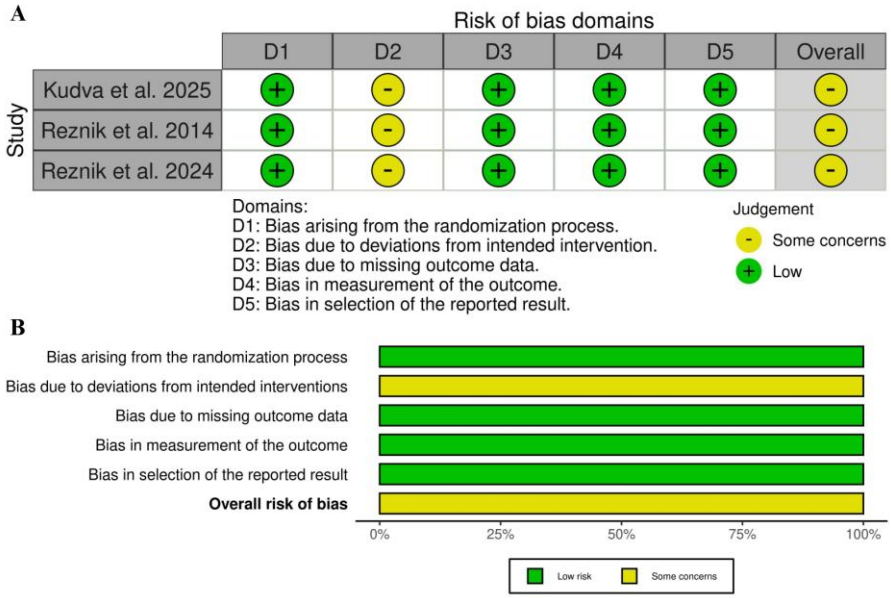
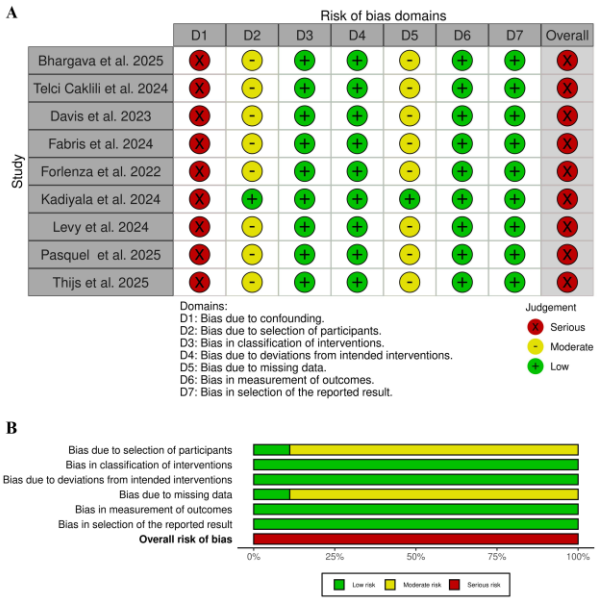


Supplementary Figure 1 Some concerns about bias were also identified in all three parallel-group RCTs, which stemmed from deviations from the intended interventions. A: Risk of bias summary. Review authors' judgments about each risk of bias item for each included parallel-group randomized controlled trials using the Cochrane risk of bias tool for randomized trials version 2; B: Risk of bias graph. Review authors' judgments about each risk of bias item presented as percentages across all included studies.



Supplementary Figure 2 All nine single-arm studies exhibited significant risk of bias, mainly due to confounding bias, as assessed by the Risk of Bias in Non-randomized Studies of Interventions tool. A: Risk of bias summary. Review authors'

judgments about each risk of bias item for each included single-arm studies using the Risk of Bias in Non-randomized Studies of Interventions version 2; B: Risk of bias graph. Review authors' judgments about each risk of bias item presented as percentages across all included studies.

