Appendix: Connected Pens – Clinical Studies Table

Study, Year	Device Studied	Type of insulin/company (number of users)	Participants	Study Design	Results
Adolfsson (2020)[26]	NovoPen 6	Basal insulin: degludec (n=21), detemir (n=1) Bolus insulin: aspart (n=79), human insulin (n=1), faster-acting insulin aspart (n=1)	94 participants (48 men & 46 women; mean age of 40.1 years; baseline TIR of 41.4%) with type 1 diabetes NovoPen 6 used for bolus insulin only (n=64), for both basal and bolus insulin (n=17), or basal insulin only (n=5)	Multicenter prospective, observational, proof-of-concept study; participants used CGM and administered bolus and/or basal insulin with NovoPen 6; Pen & CGM data downloaded during each HCP visit	TIR increased +1.9 hour/day ($p<0.001$) from baseline to follow-up period with a reduction in time in hyperglycemia (-1.8 hour/day, p=0.003) and L2 (<2.0 mmol/L) hypoglycemia (-0.3 hour/day, p=0.005). Missed bolus done (MBD) injections (meals without bolus injection within -15 and +60 min from start of meal) decreased by 43% over the study (p=0.002).
Gomez-Peralta (2020)[30]	Insulclock	N/A	16 participants (9 men & 7 women; mean age 40.1 years) with type 1 diabetes (10 received reminders and app alerts from Insulclock; 6 were in the Masked group and did not receive reminders or app alerts)	Randomized, single-center pilot study; participants used Insulclock for four weeks, with or without alerts and reminders	Insulclock use was associated with a decrease in mean glucose of −27.0 mg/dL [1.5 mmol/L] ($p = 0.013$). Time Above Range decreased by 3 hours/day (-12.5%; p=0.0026). Time in Range increased by 1.7 hours/day (+7%, p=0.038). Missed and mis-timed insulin doses per month were reduced by -3.9

					(p=0.1352) and -5.4 (p=0.032), respectively.
Jendle (2021)[19]	NovoPen 6	Basal insulin: degludec (n=21), detemir (n=1) Bolus insulin: aspart (n=79), human insulin (n=1), faster-acting insulin aspart (n=1)	94 participants (48 men & 46 women; mean age of 40.1 years; baseline TIR of 41.4%) with type 1 diabetes	Continuation of Adolfsson et al., 2020; multicenter prospective, observational, proof-of-concept study; clinical and healthcare costs projected to estimate cost-effectiveness of smart insulin pen use over participants' lifetime	NovoPen 6 use associated with +0.90 years in mean discounted life expectancy & +1.15 years in quality-adjusted life expectancy. Smart injectors were source of cost savings (direct SEK 124,270, indirect SEK 373,725) in comparison to standard care.
Vigersky (2021)[28]	InPen	Bolus insulin	529 individuals with non-optimal glycemic control; GMI >8.0% (n=423), GMI >9.5% (n=106)	Observational study; CGM data collected & compared before and up to 90 days after initiating InPen use	GMI >8.0% group had TIR increase of +0.6 hour/day (+2.3%), -0.1% reduction in GMI, mean sensor glucose -4.3 mg/dL, TAR -2.4% compared to pre-InPen use. GMI >9.5% group had TIR increase of +1.2 hour/day (+5%), -0.4% in GMI, -14.9 mg/dL mean sensor glucose, TAR -1.2 hour/day (-5.1%). Total rapid acting daily dose of insulin increased (from 26.29 to 27.19 u/day and 27.57 to 29.24 u/day, respectively, for each group. All results statistically significant (p<0.05).
Ekberg (2022)[27]	NovoPen 6	Basal insulin: degludec	32 adults (17 men & 15	One-arm, prospective,	Each missed basal insulin

		(n=32) Bolus insulin (n=28): aspart (n=26), faster aspart (n=1), faster-acting insulin aspart (n=1)	women; mean age of 35.6 years, average GMI of 8.2%) with type 1 diabetes	proof-of-concept, real-world study; participants used CGM and administered bolus and/or basal insulin with NovoPen 6; Pen & CGM data downloaded during each HCP visit; probability of missing basal insulin dose was estimated based on a cumulative linked mixed model	dose was associated with an increase in mean glucose level (p<.001), reduced TIR (p=0.005), increased TAR L2 (>250 mg/dL, p=0.002), and higher GMI (p<.001). Each missed basal dose corresponds to TIR reduction of -0.6 hour/day (2.6%) & mean glucose increase of 0.44 mmol/L. Probability that patient missed at least one basal dose (≥40 hours between two basal injections) was 22%.
Galindo (2023)[29]	Insulclock	Glargine U100 (Lantus SoloStar)	80 individuals (36 men & 44 women; mean age of 55.7 years, mean A1c of 9.2%) with type 2 diabetes on basal insulin	Randomized, cross-over pilot study; 12-week active phase receiving alarms & a 12-week control phase without feedback	Reduction in proportion of missed doses (22% vs 24%, p=0.04) when using smart pen with alarms vs no feedback. Smart pen with feedback associated with A1c reduction of 0.98% (9.3% to 8.2%) in group that started with feedback and A1c reduction of 0.70% (9.1% to 8.4%).
Chien (2023)[20]	InPen	Bolus insulin	1,681 individuals (n=397 <18 years, n=957 age 18-64 years, n=166 age ≥65 years, n=161 age NA) with	Retrospective, real-world analysis; participants used CGM and InPen smart insulin pen system;	Mean number of severe hypoglycemic events per week decline by 13% (0.67 to 0.58, p=0.008). Total estimated cost

			type 1 or type 2 diabetes	CGM data collected & compared before and up to 90 days after initating InPen use	reduction per month associated with reduced sensor-detected severe hypoglycemic events for this cohort is $19,234-$98,915 (assuming 5%-25% of sensor-detected severe hypoglycemic events result in a clinical event. Estimated cost reduction associated with reduced severe hypoglycemic events was $12-$59 per month & $110-$551 per year for each InPen user.
Baliga (2023)[31]	Bigfoot Unity	N/A	58 participants (mean age of 62 years; mean diabetes duration of 17.2 years) with type 1 diabetes (n=9) or type 2 diabetes (n=49)	Multicenter, retrospective, real-world study of Bigfoot Unity Diabetes Management System in adults with T1D or T2D over six months	Using the glucose management indicator (GMI) as a proxy for A1c, there was an 1% improvement GMI (P < 0.001). Participants with higher baseline A1c had the largest average decrease in GMI. Overall Time <70 mg/dL and <54 mg/dL on average, were 1.4% and 0.2%, respectively in the sixth month of pen cap system use.