY 2.

Research personnel conducted the exercise challenge without announcing it to the system as follows: (1) research personnel started challenge only if BG was between 100 and 200 mg/dL and (2) participants exercised on a treadmill or stationary bike with moderate intensity for up to 60 min, with breaks allowed. For STUDY 1, the exercise challenge occurred before breakfast and research personnel provided breakfast ~ 1 h after completion of exercise; for STUDY 2, the exercise challenge occurred after dinner. During unannounced exercise, there were no changes in how the algorithm regulated insulin delivery.

At the conclusion of the inpatient period, participants resumed using their personal pump, CGM, and insulin.

Hypoglycemia classification

Hypoglycemia events were classified as Level 1 or Level 2.¹⁰ A Level 1 event based on CGM was defined as ≥ 15 min of sensor glucose readings < 70 mg/dL. A Level 2 hypoglycemic event was defined as ≥ 15 min of sensor glucose readings < 54 mg/dL. Hypoglycemia events within 15 min of another were classified as the same event.

Meals and snacks

Meals were provided to study participants by the site. No restrictions were placed on meal content. Study staff members were responsible for estimating CHO content. Snacks, restricted to < 15 g, were discouraged, limited to outside of the challenge period, and not announced to the system. Participants selected breakfast, lunch, and dinner meals, which were subsequently repeated on each day of the inpatient period.

Rescue carbohydrates

Investigators were instructed to provide rescue CHOs to study participants for self-monitored blood glucose (SMBG) values < 60 mg/dL if the participant was symptomatic, or if the SMBG value was < 54 mg/dL regardless of symptoms, or if needed for participant safety at investigator discretion or at participant request. Rescue CHOs were repeated every 15 min until SMBG value was ≥ 70 mg/dL.

Statistical analysis

As the primary objectives for the studies were performance and safety, sample size was not determined. The prespecified statistical analyses were performed for all participants who entered the study ($n = 10$ in each study; $n = 20$ combined).

Continuous demographic and clinical information are presented as mean and standard deviation and/or median (range) as determined by the distribution of the data. Categorical demographic information is presented as n (% of participants).

Endpoints for performance were the percentage of time CGM glucose readings were < 54 mg/dL, < 70 mg/dL, 70–180 mg/dL (TIR), > 180 mg/dL, and > 250 mg/dL, and the number of hypoglycemia occurrences based on CGM readings.

Endpoints for safety were the occurrence of adverse events (AEs), severe adverse events (SAEs), including severe hypoglycemia, or unanticipated adverse device effects (UADEs) while on the AID system.

Endpoints for performance were summarized across various prespecified periods during the inpatient visit: "Overall," "Nocturnal (midnight to 6 am)," "Postprandial," "Outside of Challenges," and then separately within each challenge: "Delayed Bolus Challenge," "Over Bolus Challenge," and "Exercise Challenge." Each challenge period began at the BG reading ~ 15 min before the challenge meal or the start of exercise and ended ~ 4 h later or at the start of the next meal. The "Postprandial" period included the start of each nonchallenge meal until 4 h later.

Results

Participants

A total of 20 people with T1D, 10 at each site, participated in these early feasibility studies at Ranier Clinical Research Center, Renton, WV (STUDY 1) and Diablo Clinical Research, Walnut Creek, CA (STUDY 2). Demographic and baseline characteristics of participants are given in Table 1. A1C levels ranged between 6.1% and 9.0% (mean A1C: 7.2%), with 45% of participants having levels below the American Diabetes Association target of $< 7.0\%$.¹¹ All

