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Emerging evidence in type 2 diabetes

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Disclosures

- Payments for Speaking and Advisory boards
  - Abbott Diabetes Care, Dexcom, Insulet, Lilly Diabetes, Medtronic, Menarini, Novo Nordisk, Sanofi
- Institutional Research Support
  - Abbott Diabetes Care, Novo Nordisk
- Positions held
  - Chair, Diabetes Technology Network-UK
  - Member of EXTOD executive

Plan

- Current state of play for people with type 2 diabetes
- Evidence of benefit of automated insulin delivery (AID) systems in people with type 2 diabetes
  - Benefit of AID over standard treatment
  - Benefit of using AID over open loop pump therapy
  - Fully closed loop AID systems
  - Benefit occurs irrespective of c-peptide level
- Where might we use AID systems in type 2 diabetes in the future?

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Current situation for people with type 2 diabetes

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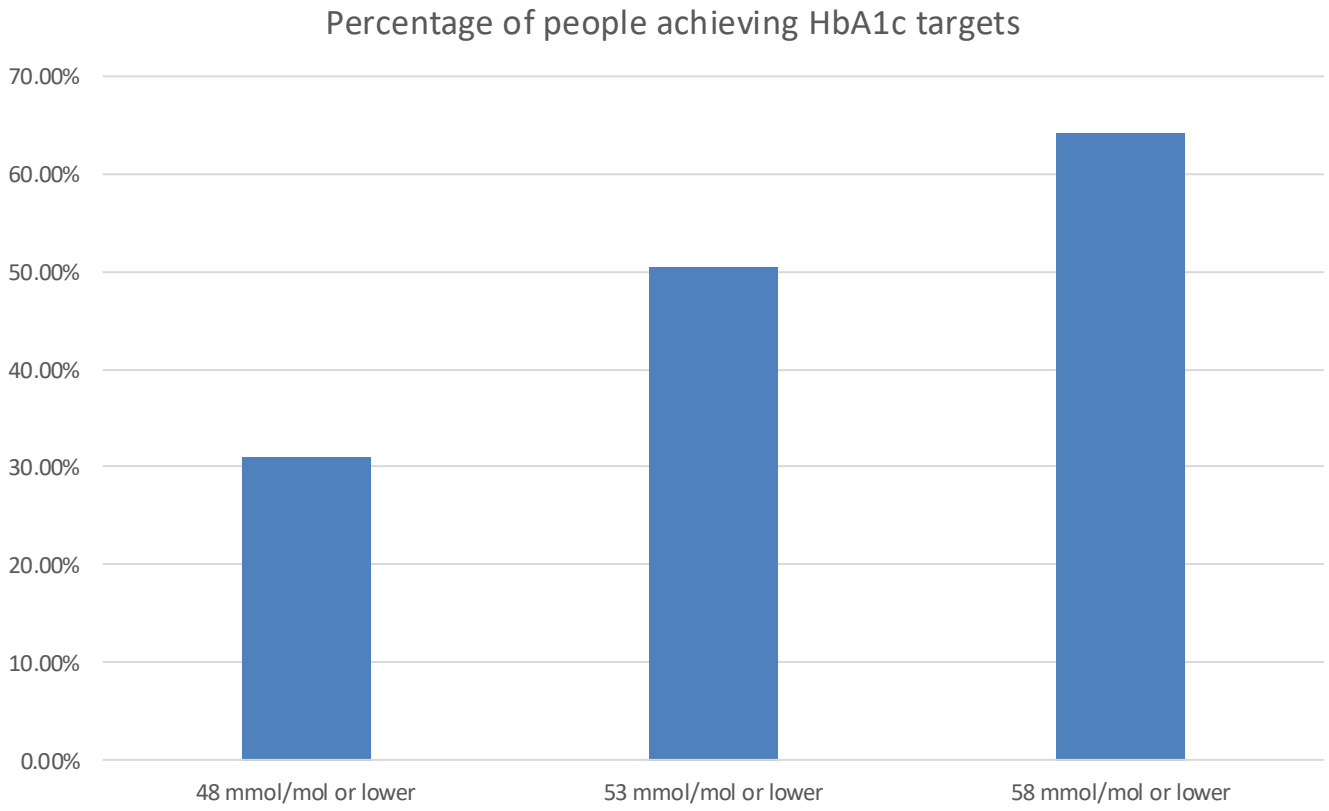
NDA data 2023-24



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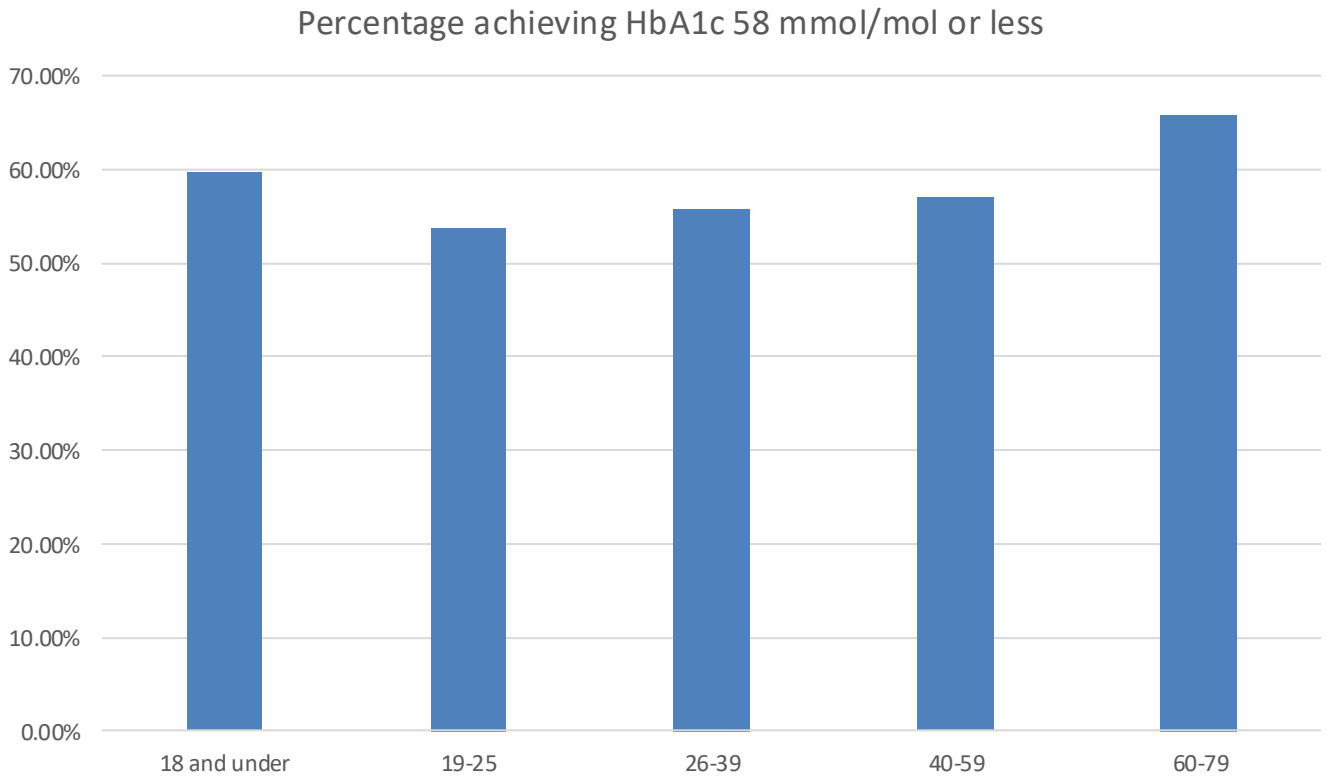
NDA data 2023-24 by age



Mortality by age of diagnosis

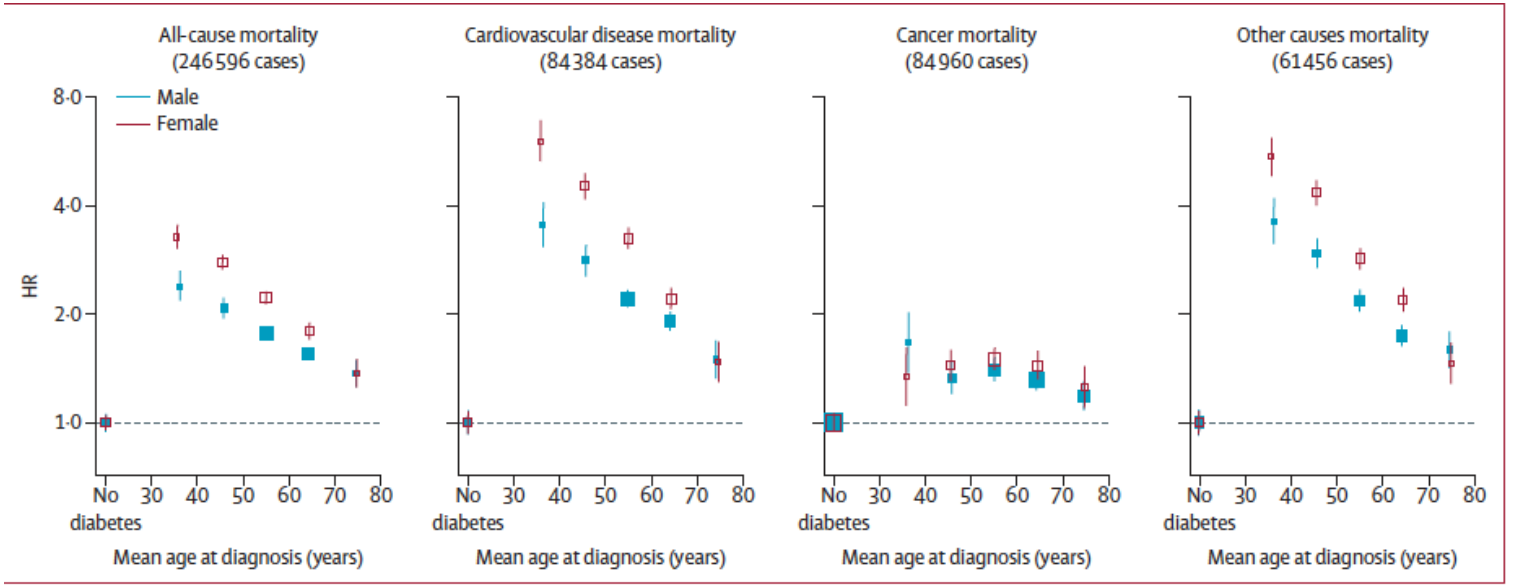


Figure 1: **Sex-specific HRs for all-cause and cause-specific mortality according to age at diagnosis of type 2 diabetes**
The mean age at diagnosis for the categories 30 to <40 years, 40 to <50 years, 50 to <60 years, 60 to <70 years and ≥70 years is plotted on the x axis. HRs are adjusted for age, and the reference (1·0) is people without diabetes. Studies with fewer than ten events of any outcome were excluded from the analysis of that outcome. The sizes of the boxes are proportional to the inverse of the variance of the log-transformed HRs. Vertical lines represent 95% CIs. HR=hazard ratio.

