

Update on Diabetes Technologies

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Disclosures

- Erin Cobry:
 - Research: Medtronic, Dexcom, Tandem, Insulet, Beta Bionics, and Lilly
 - Speaking, Ad Board: Dexcom, Insulet
- Halis Kaan Akturk:
 - Research: Medtronic, Dexcom, Tandem, Jaeb Center, Beatson Foundation
 - Consultant: Medtronic, Dexcom, Tandem
- Gregory Forlenza:
 - Research: Medtronic, Dexcom, Abbott, Tandem, Insulet, Beta Bionics, Sequel, Cambridge, and Lilly
 - Speaking/Consulting/Ad Board: Medtronic, Dexcom, Abbott, Tandem, Insulet, Beta Bionics, Sequel, and Lilly



Overview

- Background and Terminology
- Continuous Glucose Monitors and Smart Insulin Pens
- Automated Insulin Delivery Systems
- Technologies in Type 2 Diabetes



Background and Overview of Terms



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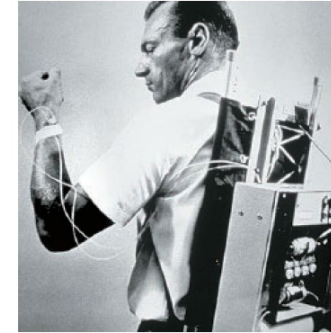


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Diabetes Technology History

- Portable insulin pumps introduced in early 1970's.
 - First insulin pump invented by Dean Kamen in his parents' garage.
 - Improved glycemic control in early studies.
 - Uptake increased after DCCT in mid 1990's.

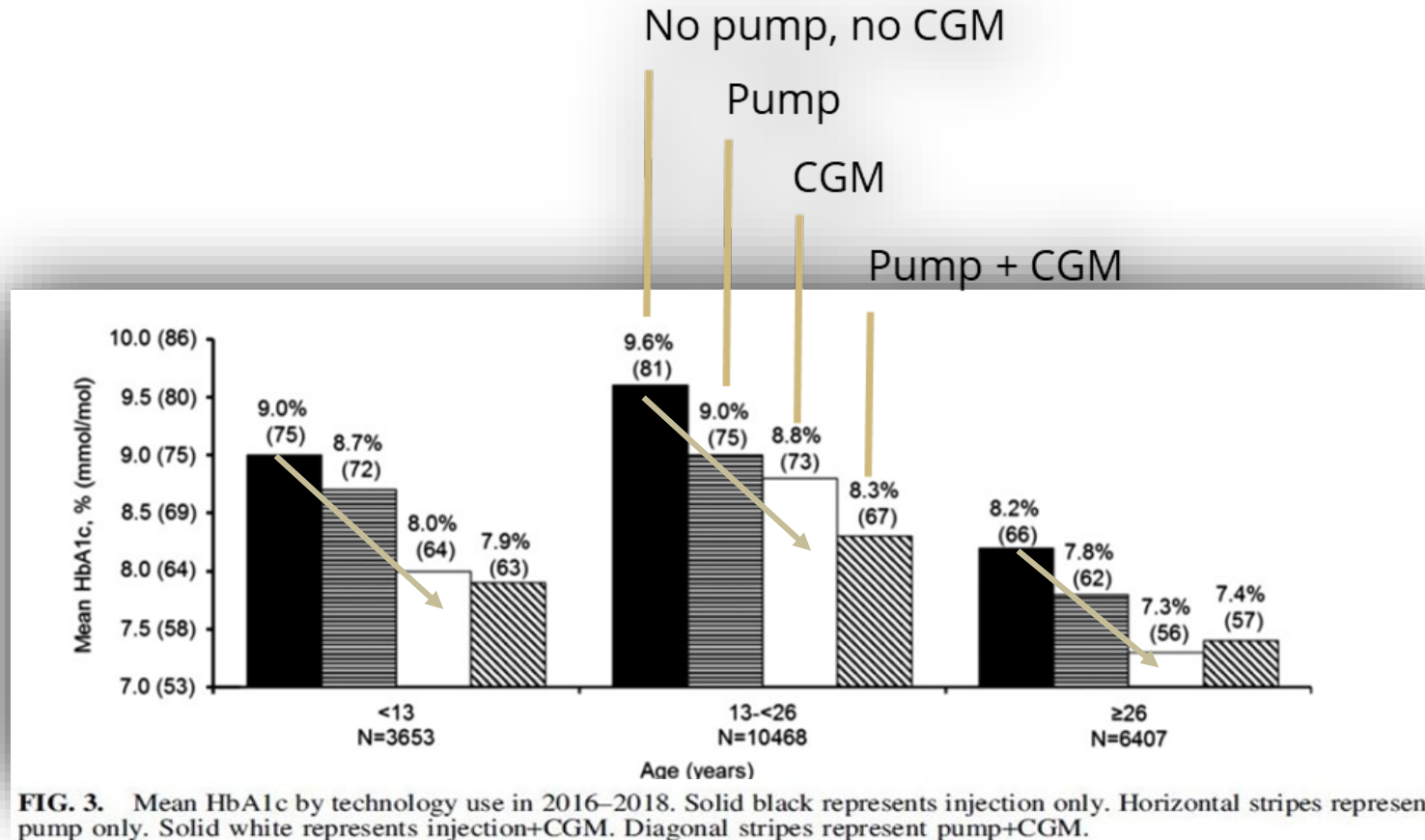
- Continuous glucose monitor (CGM) approved in 1999.
 - Medtronic (not real-time)
 - GlucoWatch
 - Data for management, did not replace fingerstick glucose.