TABLE 1. DEMOGRAPHICS AND BASELINE CHARACTERISTICS

	STUDY 1 n = 10	STUDY 2 n = 10	Combined n = 20
Male	2 (20)	3 (30)	5 (25)
Age (years)	52.1 ± 10.7	37.3 ± 13.8	44.7 ± 14.2
Median (range)	57.0 (36–64)	32.0 (24–62)	44.5 (24–64)
Race			
Asian	0	1 (10)	1 (5)
White	10 (100)	9 (90)	19 (95)
Hispanic or Latino	0	1 (10)	1 (5)
Diabetes duration (years)	34.5 ± 10.2	25.9 ± 10.8	30.2 ± 11.1
Median (range)	38.0 (18–49)	24.0 (12–52)	27.0 (12–52)
A1C (%)	7.10 ± 0.77	7.32 ± 0.86	7.21 ± 0.80
Median (range)	6.95 (6.3–8.7)	7.05 (6.1–9.0)	7.00 (6.1–9.0)
BMI (kg/m ²)	27.5 ± 4.74	28.0 ± 5.34	27.8 ± 4.92
Insulin dose [U/(kg·day)]	0.49 ± 0.25	0.57 ± 0.15	0.53 ± 0.21

Data are *n* (%) or mean ± SD.

BMI, body mass index; SD, standard deviation.

participants successfully completed the lead-in period and the entire 47–52 h inpatient period analyzed here.

Glycemic outcomes

Glycemic outcomes were similar across the two studies. Overall, participants had CGM values within range (70–180 mg/dL) 81.2% of time, with 3.1% of the time <70 mg/dL, and 15.7% of the time >180 mg/dL (Table 2). Mean sensor glucose was 136 mg/dL. Rescue CHOs were administered 32 times across 19 subjects.

In the time periods outside of challenge periods, including insulin bolus challenges and unannounced exercise challenges, TIR was greater overall (85.2% of time between 70 and 180 mg/dL) with a similar percentage time <70 mg/dL (3.1% of time) and less time >180 mg/dL (11.7%) than the overall glycemic values with a mean sensor glucose of 132 mg/dL (Table 2).

Participants consumed 44.1 ± 12.3 (12–67) grams of CHOs during meals. During the postprandial period (4 h after the start of a nonchallenge meal or until the start of the next meal, whichever occurs first), TIR 70–180 mg/dL was lower (74.5%) with greater time in hyperglycemia >180 mg/dL (20.8%) and somewhat greater time in hypoglycemia (4.7%

for <70 mg/dL and 0.8% for <54 mg/dL) than during the other periods (Table 2). Mean sensor glucose was 140 mg/dL.

Insulin bolus-related challenges

During the insulin overbolus challenge, participants received 30.0% (±0.08%) more insulin than the dose recommended by the bolus calculator, yielding a total mean bolus dose of 5.8 ± 3.1 U. The insulin overbolus challenge did not result in greater time in hypoglycemia (3.0% of time <70 mg/dL and 0.5% of time <54 mg/dL) than the nonchallenge postprandial periods but was associated with greater time in hyperglycemia >180 mg/dL (31.6%) (Fig. 2A and Table 2). Mean sensor glucose was 154 mg/dL. Rescue CHOs were required in five instances across three participants.

During the delayed bolus challenge, participants received insulin after their glucose values had increased postprandially, resulting in an average of 35.8% (±36.8) more insulin than they would have received for CHOs alone. The insulin delayed bolus resulted in late postprandial hypoglycemia <70 mg/dL in 7 out of 20 participants (Fig. 2B). The algorithm responded appropriately by increasing insulin administration early in this period before delivery of the bolus and decreasing insulin administration late in this period.