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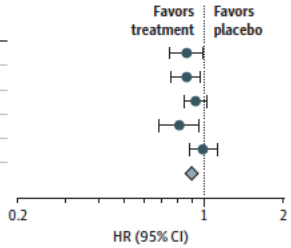
Is insulin still important in the era of SGLT2i and GLP-1RA?

SGLT2i – Cardiovascular benefits

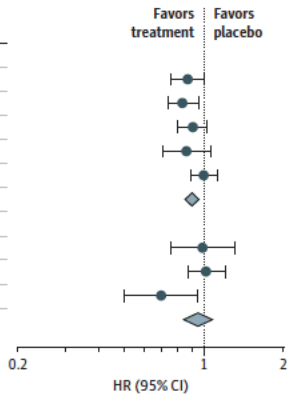
A Overall MACEs

	Treatment		Placebo				
	No./total No.	Rate/1000 patient-years	No./total No.	Rate/1000 patient-years	Hazard ratio (95% CI)	Favors treatment / Favors placebo	Weight, %
EMPA-REG OUTCOME	490/4687	37.4	282/2333	43.9	0.86 (0.74-0.99)		15.72
CANVAS program	NA/5795	26.9	NA/4347	31.5	0.86 (0.75-0.97)		20.12
DECLARE-TIMI 58	756/8582	22.6	803/8578	24.2	0.93 (0.84-1.03)		32.02
CREDENCE	217/2202	38.7	269/2199	48.7	0.80 (0.67-0.95)		10.92
VERTIS CV	735/5499	40.0	368/2747	40.3	0.99 (0.88-1.12)		21.23
Fixed-effects model (Q = 5.22; *df* = 4; *P* = .27; I^2 = 23.4%)					0.90 (0.85-0.95)		



B MACEs by ASCVD status

	Treatment		Placebo				
	No./total No.	Rate/1000 patient-years	No./total No.	Rate/1000 patient-years	Hazard ratio (95% CI)	Favors treatment / Favors placebo	Weight, %
Patients with ASCVD							
EMPA-REG OUTCOME	490/4687	37.4	282/2333	43.9	0.86 (0.74-0.99)		19.19
CANVAS program	NA/3756	34.1	NA/2900	41.3	0.82 (0.72-0.95)		21.16
DECLARE-TIMI 58	483/3474	36.8	537/3500	41.0	0.90 (0.79-1.02)		24.90
CREDENCE	155/1113	55.6	178/1107	65.0	0.85 (0.69-1.06)		8.82
VERTIS CV	735/5499	40.0	368/2747	40.3	0.99 (0.88-1.12)		25.93
Fixed-effects model (Q = 4.53; *df* = 4; *P* = .34; I^2 = 11.8%)					0.89 (0.84-0.95)		
Patients without ASCVD							
CANVAS program	NA/2039	15.8	NA/1447	15.5	0.98 (0.74-1.30)		21.70
DECLARE-TIMI 58	273/5108	13.4	266/5078	13.3	1.01 (0.86-1.20)		62.07
CREDENCE	62/1089	22.0	91/1092	32.7	0.68 (0.49-0.94)		16.23
Fixed-effects model (Q = 4.59; *df* = 2; *P* = .10; I^2 = 56.5%)					0.94 (0.83-1.07)		

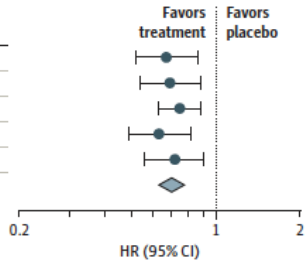


JAMA Cardiol. 2021;6(2):148-158

SGLT2i – HF benefits

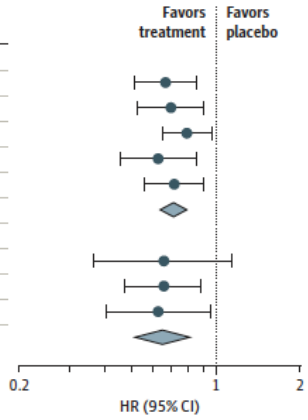
A Overall HHF

	Treatment		Placebo				
	No./total No.	Rate/1000 patient-years	No./total No.	Rate/1000 patient-years	Hazard ratio (95% CI)	Favors treatment / Favors placebo	Weight, %
EMPA-REG OUTCOME	126/4687	9.4	95/2333	14.5	0.65 (0.50-0.85)		16.09
CANVAS program	NA/5795	5.5	NA/4347	8.7	0.67 (0.52-0.87)		17.10
DECLARE-TIMI 58	212/8582	6.2	286/8578	8.5	0.73 (0.61-0.88)		33.72
CREDENCE	89/2202	15.7	141/2199	25.3	0.61 (0.47-0.80)		16.01
VERTIS CV	139/5499	7.3	99/2747	10.5	0.70 (0.54-0.90)		17.08
Fixed-effects model ($Q = 1.39$; $df = 4$; $P = .85$; $I^2 = 0.0\%$)					0.68 (0.61-0.76)		



B HHF by ASCVD status

	Treatment		Placebo				
	No./total No.	Rate/1000 patient-years	No./total No.	Rate/1000 patient-years	Hazard ratio (95% CI)	Favors treatment / Favors placebo	Weight, %
Patients with ASCVD							
EMPA-REG OUTCOME	126/4687	9.4	95/2333	14.5	0.65 (0.50-0.85)		19.62
CANVAS program	NA/3756	7.3	NA/2900	11.3	0.68 (0.51-0.90)		17.13
DECLARE-TIMI 58	151/3474	11.1	192/3500	14.1	0.78 (0.63-0.97)		29.66
CREDENCE	59/1113	20.6	92/1107	33.2	0.61 (0.44-0.85)		12.74
VERTIS CV	139/5499	7.3	99/2747	10.5	0.70 (0.54-0.90)		20.84
Fixed-effects model ($Q = 1.97$; $df = 4$; $P = .74$; $I^2 = 0.0\%$)					0.70 (0.62-0.78)		
Patients without ASCVD							
CANVAS program	NA/2039	2.6	NA/1447	4.2	0.64 (0.35-1.15)		16.38
DECLARE-TIMI 58	61/5108	3.0	94/5078	4.6	0.64 (0.46-0.88)		55.07
CREDENCE	30/1089	10.6	49/1092	17.5	0.61 (0.39-0.96)		28.56
Fixed-effects model ($Q = 0.03$; $df = 2$; $P = .99$; $I^2 = 0.0\%$)					0.63 (0.50-0.80)		

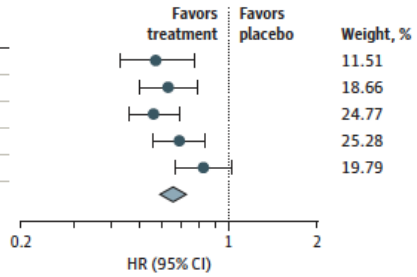


JAMA Cardiol. 2021;6(2):148-158

SGLT2i – Renal benefits

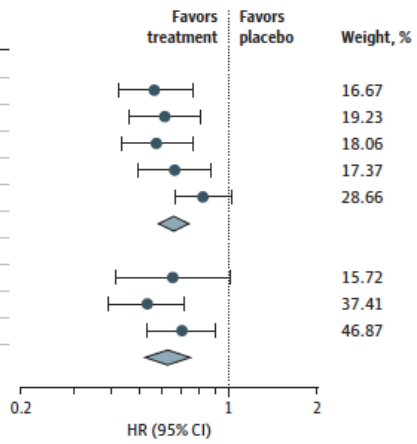
A Overall kidney outcomes

	Treatment		Placebo		Hazard ratio (95% CI)
	No./total No.	Rate/1000 patient-years	No./total No.	Rate/1000 patient-years	
EMPA-REG OUTCOME	81/4645	6.3	71/2323	11.5	0.54 (0.40-0.75)
CANVAS program	NA/5795	5.5	NA/4347	9.0	0.60 (0.47-0.77)
DECLARE-TIMI 58	127/8582	3.7	238/8578	7.0	0.53 (0.43-0.66)
CREDENCE	153/2202	27.0	224/2199	40.4	0.66 (0.53-0.81)
VERTIS CV	175/5499	9.3	108/2747	11.5	0.81 (0.64-1.03)
Fixed-effects model (Q = 7.96; *df* = 4; *P* = .09; I^2 = 49.7%)					0.62 (0.56-0.70)



B Kidney outcomes by ASCVD status

	Treatment		Placebo		Hazard ratio (95% CI)
	No./total No.	Rate/1000 patient-years	No./total No.	Rate/1000 patient-years	
Patients with ASCVD					
EMPA-REG OUTCOME	81/4645	6.3	71/2323	11.5	0.54 (0.40-0.75)
CANVAS program	NA/3756	6.4	NA/2900	10.5	0.59 (0.44-0.79)
DECLARE-TIMI 58	65/3474	4.7	118/3500	8.6	0.55 (0.41-0.75)
CREDENCE	69/1113	24.1	102/1107	36.5	0.64 (0.47-0.87)
VERTIS CV	175/5499	9.3	108/2747	11.5	0.81 (0.64-1.03)
Fixed-effects model (Q = 6.09; *df* = 4; *P* = .19; I^2 = 34.4%)					0.64 (0.56-0.72)
Patients without ASCVD					
CANVAS program	NA/2039	4.1	NA/1447	6.6	0.63 (0.39-1.02)
DECLARE-TIMI 58	62/5108	3.0	120/5078	5.9	0.51 (0.37-0.69)
CREDENCE	84/1089	29.9	122/1092	44.3	0.68 (0.51-0.89)
Fixed-effects model (Q = 1.86; *df* = 2; *P* = .40; I^2 = 0.0%)					0.60 (0.50-0.73)