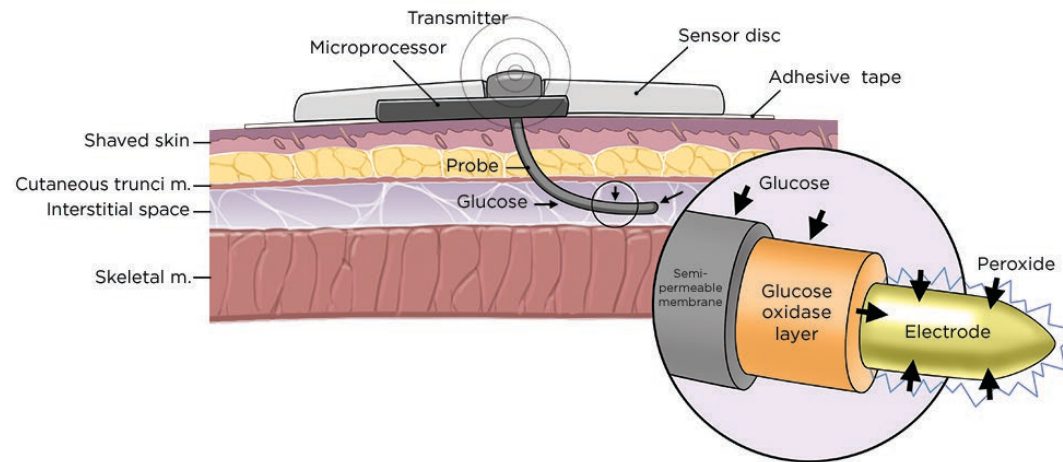
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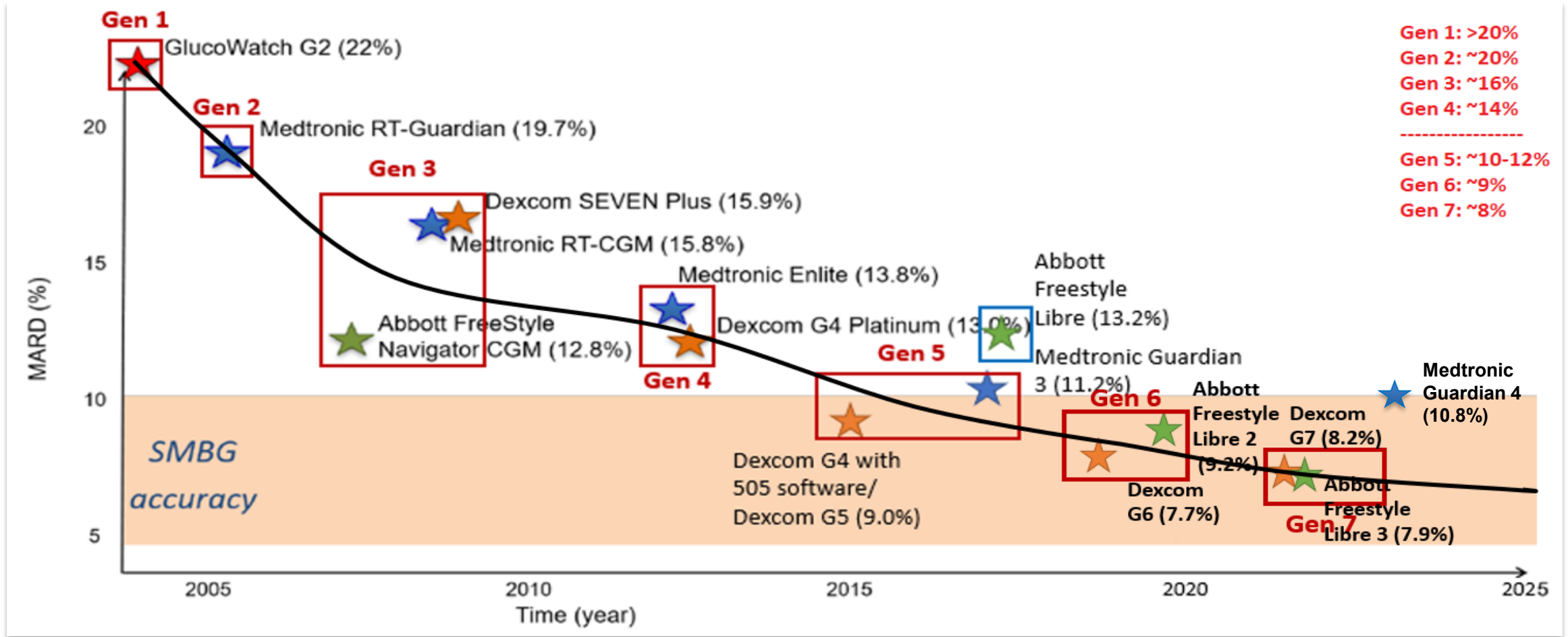
Diabetes Control by Device



Continuous Glucose Monitors



CGM Accuracy



Adapted from Facchinetti, Sensors 2016 and various publications.