TABLE 2. CONTINUOUS GLUCOSE MONITOR GLUCOSE METRICS FOR STUDY 1 AND STUDY 2 COMBINED

Study periods	% Time in glucose ranges, mean ± SD					Mean sensor glucose
	70–180 mg/dL	<54 mg/dL	<70 mg/dL	>180 mg/dL	>250 mg/dL	
Overbolus challenge	65.4 ± 29.2	0.5 ± 2.3	3.0 ± 8.6	31.6 ± 31.3	4.8 ± 11.6	154 ± 51
Delayed bolus challenge	57.1 ± 25.1	0.9 ± 2.5	4.3 ± 7.3	38.6 ± 25.9	10.1 ± 20.2	166 ± 62
Exercise challenge	89.6 ± 19.9	0.0 ± 0.0	1.3 ± 3.1	9.1 ± 19.6	0.0 ± 0.0	128 ± 30
Overall ^a	81.2 ± 8.4	0.4 ± 0.8	3.1 ± 3.5	15.7 ± 8.4	2.8 ± 4.2	136 ± 48
Outside of challenges	85.2 ± 8.1	0.4 ± 0.8	3.1 ± 3.2	11.7 ± 7.7	2.0 ± 4.6	132 ± 45
Postprandial ^b	74.5 ± 16.2	0.8 ± 1.9	4.7 ± 7.0	20.8 ± 16.6	4.0 ± 7.6	140 ± 54
Nocturnal (12 am–6 am)	97.3 ± 5.3	0.1 ± 0.3	0.8 ± 1.5	1.9 ± 5.1	0.0 ± 0.0	122 ± 29

^aOverall includes the entire time from when the system was placed in HCL until the conclusion of the study period.

^bPostprandial is the time from the start of the meal for all nonchallenge meals until 4 h later or the start of the next meal or challenge. HCL, hybrid closed-loop.

