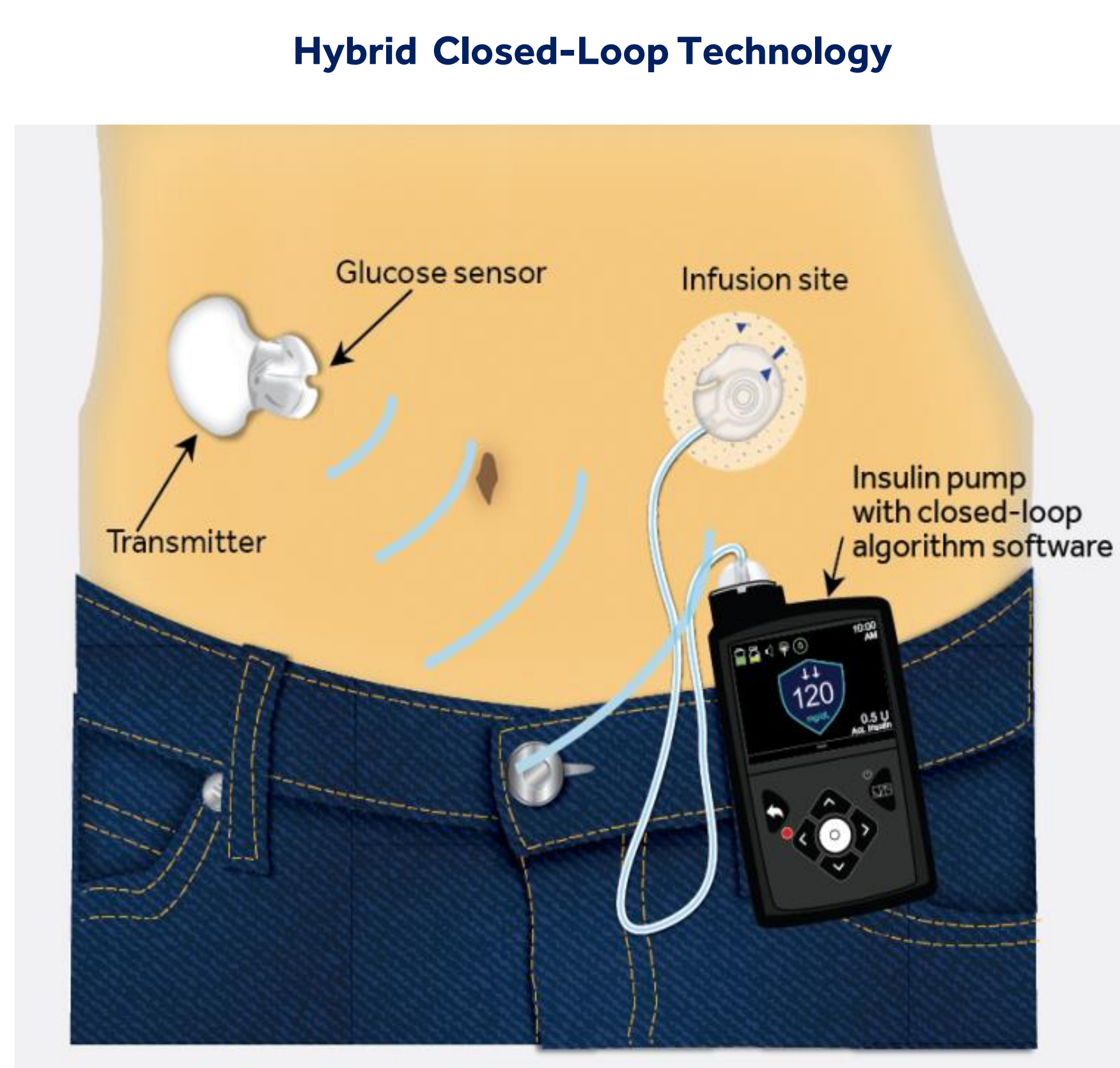


FACTORS THAT INFLUENCE THE PERFORMANCE OF A HYBRID CLOSED-LOOP (HCL) SYSTEM

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MINIMED™ 670G: HCL SYSTEM



Components:

- MiniMed 670G Insulin Pump
 - HCL algorithm (Medtronic proprietary)
- Guardian™ Sensor 3 sensor
- Guardian™ Link 3 transmitter
- CONTOUR®NEXTLINK 2.4 blood glucose meter (calibrates sensor)
- New CareLink™ Reports