Dexcom

- Approved for 2 years-old and above
- Every 5 min values
- 10-day wear
- No calibrations
- Can be used to dose insulin
- Share feature
- No acetaminophen interference

- **Dexcom G6:**
 - Works w/ Tandem Control-IQ/Basal-IQ, Insulet Omnipod 5, Beta Bionics iLet.

- **Dexcom G7:**
 - Works w/ Tandem Control-IQ, Beta Bionics iLet only currently.



Abbott Freestyle Libre Systems

- Approved for people 2 years-old and above
- Every 1 min values
- 14-day wear
- No calibrations
- Can be used to dose insulin
- No acetaminophen interference

- **Freestyle Libre 2:**
 - Realtime alerts but must be scanned to get values
 - Freestyle Libre 2 Plus integrates with Tandem Control-IQ

- **Freestyle Libre 3:**
 - Realtime data to phone or receiver
 - Share feature
 - Not integrated with automated systems yet



Medtronic

- Every 5-minute values
- 7-day wear
- Works with Medtronic automated pumps
- **Guardian Sensor 3:**
 - Approved for people 2 years-old +
 - Requires 2-3 calibrations per day
 - Not approved for insulin dosing
 - Remote monitoring with 770G/780G pump
 - Can't take acetaminophen
 - Standalone version is **Guardian Connect**

- **Guardian Sensor 4:**
 - Approved for people 7 years-old +
 - Can use for insulin dosing
 - About 1 calibration per week
 - Remote Monitoring via phone app
 - Works with 780G pump
 - No acetaminophen interference
 - No standalone version
- **Simplera**
 - One piece, disposable, 10-day
 - No calibrations
 - Will work with 780G pump
 - **Simplera** (stand-alone) has also been called **Synergy** (algorithm) and **Instinct** (automated version)



Eversense

- Implantable real-time CGM, 180-day wear (soon 1-year)
- Alerts by cell phone and vibrating wearable transmitter
- In clinic insertion and removal
- Different vibrating tones for high and low alerts
- Approved ≥ 18 -year-old
- Silicone taping, hypoallergenic
- Sensor powered wirelessly by wearable transmitter
- For most MRI imaging, sensor can be kept in
- One calibration per day (two per day during first 21 days), 24-hour warm up
- Tetracycline and mannitol interference



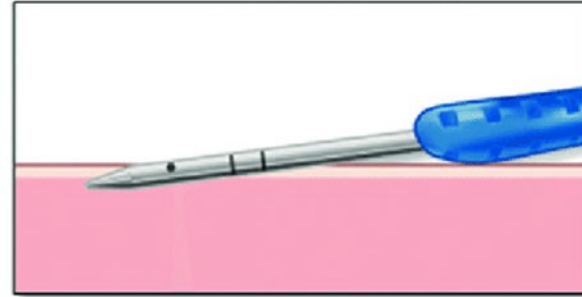
Eversense E3 Insertion Procedure

1 Make incision



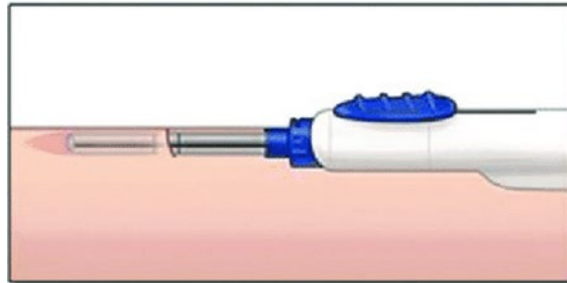
5-8 mm incision upper arm (Lidocaine)

2 Create subcutaneous pocket



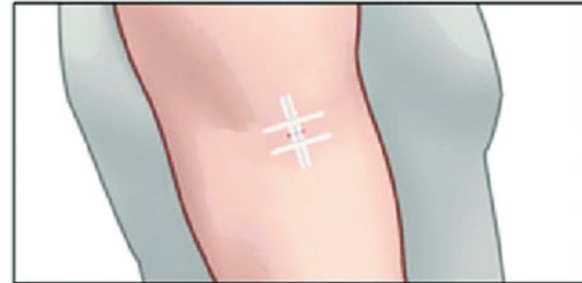
Approximately 3-5 mm below skin surface

3 Insert sensor

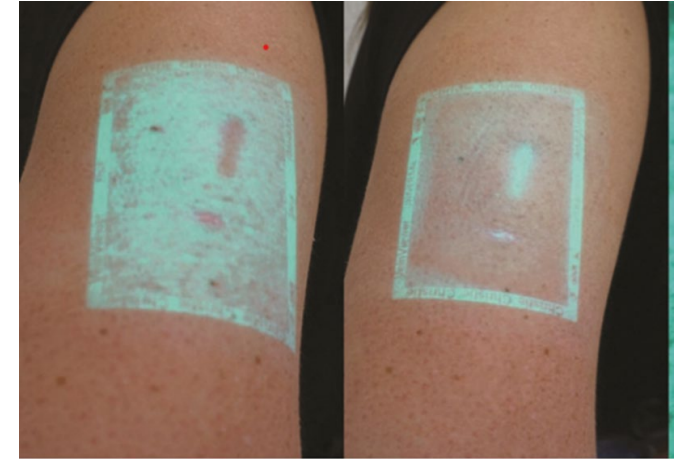


Sensor placed with custom Inserter

4 Close incision



Steri-Strips™ to close



- Near-infrared light (NIL) easy to use, faster, cheaper than ultrasound, and used for blood draws
- NIL located 80% of nonpalpable sensors, decreased procedure time from 20 to 2 minutes in 30 patients
- NIL failed in areas of tattoos or freckles