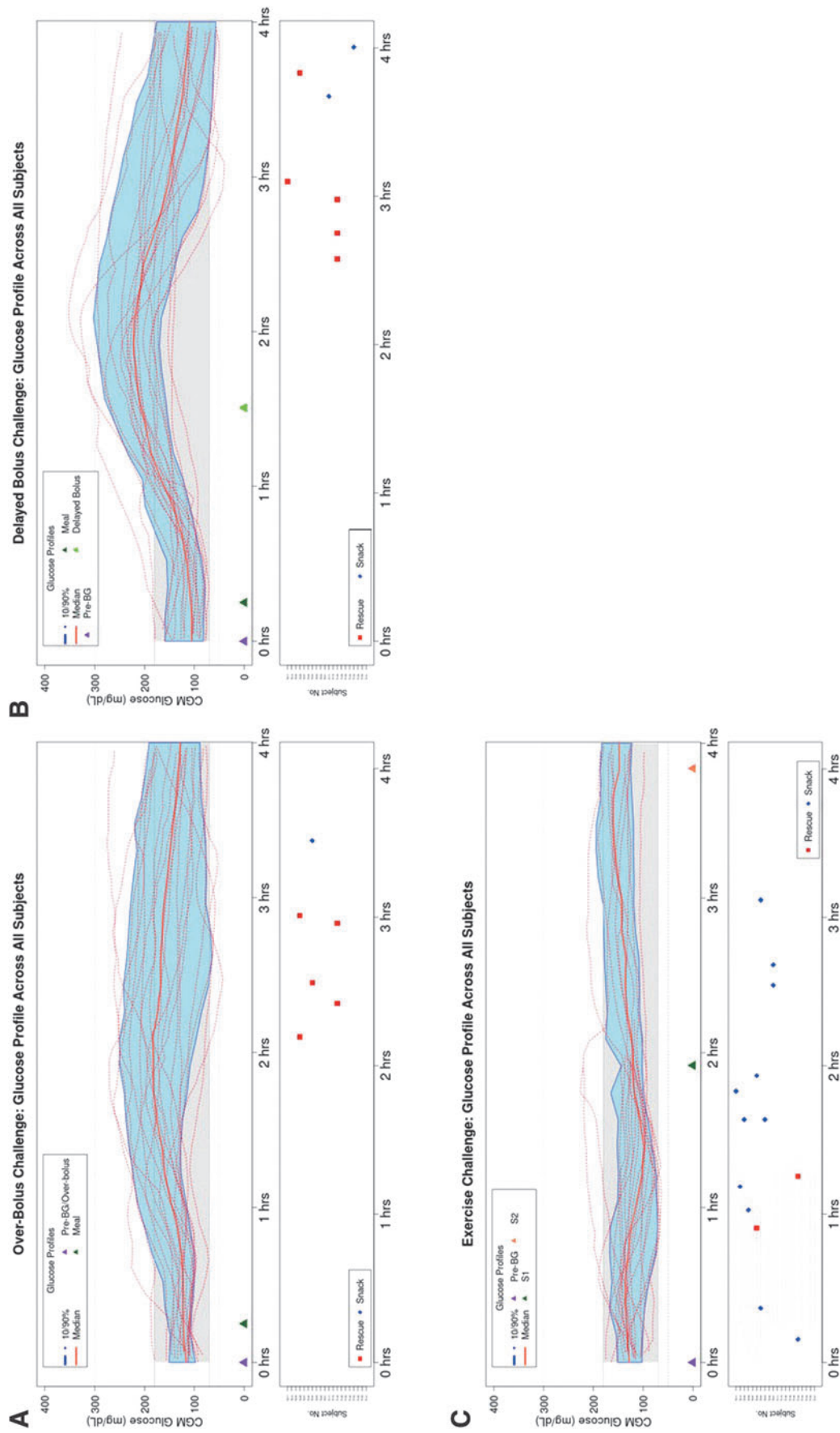


FIG. 2. Glucose profiles. The glucose profiles and CHO rescue and snacks for STUDY 1 and STUDY 2 are shown for each of the challenges: Over Bolus, Delayed Bolus, and Exercise. In the top panel, the median, 10th and 90th percentiles (shaded in gray) and the 70–180 mg/dL target range (shaded in blue) are shown for the CGM glucose values. The individual subject glucose profiles are dashed red lines. The bottom panel shows CHO rescues and snacks for individual subjects. (A) Overbolus challenge: rescue CHOs were administered in five instances (three subjects) ~2–3 h after the overbolus. (B) Delayed bolus challenge: the light green triangle depicts the median time of delivery of the delayed bolus for subjects in STUDY 1 and STUDY 2. Rescue CHOs were administered in five instances (three subjects). (C) The exercise challenge periods were predefined in the study protocols. The green triangle (S1) depicts the end of the challenge period for STUDY 1 wherein breakfast was served an hour after the conclusion of exercise. The orange triangle (S2) depicts the end of the challenge period for STUDY 2, which concluded 4 h after the start of exercise. Horizontal gray lines represent the individual exercise periods. Rescue CHOs were administered in two instances (two subjects).

During this challenge, TIR 70–180 mg/dL declined to 57.1% with 38.6% of time >180 mg/dL and 4.3% of time <70 mg/dL with a mean sensor glucose of 166 mg/dL (Table 2). Rescue CHOs were required in five instances across three participants.

Glycemia during and after unannounced exercise

Participants exercised for a duration of 56.9 ± 8.7 min per session. During exercise, 89.6% of time was in range 70–180 mg/dL, with 1.3% of time <70 mg/dL, and 9.1% of time >180 mg/dL with a mean sensor glucose of 128 mg/dL (Fig. 2C and Table 2). Less than 1% of time was spent with glucose <54 or >250 mg/dL during exercise. Rescue CHOs were required twice across two participants.

Nocturnal glycemia

During the overnight period, TIR 70–180 mg/dL was high (97.3%), with limited time in hypoglycemia (0.8% for <70 mg/dL) and hyperglycemia (1.9% for >180 mg/dL) (Table 2). Mean sensor glucose was 122 mg/dL during this period. There was one instance wherein a participant was given CHOs when they met the definition of Level 1 hypoglycemia by CGM. Additional CGM glucose metrics by study are provided in Table S1.

Safety

Multiple episodes of Level 1 hypoglycemia and Level 2 hypoglycemia occurred across the two studies (Table 3). No severe hypoglycemia involving cognitive impairment requiring external assistance for recovery was experienced by any participant. No participant stopped study participation secondary to prolonged hypoglycemia.