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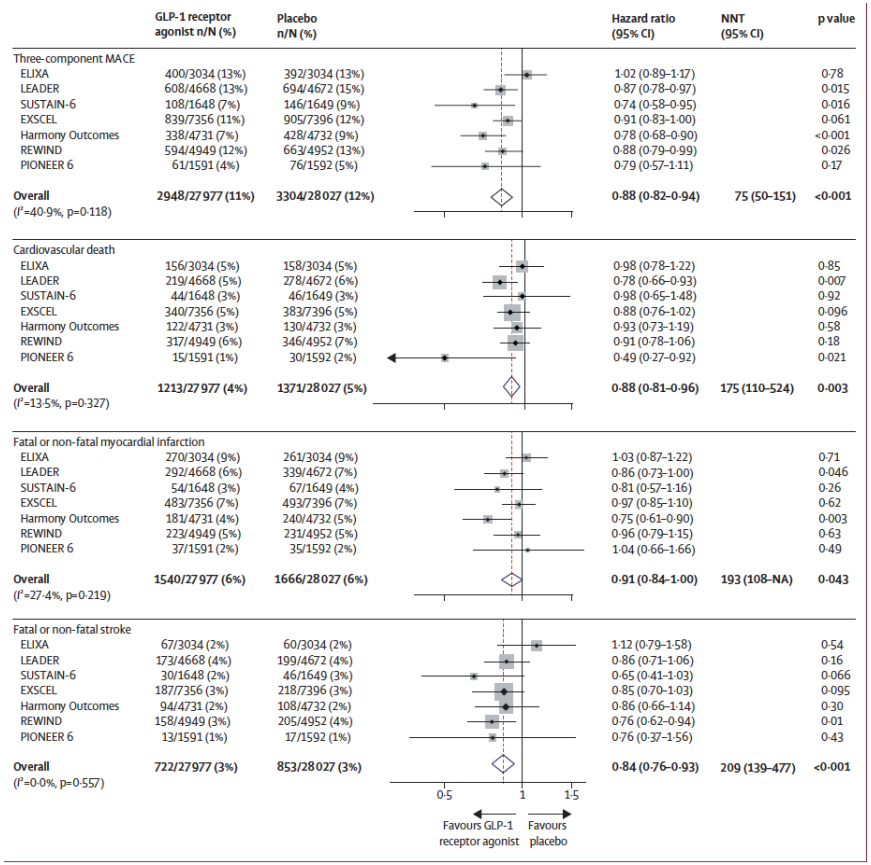
GLP-1RA – cardiovascular benefits

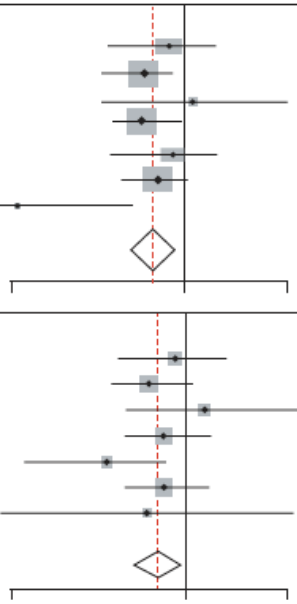


	GLP-1 receptor agonist n/N (%)	Placebo n/N (%)	Hazard ratio (95% CI)	NNT (95% CI)	p value
Three-component MACE					
ELIXA	400/3034 (13%)	392/3034 (13%)	1·02 (0·89–1·17)		0·78
LEADER	608/4668 (13%)	694/4672 (15%)	0·87 (0·78–0·97)		0·015
SUSTAIN-6	108/1648 (7%)	146/1649 (9%)	0·74 (0·58–0·95)		0·016
EXSCEL	839/7356 (11%)	905/7396 (12%)	0·91 (0·83–1·00)		0·061
Harmony Outcomes	338/4731 (7%)	428/4732 (9%)	0·78 (0·68–0·90)		<0·001
REWIND	594/4949 (12%)	663/4952 (13%)	0·88 (0·79–0·99)		0·026
PIONEER 6	61/1591 (4%)	76/1592 (5%)	0·79 (0·57–1·11)		0·17
Overall (I^2=40·9%, p=0·118)	**2948/27 977 (11%)**	**3304/28 027 (12%)**	**0·88 (0·82–0·94)**	**75 (50–151)**	**<0·001**
Cardiovascular death					
ELIXA	156/3034 (5%)	158/3034 (5%)	0·98 (0·78–1·22)		0·85
LEADER	219/4668 (5%)	278/4672 (6%)	0·78 (0·66–0·93)		0·007
SUSTAIN-6	44/1648 (3%)	46/1649 (3%)	0·98 (0·65–1·48)		0·92
EXSCEL	340/7356 (5%)	383/7396 (5%)	0·88 (0·76–1·02)		0·096
Harmony Outcomes	122/4731 (3%)	130/4732 (3%)	0·93 (0·73–1·19)		0·58
REWIND	317/4949 (6%)	346/4952 (7%)	0·91 (0·78–1·06)		0·18
PIONEER 6	15/1591 (1%)	30/1592 (2%)	0·49 (0·27–0·92)		0·021
Overall (I^2=13·5%, p=0·327)	**1213/27 977 (4%)**	**1371/28 027 (5%)**	**0·88 (0·81–0·96)**	**175 (110–524)**	**0·003**
Fatal or non-fatal myocardial infarction					
ELIXA	270/3034 (9%)	261/3034 (9%)	1·03 (0·87–1·22)		0·71
LEADER	292/4668 (6%)	339/4672 (7%)	0·86 (0·73–1·00)		0·046
SUSTAIN-6	54/1648 (3%)	67/1649 (4%)	0·81 (0·57–1·16)		0·26
EXSCEL	483/7356 (7%)	493/7396 (7%)	0·97 (0·85–1·10)		0·62
Harmony Outcomes	181/4731 (4%)	240/4732 (5%)	0·75 (0·61–0·90)		0·003
REWIND	223/4949 (5%)	231/4952 (5%)	0·96 (0·79–1·15)		0·63
PIONEER 6	37/1591 (2%)	35/1592 (2%)	1·04 (0·66–1·66)		0·49
Overall (I^2=27·4%, p=0·219)	**1540/27 977 (6%)**	**1666/28 027 (6%)**	**0·91 (0·84–1·00)**	**193 (108–NA)**	**0·043**
Fatal or non-fatal stroke					
ELIXA	67/3034 (2%)	60/3034 (2%)	1·12 (0·79–1·58)		0·54
LEADER	173/4668 (4%)	199/4672 (4%)	0·86 (0·71–1·06)		0·16
SUSTAIN-6	30/1648 (2%)	46/1649 (3%)	0·65 (0·41–1·03)		0·066
EXSCEL	187/7356 (3%)	218/7396 (3%)	0·85 (0·70–1·03)		0·095
Harmony Outcomes	94/4731 (2%)	108/4732 (2%)	0·86 (0·66–1·14)		0·30
REWIND	158/4949 (3%)	205/4952 (4%)	0·76 (0·62–0·94)		0·01
PIONEER 6	13/1591 (1%)	17/1592 (1%)	0·76 (0·37–1·56)		0·43
Overall (I^2=0·0%, p=0·557)	**722/27 977 (3%)**	**853/28 027 (3%)**	**0·84 (0·76–0·93)**	**209 (139–477)**	**<0·001**

Lancet Diabetes Endocrinol 2019;7:776–785

GLP-1RA – mortality and HF benefits

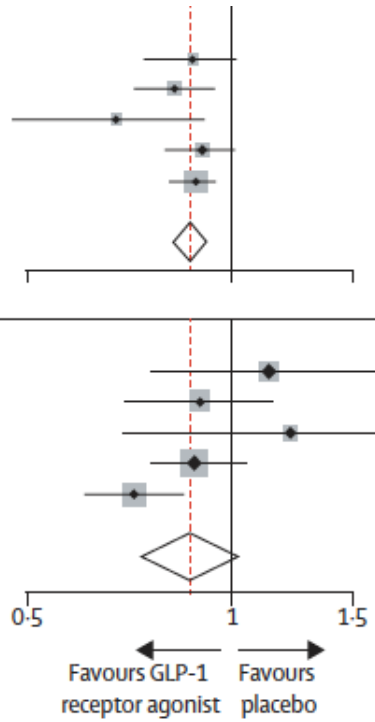
	GLP-1 receptor agonist n/N (%)	Placebo n/N (%)	Hazard ratio (95% CI)	NNT (95% CI)	p value
All-cause mortality					
ELIXA	211/3034 (7%)	223/3034 (7%)	0·94 (0·78–1·13)		0·50
LEADER	381/4668 (8%)	447/4672 (10%)	0·85 (0·74–0·97)		0·02
SUSTAIN-6	62/1648 (4%)	60/1649 (4%)	1·05 (0·74–1·50)		0·79
EXSCEL	507/7356 (7%)	584/7396 (8%)	0·86 (0·77–0·97)		0·016*
Harmony Outcomes	196/4731 (4%)	205/4732 (4%)	0·95 (0·79–1·16)		0·64
REWIND	536/4949 (11%)	592/4952 (12%)	0·90 (0·80–1·01)		0·067
PIONEER 6	23/1591 (1%)	45/1592 (3%)	0·51 (0·31–0·84)		0·008
Overall (I^2=16·5%, p=0·304)	**1916/27 977 (7%)**	**2156/28 027 (8%)**	**0·88 (0·83–0·95)**	**113 (80 to 271)**	**0·001**
Hospital admission for heart failure					
ELIXA	122/3034 (4%)	127/3034 (4%)	0·96 (0·75–1·23)		0·75
LEADER	218/4668 (5%)	248/4672 (5%)	0·87 (0·73–1·05)		0·14
SUSTAIN-6	59/1648 (4%)	54/1649 (3%)	1·11 (0·77–1·61)		0·57
EXSCEL	219/7356 (3%)	231/7396 (3%)	0·94 (0·78–1·13)		0·51
Harmony Outcomes	79/4731 (2%)	111/4732 (2%)	0·71 (0·53–0·94)		0·019
REWIND	213/4949 (4%)	226/4952 (5%)	0·93 (0·77–1·12)		0·46
PIONEER 6	21/1591 (1%)	24/1592 (2%)	0·86 (0·48–1·55)		0·59
Overall (I^2=0·0%, p=0·595)	**931/27 977 (3%)**	**1021/28 027 (4%)**	**0·91 (0·83–0·99)**	**311 (164 to 2797)**	**0·028**



Lancet Diabetes Endocrinol 2019;7:776–785

GLP-1RA – renal benefits

Composite kidney outcome including macroalbuminuria					
ELIXA	172/2647 (6%)	203/2639 (8%)	0·84 (0·68–1·02)		0·083
LEADER	268/4668 (6%)	337/4672 (7%)	0·78 (0·67–0·92)		0·003
SUSTAIN-6	62/1648 (4%)	100/1649 (6%)	0·64 (0·46–0·88)		0·006
EXSCEL	366/6256 (6%)	407/6222 (7%)	0·88 (0·76–1·01)		0·065
REWIND	848/4949 (17%)	970/4952 (20%)	0·85 (0·77–0·93)		<0·001
Overall (I^2=0·0%, p=0·413)	**1716/20168 (9%)**	**2017/20134 (10%)**	**0·83 (0·78–0·89)**	**62 (48 to 96)**	**<0·001**
Worsening of kidney function					
ELIXA	41/3031 (1%)	35/3032 (1%)	1·16 (0·74–1·83)		0·513
LEADER	87/4668 (2%)	97/4672 (2%)	0·89 (0·67–1·19)		0·43
SUSTAIN-6	18/1648 (1%)	14/1649 (1%)	1·28 (0·64–2·58)		0·48
EXSCEL	246/6456 (4%)	273/6458 (4%)	0·88 (0·74–1·05)		0·164
REWIND	169/4949 (3%)	237/4952 (5%)	0·70 (0·57–0·85)		<0·001
Overall (I^2=42·7%, p=0·137)	**561/20752 (3%)**	**656/20763 (3%)**	**0·87 (0·73–1·03)**	**247 (119 to –1072†)**	**0·098**



Lancet Diabetes Endocrinol 2019;7:776–785

Is insulin still important in type 2 diabetes?