- In-clinic insertion and removal
- Certification is required to do procedures
- Local anesthetic used, no stitches

Pictures: Courtesy of Dr. Akturk

Christiansen MP, Klaff LJ, Brazg R, et al. Diabetes Technol Ther 2018;20:197-206



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Smart Insulin Pens, Pen Caps, and Digital Systems



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NovoPen Echo

- Works with Novolog cartridges
- Half unit dosing available
- Memory function tracks last dose and time since dose
- Battery up to 5 years
- No dosing advise
- No active insulin tracking



<https://www.novonordisk.com/our-products/pens-and-needles/novopen-echo.html>



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InPen

- Smart Pen sleeve is paired with smart phone app
- Used with Novolog and Fiasp in Novolog Pen and Humalog in Humalog Pen
- Comes in three colors, blue, pink, and gray
- Mimics insulin pumps by using carb ratio, correction factor, insulin on board, active insulin time
- Can be used for fixed doses
- Insulin dose tracking, reminders
- Can be used with Dexcom G6 (delayed values) and Medtronic Guardian 3 CGM
- Downloadable reports that can be shared
- Once a year replacement



Pictures: <https://consumerguide.diabetes.org/collections/cgm>



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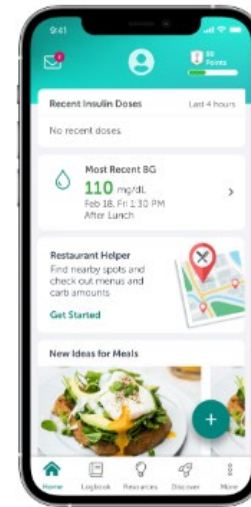
Bigfoot Unity

- Smart Pen cap is paired with smart phone app
- Basal (black cap) and bolus (white cap) pen cap
- Bolus pen cap can be used with Freestyle Libre 2 CGM (pen can scan the sensor)
- Clinic based prescription model- Abbott acquired, will change
- No half units
- Compatible with almost all insulin pens
- Rechargeable

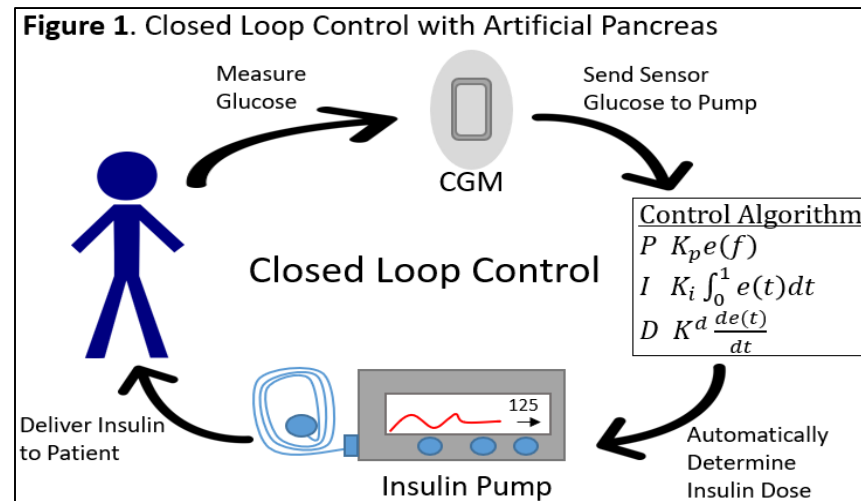


Tempo

- Reusable smartpen cap works with Lilly insulins (Basaglar, Humalog, Lyumjev)
- Connects to app with Bluetooth
- Integration with BGMs and CGM (Dexcom)
- Battery up to 8 months
- No half units
- New feature of dosing calculation-recently



Automated Insulin Delivery



BDC Diabetes Control 2018-2020

Glycemic Control in Relation to Technology Use in a Single-Center Cohort of Children with Type 1 Diabetes

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Gregory P. Forlenza, MD,³ and Guy Todd Alonso, MD³

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TABLE 3. COMPARISON OF HEMOGLOBIN A1C BETWEEN NONHYBRID CLOSED-LOOP USERS AND HYBRID CLOSED-LOOP USERS AMONG PUMP AND CGM COMBINED USERS

	<i>Pump/CGM without HCL</i> (n = 1287)	<i>Pump/CGM with HCL</i> (n = 706)
Age group (n)		
Mean HbA1c [SD]	8.3 [1.8]	7.6 [1.2]****
Met goal HbA1c % <6 (106)	19.4	29.9***
	7.5 [1.2]	7.1 [0.7]
	30.2	40.0
6 to <12 (554)	8.0 [1.4]	7.5 [0.9]****
	20.4	30.5**
12 to <18 (939)	8.5 [1.9]	7.8 [1.3]****
	17.6	25.9***
18 to <22 (394)	8.6 [2.1]	7.4 [1.2]****
	18.4	38.4***