For hyperglycemia rescue events, three participants who required infusion set changes due to suspected occlusions on day 1 had BG >300 mg/dL. There were no serious AEs associated with hyperglycemia.

No episodes of AEs were observed while participants were using the system. Four AEs were reported across three par-

ticipants in the lead-in period of the study. No SAEs or UADEs occurred during this study.

Discussion

Results of these inpatient multicenter early feasibility studies in adults with T1D compare favorably with other similar highly supervised studies of HCL systems with 81.2% TIR (70–180 mg/dL), 15.7% time >180, and 3.1% time <70 mg/dL inclusive of challenge periods of unannounced exercise, delayed bolus, and overbolus. Results also compare favorably with the recommendations for international consensus on time in range that recommended >70% TIR 70–180 mg/dL, <25% time >180 mg/dL, and <4% time below 70 mg/dL.¹² Safety objectives were met in these early studies; there were no serious AEs or unexpected adverse device events and there were eight events of Level 2 hypoglycemia.

Although comparison with other studies are inherently limited by differences in lead-in periods, participant populations, and study design, our results are comparable when benchmarking against other HCL systems tested in adults with T1D in supervised settings with regard to TIR. Although time <70 mg/dL was higher in our study than another system, differences among the methods of these studies limit the ability to draw conclusions.^{13,14} Although there are numerous limitations in extrapolating from inpatient performance to outpatient use, benchmarking against the pivotal trials of the two commercially available HCL systems in the United States also suggests that our system is ready for outpatient evaluation.^{15,16}

Challenge scenarios in our studies focused on common behaviors that impact glycemic control. An overbolus of 30% more insulin than a meal bolus calculation might occur in situations when CHO content is uncertain or the person does not eat all the CHOs anticipated, potentially leading to hypoglycemia. In our overbolus challenge, only three participants experienced hypoglycemia <70 mg/dL and required rescue CHOs, and just one reached sensor values <54 mg/dL, suggesting that the HCL system successfully attenuated basal

TABLE 3. SUMMARY OF HYPOGLYCEMIA EVENTS

	STUDY 1 (n = 10)		STUDY 2 (n = 10)		Combined (n = 20)	
	n (%)	No. of events	n (%)	No. of events	n (%)	No. of events
Level 1 hypoglycemia (<70 mg/dL)						
Overbolus challenge	1 (10)	1	1 (10)	1	2 (10)	2
Delayed bolus challenge	1 (10)	1	4 (40)	4	5 (25)	5
Exercise challenge	0	0	1 (10)	1	1 (5)	1
Outside of challenges ^a	6 (60)	9	8 (80)	13	14 (70)	22
Postprandial ^b	0	0	5 (50)	9	5 (25)	9
Nocturnal (12 am–6 am)	1 (10)	1	2 (20)	2	3 (15)	3
Level 2 hypoglycemia (<54 mg/dL)						
Overbolus challenge	0	0	1 (10)	1	1 (5)	1
Delayed bolus challenge	1 (10)	1	1 (10)	1	2 (10)	2
Exercise challenge	0	0	0	0	0	0
Outside of challenges ^a	3 (30)	3	1 (10)	2	4 (20)	5
Postprandial ^b	0	0	1 (10)	1	1 (5)	1
Nocturnal (12 am–6 am)	0	0	0	0	0	0

^aThe time from when the system was placed in HCL until the conclusion of the study period, exclusive of the challenge periods. The “Postprandial” and “Nocturnal” periods are included within the “Outside of Challenges” period.