- The advent of newer agents for type 2 diabetes has had a significant influence on outcomes for people with the condition
- Both SGLT2i and GLP-1RA medications are now well established in treatment pathways and are associated with HbA1c lowering as well as a variety of additional benefits
- Importantly however, not everybody with type 2 diabetes is able to benefit from these medications (adverse effects and contraindications)
- Also, some taking them will still not meet treatment targets

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Benefits of AID systems in people with type 2 diabetes

OP5 in type 2 diabetes

- Non-randomized, single-arm prospective trial
- 305 participants, aged 18-75, in 21 centres in the USA
- Treated with insulin at least 3 months prior to inclusion
- 14 day run-in period, followed by 13 week (3 month) intervention
- Primary outcome change in HbA1c with OP5

JAMA Network Open. 2025;8(2):e2459348

Participant characteristics

- 57% F, 43% M
- Mean age 57, mean duration of diabetes 17 years
- 50% White, 24% Black, 22% Hispanic or Latino
- Mean HbA1c 8.2%
- Mean BMI 35
- Varied education and income

JAMA Network Open. 2025;8(2):e2459348

Prior treatment

- 62% using CGM at baseline
- 55% using GLP-1RA (16% of these HbA1c < 7.0% at baseline)
- 44% using SGLT2i (15% of these HbA1c < 7.0% at baseline)
- 72% using either SGLT2i or GLP-1RA, 27% using both
- 73% MDI, 21% basal only, 5.6% insulin pump
- Mean TDD insulin 0.8 units/kg

JAMA Network Open. 2025;8(2):e2459348

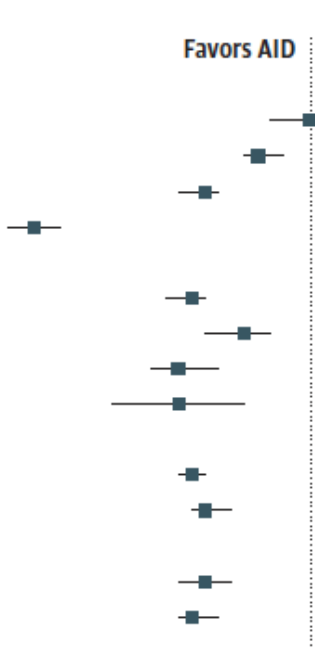
Outcomes – HbA1c and TIR

Outcome	Mean (SD)		Mean difference (95% CI)[b]	*P* value
	Baseline or ST (2 weeks)[a,b]	End of treatment or treatment phase (13 weeks)[a,b]		
Primary outcome				
HbA_{1c}, %				
Overall	8.2 (1.3)	7.4 (0.9)	−0.8 (−1.0 to −0.7)[c]	<.001[c,d]
Prior MDI users[e]	8.2 (1.4)	7.4 (0.9)	−0.8 (−0.9 to −0.7)	<.001[f]
Prior basal insulin only users	8.6 (1.2)	7.5 (0.8)	−1.2 (−1.5 to −0.9)	<.001[f]
Secondary outcomes in prespecified hierarchical order[g]				
Mean sensor glucose, mg/dL	202 (50)	170 (24)	−32 (−37 to −28)	<.001
Time in glucose range, %				
70-180 mg/dL	45 (25)	66 (17)	20 (18 to 22)	<.001
70-140 mg/dL	21 (18)	33 (17)	12 (10 to 13)	<.001
≥300 mg/dL[h]	8 (10)	2 (2)	−5 (−6 to −4)	<.001
>250 mg/dL[h]	20 (22)	7 (8)	−12 (−14 to −11)	<.001
>180 mg/dL	54 (25)	34 (17)	−20 (−22 to −18)	<.001
<70 mg/dL[i]	0.2 (0.3)	0.2 (0.2)	0.0 (−0.1 to 0.0)	<.001
<54 mg/dL[i]	0.01 (0.02)	0.04 (0.05)	0.01 (0.00 to 0.01)	<.001

JAMA Network Open. 2025;8(2):e2459348

Impact of baseline HbA1c, race, therapy

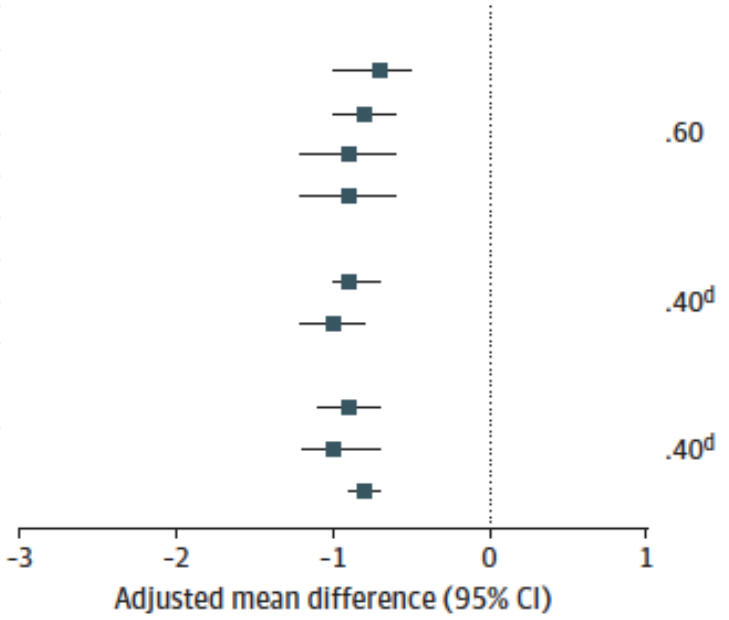
Source	Adjusted mean difference (95% CI)[a]	Interaction *P* value[b]
Baseline HbA_{1c}, %		
<7.0 (n = 42)	-0.0 (-0.3 to 0.2)	
7.0-7.9 (n = 104)	-0.4 (-0.5 to -0.2)	
8.0-8.9 (n = 82)	-0.8 (-1.0 to -0.7)	<.001
≥9.0 (n = 68)	-2.1 (-2.3 to -1.9)	
Race and ethnicity		
White, not Hispanic/Latino (n = 148)	-0.9 (-1.1 to -0.8)	
Black, not Hispanic/Latino (n = 69)	-0.5 (-0.8 to -0.3)	
Hispanic or Latino (n = 65)	-1.0 (-1.2 to -0.7)	.004
Other (n = 14)	-1.0 (-1.5 to -0.5)	
GLP-1RA Use		
Yes (n = 164)	-0.9 (-1.0 to -0.8)	.50
No (n = 132)	-0.8 (-0.9 to -0.6)	
SGLT-2i Use		
Yes (n = 130)	-0.8 (-1.0 to -0.6)	.50
No (n = 166)	-0.9 (-1.0 to -0.7)	



JAMA Network Open. 2025;8(2):e2459348

Impact of baseline insulin, CGM use

Pretrial mealtime insulin regimen	
Carbohydrate counting (n = 49)	-0.7 (-1.0 to -0.5)
Fixed dose (n = 108)	-0.8 (-1.0 to -0.6)
Sliding scale (n = 46)	-0.9 (-1.2 to -0.6)
Small/medium/large (n = 30)	-0.9 (-1.2 to -0.6)
Insulin therapy[c]	
MDI (n = 216)	-0.9 (-1.0 to -0.7)
Basal-only injections (n = 62)	-1.0 (-1.2 to -0.8)
CGM use[c]	
Never (n = 72)	-0.9 (-1.1 to -0.7)
In the past (n = 41)	-1.0 (-1.2 to -0.7)
Current (n = 183)	-0.8 (-0.9 to -0.7)



JAMA Network Open. 2025;8(2):e2459348

OP5 summary

- Non-randomized trial – comparison of pre- and post-treatment
- Diverse cohort, benefits accrued across all groups
- Greater benefit in those with higher baseline HbA1c – mean adjusted reduction 0.8%, rising to 2.1% for those 9.0% or above at baseline
- TIR increased from 45 to 66%, driven by a decrease in TAR
- Well tolerated – 90% would recommend
- 1 severe hypo, no DKA/HHS

780G in people with type 2 diabetes

- Non-randomized, single-arm, open-label study
- 95 participants in 13 centres in the USA
- Diagnosed at least 2 years prior to inclusion
- 21 day run-in period, followed by 90-day study period

DOI: 10.1089/dia.2024.0586

Baseline characteristics

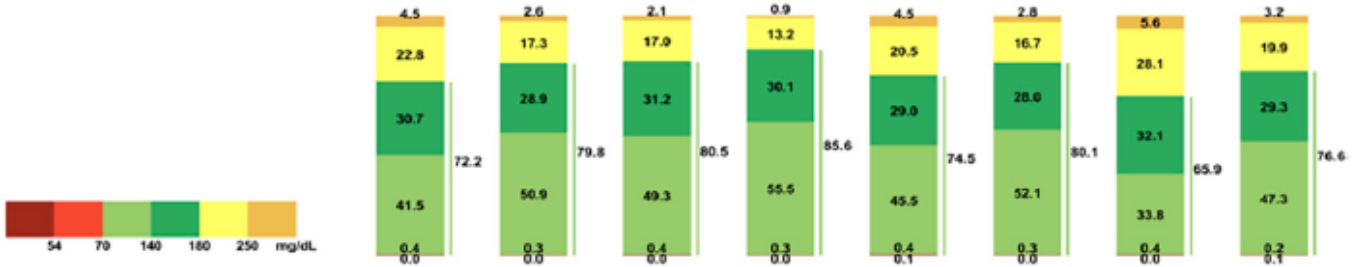
TABLE 1. PARTICIPANT DEMOGRAPHICS AND BASELINE CHARACTERISTICS

	Overall group (N = 95)
Age, years	60.3 ± 10.8
Female, *N* (%)	47 (49.5)
HbA1c, %	7.9 ± 1.0
HbA1c, mmol/mol	62.4 ± 10.4
Diabetes duration, years	18.6 ± 8.6
Weight, kg	105.8 ± 21.8
BMI, kg/m^2	36.0 ± 7.4
Insulin delivery method, *N* (%)	
MDI	58 (61.1)
CSII with CGM	19 (20.0)
CSII	9 (9.5)
Automated insulin delivery pump	7 (7.4)
Other	2 (2.1)
Race, *N* (%)	
White	76 (80.0)
Black or African American	16 (16.8)
Asian	2 (2.1)
Asian/White	1 (1.1)
Ethnicity, *N* (%)	
Hispanic/Latino	5 (5.3)
Non-Hispanic/Latino	89 (93.7)
Not reported	1 (1.1)