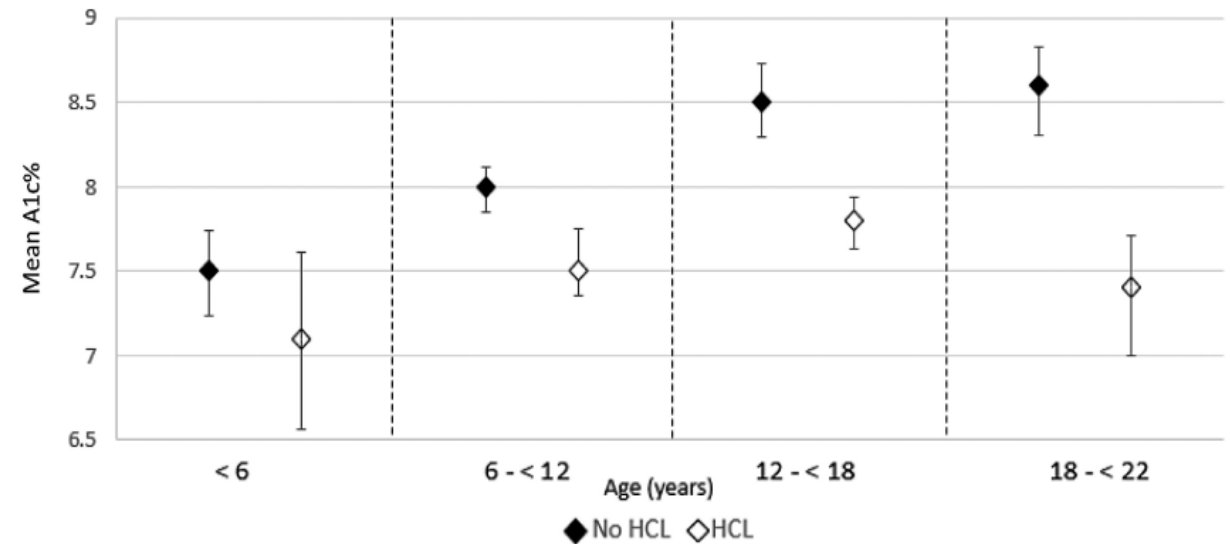


FIG. 2. Mean HbA1c compared between pump/CGM users without HCL and pump/CGM users with HCL using ANCOVA and controlling for diabetes duration, race, and insurance (Medicaid/not). *P*-value is <0.0001 for comparisons within the 6 to <12, 12 to <18, and 18 to <22 years groups, but >0.05 in the <6-year age group. Error bars represent 95% CI. HCL, hybrid closed-loop.



Medtronic 780G – Advanced Hybrid Closed Loop

- FDA Approved April 2023 for 7 years-old and up.
- Less exits from Auto Mode.
- System automatically adjusts basal insulin.
- Programmed insulin:carb ratios and carbohydrate entry to bolus for meals, “auto bolus” for high blood sugar reduction.
- Can do temporary targets for exercise.
- Recommended target is 100mg/dL and insulin action time is 2 hours.
- Works with Medtronic Guardian Sensor 4 (no/minimal calibration), will work with the Medtronic Simpler/Instinct sensor, likely in 2024.



Tandem Control-IQ

- FDA approved 14 years-old + in December 2019.
 - Approved 6-13 years-old in June 2020.
 - Trials 2-5 years-old completed 2022.
 - Tandem Mobi approved for 6 years-old + July 2023.
- Automatically adjusts the basal insulin, but still bases the basal on settings.
- Insulin:Carb ratio and correction factor (CF) are programmed, administers automated corrections (~60% of a correction bolus).
- The target (110mg/dL) and Insulin On Board time (5 hours) are fixed.
- Includes two modes: Sleep and Exercise for temporary adjustments in target ranges.
- T:slim X2 pump (G6, G7, or Libre 2+) and Tandem Mobi (G6, G7).



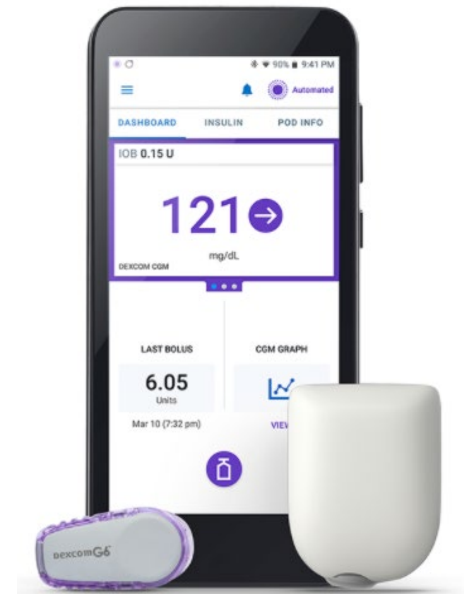
Insulet Omnipod 5

- FDA approved January 2022 for 6 years-old and up and in August 2022 for 2-5 years-old as the first tubeless automated system.
- Phone app/PDM commands boluses.
 - iPhone app approved, pending release in app store in 2024
- CGM communicates directly to pod.
- Control algorithm adjusts basal insulin, no autocorrection.
- Programmed insulin:carb ratios and correction factors for meal and high glucose dosing.
- Can program different targets throughout day (between 110mg/dL and 150mg/dL) and can do an exercise/activity mode (150mg/dL).
- Works with Dexcom G6 (Dexcom G7 coming 2024).