^bPostprandial is the time from the start of the meal for all nonchallenge meals until 4 h later or the start of the next meal or challenge.

insulin and limited hypoglycemia. In 12 adults using an investigational Omnipod HCL system who received a 30% insulin overbolus, results were comparable with two subjects experiencing a BG <70 mg/dL and three subjects consuming supplemental CHOs.¹³ A 30% insulin overbolus at breakfast in 40 subjects with T1D led to only 5% of subjects with a BG ≤70 mg/dL; however, 20% of subjects were pre-emptively treated with CHOs after an algorithm warned that hypoglycemia would be unavoidable.¹⁷ This suggests that excess prandial insulin boluses can sometimes be challenging for HCL systems without use of supplemental CHOs.

Insulin boluses that are delayed, occurring during or after a meal, are another common clinical scenario. We tested the “worst case” of a person giving the full meal bolus plus a correction dose based on the bolus calculation glucose reading 1 h after a meal had started. This resulted in greater insulin bolus over delivery, on average, than our designated overbolus scenario. Notably, the results of this challenge were dependent upon time of day, with a greater glycemic rise after the breakfast delayed bolus than after the dinner delayed bolus. Four of 10 participants experienced postprandial hyperglycemia (sensor >250 mg/dL) and 5 of 10 participants experienced postprandial hypoglycemia (sensor <70 mg/dL) when the challenge occurred at breakfast time, as compared with 1 of 10 and 2 of 10, respectively, when the challenge occurred at dinner time. These differences also demonstrate the importance of considering the impact of time of day when interpreting results of some challenge scenarios.

Nocturnal performance in our studies was notable with a median of 100% TIR 70–180 mg/dL. Other supervised studies have likewise shown increased percentages of TIR during the overnight periods^{13,14,18} and this trend continued in less closely supervised outpatient trials.^{3,15,16} Although few studies across any setting have achieved a median of 100% TIR 70–180 mg/dL, the structure of our protocol and attentiveness of the clinical investigators likely helped facilitate this outcome.

We also tested the system during unannounced structured exercise. During STUDY 1, exercise was conducted in the morning, and during STUDY 2, exercise was conducted after dinner. Although TIR was high and time in hypoglycemia was minimal during these challenges, seven participants received supplemental CHOs during exercise later in the day whereas only one participant received supplemental CHOs during prebreakfast exercise. This was possibly related to greater resistance to exercise-related hypoglycemia or greater insulin on board in the postdinner period.^{19,20}

This inpatient early feasibility study has several limitations. Participants in both studies had reasonably well-controlled diabetes with a mean A1C <7.5%, and the lead-in period offered multiple opportunities for pump setting changes. We do not have CGM metrics available during the lead-in period for comparison purposes. Participants were always highly supervised and did not interact with the user interface. Participants could have taken breaks or stopped exercise early secondary to impending hypoglycemia; however, the 20 participants exercised for an average of 56.9 ± 8.7 min, suggesting this was infrequently the case. Although structured challenges were introduced to better understand how the system responded to a variety of potentially difficult conditions, the frequent unpredictable challenges that come from real-world use could not be assessed.

In summary, in these inpatient trials, the Lilly HCL system performed safely and comparably with other HCL systems. The system mitigated some of the expected effects of meal and exercise-related challenges. Additional testing of the system in outpatient settings where participants are able to interact with the system will allow further development and refinement. More learning is expected as the system is evaluated in populations with greater variability in demographic and clinical characteristics. This HCL system performed well in an inpatient setting and is ready for outpatient testing for adults with T1D.

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Authors' Contributions

Conception of the study was done by A.B., A.L., R.J., and H.W.; design of the study was carried out by A.B., A.L., R.J., and H.W.; acquisition of data was performed by M.C. and R.B.; analysis of data was by A.L.; interpretation of data was performed by all authors; drafting the article was carried out by A.B., A.L., and M.K. and critical revision of the article for important intellectual content was by all authors.

Author Disclosure Statement

A.B., A.L., R.E.J., M.K., and H.W. are employees and shareholders of Eli Lilly and Company.

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Disclaimer

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Supplementary Material

Supplementary Data
Supplementary Table S1

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