DOI: 10.1089/dia.2024.0586

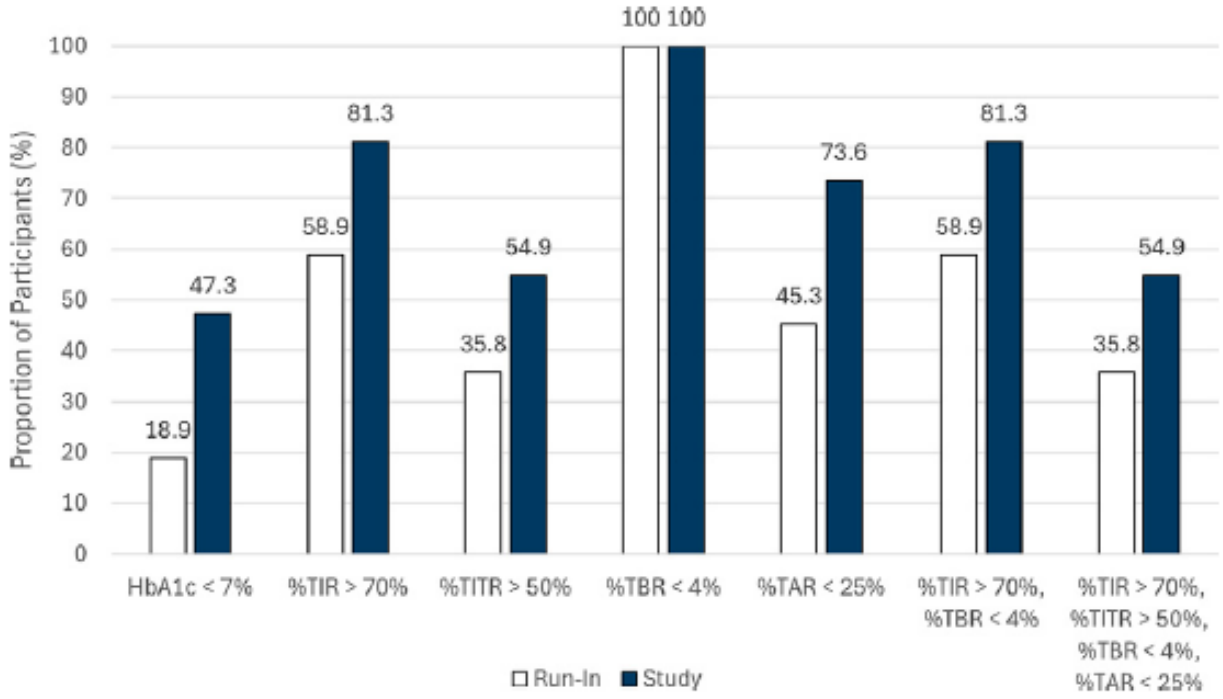
Glycaemic outcomes

	Overall Group		Baseline HbA1c					
			<7.0%		7.0% - 8.0%		>8.0%	
	Run-in (N=95)	Study (N=91)	Run-in (N=18)	Study (N=17)	Run-in (N=39)	Study (N=39)	Run-in (N=38)	Study (N=35)
Time in AHCL, %	--	91.2 ± 16.8	--	94.0 ± 8.6	--	93.9 ± 11.0	--	86.8 ± 23.3
CGM use, %	94.2 ± 5.5	92.9 ± 9.0	95.4 ± 3.1	94.8 ± 4.3	94.8 ± 4.5	93.7 ± 8.2	93.0 ± 7.0	91.1 ± 11.3
HbA1c, %	7.9 ± 1.0	7.2 ± 0.7[a]	6.5 ± 0.4	6.7 ± 0.3[b]	7.6 ± 0.3	7.1 ± 0.8[c]	8.8 ± 0.5	7.4 ± 0.7[d]
Mean SG, mg/dL	157.1 ± 22.4	147.5 ± 15.2	146.9 ± 19.1	141.5 ± 7.2	154.0 ± 22.9	146.8 ± 18.0	165.1 ± 21.2	151.3 ± 13.8
SD of SG, mg/dL	41.3 ± 10.3	39.6 ± 8.7	36.5 ± 7.6	34.9 ± 5.7	41.5 ± 12.1	39.4 ± 9.3	43.3 ± 8.9	42.1 ± 8.3
CV of SG, %	26.1 ± 4.4	26.7 ± 3.9	24.8 ± 3.5	24.7 ± 3.5	26.7 ± 4.7	26.6 ± 3.9	26.3 ± 4.5	27.7 ± 3.9
GMI, %	7.1 ± 0.5	6.8 ± 0.4	6.8 ± 0.5	6. 7 ± 0.2	7.0 ± 0.5	6.8 ± 0.4	7.3 ± 0.5	6.9 ± 0.3
TDD, U	77.4 ± 38.5	91.8 ± 49.3	75.3 ± 32.8	81.4 ± 39.6	74.7 ± 41.2	84.2 ± 42.6	81.2 ± 38.8	105.3 ± 58.0
Total basal, U	46.0 ± 21.9	50.1 ± 26.6	47.4 ± 22.9	46.1 ± 23.0	45.1 ± 23.2	45.2 ± 22.9	46.4 ± 20.5	57.5 ± 30.7
Total bolus, U	31.4 ± 25.1	41.7 ± 28.8	27.9 ± 20.7	35.3 ± 22.0	29.6 ± 27.2	39.0 ± 23.8	34.8 ± 25.0	47.8 ± 35.7
Auto correction, U	--	12.7 ± 10.8	--	10.5 ± 7.1	--	11.3 ± 8.4	--	15.2 ± 14.0
Auto correction, %TB	--	34.4 ± 22.5	--	33.2 ± 20.9	--	35.0 ± 25.9	--	34.2 ± 19.7
Daily user-initiated boluses, N/day	3.9 ± 1.9	3.2 ± 1.8	4.1 ± 2.2	3.5 ± 1.9	3.8 ± 2.0	3.0 ± 1.5	3.8 ± 1.8	3.3 ± 2.0



DOI: 10.1089/dia.2024.0586

Target achievement



DOI: 10.1089/dia.2024.0586

780G in people with type 2 diabetes

- Again see a reduction in HbA1c, greater in those with higher baseline HbA1c
- Increase in TIR driven by a decrease in TAR

- Increase in TDD insulin, no measured increase in CHO intake or weight

- No severe hypo/DKA/HHS

DOI: 10.1089/dia.2024.0586

Oxford University Hospitals NHS
NHS Foundation Trust

Closed loop v CSII with CGM

Diabetes Care
American Diabetes Association

Closed-Loop Insulin Therapy for People With Type 2 Diabetes Treated With an Insulin Pump: A 12-Week Multicenter, Open-Label Randomized, Controlled, Crossover Trial

Anne-Laure Borel, Sandrine Lablanche, Christine Waterlot, Eloïse Joffray, Céline Barra, Nathalie Arnol, Hafid Amougay, and Pierre-Yves Benhamou

Diabetes Care 2024;47(10):1778–1786 | https://doi.org/10.2337/dc24-0623

Diabetes Care 2024;47(10):1778–1786

Closed loop v CSII with CGM

- Crossover trial, open-loop to closed-loop or vice versa
- Smaller study – 17 people recruited from 3 hospitals in France
- 12 weeks total which resulted in 6 weeks in each trial arm
- Mean age 63, 65% male
- 41.2% GLP-1RA, 29.6% SGLT2i

Diabetes Care 2024;47(10):1778–1786

Glycaemic outcomes

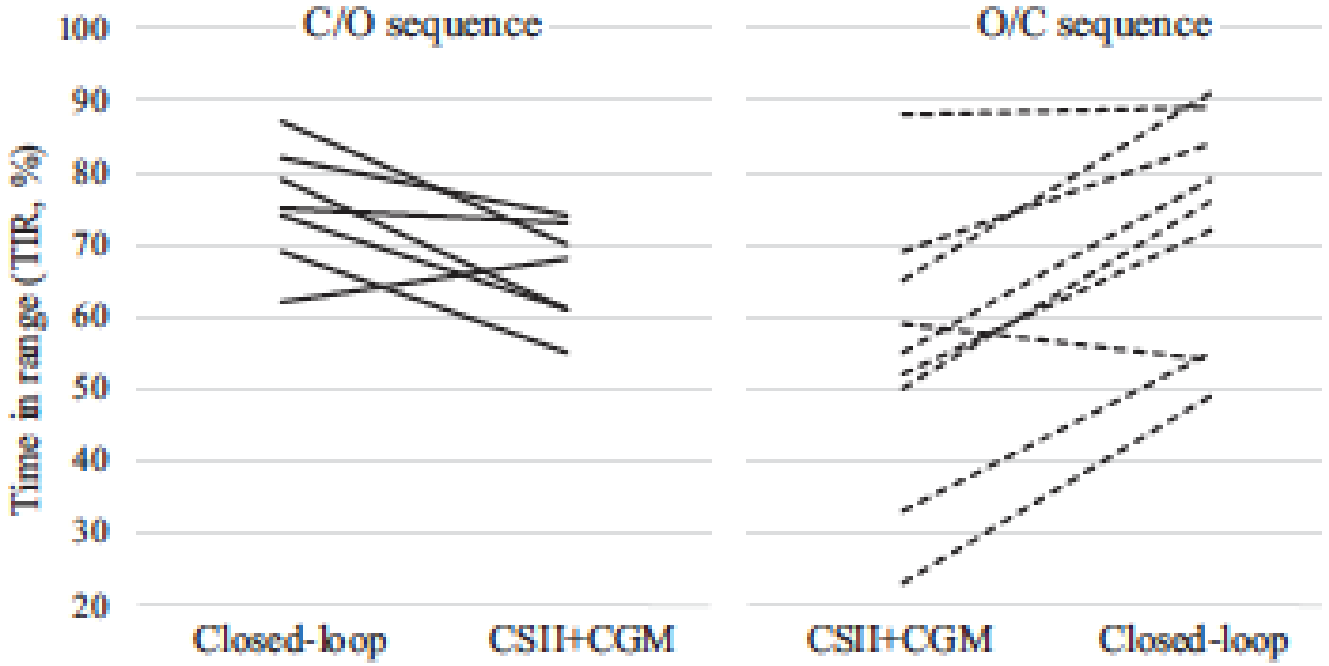
Table 2—Main and secondary outcomes for the differences between closed-loop system and CSII with CGM