Open Loop (Manual Mode)

- Need all the traditional pump settings
- Basal rates, Bolus Wizard™ settings, alerts for high and low glucose
- Can set Suspend on low or Suspend before low



Closed Loop (Auto Mode)

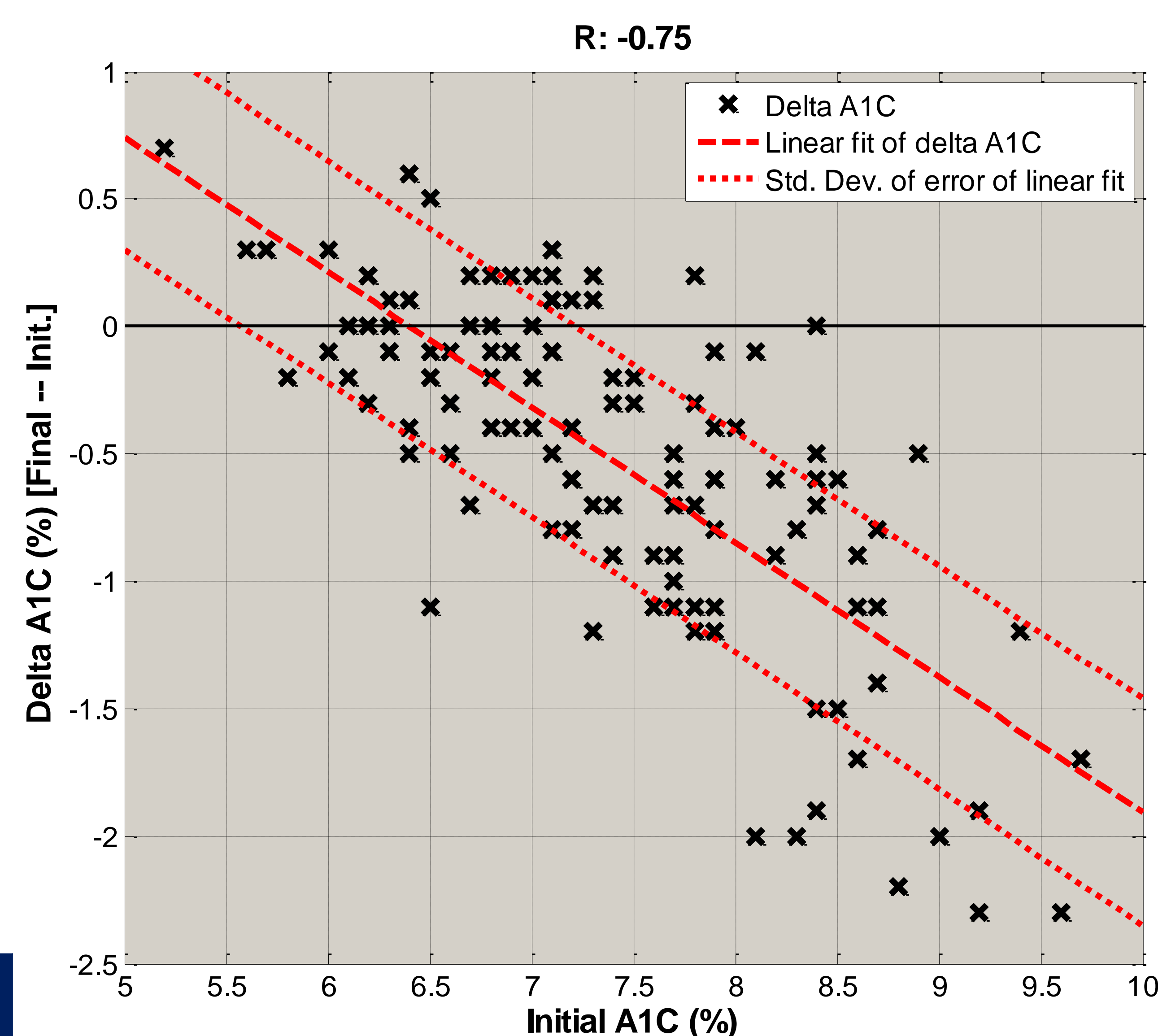
- Two adjustable settings:
 - Insulin to carb ratio
 - Active insulin action time
- Algorithm Targets 120 mg/dL
 - Temporary target can be set by user to 150 mg/dL for exercise
- Daily use:
 - Patient calibrates sensors, determines meal carbohydrate for pre-meal bolus, confirms correction bolus
 - Auto Mode exit can occur due to: Sustained hyperglycemia, prolonged delivery of maximum or minimum insulin, sensor issues (calibrations, missed transmission), self-diagnostic issues