Multicenter Trial of a Tubeless, On-Body Automated Insulin Delivery System With Customizable Glycemic Targets in Pediatric and Adult Participants With Type 1 Diabetes

Diabetes Care 2021;44:1–11 | <https://doi.org/10.2337/dc21-0172>

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Beta Bionics iLet

- FDA approved May 2023 for 6 years-old and up.
- “No numbers” automated system.
- Simplified to be **initialized with only the weight.**
- Other parameters are adapted based on feedback from the CGM.
- Must have CGM data to operate.
- Meal boluses are based on usual size of meals, not carb counting.
- Cannot administer corrections or do temporary targets.



Novel and Upcoming Designs



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Dual Hormone iLet

- Same core as the insulin-only iLet but allows for glucagon delivery.
- Study with 10 adults using for 7 days:
 - Time <70mg/dL decreased from 4% (insulin only) to 2% (dual hormone).
 - Time in range (70-180mg/dL) increased from 72% (insulin only) to 79% (dual hormone)

Performance of the Insulin-Only iLet Bionic Pancreas and the Bihormonal iLet Using Dasiglucagon in Adults With Type 1 Diabetes in a Home-Use Setting

Diabetes Care 2021;44:e118–e120 | <https://doi.org/10.2337/dc20-1086>

Luz E. Castellanos,¹ Courtney A. Balliro,¹ Jordan S. Sherwood,¹ Rabab Jafri,¹ Mallory A. Hillard,¹ Evelyn Greaux,¹ Rajendranath Selagamsetty,² Hui Zheng,³ Firas H. El-Khatib,² Edward R. Damiano,^{2,4} and Steven J. Russell¹



Caution - THE iLet IS AN INVESTIGATIONAL DEVICE, LIMITED BY FEDERAL LAW TO INVESTIGATIONAL USE



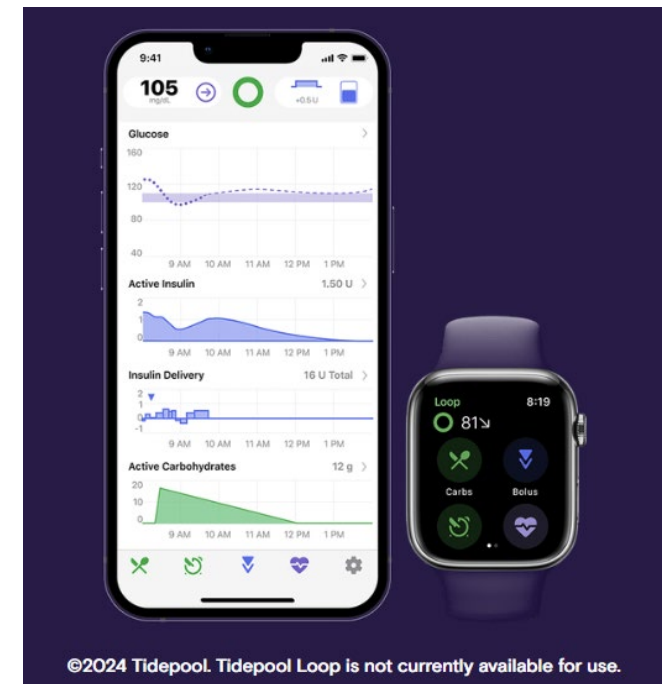
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Sequel Med Tech and Tidepool Loop

- FDA clearance in March 2024
 - Combines the novel twist pump, the Dexcom G6 CGM, and the Tidepool Loop Algorithm (FDA approved 01/23)
 - Not yet commercially available
 - Studies coming this year



Luna Insulin Delivery System

- Used with multiple daily injections (T1D and T2D).
- Overnight “hyperglycemia minimization.”
- Placed at night, removed in the morning.
- 10u of rapid acting insulin.
- Communicates with a CGM (Dexcom G6 currently).
- Outpatient studies this summer.



Rocket AP System Fully Closed Loop

Advanced Closed-Loop Control System Improves Postprandial Glycemic Control Compared With a Hybrid Closed-Loop System Following Unannounced Meal

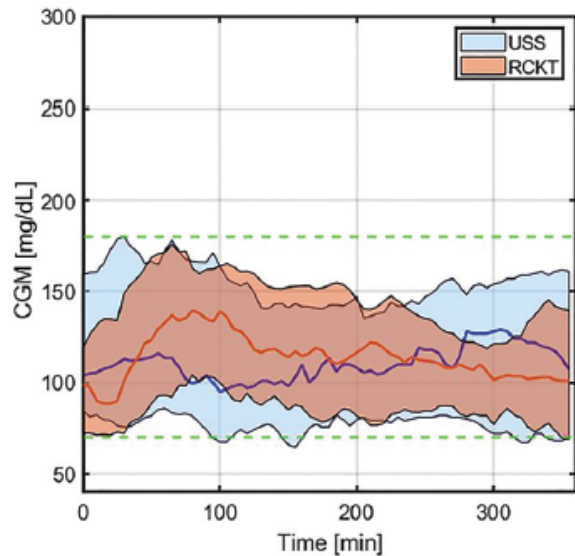
Jose Garcia-Tirado,¹ Jenny L. Diaz,¹ Rebeca Esquivel-Zuniga,² Chaitanya L.K. Koravi,¹ John P. Corbett,¹ Martha Dawson,¹ Christian Wakeman,¹ Charlotte L. Barnett,¹ Mary C. Oliveri,¹ Helen Myers,¹ Katie Krauthouse, Marc D. Breton,¹ and Mark D. DeBoer^{1,2}

