eSwiss
MEDICAL & SURGICAL CENTER

AID systems – in research and practice

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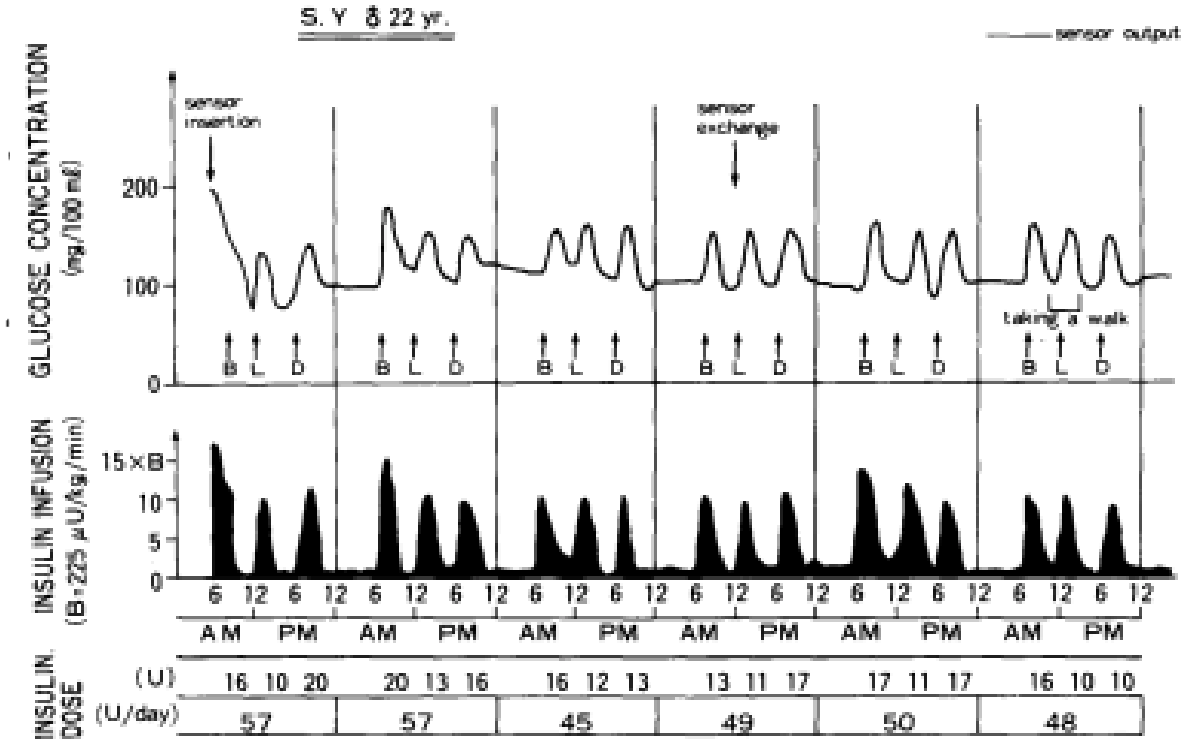
Specialist in Endocrinology & Diabetes and General Internal Medicine

2 Slides on the History of AIDs

AID 1963 to 2015

- A H Kadish (Biomed Sci Instrum 1963;1:171-6) - "Servomechanism for blood glucose control"
- E F Pfeiffer (MMW 1975 May 16;117(20):849)
- Commercialization 1977: Biostator
- S S Schwartz (Diabetologia 1979; 16, 157-164) - "Use of a Glucose Controlled Insulin Infusion System (artificial beta cell) to control diabetes during surgery"
- M Shichiri (Lancet 1982; 2:1129-31) - "Wearable Artificial Endocrine Pancreas With Needle-Type Glucose Sensor"
- JDRF "Artificial pankreas project" 2005
- Studies under controlled conditions
  - 2008 - Medtronic
  - 2010/11 - Deltec Cozmo Pump, FreeStyle Navigator, APCam01
- MiniMed VEO (Medtronic)
- #WeAreNotWaiting – movement, Tidepool

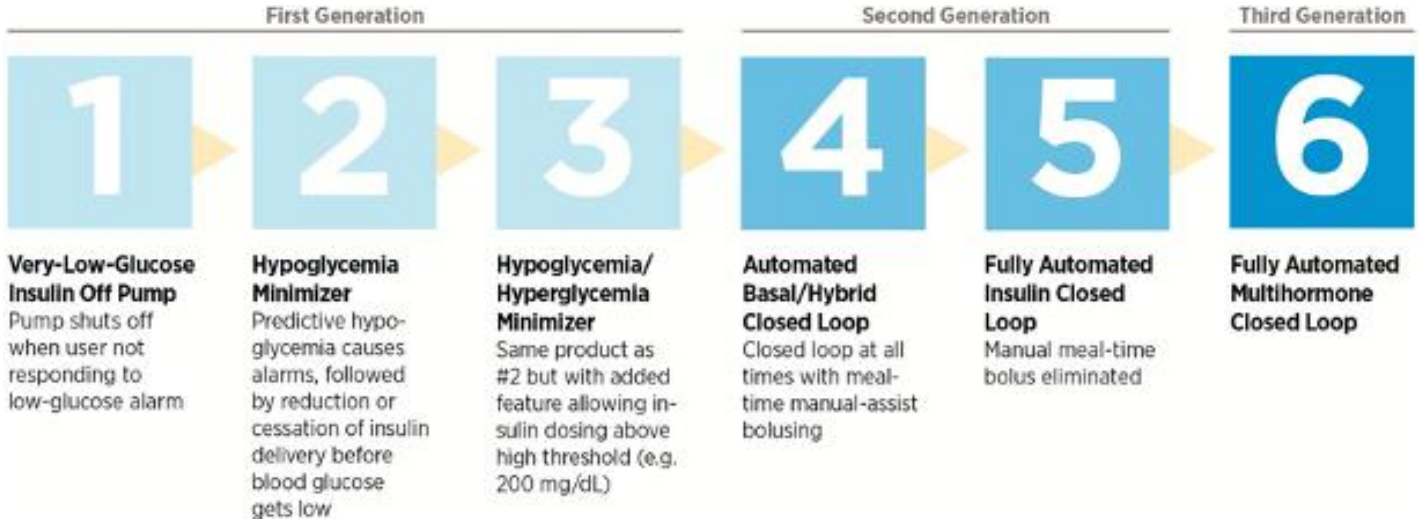


S Templer, Front. Endocrinol. 13:919942.
M Shichiri et al. DIABETES, VOL. 33, DECEMBER 1984

S Weinzimmer et al. Diabetes Care 31:934–939, 2008
R. Hovorka et al. BMJ, 2011; 342: d1855 und Lancet 2010; 375: 743–51

AID 2015 to 2023 (in Switzerland)

- Open source: OpenAPS, Tidepool Loop (FDA approved)
- MiniMed VEO -> 640G -> 670G -> 780G (Medtronic) - for SmartWatch
- Accu-Chek Insight with DBLG1 (Roche, Diabeloop, Dexcom)
- t:slim X2 with control-IQ technology (Tandem Diabetes Care, Dexcom)
- YpsoPump with CamAPS FX (Ypsomed, CamDiab, Dexcom, Abbott)
- OmniPod 5 with SmartAdjust™ (Insulet, Dexcom) - still not in CH
- Solo (Roche) with ? - re-launch imminent



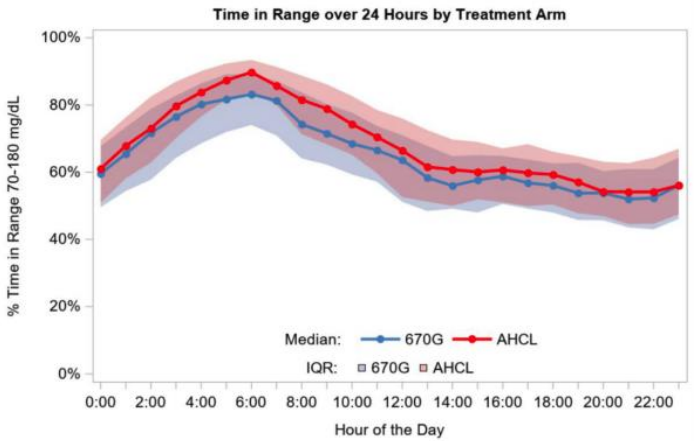
https://www.jdrf.org/

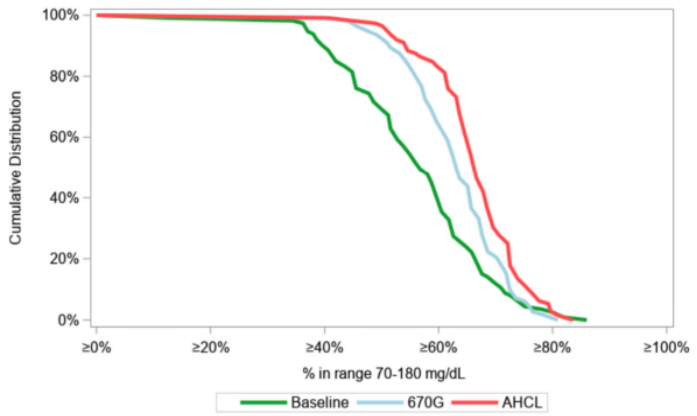
Evidence

- For each system + open source
- Increasingly based on real life data
- Rather similar results

