

Supplementary Table 2. Adverse events of closed-loop systems in major clinical trials

Study	Comparison	Age, yr	No.	TBR < 54 mg/dL	Severe hypoglycemia (events)	Diabetic ketoacidosis (events)
Control-IQ, TypeZero group						
Brown et al. (2019) [45]	HCL vs. SAP	14–72	168	0.29% vs. 0.35%, $P=0.02$	0 vs. 0, $P=NA$	1 vs. 0, $P=NA$
Brown et al. (2020) [82]	HCL vs. PLGS SAP	14–72	109	0.20% vs. 0.22%, $P=NA$	0 vs. 0, $P=NA$	0 vs. 0, $P=NA$
Bretton et al. (2020) [83]	HCL vs. SAP	6–13	101	0.2% vs. 0.3%, $P=NA$	0 vs. 0, $P=NA$	0 vs. 0, $P=NA$
Florence (pre-stage of CamAPS FX), CamDiab group						
Bally et al. (2017) [77]	HCL vs. CSII	≥18	29	0.3% vs. 1.0% ^a , $P<0.01$	0 vs. 0, $P=NA$	0 vs. 0, $P=NA$
Tauschmann et al. (2018) [78]	HCL vs. SAP	≥6	86	0.3% vs. 0.5% ^a , $P=0.11$	0 vs. 0, $P=NA$	1 vs. 0, $P=NA$
Minimed 670G, Medtronic group						
Bergental et al. (2016) [24]	HCL vs. CSII (single arm)	14–75	124	0.6% vs. 1.0% ^a , $P=NA$	0 vs. 0, $P=NA$	0 vs. 0, $P=NA$
McAuley et al. (2020) [76]	HCL vs. MDI or CSII	25–75	120	0.2% vs. 0.9%, $P<0.01$	8 vs. 7, $P=NA$	1 vs. 2, $P=NA$
Minimed 780G, Medtronic group						
Collins et al. (2021) [37]	AHCL vs. PLGS SAP	7–80	60	0.4% vs. 0.5%, $P=0.03$	0 vs. 0, $P=NA$	0 vs. 1, $P=NA$
Bergental et al. (2021) [38]	AHCL vs. HCL	14–29	113	0.46% vs. 0.50%, $P<0.01$ ^b	1 vs. 0, $P=NA$	0 vs. 0, $P=NA$
DBLG1, Diabeloop group						
Benhamou et al. (2019) [47]	HCL vs. SAP	≥18	63	0.2% vs. 0.7% ^a , $P<0.01$	5 vs. 3, $P=NA$	0 vs. 0, $P=NA$
Amadou et al. (2021) [88]	HCL vs. SAP (single arm)	≥22	25	0.24% vs. 0.32%, $P=0.42$	0 vs. 0, $P=NA$	NA
Beta Bionics group						
El-Khatib et al. (2017) [111]	Dual HCL vs. CSII or SAP	≥18	43	0.6% vs. 1.9% ^c , $P<0.01$	0 vs. 1, $P=NA$	NA
Castellanos et al. (2021) [54]	Dual HCL vs. HCL	≥18	10	0.2% vs. 0.6%, $P=NA$	0 vs. 0, $P=NA$	0 vs. 0, $P=NA$
Inreda group						
Blauw et al. (2021) [50]	Dual FCL vs. HCL	≥18	23	0% vs. 0.5% ^c , $P<0.01$	0 vs. 0, $P=NA$	0 vs. 0, $P=NA$

TBR, time below range; HCL, hybrid closed-loop system; SAP, sensor augmented pump; NA, not available; PLGS, predictive low glucose suspension; CSII, continuous subcutaneous insulin infusion; MDI, multiple daily insulin injection; AHCL, advanced hybrid closed-loop; FCL, full closed-loop system.

^aTBR < 50 mg/dL was presented as outcome, instead of TBR < 54 mg/dL, ^b P value of non-inferiority test, ^cTBR < 60 mg/dL was presented as outcome, instead of TBR < 54 mg/dL.