METHODS

- Pivotal Trial¹
 - 10 sites (9 US, 1 Israel)
- Type 1 > 2 yrs
 - A1C < 10%
 - Adolescent: 14 – 21 yrs
 - Adult: 22 – 75 yrs
- Pump ≥ 6 months; +/- CGM
- Run-in Phase: Open loop (Manual Mode) 2-weeks
- Study Phase: Closed loop (Auto Mode) 3 months
 - 6-day / 5-night hotel stay
 - 24 hour reference i-STAT

Characteristic	Adolescents (n=30)	Adults (n=94)
Sex	16F / 14M	53F / 41M
Age (years)	16.5 ± 2.3	44.6 ± 12.8
Weight (kg)	67.4 ± 13.0	79.9 ± 18.2
BMI (kg/m ²)	23.7 ± 3.8	27.1 ± 5.4
Duration of diabetes (years)	7.7 ± 4.2	26.4 ± 12.4
Total daily dose of insulin (units/kg/day)	0.8 ± 0.2	0.6 ± 0.2
HbA1C at screening (%)	7.7 ± 0.8	7.3 ± 0.9
	Means ± SD	

Delta A1C (Final – Initial) v/s Initial A1C



RESULTS

Items	No-change in A1C	Rise in A1C	Drop in A1C	p-value
Number of patients (%)	3 (6%)	13 (25%)	35 (69%)	--
Average age, yrs	32.3 ± 6.1	40.0 ± 22.3	43.9 ± 14.1	0.5235
Average initial A1C, %	6.8 ± 0.2	7.0 ± 0.2	7.0 ± 0.3	0.8134
Average final A1C, %	6.8 ± 0.2	7.2 ± 0.2	6.6 ± 0.4	<0.0001
Average total daily dose, U/day	35 ± 8	38 ± 12	48 ± 33	0.2681
Average daily total number of meals entered	7.7 ± 2.7	5.0 ± 1.1	5.6 ± 1.8	0.2204
Average daily total carbohydrate input, grams/day	162 ± 52	167 ± 47	189 ± 60	0.2341
Average carb-to-insulin ratio, grams/unit	9.9 ± 2.6	10.9 ± 2.9	9.2 ± 3.1	0.08
Percentage daily insulin from meal bolus, %	46 ± 6.3	42 ± 6.9	50 ± 9.1	0.0082
Overnight (0000 – 0600 hrs) mean sensor glucose, mg/dL	137 ± 13	144 ± 12	142 ± 16	0.6266
Average sensor glucose value at wake-up time (0600 hrs), mg/dL	132 ± 15	135 ± 12	136 ± 15	0.8885
Daytime (0600 – 0000 hrs) mean sensor glucose, mg/dL,	147 ± 11	154 ± 10	147 ± 11	0.0434

- Significant inverse correlation observed between initial A1C and delta A1C (R = -0.75)
- A total of 51 subjects (out of 124) with initial A1C between 6.5 – 7.5% were divided into 3 groups
 - No-change in A1C
 - Rise in A1C
 - Drop in A1C
- No difference in total daily insulin and avg. daily carb input observed among 'Rise' and 'Drop' groups
- However, percentage of daily insulin from meal-bolus was significantly higher for the 'Drop' group
 - Mainly due to lower carb-insulin ratio
- No difference in overnight mean glucose existed indicating equivalent effectiveness of the HCL system without meal disturbance

CONCLUSIONS

- The analysis of a subgroup of subjects in the HCL pivotal trial indicates a significant effect of aggressive carb-insulin ratio on daytime glucose values
- Overall, the system is proven to be safe and demonstrated a positive effect of automating insulin delivery

REFERENCES

- ClinicalTrials.gov; Hybrid Closed Loop Pivotal Trial in Type 1 Diabetes (NCT02463097). <https://clinicaltrials.gov/ct2/show/NCT02463097>. Accessed February 4, 2017.