MiniMed™ 780G

- n = 113, T1DM, many with MDI and without CGM
- Multi-national, cross-over, 3 months each
- 670G vs. 780G
- Tightening of targets during ongoing study
- More Insulin (less basal, more bolus)

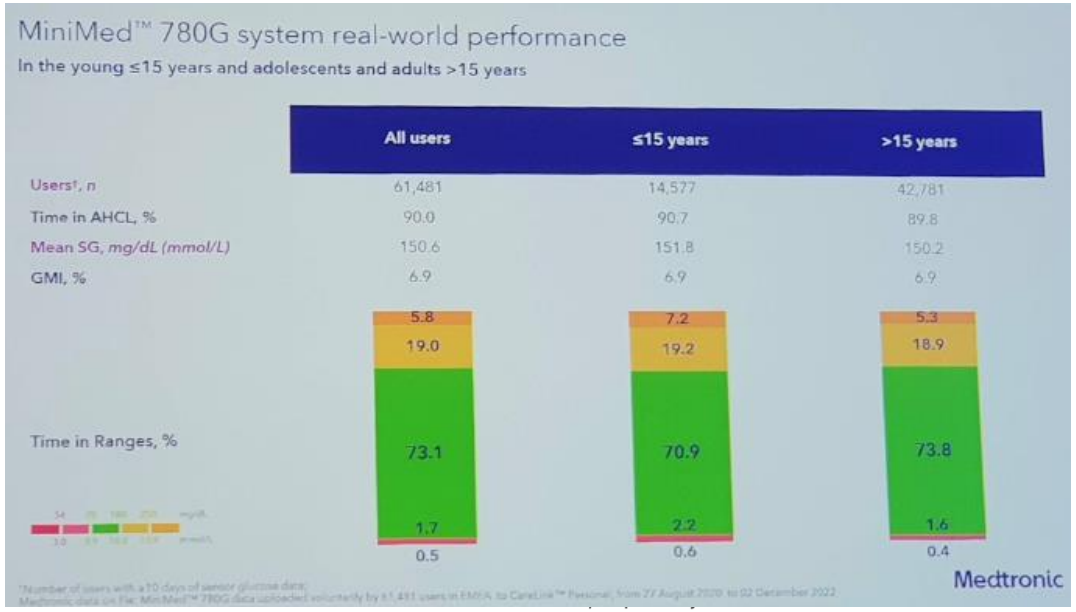




Bergenstal et al. Lancet. 2021 Jan 16;397(10270):208-219.

› Diabetes Technol Ther. 2021 Sep 15. doi: 10.1089/dia.2021.0203. Online ahead of print.

Real-world Performance of the MiniMed™ 780G System: First Report of Outcomes from 4'120 Users



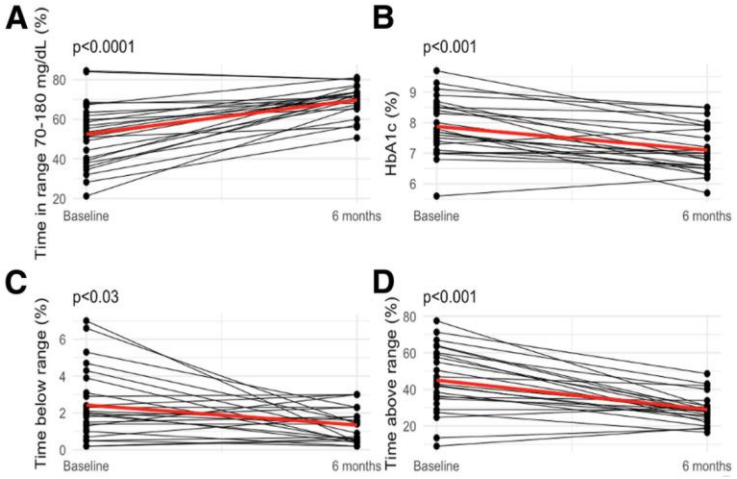
comparison with pre-AHCL was possible (N=812) reduced their GMI by 0.4±0.4% (p=0.005) and increased their TIR by 12.1±10.5% (p<0.0001), post-AHCL initiation. More users achieved the glycemic treatment goals of GMI <7.0% (37.6% vs 75.2%, p<0.0001) and TIR >70% (34.6% vs 74.9%, p<0.0001) when compared to pre-AHCL initiation.

Conclusion: Most MiniMed™ 780G system users achieved TIR >70% and GMI <7%, while minimizing hypoglycemia, in a real-world condition.

https://www.diabetotech.com/blog/updates-on-aid-systems-attd2023

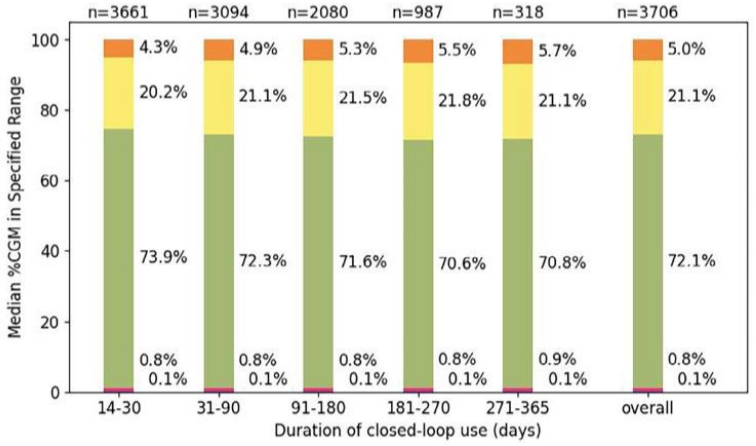
Accu-Chek Insight with DBLG1

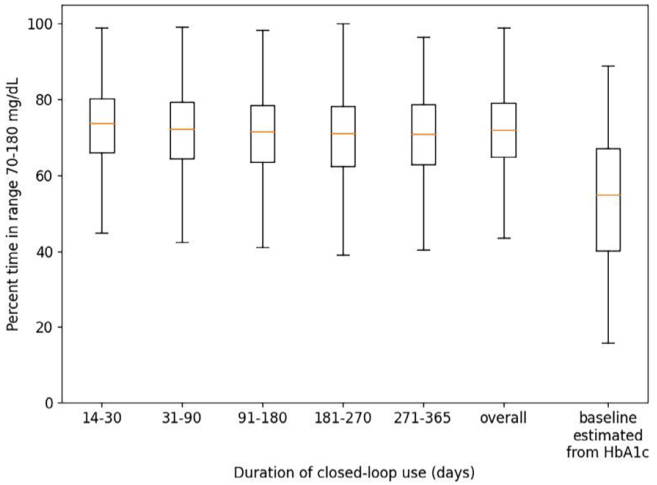
- n = 25, T1DM
- CSII and CGM for more than 1 year
- 1 week run-in, then 6 months DBLG 1
- Before vs. after



Diabeloop DBLG1 Closed-Loop System Enables Patients With Type 1 Diabetes to Significantly Improve Their Glycemic Control in Real-Life Situations Without Serious Adverse Events: 6-Month Follow-up. Coralie Amadou. Diabetes Care 2021 Mar; 44(3): 844-846.

- n = "first" 3700, T1DM, start of Tx prior April 2022
- Retrospective analysis ("DBLG-1 Cloud" data)
- 365 Tage

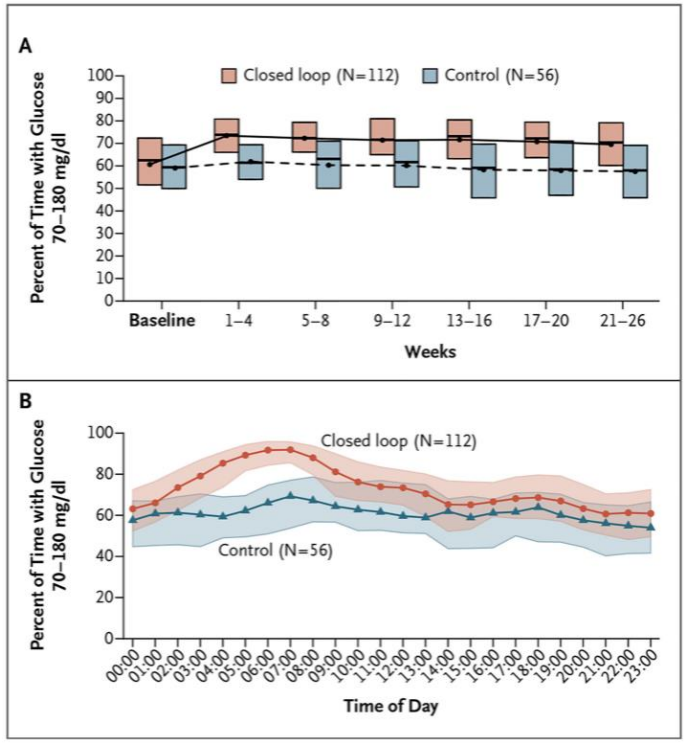




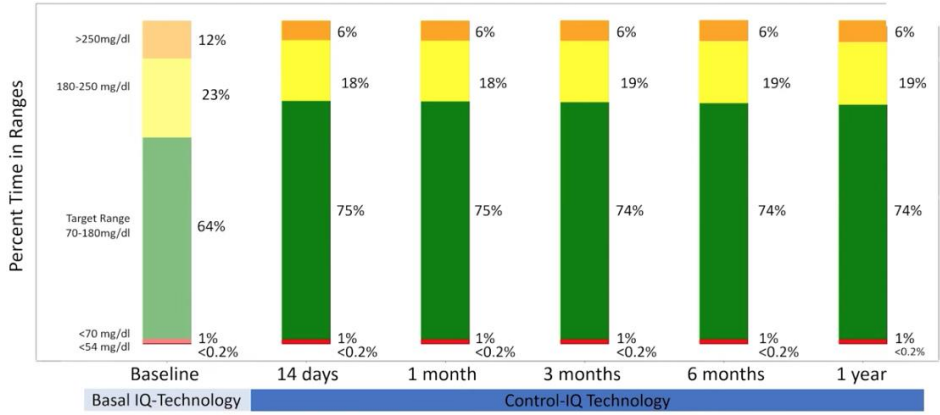
Pierre-Yves B. et al. Diabetes Obes Metab. 2023;25:1607–1613