Search strategy

PubMed: ("type 2 diabetes mellitus"[Title/Abstract] OR "type 2 diabetes"[Title/Abstract] OR "non-insulin dependent diabetes mellitus"[Title/Abstract] OR "T2DM"[Title/Abstract] OR "T2D"[Title/Abstract]) AND ("automated insulin delivery"[Title/Abstract] OR "closed loop insulin"[Title/Abstract] OR "artificial pancreas"[Title/Abstract] OR "hybrid closed loop"[Title/Abstract] OR "continuous subcutaneous insulin infusion"[Title/Abstract] OR "insulin pump"[Title/Abstract]).

Scopus: (TITLE-ABS-KEY (type 2 diabetes AND mellitus) OR TITLE-ABS-KEY (type 2 diabetes) OR TITLE-ABS-KEY (non-insulin AND dependent AND diabetes AND mellitus) OR TITLE-ABS-KEY (t2dm) OR TITLE-ABS-KEY (t2d) AND TITLE-ABS-KEY (automated AND insulin AND delivery) OR TITLE-ABS-KEY (closed AND loop AND insulin) OR TITLE-ABS-KEY (artificial AND pancreas) OR TITLE-ABS-KEY (hybrid AND closed AND loop) OR TITLE-ABS-KEY (continuous AND subcutaneous AND insulin AND infusion) OR TITLE-ABS-KEY (insulin AND pump)).

Web of Science: ((((((((((TI=(type 2 diabetes)) OR TI=(type 2 diabetes mellitus)) OR TI=(non-insulin dependent diabetes mellitus)) OR TI=(T2DM)) OR TI=(t2d)) AND TI=(automated insulin delivery)) OR TI=(closed loop insulin)) OR TI=(artificial pancreas)) OR TI=(hybrid closed loop)) OR TI=(continuous subcutaneous insulin infusion)) OR TI=(insulin pump) AND ((((((((((AB=(type 2 diabetes)) OR AB=(type 2 diabetes mellitus)) OR AB=(non-insulin dependent diabetes mellitus)) OR AB=(T2DM)) OR AB=(t2d)) AND AB=(automated insulin delivery)) OR AB=(closed loop insulin)) OR AB=(artificial pancreas)) OR AB=(hybrid closed loop)) OR AB=(continuous subcutaneous insulin infusion)) OR AB=(insulin pump))).

Supplementary Table 1 Summary of the excluded studies

Ref.	Reason for exclusion	Study design	Summary of outcomes
Lakshman *et al*[38], 2023	Letter to the editor and post hoc analysis of the study, Daly *et al*[25], 2023	Cross-over randomized trial. Sample size: 25. Aimed to characterize changes in insulin requirements associated with improvements in glycemic control during the eight-week closed loop period	Mean glucose levels fell significantly from weeks 1-2 to weeks 5-6 of closed-loop (9.3-8.8 mmol/L, P = 0.04) and this was sustained in weeks 7-8. Associated with this improvement in glucose control, relative insulin requirements peaked at weeks 3-4 (108% of 8-week period average) followed by a non-significant trend to decrease in weeks 5-6 and 7-8 (down to 104% and 91% of 8-week period average, respectively, P = 0.08). Absolute total insulin dose [median (interquartile range)] peaked at 133 (76, 217) units at weeks 3-4, falling to 122 (64, 197) units at 5-6 weeks and 103 (61, 160) units by weeks 7-8 (a decrease of 8% and 23%, respectively)
Davis *et al*[39], 2025	Report of the extension phase of the study, Davis *et al*[31], 2023	Single-arm prospective study. Sample size: 24. Aimed to build confidence in the durability of these results over a longer period of use, we evaluated the safety and effectiveness of the Omnipod 5 automated insulin delivery System for an additional	During the initial 8-week study, participants achieved a decrease in percentage of time ≥ 250 mg/dL from 27.4% ± 21.0% to 10.5% ± 8.8% (P < 0.0001), which further decreased to 9.7% ± 9.2% during the extension phase (P = 0.0002 *vs* standard therapy). Percentage of time < 54 mg/dL remained low from standard therapy through extension [median (interquartile range)] 0.00% (0.00%, 0.06%) *vs* 0.02% (0.00%, 0.05%), P > 0.05). HbA1c decreased by 1.6% ± 1.2% (15.5 ± 13.1 mmol/mol, P < 0.0001) and time in range increased by 22.4% ± 19.2% (P < 0.0001) from standard therapy through extension. No significant change in body mass index or total daily insulin