Diabetes Care

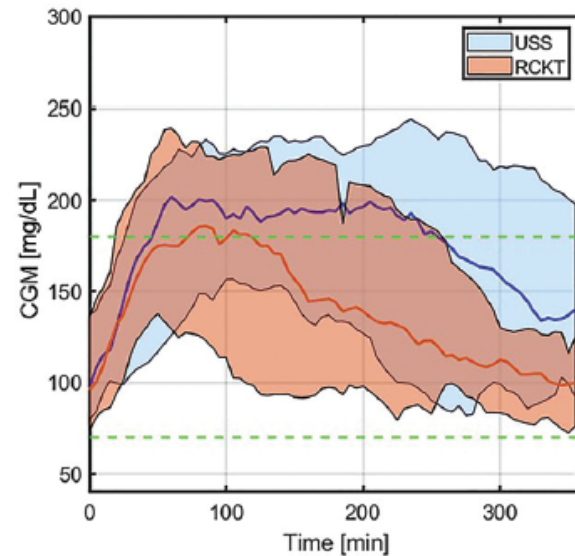
<https://doi.org/10.2337/dc21-0932>

- Randomized Crossover study comparing the “legacy UVA HCL system” (aka CIQ) against a novel fully automated CLC system (RocketAP) during 2 46-h supervised admissions.