t:slim X2 with control-IQ technology

- n = 168, T1DM with CSII or MDI
- 8 weeks run-in
- 2:1 HCLP vs. SAP
- 26 Wochen



- n = 9451, T1DM or T2DM
- Retrospective
- «Tandem's Cloud» data
- 2 weeks before vs. 12 months with control IQ



N = 9,010 participants who had >75% CGM data available	Baseline (Basal-IQ)	12-month Control-IQ use	Control-IQ - Baseline Difference	p-value
GMI [%]	**7.2%**	**6.9%**	**-0.3%**	**<0.001**
Time Below Range <70mg/dL	0.9%	1.05%	+0.15%	n.s.
Time Above Range >180mg/dL	33.2%	24.3%	-9.0%	<0.001
Mean Sensor Glucose	164 mg/dL	152 mg/dL	-12 mg/dL	<0.001

People At Worst Control At Baseline Improved Most (Analysis Suggested by Dr. Gregory Forlenza, BDC)

Select N=242 participants with Baseline GMI >= 9 %	Baseline (Basal-IQ)	12-month Control-IQ use	Control-IQ - Baseline Difference	p-value
GMI [%]	**9.5%**	**8.1%**	**-1.4%**	**<0.001**
Time in Range 70-180mg/dL	19.6%	46.7%	+27.1%	<0.001
Time Below Range <70mg/dL	0.3%	0.5%	+0.2%	N/A
Time Above Range >180mg/dL	80.1%	52.8%	-27.3%	<0.001
Mean Sensor Glucose	258.2 mg/dL	200.9 mg/dL	-57.2 mg/dL	<0.001

Six-Month Randomized, Multicenter Trial of Closed-Loop Control in Type 1 Diabetes. S.A. Brown, N Engl J Med. 2019 October 31; 381(18): 1707–1717

One Year Real-World Use of the Control-IQ Advanced Hybrid Closed-Loop Technology. Marc D B et al. Diabetes Technol Ther. 2021 Sep;23(9):601-60 8.

YpsoPump with CamAPS FX

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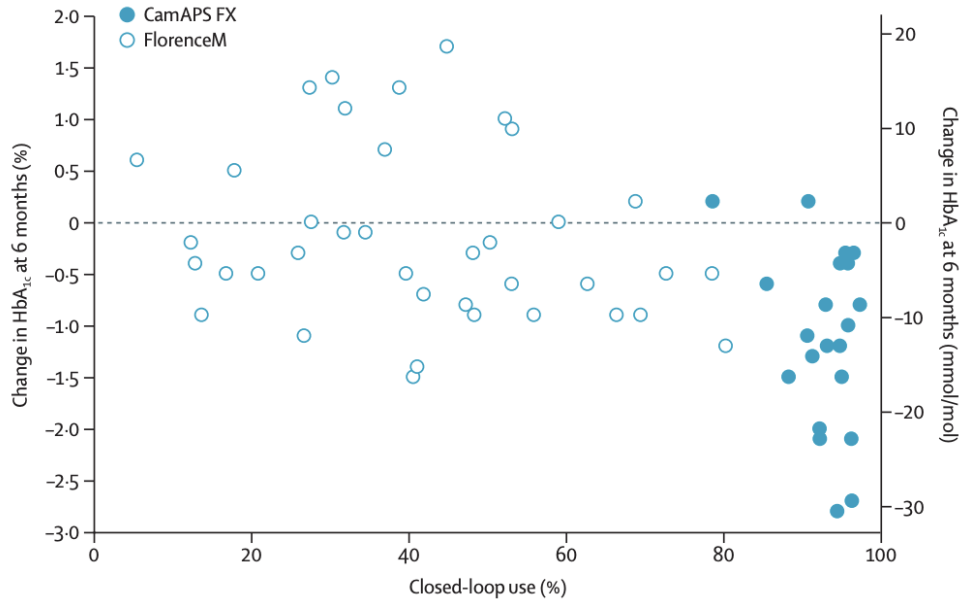
- No studies, but good evidence mit CamAPS FX
- Prof. R Hovorka: "How a mathematician built the artificial pancreas"

R Hovorka et al. Lancet 2010 Feb 27;375(9716):743-51 R Hovorka. BMJ. 2011; 342: d1855.

- n = 133, average age 13, T1DM with suboptimal DM control, CSII for more than 3 months
- Multi-centre, multi-national, parallel, randomized
- "Usual care with insulin pump" vs. "closed loop", 6 months

	Baseline		3 months		6 months		Adjusted difference at 6 months (95% CI)*	p value†
	Closed-loop group	Control group	Closed-loop group	Control group	Closed-loop group	Control group		
Primary endpoint								
Number of participants	65	68	59	62	57	62	..	..
HbA_{1c}, mmol/mol; HbA_{1c} %	66 (8); 8·2% (0·7)	67 (8); 8·3% (0·7)	60 (11); 7·6% (1·0)	66 (9); 8·2% (0·8)	60 (12); 7·6% (1·1)	64 (8); 8·1% (0·8)	−3·5 (−6·5 to −0·5); −0·32 pp (−0·59 to −0·04)	0·023
Day and night (key endpoints)‡								
Number of participants	65	67	54	62	52	62	..	..
Percentage of time with glucose level 3·9–10·0 mmol/L	47% (12)	46% (13)	57% (15)	46% (12)	54% (17)	47% (12)	6·7 pp (2·2 to 11·3)	0·0043‡
Mean glucose (mmol/L)	10·3 (1·8)	10·4 (2·0)	9·0 (2·6)	10·4 (1·8)	9·7 (2·9)	10·1 (1·8)	−0·33 (−1·08 to 0·43)	0·39‡
Percentage of time with glucose level								
>10·0 mmol/L	46% (15)	47% (16)	33% (19)	47% (15)	38% (20)	46% (15)	−7·0 pp (−12·5 to −1·5)	..
<3·9 mmol/L (median)	6·1% (2·7 to 9·5)	4·9% (2·0 to 9·4)	6·2% (3·0 to 12·7)	3·8% (2·1 to 9·9)	6·1% (3·0 to 12·1)	5·4% (2·0 to 12·0)	0·53 pp (−1·78 to 2·83)	..



https://jdrf.org.uk/stories/professor-roman-hovorka-how-a-mathematician-built-the-artificial-pancreas-for-type-1-diabetes/