	N	Closed loop	CSII + CGM	Difference of closed loop minus CSII + CGM	*P* value treatment effect	Statistical test for treatment effect	*P* value for normality test of the treatment effect	*P* value for interaction test order x intervention
Main outcome								
TIR 70–180 mg/dL (%)	17	76.0 (69.0–84.0)	61.0 (55.0–70.0)	15.0 (8.0–22.0)	<0.001	Mann-Whitney	0.013	0.18
Secondary outcomes								
CGM metrics								
Mean sensor glucose (mg/dL)	17	158.8 ± 17.3	172.2 ± 20.8	−13.2 (−20.8 to −5.6)	0.002	Student	0.12	0.19
TAR >180 mg/dL (%)	17	24.0 (16.0–30.0)	38.0 (30.0–45.0)	−15.0 (−22.0 to −8.0)	<0.001	Mann-Whitney	0.007	0.18
Level 2 hyperglycemia, >250 mg/dL	17	2.3 (1.0–5.3)	7.0 (3.7–9.6)	−3.3 (−6.9 to 0.7)	0.014	Student	0.71	0.16
TBR <70 mg/dL (%)	17	0.1 (0.0–0.4)	0.3 (0.2–1.0)	−0.2 (−0.2 to 0.0)	0.13	Mann-Whitney	0.001	0.38
Level 2 hypoglycemia, <54 mg/dL	17	0.00 (0.00–0.05)	0.00 (0.00–0.02)	0.00 (−0.02 to 0.03)	0.89	Mann-Whitney	<0.001	0.81
Variation coefficient (%)	17	23.0 (3.3)	25.1 (2.9)	−2.1 (95% CI −3.6 to 0.7)	0.006	Student	0.30	0.83
SD (g/L)	17	0.43 (0.11)	0.50 (0.08)	−0.07 (95% CI −0.11 to 0.02)	0.005	Student	0.20	0.54
GMI (%)	17	7.1 (0.4)	7.4 (0.5)	−0.3 (95% CI −0.5 to 0.1)	0.002	Student	0.12	0.16
CGM use (% of 24 h)	17	99.0 (96.9–99.0)	95.0 (93.0–98.0)	2.0 (0.0–5.0)	0.016	Mann-Whitney	0.006	0.65
Insulin doses								
Daily total insulin (IU/day)	17	103.7 (76.1–122.8)	78.0 (59.3–95.3)	10.0 (3.3–30.6)	0.003	Mann-Whitney	<0.001	0.36
DTSQs								
Treatment satisfaction scale total	17	31.0 (28.0–35.0)	32.0 (28.0–35.0)	−1.0 (−6.0 to 4.0)	0.89	Student	0.15	0.43
Perceived frequency of								
Hyperglycemia (*n*/day)	17	1.0 (1.0–3.0)	3.0 (1.0–5.0)	−2.0 (−3.0 to 1.0)	0.045	Student	0.19	0.65
Hypoglycemia (*n*/day)	17	1.0 (0.0–2.0)	1.0 (0.0–2.0)	0.0 (−1.0 to 1.0)	0.84	Student	0.15	0.27
Actimetry								
Mean daily physical activity (METs)	16	1.07 (1.04–1.09)	1.06 (1.05–1.08)	0.01 (−0.01 to 0.02)	0.16	Mann-Whitney	0.044	0.50
Mean daily total sleep time (min)	16	369 (64)	371 (72)	−2 (−51 to 47)	0.93	Student	0.21	0.64
Mean daily sleep fragmentation index	16							0.038

Results are expressed as means and SD and differences between periods by means and 95% CIs if the data are normally distributed. Quantitative variables and differences between periods are reported by median and interquartile range if the data are not normally distributed. Mean differences represent the means of the individual differences between the two periods of the study. If the differences were normally distributed, a Student test was realized to look for treatment effect; if not, a Mann-Whitney test was realized.

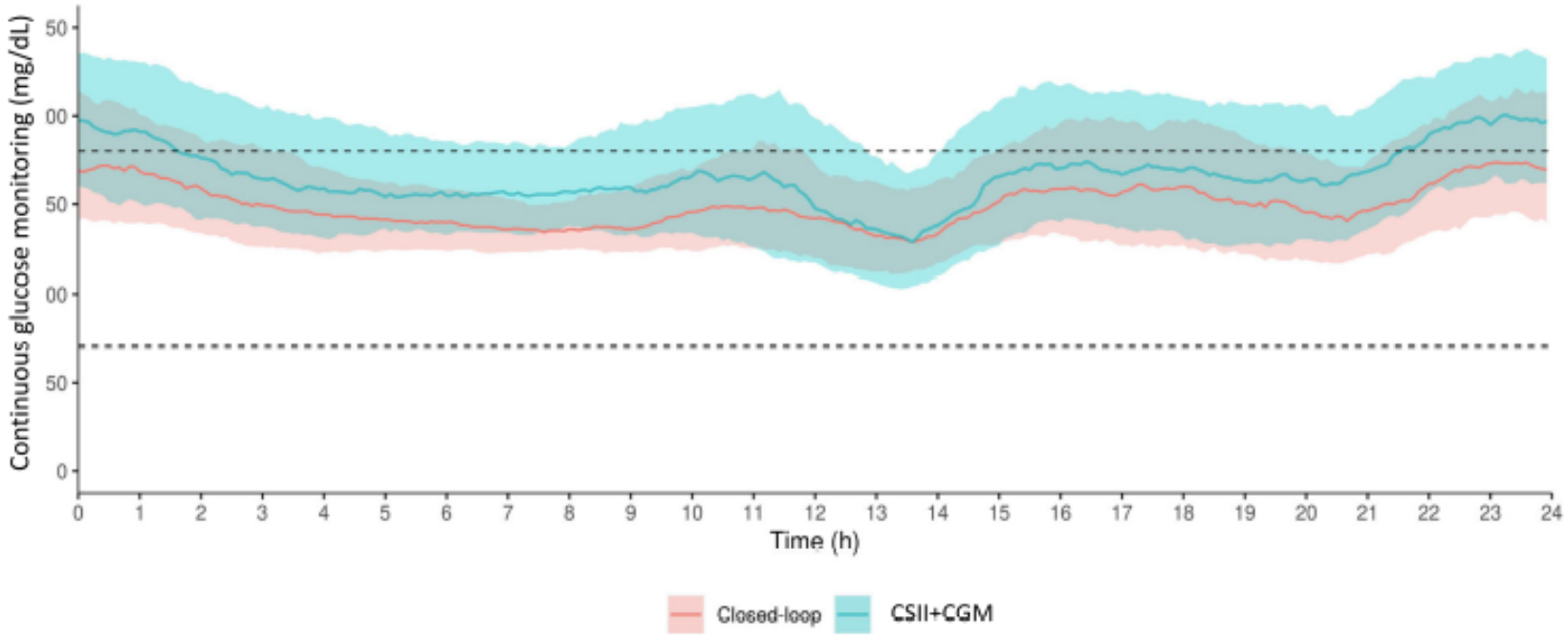
Diabetes Care 2024;47(10):1778–1786

Closed loop v CSII with CGM



Diabetes Care 2024;47(10):1778–1786

Closed loop v CSII with CGM



Diabetes Care 2024;47(10):1778–1786

CampAPS HX – fully closed loop

- Open-label, single-centre, randomized crossover study
- 26 adults, mean age 59, 73% M 27% F
- 8 week intervention periods, 2-4 week washout in between
- Comparing CamAPS HX fully-closed loop system with standard insulin therapy
- Primary endpoint TIR (3.9 – 10.0 mmol/l)

Nat Med 2023;29:203–208

Baseline characteristics

Table 1 | Baseline characteristics

Characteristic	Overall[a] (*n*=26)	Closed-loop therapy first (*n*=14)	Control therapy first[a] (*n*=12)
Age (years)	59 (11)	59 (12)	59 (10)
Female sex, *n* out of total *n* (%)	7 out of 26 (27)	3 out of 14 (21)	4 out of 12 (33)
Ethnic origin, *n* (%)			
White	25 (96)	14 (100)	11 (92)
Black	0 (0)	0 (0)	0 (0)
Asian	1 (4)	0 (0)	1 (8)
BMI ($kg\,m^{-2}$)	35.3 (8.6)	37.4 (9.1)	33.0 (7.7)
HbA1c ($mmol\,mol^{-1}$)	75 (15)	76 (12)	74 (19)
HbA1c (%)	9.0 (1.4)	9.1 (1.1)	9.0 (1.8)
Duration of diabetes (years)	17.5 (8.2)	17.2 (7.3)	17.8 (9.5)
Duration of insulin therapy (years)	8.5 (6.9)	7.9 (7.0)	9.3 (7.0)
Total daily insulin dose ($U\,kg^{-1}$)	0.70 (0.54–1.31)	0.69 (0.38–1.32)	0.83 (0.58–1.36)
Prior CGM or flash glucose monitor use, *n* (%)	3 (12)	1 (4)	2 (8)
Charlson comorbidity index	4 (2–5)	4 (2–6)	4 (2–4)

Nat Med 2023;29:203–208

Glycaemic outcomes

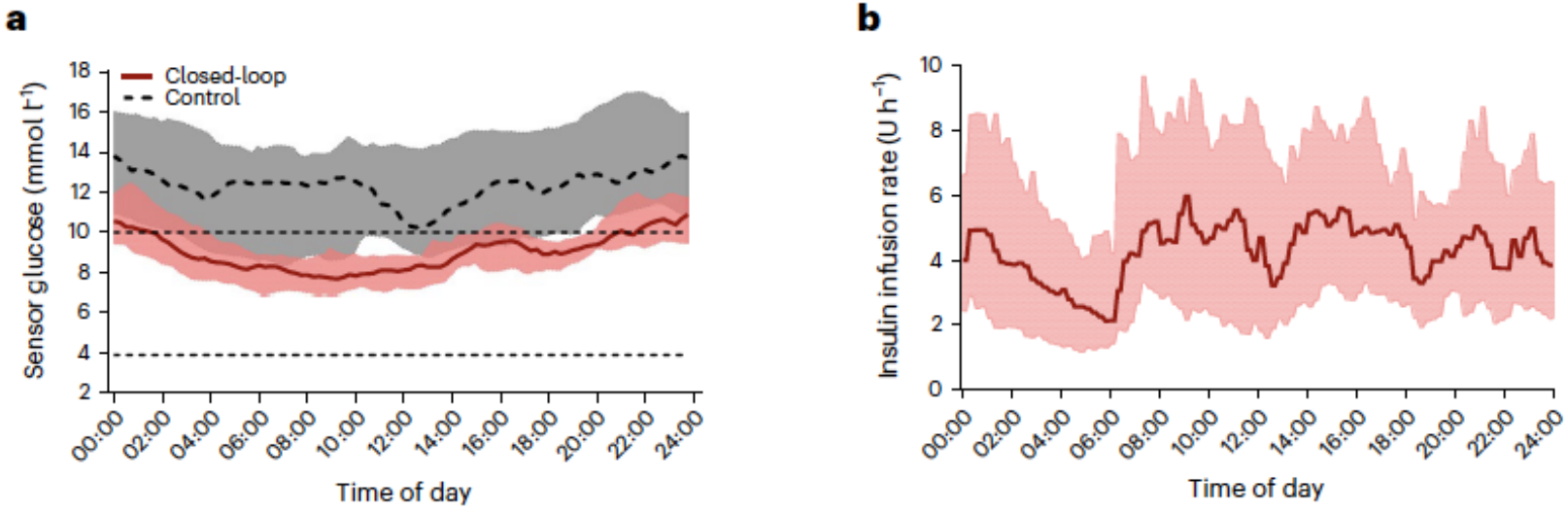
Table 2 | Primary and secondary endpoints during the closed-loop and control therapy periods