	6 months beyond the initial study phase requirements

Supplementary Table 2 Review authors' judgments about each risk of bias item for each included randomized crossover trials using the Cochrane risk of bias tool for randomized trials version 2

Ref.	Domain 1: Risk of bias arising from the randomization process	Domain S: Risk of bias arising from period and carryover effects	Domain 2: Risk of bias due to deviations from the intended interventions	Domain 3: Risk of bias due to missing outcome data	Domain 4: Risk of bias in measurement of the outcome	Domain 5: Risk of bias in selection of the reported result	Overall
Borel *et al*[23], 2024	Low	Low	Some concerns	Low	Low	Low	Some concerns
Boughton *et al*[24], 2021	Some concerns	Low	Low	Low	Low	Low	Some concerns
Daly *et al*[25], 2023	Low	Some concerns	Some concerns	Low	Low	Low	Some concerns

Supplementary Table 3 Summary of findings table

Outcomes	Anticipated absolute effects[1] (95%CI)		Number of participants (studies)	Certainty of the evidence (GRADE)
	Risk with control	Risk with automated insulin delivery		
HbA1c (%)	The mean HbA1c at the end of the study was	MD 0.89% lower (1.32% lower to 0.46%	718 (4 RCTs)	⊕⊕◯◯ Low[2]

	8.31%	lower)		
TIR (3.9-10 mmol/L)	The mean TIR at the end of the study was 47.78%	MD 19.25% higher (11.43% higher to 27.06% higher)	480 (5 RCTs)	⊕⊕⊕◯ Moderate[3]
TAR > 10 mmol/L	The mean TAR > 10 mmol/L at the end of the study was 51.92%	MD 19.48% lower (27.14% lower to 11.82% lower)	480 (5 RCTs)	⊕⊕⊕◯ Moderate[3]
TAR > 13.9 mmol/L	The mean TAR > 13.9 mmol/L at the end of the study was 16.54%	MD 8.33% lower (12.89% lower to 3.77% lower)	428 (4 RCTs)	⊕⊕⊕◯ Moderate[3]
TBR < 3.9 mmol/L	The mean TBR < 3.9 mmol/L at the end of the study was 0.43%	MD 0.07% lower (0.21% lower to 0.08% higher)	480 (5 RCTs)	⊕⊕⊕⊕ High
TBR < 3 mmol/L	The mean TBR < 3 mmol/L at the end of the study was 0.09%	MD 0.01% lower (0.03% lower to 0.02% higher)	480 (5 RCTs)	⊕⊕⊕⊕ High
Mean sensor glucose (mmol/L)	The mean mean sensor glucose at the end of the study was 10.24 mmol/L	MD 1.21 mmol/L lower (1.93 mmol/L lower to 0.49 mmol/L lower)	786 (5 RCTs)	⊕⊕◯◯ Low[2]

[1]**The risk in the intervention group** (and its 95%CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

[2]High heterogeneity among the studies is present.

[3]Moderate heterogeneity among the studies is present.

GRADE Working Group grades of evidence: (1) High certainty: We are very confident that the true effect lies close to that of the estimate of the effect; (2) Moderate certainty: We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different; (3) Low certainty: Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect; and (4) Very low certainty: We have very little confidence in the effect estimate: the true effect is likely to be

substantially different from the estimate of effect. HbA1c: Glycated hemoglobin; MD: Mean difference; RCTs: Randomized controlled trials; TAR: Time above range; TBR: Time below range; TIR: Time in range.