J Ware et al. Lancet Digit Health 2022; 4: e245–55

YpsoPump mit CamAPS FX

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ATTD 2023 Berlin

- n = 1805 data sets
- Retrospective
- "CamAPS Fx Cloud" data
- 95% in Auto Mode

CamAPS FX: Real world analysis

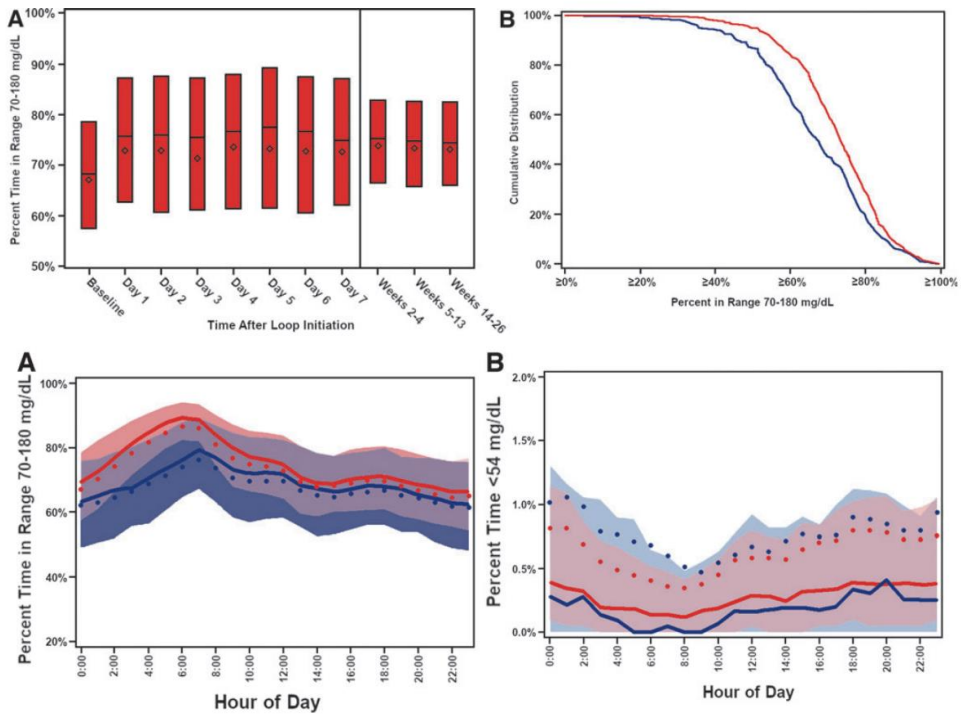
	Overall	≤ 6 years	7 – 14 years	15 – 21 years	22 – 64 years	≥ 65 years
Users (n)	1805	214	203	95	820	43
Observation period (days)	84.0 (54.0,118.0)	95.0 (61.0,122.0)	84.0 (55.5, 117.0)	77.0 (47.5, 116.0)	88.0 (58.0, 124.0)	81.0 (59.5, 127.0)
Age (years)	30.2±19.3	3.8±1.5	10.3±2.2	17.3±2.0	41.4±10.9	69.2±3.4
Total daily insulin (U/day)	37.3 (20.8, 5.2)	11.2 (7.6, 16.0)	30.8 (21.7, 43.3)	55.9 (43.4, 76.6)	42.8 (29.9, 62.3)	42.3 (30.4, 54.4)
Time using closed-loop (%)	94.7 (90.0, 96.9)	95.6 (92.6,97.1)	93.9 (89.0, 96.4)	93.2 (84.5, 95.0)	94.9 (90.4, 96.9)	96.1 (93.7, 97.4)
Mean glucose (mmol/L)	8.4±1.1	8.8±1.1	8.5±1.1	8.7±1.2	8.2±1.1	7.7±0.8
Glucose SD (mmol/L)	3.1±0.7	3.4±0.7	3.3±0.8	3.5±0.9	2.9±0.7	2.4±0.5
Glucose CV (%)	36.2±5.5	38.7±4.5	38.9±5.5	39.5±5.9	35.1±5.1	30.9±4.1
GMI (%)	6.9	7.1	7	7.1	6.9	6.6
Percentage of time with glucose						
3.9-10.0 mmol/L	72.6±11.5	66.9±11.7	70.5±10.4	68.9±11.2	74.2±11.3	81.8±8.7
>10.0 mmol/L	24.7±11.8	29.7±12.0	26.3±10.7	28.5±11.5	23.3±11.8	16.4±9.1
>13.9 mmol/L	5.2 (2.5, 9.4)	7.9 (4.2, 13.4)	7.1 (3.9, 10.5)	8.6 (4.6, 13.7)	4.3 (1.9, 7.8)	1.8 (0.8, 3.2)
<3.9 mmol/L	2.3 (1.3, 3.6)	3.0 (1.8, 4.5)	2.9 (1.8, 4.3)	2.2 (1.3, 3.5)	2.1 (1.1, 3.3)	1.3 (0.7, 2.6)
<3.0 mmol/L	0.4 (0.2, 0.7)	0.5 (0.3, 0.9)	0.5 (0.3,0.9)	0.4 (0.2, 0.7)	0.3 (0.1, 0.6)	0.1 (0.1, 0.4)

Data are mean±SD or median (IQR). SD=standard deviation. CV=coefficient o[illegible]on. GMI=glucose management indicator.

https://www.diabetotech.com/blog/updates-on-aid-systems-attd2023

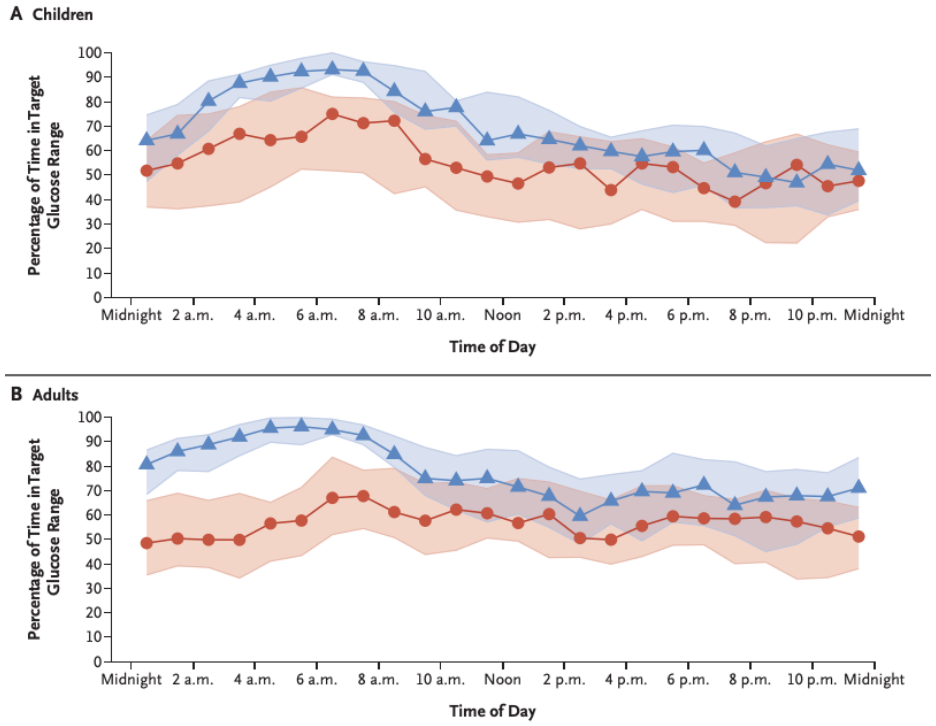
Open Source

- n = 558, T1DM, including children
- No real-life contact with participants (online meetings)
- Prospective, observational, real-life
- Baseline with SAP vs. 1-6/12 mit AHCLP ("Loop")
- No DKA or severe hypoglycemia
- Slightly higher hypoglycemia rate



Lum et al, DIABETES TECHNOLOGY & THERAPEUTICS Volume 23, Number 5, 2021

- n = 97, T1DM, 50% children, 24 weeks
- Open-label, randomized (1:1), controlled
- SAP vs. open source AHCLP (OpenAPS)
- No DKA or severe hypoglycemia
- No increase in AEs



Burnside et al. N Engl J Med 2022;387:869-81

OmniPod 5 with SmartAdjust™

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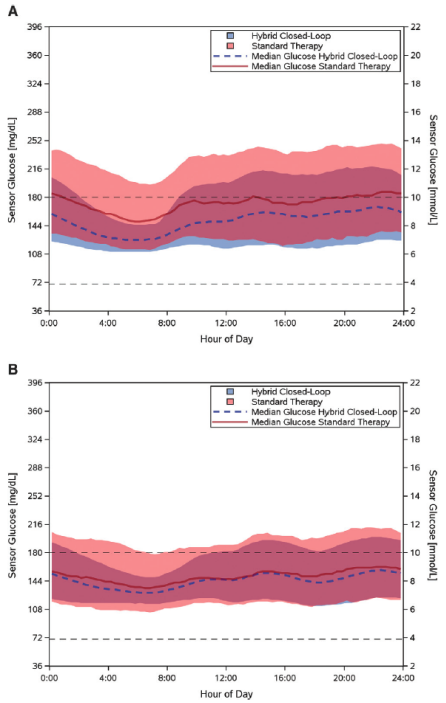
- n = 251, T1DM, OmniPod users
- Mutlti-centre (17 diabetes centres in the US)
- 2 weeks without vs. 3 months with SmartAdjust™
- Sport allowed (moderate intensity)



ATTD 2023 Berlin

- n = "first" 31.691 data sets ("OmniPod 5 Cloud", US data)
- Retrospective
- TIR dependent on target setting:
  55/63/71% for 7.2-8.3/6.7/6.1mmol/l
- TBR under 1.2% (even with 6.1 mmol/l target setting)
- TIR 65% among adolescents
- Better results with at least 4 boli daily

Multicenter Trial of a Tubeless, On-Body Automated Insulin Delivery System With Customizable Glycemic Targets in Pediatric and Adult Participants With Type 1 Diabetes. Sue A. Brown et al. Diabetes Care 2021;44:1–11

https://www.diabetotech.com/blog/updates-on-aid-systems-attd2023

Our Experience

"Diabetes Technology Centre"

- T1DM n = 319
  - CGM/FGM: n = 272 (85%)
  - CSII: n = 252 (79%)
  - AHCL: n = 102 (32%)