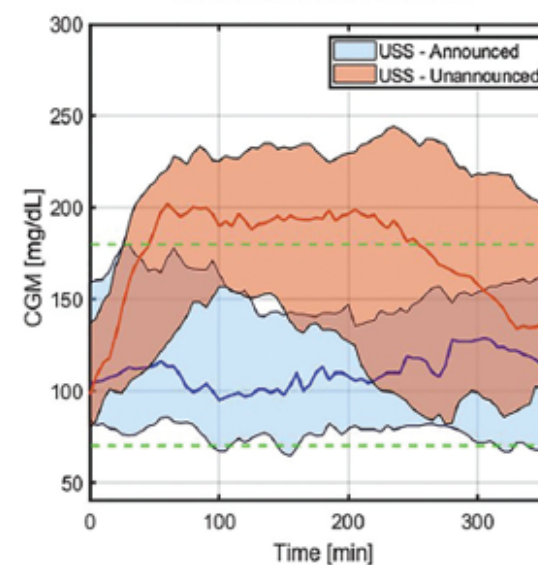
A Announced dinner: RCKT vs. USS



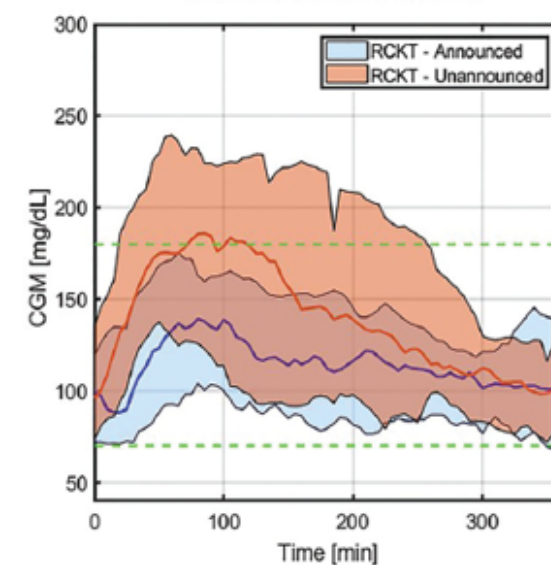
B Unannounced dinner: RCKT vs. USS



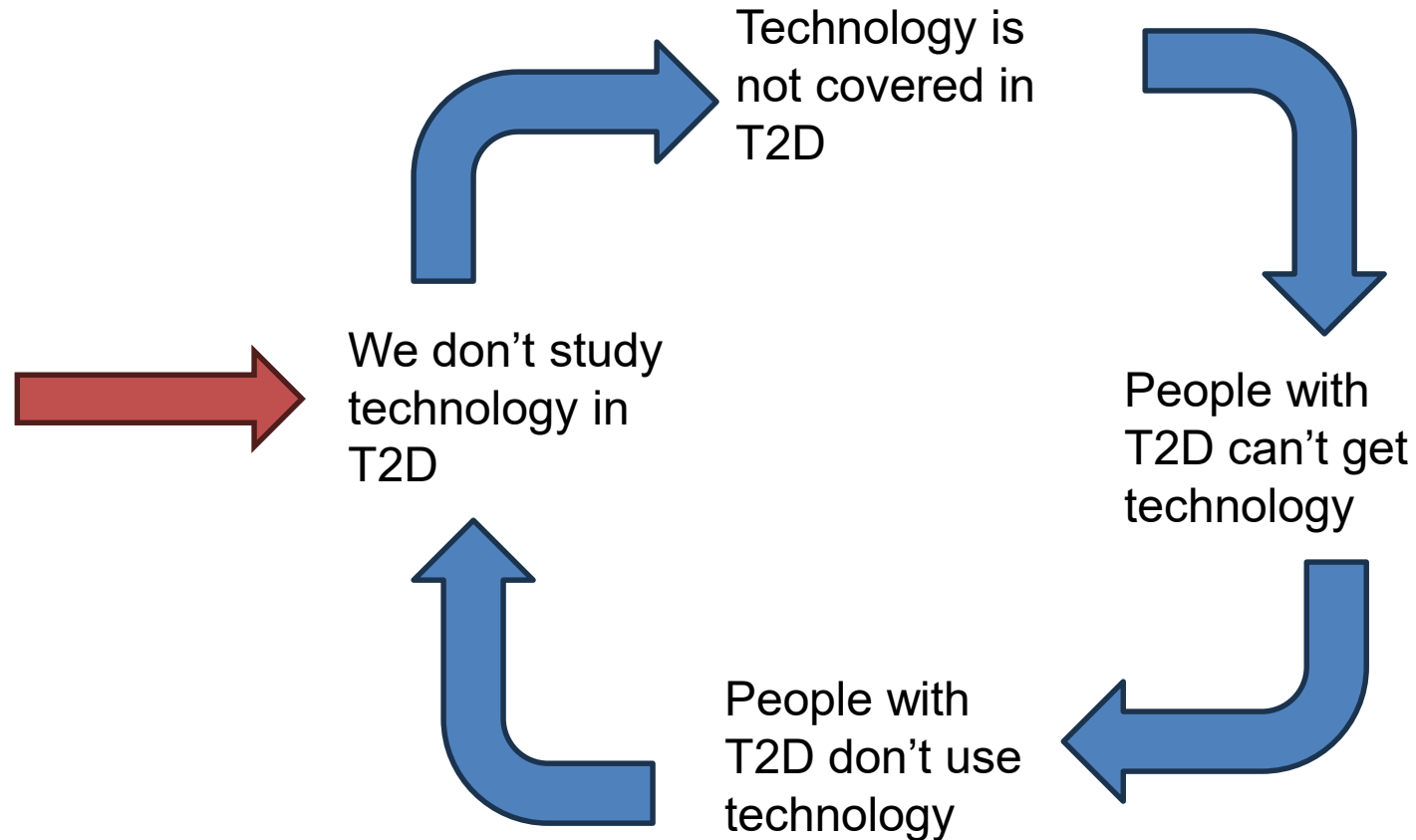
C USS: Announced vs. unannounced dinner



D RCKT: Announced vs. unannounced dinner



History of Technology (CSII, CGM, AID) for T2D



Evidence for AID in T2D

- Reviewed 5 published Randomized Controlled Trials (RCTs) on AID use in T2D.
- Design of trials similar to AID studies of early 2010's
 - Limited duration
 - Highly supervised
 - Control group on MDI therapy



Automated Insulin Delivery Systems as a Treatment for Type 2 Diabetes Mellitus: A Review

Alexander B. Karol, MD, Grenye O'Malley, MD, Reshmitha Fallurin, MD, Carol J. Levy, MD, CDCES*

Division of Endocrinology, Diabetes, and Metabolism, Icahn School of Medicine at Mount Sinai, New York, New York

Evidence for AID in T2D

Table. AID RCTs in T2D

Study	System	Duration of AID	Control Group	Target Range	Time in target improvement
Kumareswaran 2014	Hovorka	24h	Usual Care	70-144	+16% (40 v 24%)
Thabit 2017	Hovorka	72h	Conventional SQ	100-180	+21.8% (59.8 v 38.1%)
Bally 2018	Hovorka	up to 15d	Conventional SQ	100-180	+24.3% (65.8 v 41.5%)
Taleb 2019	Haidar	24h	MDI	72-180	+23% Overnight (100 v 78%)
Boughton 2021	Hovorka	20d	MDI	100-180	+15.1% (52.8 v 37.7%)
Peters 2022	OP5	8 wk	MDI	70-180	+15.1% (52.8 v 37.7%)



Automated Insulin Delivery Systems as a Treatment for Type 2 Diabetes Mellitus: A Review

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Division of Endocrinology, Diabetes, and Metabolism, Icahn School of Medicine at Mount Sinai, New York, New York

Evidence for AID in T2D

- Furthermore, 2 of the trials conducted patient satisfaction surveys and both found that 100% of participants would recommend use of the device to other people with T2D.
- Note that the TIR improvements were 15-25%, while for T1D AID studies we usually see 10-12% improvement!



Summary of T2D RWE

Table 2. Type 2 Diabetes Device Evidence

Device	Source	TIR 70-180 mg/dL (%)	Change in TIR (%)	Mean SG (mg/dL)	HbA1c/ GMI (%)	TBR <70 mg/dL (%)	TBR <54 mg/dL (%)
Medtronic 780G	Van Den Heuvel ATTD 2024	75.1		150.5	6.9	1.4	0.3
Tandem CIQ	Forlenza DTT 2022	72	8	158.4	7.1	0.34	0.06
Insulet OP5	Davis DC 2023	58.6	21.9	179	8.1	0.06	
CamAPS HX	Daly Nat Med 2023	66.3	35.3	165.6	7.3		0.04
Loop	Bauza DTT 2024	93	9.9	124	6	0.63	0.09



Impact of GLP-1's

- GLP-1 Receptor Agonists can significantly reduce insulin needs for PwD requiring insulin while improving glycemic control.
- They may aid AID systems in improving glycemic control or remove the need for insulin for some people with T2D.
- More research is needed in this area to draw conclusions on this question.



Conclusions

- There is a growing body of evidence to support the safety and efficacy of AID to benefit people with T2D.
- Both RCTs and real-world data demonstrate the success of these system in improving glycemic control.
- User surveys and real-world data support the robustness of system use in adults with T2D.