Endpoint	Closed-loop (n=26)	Control (n=25)[a]	Mean difference (95% CI for treatment difference[b])	P value
Primary endpoint				
Proportion of time with glucose 3.9–10.0 mmol l^{-1} (%)	66.3 (14.9)	32.3 (24.7)	35.3 (28.0 to 42.6)	<0.001
Key endpoints[c]				
Proportion of time with glucose > 10.0 mmol l^{-1} (%)	33.2 (14.8)	67.0 (25.2)	−35.2 (−42.8 to −27.5)	<0.001
Mean glucose (mmol l^{-1})	9.2 (1.2)	12.6 (3.0)	−3.6 (−4.6 to −2.5)	<0.001
HbA1c (mmol mol^{-1})	57 (9)	72 (13)	−15 (−20 to −11)	<0.001
HbA1c (%)	7.3 (0.8)	8.7 (1.2)	−1.4 (−1.8 to −1.0)	<0.001
Proportion of time with glucose < 3.9 mmol l^{-1} (%)	0.44 (0.19–0.81)	0.08 (0.00–1.05)	−0.10 (−0.36 to 0.16)	0.43
Secondary endpoints				
Proportion of time with glucose > 16.7 mmol l^{-1} (%)	1.8 (0.6–3.3)	12.5 (3.6–31.3)	NA	NA
Proportion of time with glucose > 20.0 mmol l^{-1} (%)	0.2 (0.0–0.5)	3.2 (0.2–9.7)	NA	NA
Proportion of time with glucose < 3.0 mmol l^{-1} (%)	0.04 (0.01–0.08)	0.03 (0.00–0.32)	NA	NA
s.d. of glucose (mmol l^{-1})	3.0 (0.8)	3.4 (1.0)	NA	NA
Coefficient of variation of glucose (%)	32.2 (5.7)	27.7 (8.5)	NA	NA
Total daily insulin dose (U per day)	108 (73–188)	84 (54–129)	NA	NA
Total daily insulin dose (U kg^{-1} per day)	0.90 (0.72–1.63)	0.71 (0.56–1.26)	NA	NA
Proportion of time with sensor glucose availability (%)	98.1 (96.8–98.5)	92.6 (89.8–98.0)	NA	NA
Proportion of time spent with closed-loop active (%)	92.3 (87.6–96.4)	NA	NA	NA

Nat Med 2023;29:203–208

Oxford University Hospitals NHS
NHS Foundation Trust

Glucose and insulin graphs



Nat Med 2023;29:203–208

Safety outcomes

Table 3 | Adverse events and safety analyses

Adverse event	Overall (*n*=30)	Prerandomization (*n*=30)	Closed-loop (*n*=26)	Control (*n*=25)	Washout (*n*=25)
No. of severe hypoglycemic events	0	0	0	0	0
No. (%) of participants with severe hypoglycemic events	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
No. of SAEs Study related Nonstudy related	8 1 7	2 0 2	4 1 3	2 0 2	0 0 0
No. (%) of participants with SAEs	6 (20)	1 (3)	3 (12)	1 (4)	0 (0)
No. of other adverse events	11	0	5	5	1
No. (%) of participants with adverse events	11 (37)	0 (0)	5 (19)	5 (20)	1 (4)
No. of device deficiencies	6	0	6	0	0
Pump related	4	0	4	0	0
Sensor related	1	0	1	0	0
Smartphone related	1	0	1	0	0
No. (%) of participants with device deficiencies	5 (17)	0 (0)	5 (19)	0 (0)	0 (0)

Nat Med 2023;29:203–208

Control IQ+ in type 2 diabetes

- Multi-centre randomized, controlled trial
- 319 participants across 21 centres in the USA and Canada
- Randomized 2:1 to receive automated insulin delivery (AID) with Control IQ+ or standard care
- 13 week intervention
- Primary outcome HbA1c at 13 weeks

N Engl J Med 2025;392:1801–1812

Baseline characteristics

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	AID Group (N=215)	Control Group (N=104)
Age — yr		
Mean	59±12	57±12
Range	19–87	23–80
Female sex — no. (%)	105 (49)	49 (47)
Race or ethnic group — no. (%)†		
White	148 (69)	74 (71)
Black	45 (21)	24 (23)
Asian	10 (5)	3 (3)
Native Hawaiian or other Pacific Islander	2 (1)	0
American Indian or Alaska Native	1 (<1)	1 (1)
More than one race or ethnic group	6 (3)	2 (2)
Unknown or not reported	3 (1)	0
Hispanic or Latino — no. (%)†		
Yes	23 (11)	11 (11)
No	190 (88)	93 (89)
Unknown or not reported	2 (1)	0
Diabetes duration — yr		
Median (IQR)	18 (11–26)	18 (11–24)
Range	1–59	2–45
Body-mass index‡		
Median (IQR)	33 (29–40)	35 (29–40)
Range	19–56	20–57

Table 1. (Continued.)

Characteristic	AID Group (N=215)	Control Group (N=104)
Glycated hemoglobin level§		
Distribution — no. (%)		
<7.0%	28 (13)	15 (14)
7.0 to <8.0%	73 (34)	40 (38)
8.0 to <9.0%	66 (31)	24 (23)
≥9.0%	47 (22)	25 (24)
Mean value — %	8.2±1.4	8.1±1.2
Range in values — %	5.7–14.1	5.2–12.4
Insulin delivery method — no. (%)		
Multiple daily injections	206 (96)	100 (96)
Insulin pump	9 (4)	4 (4)
Noninsulin glucose-lowering medication — no. (%)¶		
Metformin	109 (51)	61 (59)
SGLT2 inhibitor	76 (35)	41 (39)
GLP-1 receptor agonist	87 (40)	54 (52)
SGLT2 inhibitor and GLP-1 receptor agonist	44 (20)	24 (23)
Other	9 (4)	10 (10)
Use of CGM — no. (%)		
Current	147 (68)	78 (75)
In past, but not current	40 (19)	16 (15)
Never	28 (13)	10 (10)

N Engl J Med 2025;392:1801–1812

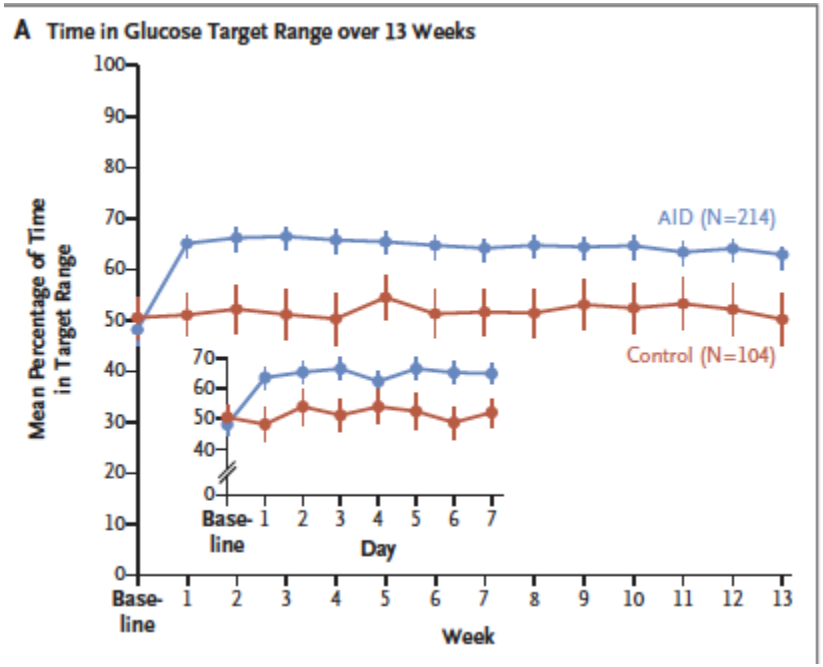
Glycaemic outcomes

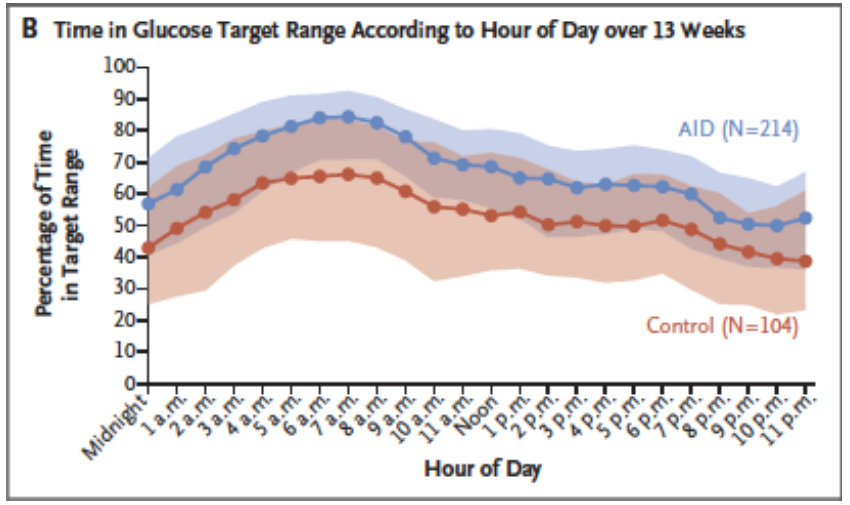
Table 2. Primary and Secondary Hierarchical Efficacy Outcomes.*

Outcome	At Baseline		At 13 Weeks		Adjusted Difference between Groups (95% CI)	P Value
	AID Group	Control Group	AID Group	Control Group		
Primary outcome						
No. of patients evaluated	214†	104	209‡	102§		
Glycated hemoglobin level — %	8.2±1.4	8.1±1.2	7.3 ±0.9	7.7 ±1.1	−0.6 (−0.8 to −0.4)	<0.001
Secondary hierarchical outcomes						
No. of patients evaluated	215	104	214¶	104		
Percentage of time with glucose level in range of 70 to 180 mg/dl	48±24	51±21	64±16	52±21	14 (11 to 17)	<0.001
Mean glucose level — mg/dl	194±43	190±35	170±23	188±34	−21 (−26 to −15)	<0.001
Percentage of time with glucose level of >180 mg/dl	51±25	49±21	35±16	48±21	−14 (−17 to −11)	<0.001
Percentage of time with glucose level of >250 mg/dl‖	19.5±17.3	15.8±13.6	9.7±7.8	16.7±14.1	−9.1 (−11.7 to −6.6)	<0.001
No. of prolonged hyperglycemia events per wk‖**	1.7±1.7	1.6±1.7	0.9±0.9	1.6±1.5	−0.7 (−1.0 to −0.4)	<0.001
Percentage of time with glucose level of <70 mg/dl‖	0.7±0.8	0.3±0.3	0.4±0.4	0.4±0.4	−0.1 (−0.4 to 0.1)	NS††
Percentage of time with glucose level of <54 mg/dl‖	0.16±0.16	0.05±0.05	0.09±0.09	0.09±0.10	−0.02 (−0.09 to 0.04)	NA
No. of CGM-measured hypoglycemia events per wk‖‡‡	0.2±0.3	0.1±0.0	0.1±0.2	0.1±0.2	0.0 (−0.1 to 0.0)	NA
Coefficient of variation in glucose levels — %	28±6	27±5	30±5	29±5	0.3 (−0.5 to 1.2)	NA

N Engl J Med 2025;392:1801–1812

Glucose graphs





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Safety outcomes

Table 3. Safety Outcomes during the 13-Week Trial Period.