Systems used at our centre

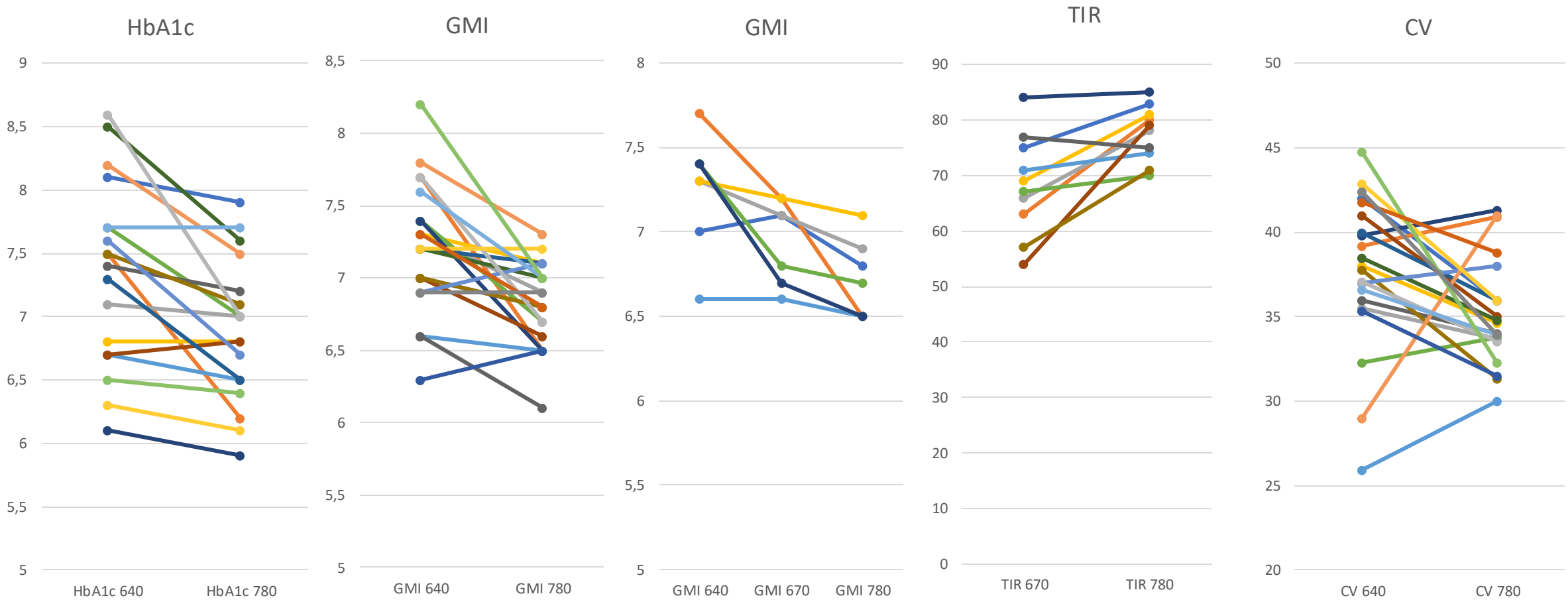
- MiniMed 780G: 47
- Insight with DBLG1: 34
- t:slim X2 with control-IQ technology: 8
- YpsoPump with CamAPS Fx: 11

- OmniPod (without SmartAdjust™): 62
- OmniPod linked with Libre 3: 2

- In T2DM: 7

MiniMed™ 780G statistics

November 2021 data



Patient selection

- Patient selection and preparation
  - Motivation is crucial
  - Willingness to enter KHs “always” and in a timely manner
  - Different starting points (de novo, switch to Loop,change of systems)
  - Adequate, but not too much preparation -> Refresher of FIT principles
- Typical reasons for declining an AID
  - Too cumbersome
  - No motivation to estimate and enter carbs
  - Optimized therapy and/or content with current treatment
  - Waiting for more advanced technologies

Challenges

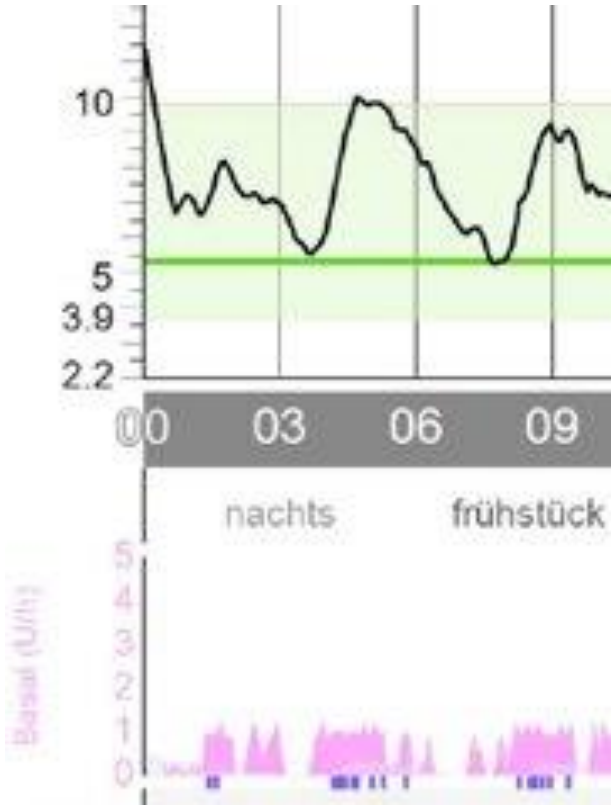
- Alarm fatigue
- More strenuous exercise
- Loss of autonomy (at the mercy of the algorithm)
- Individualisation despite a controlling algorithm
  - Adaptable targets
  - «Hypoprotect-setting», «Exercise-setting»
  - Multilayer algorithms (1. No Hypo 2. BG analysis, 3. comparing with previous data)
  - Adaptation of aggressiveness
  - Basalrate settings as basis for calculations made by algorithm

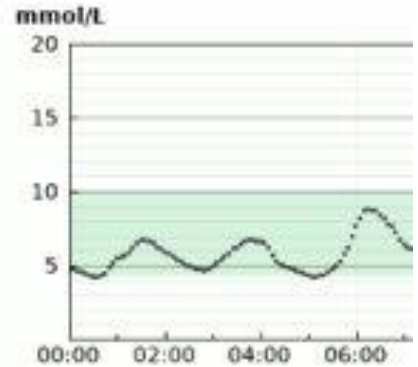
Consumer Needs

- Reliable and as small as possible
- A tape, which always works, but without skin irritation
- Changing intervals for tubing and sensors as long as possible
- Reliable 24h support
- Contradictory
  - Must be on my smartphone! - Never on my smartphone!
  - "Remote Bolusing" crucial – Bolus delivery only via my pump
  - Absolutely no tubing – Only with tubing
  - As much influence as possible - As little influence as possible

=> Matching is key!

Different algorithms





AID Systems in comparison

My personal impression, not conclusive, without judgment

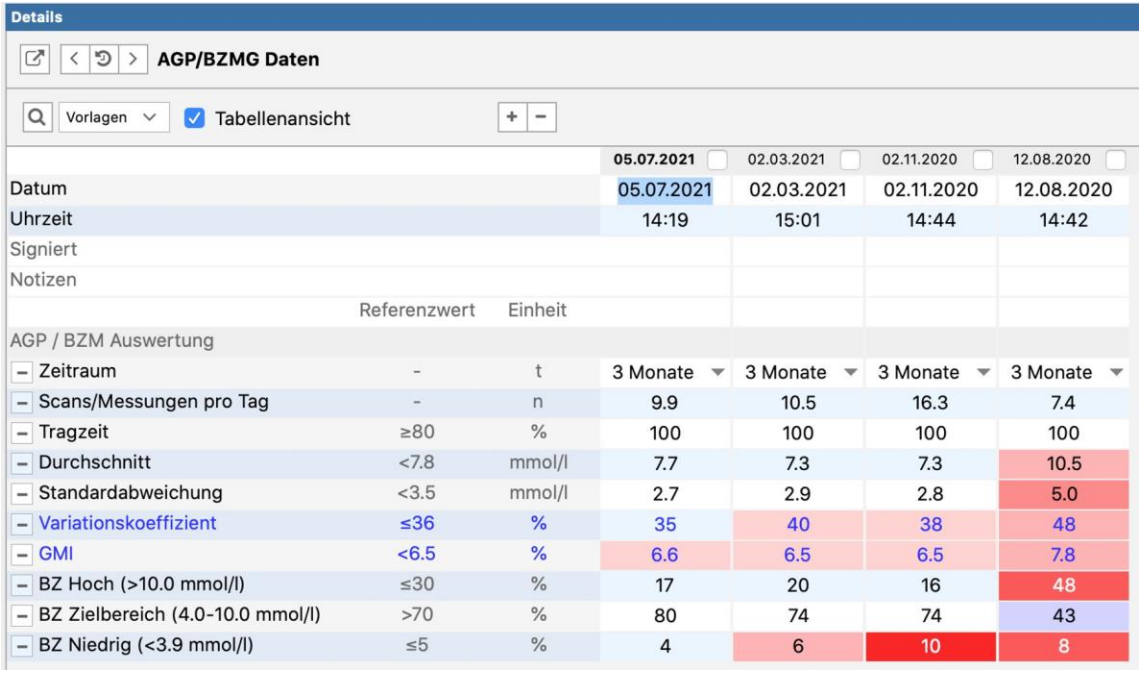
	MiniMed™ 780G	Accu-Chek Insight DBLG1	t:slim X2 Control-IQ	YpsoPump CamAPS Fx	OmniPod 5 Open Source
Properties	• Most experience • PID - restrictive • A bit clunky • Sensor only 1 week • Pump fractures • Fixed deliveries	• 3 companies • MP – adaptive • Innovativ software • Only TDD und weight • Adjustments of boli	• 2 companies • Ample experience • MP - adaptive • Algorithm based on basal rate	• 3 companies • MP - adaptiv • Handy • Innovativ (Hardware) • Nur TDD und KG • Bolus Anpassung	• Handy • MP -? adaptive • Only for loopers • Waste
USPs	• One company • 7 days tubing	• Custom built handheld • Aggressiveness concept	• Design	• With Libre 3 • Android controllable • Swiss product • Boost function • Lowest target	• No tubing