Supplementary Table 4 Leave-one-out sensitivity analysis for the main outcomes with moderate and high heterogeneity in the meta-analysis

Variable	Study omitted	Mean difference (95%CI)	*P* value	I^2 (%)
Change from baseline in glycated hemoglobin (%)	Daly *et al*[25], 2023	-0.74 (-1.14 to 0.33)	0.0004	78
	Kadva *et al*[26], 2025	-1.11 (-1.65 to 0.57)	< 0.0001	75
	Reznik et al[27], 2014	-1.03 [-1.80 to 0.25)	0.009	88
	Reznik *et al*[28], 2024	-0.76 (-1.19 to 0.33)	0.0005	82
Time in range 3.9-10 mmol/L (%)	Borel *et al*[23], 2024	21.00 (10.35-31.64)	0.0001	80
	Boughton *et al*[24], 2021	20.57 (10.86-30.29)	< 0.0001	81
	Daly *et al*[25], 2023	14.79 (9.86-19.72)	< 0.00001	31
	Kadva *et al*[26], 2025	21.84 (12.30-31.39)	< 0.00001	69
	Reznik *et al*[28], 2024	17.86 (9.37-26.35)	< 0.0001	76
TAR > 10 mmol/L (%)	Borel *et al*[23], 2024	-21.34 (-31.86 to 10.82)	< 0.0001	80
	Boughton *et al*[24], 2021	-20.98 (-30.42 to 11.53)	< 0.0001	80
	Daly *et al*[25], 2023	-14.88 (-19.29 to 10.48)	< 0.00001	20
	Kadva *et al*[26], 2025	-21.93 (-31.92 to 11.93)	< 0.0001	72
	Reznik *et al*[28], 2024	-18.14 (-26.48 to 9.80)	< 0.0001	76
TAR > 13.9 mmol/L (%)	Borel *et al*[23], 2024	-11.70 (-18.93 to 4.46)	0.0002	64
	Daly *et al*[25], 2023	-6.99 (-11.56 to 2.41)	0.003	72
	Kadva *et al*[26], 2025	-11.13 (-20.85 to 1.40)	0.02	80
	Reznik *et al*[28], 2024	-6.70 (-10.57 to 2.83)	0.0007	66
Mean sensor glucose (mmol/L)	Borel *et al*[23], 2024	-1.38 (-2.30 to 0.45)	0.004	87
	Boughton *et al*[24], 2021	-1.16 (-1.98 to 0.35)	0.005	86
	Daly *et al*[25], 2023	-0.77 (-1.23 to 0.32)	0.0009	57
	Kadva *et al*[26], 2025	-1.37 (-2.48 to 0.25)	0.02	87
	Reznik et al[27], 2014	-1.51 (-2.39 to 0.64)	0.0007	79
Coefficient of variation	Borel *et al*[23], 2024	1.55 (0.01-3.10)	0.05	30

of glucose (%)	Boughton *et al*[24], 2021	1.20 (-1.29 to 3.70)	0.35	76
	Daly *et al*[25], 2023	0.32 (-1.60 to 2.23)	0.75	65
	Kadva *et al*[26], 2025	1.12 (-1.89 to 4.12)	0.47	74
	Reznik *et al*[28], 2024	0.53 (-1.60 to 2.66)	0.62	72
Total daily dose of insulin (U)	Borel *et al*[23], 2024	-13.22 (-26.85 to 0.41)	0.06	54
	Boughton *et al*[24], 2021	-4.57 (-25.85 to 16.70)	0.67	79
	Daly *et al*[25], 2023	-9.92 (-25.96 to 6.12)	0.23	72
	Kadva *et al*[26], 2025	-1.39 (-24.42 to 21.65)	0.91	78
	Reznik et al[27], 2014	0.31 (-19.56 to 20.18)	0.98	71
	Reznik *et al*[28], 2024	-3.25 (-21.09 to 14.60)	0.72	78

TAR: Time above range.