Adverse Event	AID Group (N=215)		Control Group (N=104)	
	no. of events	*no. of patients (%)*	*no. of events*	*no. of patients (%)*
Any adverse event*	106	64 (30)	26	19 (18)
Specific event				
Severe hypoglycemia	1	1		0
Diabetic ketoacidosis or hyperosmolar hyperglycemic syndrome		0		0
Other serious adverse event†	18	16 (7)	7	7 (7)
Other adverse event				
Hyperglycemia with or without ketosis				
Related to trial device	20	13 (6)		0
Not related to trial device	1	1 (<1)	2	2 (2)
Nonsevere hypoglycemia	10	9 (4)	2	2 (2)
Other reportable adverse event	56	37 (17)	15	14 (13)

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High v low c-peptide

Diabetes Care
American Diabetes Association.

Adults With Type 2 Diabetes Benefit From Automated Insulin Delivery Irrespective of C-Peptide Level

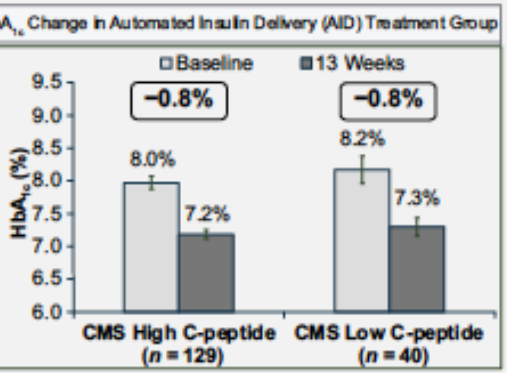
Iri B. Hirsch, Yogish C. Kudva, David T. Ahn, Thomas Blevins, Michael R. Rickels, Dan Raghinaru, John W. Lum, Craig Kollman, Jordan E. Pinsker, and Roy W. Beck, for the 2IQP Study Group

Diabetes Care 2025;48(12):2061–2066 | https://doi.org/10.2337/dc25-1125

Adults With Type 2 Diabetes Benefit From Automated Insulin Delivery Irrespective of C-Peptide Level

The Centers for Medicare & Medicaid Services (CMS) requires a low C-peptide level for insulin pump coverage, which excludes many people with type 2 diabetes.

Data from 254 adults with type 2 diabetes participating in the 2IQP trial were analyzed to assess effect of C-peptide level on AID outcomes.



The benefit of AID is present with high and low C-peptide levels. Thus, requiring a low C-peptide level as a prerequisite for AID therapy is not warranted.

Benefits of AID systems in type 2 diabetes

- People with type 2 diabetes benefit from AID systems
- Greatest benefit in those with highest baseline HbA1c
- See benefit in those on basal insulin, MDI, CSII and sensor-augmented pump, independent of c-peptide levels
- Trials are short-term, but remember benefits persist over time in trials in type 1 diabetes
- Safe, with limited concerns about serious adverse events

Oxford University Hospitals NHS
NHS Foundation Trust

So should we be using AID systems routinely now in type 2 diabetes?

Oxford University Hospitals NHS
NHS Foundation Trust

NICE Technology Appraisal 943

- Hybrid Closed loop systems are recommended as an option for managing blood glucose levels in type 1 diabetes for:
  - All children and young people
  - Pregnant women or those planning pregnancy
  - Those with HbA1c 58 mmol/mol (7.5%) or more
  - Those with disabling hypoglycaemia

NICE National Institute for Health and Care Excellence

NICE guidance

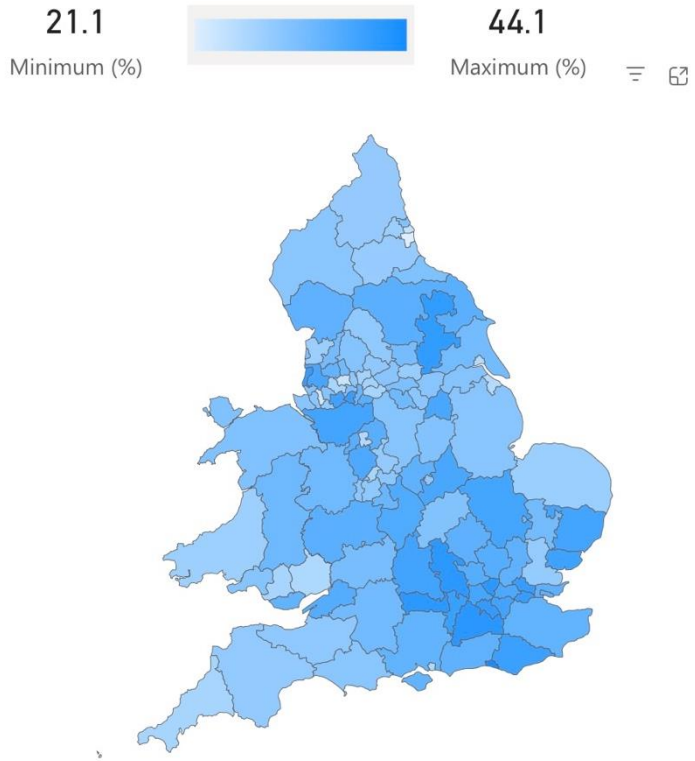
Hybrid closed loop systems for managing blood glucose levels in type 1 diabetes

Technology appraisal guidance
Published: 19 December 2023

www.nice.org.uk/guidance/ta943

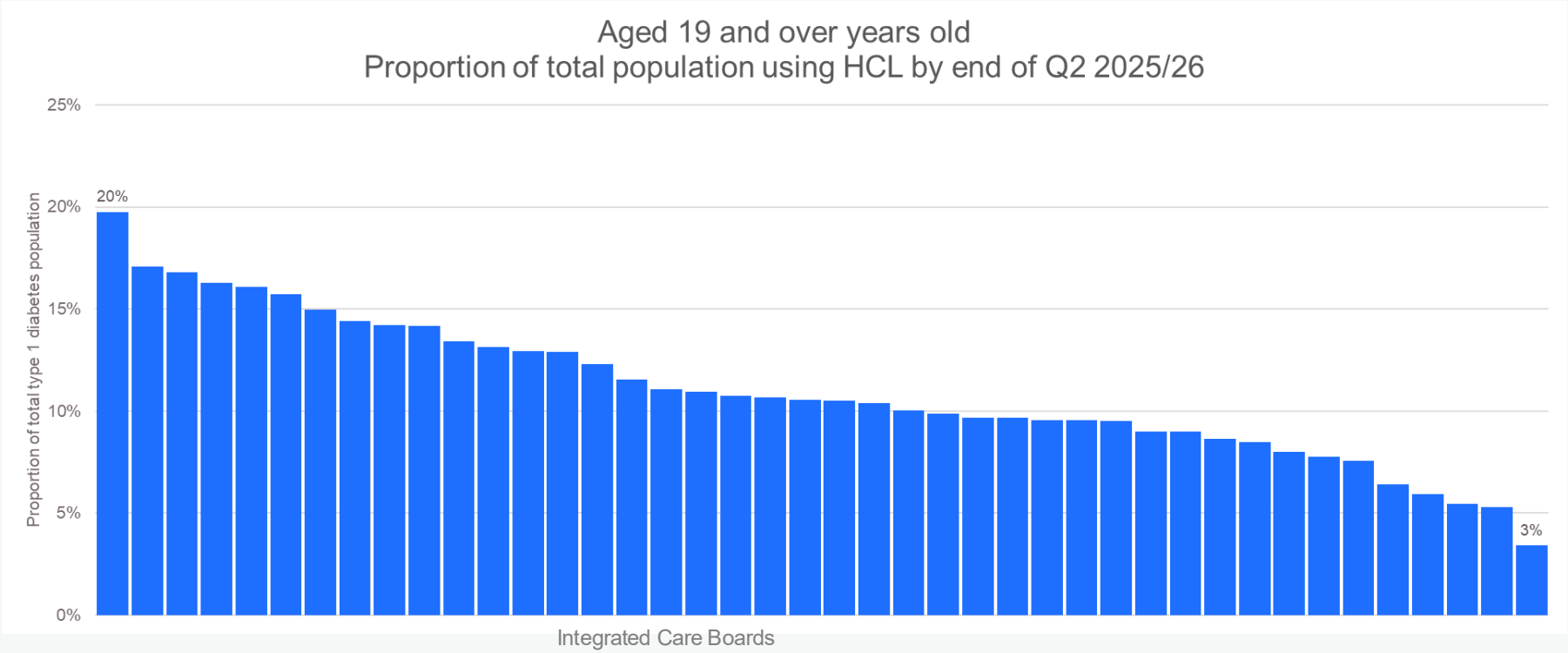
Numbers

- Last NDA type 1 diabetes audit (2021-22):
  - 227 435 adults with type 1 diabetes in England and Wales
  - 34% overall achieving HbA1c 7.5% or below
  - **Just over 150 000 adults eligible for HCL under HbA1c criteria**
  - An estimated 26 000 current insulin pump users
  - An additional 58 000 eligible under HbA1c criteria from NICE TA 151



HCL usage in Adults with type 1 diabetes

- Overall, 11% of adults aged over 19 and over were using HCL as of the end of September 2025.
- Variation exists between integrated Care Boards, ranging from 20-3%.



Source: GIRFT analysis of NDA and NPDA data. England only

Slide courtesy Verity Hawkes, NHSE

Who with type 2 diabetes should be eligible?

- Will need a proper cost-effectiveness analysis
- There are likely some individuals at high risk who could benefit
- 3360875 people with type 2 diabetes in England in NDA data reported earlier
- 35.6% not meeting HbA1c target of less than 7.5%
- Just over 1200000 people

Summary

- Current state of play for people with type 2 diabetes
- Evidence of benefit of automated insulin delivery (AID) systems in people with type 2 diabetes
  - Benefit of AID over standard treatment
  - Benefit of using AID over open loop pump therapy
  - Fully closed loop AID systems
  - Benefit occurs irrespective of c-peptide level
- Where might we use AID in type 2 diabetes in the future?

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Thanks for your attention
Any questions?