Data analysis

- Essential for health care providers
- Unfortunately not taken advantage enough by many users

Data analysis

- Software mature
  - Convenient data merging
  - Browser based
  - IT struggle
  - Privacy and usage concerns
- Important functionalities
  - Data merging (BZWs, boluses, carb ingestion)
  - Overviews (AGP, trends, standard day, individual days, pump settings)
  - Event visualization (meals, activities, infusion set changes)
  - Data sharing
- Data collection for analyis over longer time



Details

AGP/BZMG Daten

Vorlagen | Tabellenansicht

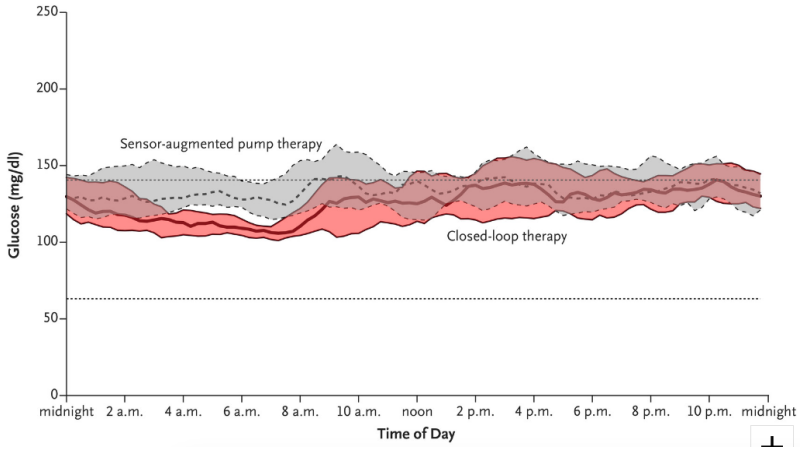
			05.07.2021	02.03.2021	02.11.2020	12.08.2020
Datum			05.07.2021	02.03.2021	02.11.2020	12.08.2020
Uhrzeit			14:19	15:01	14:44	14:42
Signiert						
Notizen						
	Referenzwert	Einheit				
AGP / BZM Auswertung						
Zeitraum	-	t	3 Monate	3 Monate	3 Monate	3 Monate
Scans/Messungen pro Tag	-	n	9.9	10.5	16.3	7.4
Tragzeit	≥80	%	100	100	100	100
Durchschnitt	<7.8	mmol/l	7.7	7.3	7.3	10.5
Standardabweichung	<3.5	mmol/l	2.7	2.9	2.8	5.0
Variationskoeffizient	≤36	%	35	40	38	48
GMI	<6.5	%	6.6	6.5	6.5	7.8
BZ Hoch (>10.0 mmol/l)	≤30	%	17	20	16	48
BZ Zielbereich (4.0-10.0 mmol/l)	>70	%	80	74	74	43
BZ Niedrig (<3.9 mmol/l)	≤5	%	4	6	10	8

Where are AIDs heading ?

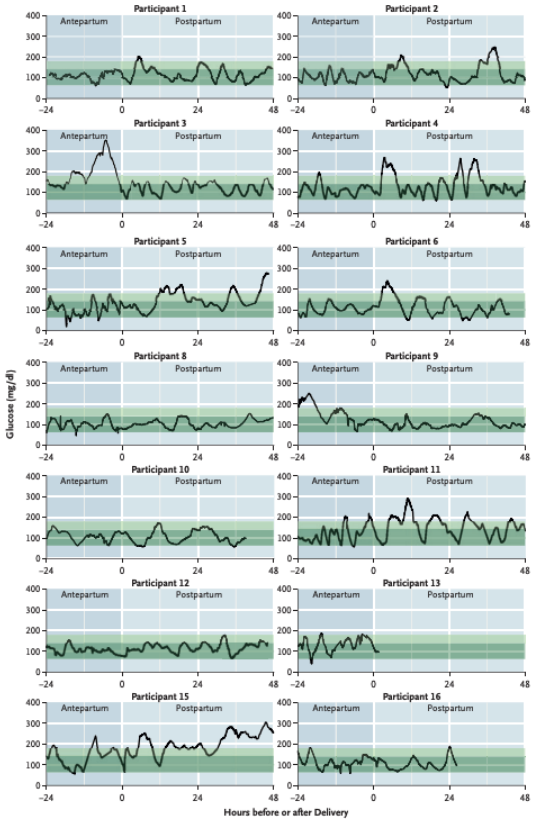
- Improvements ongoing (smaller, more precise, more convenient, more open for individualisation)
- New applications
  - In pregnancy
  - In type 2 diabetes (Basal Only Pod etc.)
  - Inpatient care
- Without carb counting (pre-entered meal settings)
- Closing the Loop
  - Automatic recognition of carb ingestions
  - Physiological counterregulation

AHCLP in pregnancy

- n = 16, T1DM, pregnant
- Open-label, randomized, cross-over
- SAP vs. nocturnal AHCLP
- Extension: Day and night (n = 14)
- No AEs in both groups



Z Stewart et al. N Engl J Med 2016; 375:644-654



- n = 124, T1DM, pregnant
- 9 sites across UK
- Open-label, randomized, controlled
- CGM + "standard insulin therapy" vs. AHCLP
- 16. gestational week to delivery
- Outcome: TIR (3.5 - 7.8 mmol/l)
  - 68% with AHCLP
  - 56% with CGM and MDI
- Baseline HbA1c 7.7%,
- HbA1c 0.31% lower with AHCLP
- severe hypoglycemia not different

T. Lee et al N Engl J Med 2023 Oct 26;389(17):1566-1578.

AHCLP in T2DM

POPULATION

24 patients with type 2 diabetes, mean age 61 years, & baseline HbA_{1c} ≥8%

Basal-bolus insulin users n=12

Basal-only insulin users n=12

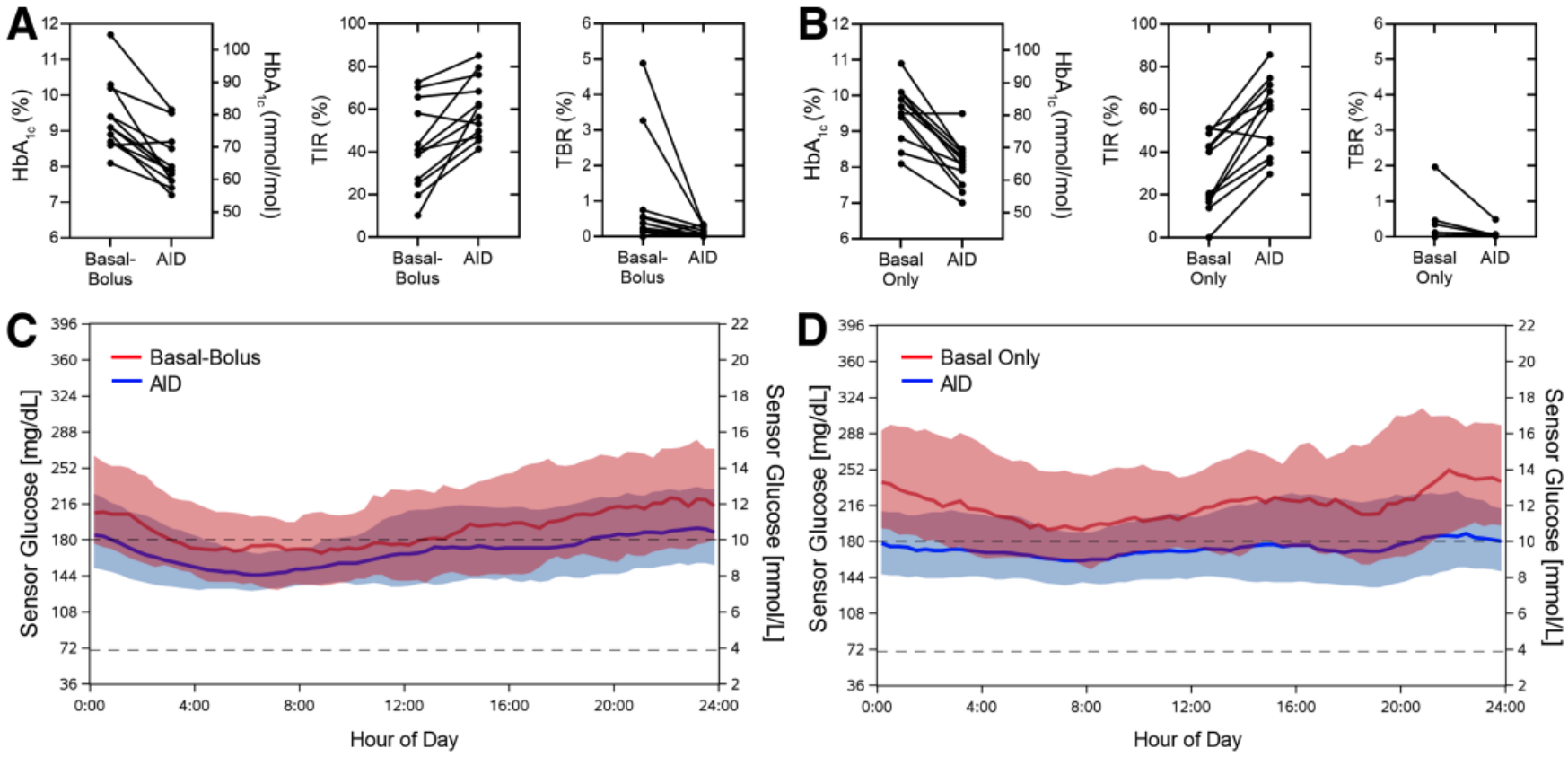
STUDY DESIGN

8-week single-arm outpatient study of automated insulin delivery

OUTCOMES

Primary: time with sensor glucose ≥250mg/dL and <54mg/dL

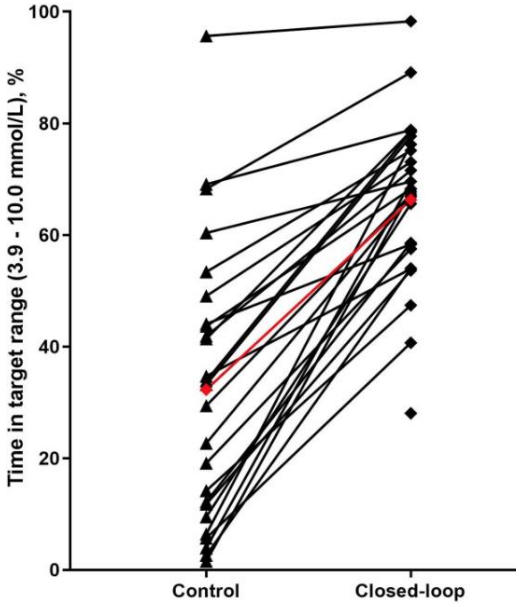
Secondary: HbA_{1c}, time in target range (70-180mg/dL)

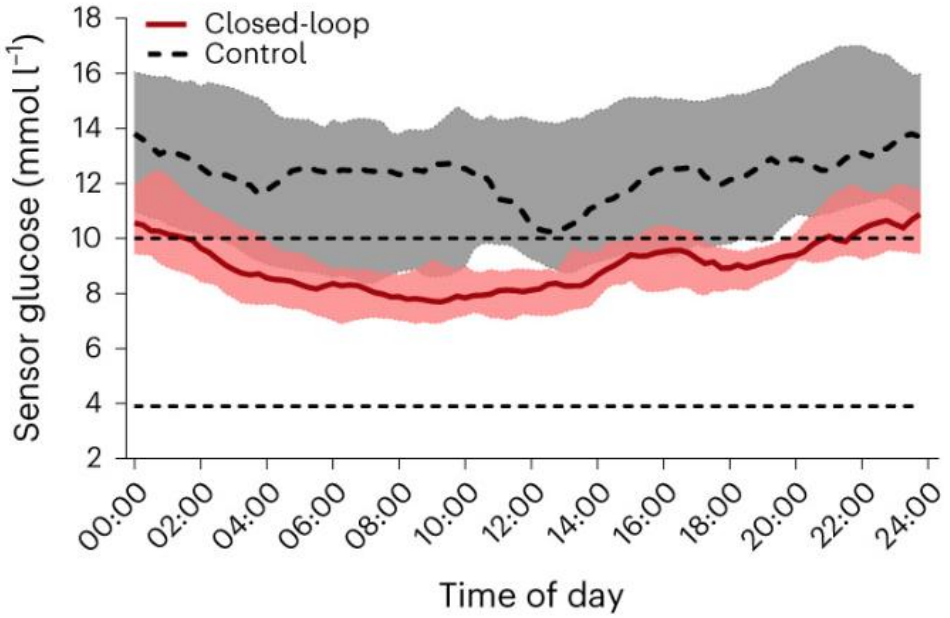


G Davis et al. Diabetes Care 2023;46(4):742–750

Fully closed loop in T2DM

- n = 26, T2DM treated with Insulin, av. HbA1c 9.0%
- Cross-over, 1:1 ratio, 8 weeks each, 2 weeks washout
- MDI vs. Closed Loop without manual meal announcement
- "Closed-Loop App" (CamAPS HX, CamDiab)
- HbA1c 8.7% vs. 7.3%

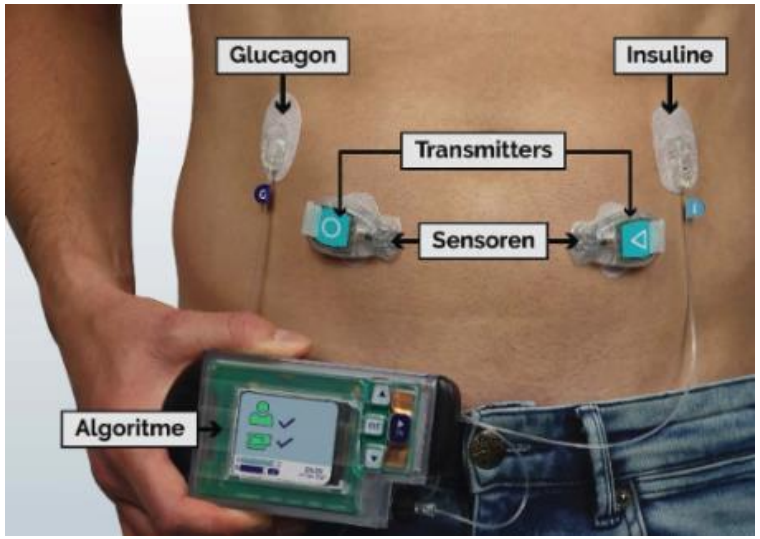




A Daly et al. Nat Med. 2023; 29(1): 203–208.

Bihormonal artificial pancreas

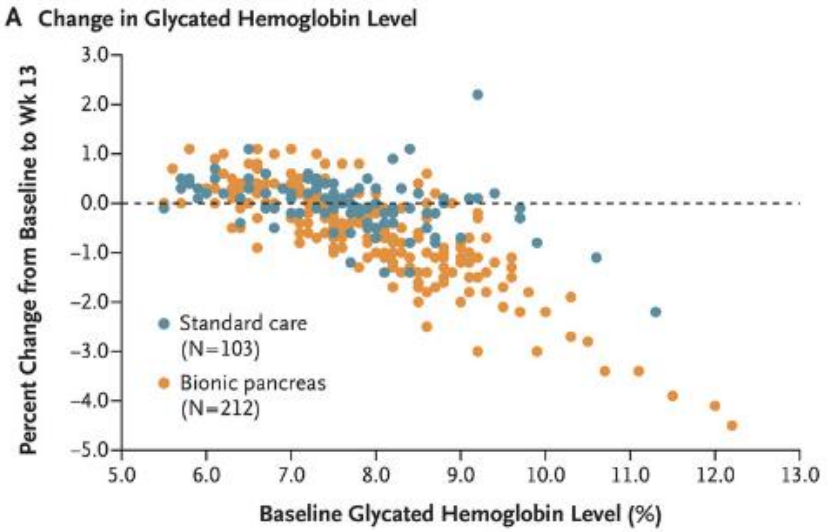
AP (INREDA)

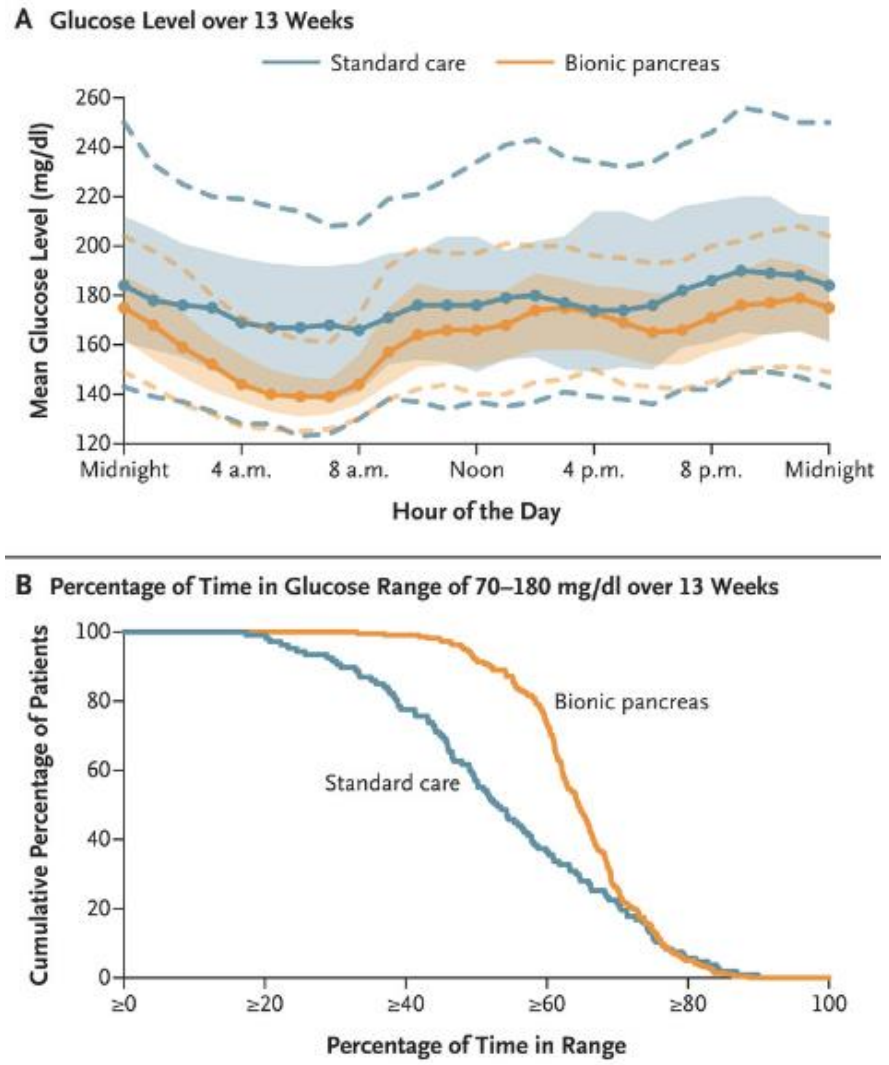


iLet (Beta Bionics)

Beta Bionics

- n = 326, T1DM, 6 - 79 years
- Multi-center, parallel-group, unblinded, randomized
- (MDI, CSII, HCLP) + CGM vs. Bionic Pancreas
- Everday life conditions without any restrictions
- 3 months duration
- No DKA
- No increase in hypoglycemia

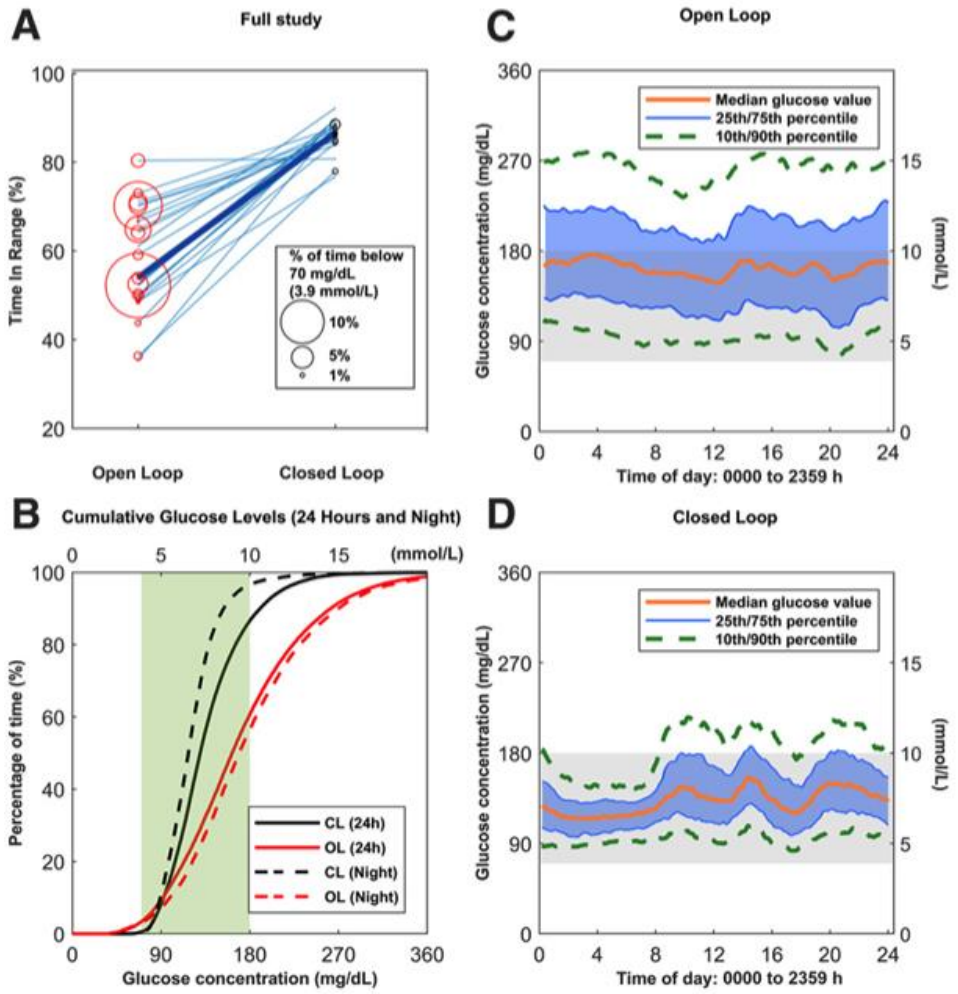




N Engl J Med 2022; 387:1161-1172

INEDRA

- n = 23, adults, T1DM
- Cross-over study
- 2 weeks each
- Bihomonal APS vs. HCLP
- TIR improved (87% vs. 54%)

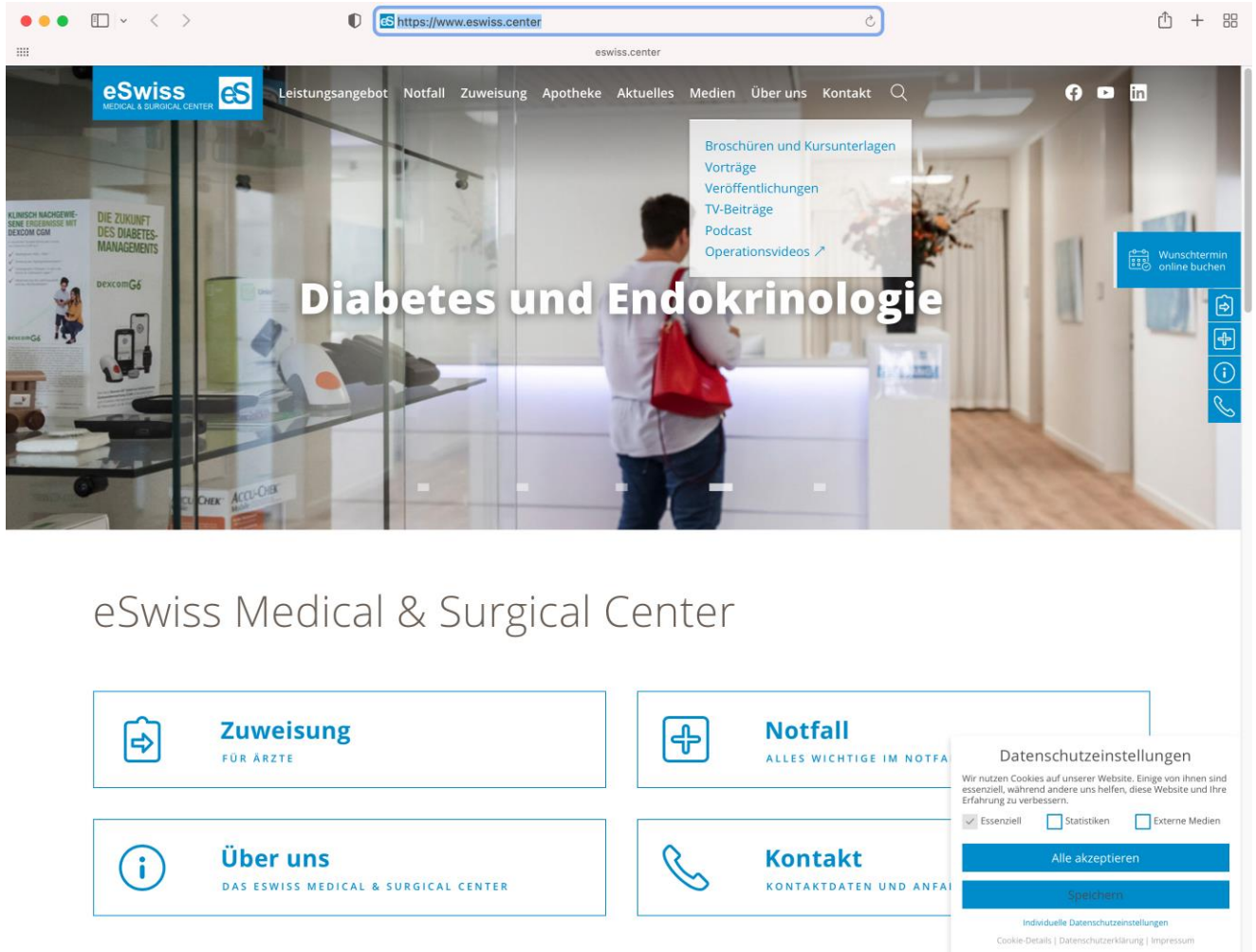


H. Blauw et al. Diabetes Care 2021;**44(3)**: 836–838

Conclusion

- AID systems took a long time to fruition, but are now set to dominate diabetes care
- The evidence for better outcome with AID systems is robust
- In practice AID systems pose new challenges, but patients profit
- There is currently a massive drive for optimisation of AID systems and an expansion in other areas of application

„eswiss.center“ – talk available as PDF



Thank you!

Any questions?