Emerging Technologies in Diabetes Care

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Conflicts to Disclose

Stock holdings:

Emisphere Technologies
Novo Nordisk
Abbott Laboratories

"2019 is ***The Year*** to have a diagnosis of diabetes…"

"…because we've never had technology like we have now."

- Me

Objectives

- **The options to treat diabetes are as varied as the patients we share**
- Review current available options for diabetes care
  - Novel insulins
  - CGMs
  - Insulin pumps
  - Patch pumps
  - Smart pens
- Consider how embracing technology can improve outcomes by reducing burden of care
- Review outcome data for various approaches to management
- Outline what is on the horizon in the next 1-2 years
- Provide resources for quick reference

Why Do We Care?

- 33-49% of patients still do not meet targets for A1C, blood pressure, or lipids
- Only14% of patients meet targets for all A1C, BP, lipids, and nonsmoking status
- Progress in CVD risk factor control is slowing
- System-level improvements are needed

x Improving Care and Promoting Health in Populations: *Standards of Medical Care in Diabetes - 2019. Diabetes Care* 2019;42(Suppl. 1):S7-S12

American Diabetes Association.

Diabetes Technology: What You Will See

Glucose Monitors

- In 2016, FDA required that all home glucometers had to be within 20% of the true glucose 99% of the time.
- If venous glucose = 100
  - CBG can be 80-120 and be acceptable

NUMBER AND PERCENT OF VALUES WITHIN SPECIFIED ERROR LIMITS

				Distance from the Reference Value*									
Brand	Blood Glucose Monitor	Test Strip	Valid Trials	Within +/- 5%		Within +/- 10%		Within +/- 15%†		Within +/- 20%		>20%	
Bayer	Contour Next	Contour Next	312	212	68%	302	97%	311	100%	311	100%	1	0.3%
Roche	ACCU-CHEK AVIVA Plus	ACCU-CHEK AVIVA Plus	311	161	52%	272	87%	306	98%	311	100%	0	0.0%
Arkray	Walmart ReliOn Confirm (Micro)	ReliOn Confirm/micro	317	167	53%	276	87%	307	97%	314	99%	3	0.9%
Agamatrix	CVS Advanced	CVS Advanced	318	172	54%	272	86%	307	97%	317	100%	1	0.3%
Abbott	FreeStyle Lite	FreeStyle Lite	312	95	30%	238	76%	298	96%	306	98%	6	1.9%
Roche	Accu-Chek Smart View	ACCU-CHEK SmartView	320	133	42%	251	78%	305	95%	317	99%	3	0.9%
Arkray	Walmart ReliOn Prime	ReliOn Prime	312	121	39%	224	72%	288	92%	305	98%	7	2.2%
LifeScan	OneTouch Verio	OneTouch Verio	319	139	44%	239	75%	294	92%	315	99%	4	1.3%
Prodigy	Prodigy Auto Code	Prodigy No Coding	312	135	43%	229	73%	282	90%	304	97%	8	2.6%
LifeScan	OneTouch Ultra2	OneTouch Ultra	311	127	41%	230	74%	280	90%	302	97%	9	2.9%
Abbott	Walmart ReliOn Ultima	ReliOn Ultima	319	140	44%	241	76%	285	89%	302	95%	17	5.3%
Bayer	Contour Classic	Contour	320	109	34%	215	67%	284	89%	313	98%	7	2.2%
Omnis Health	Embrace	Embrace No Code	319	116	36%	230	72%	282	88%	308	97%	11	3.4%
HDI/Nipro	True Result	TrueResult	318	81	25%	188	59%	279	88%	311	98%	7	2.2%
HDI/Nipro	True Track	TrueTrack	205	57	28%	112	55%	167	81%	186	91%	19	9.3%
BioSense Medical	SolusV2	SOLUS	320	59	18%	148	46%	244	76%	297	93%	23	7.2%
Diabetic Supply of Suncoast	Advocate Redi-Code +	Advocate	319	66	21%	148	46%	241	76%	288	90%	31	9.7%
Philosys, Inc.	Gmate Smart	Gmate	320	82	26%	159	50%	226	71%	267	83%	53	16.6%

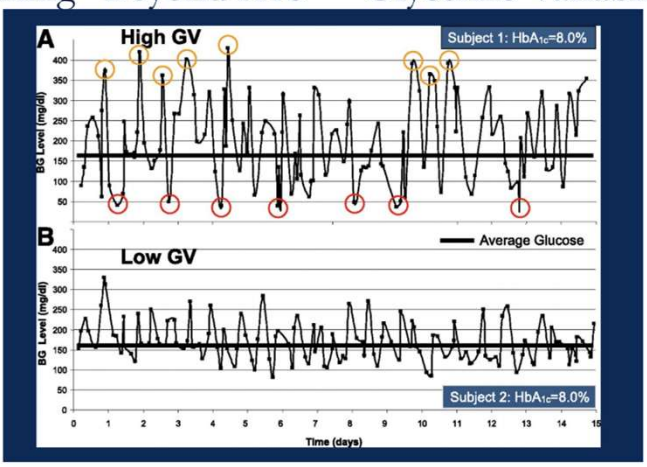
*When reference value is <100 mg/dL, then distance is absolute mg/dL rather than %.

†The percentage of data points within +/- 15% distance from the Reference Value is the same as the percentage of data points for Trials Within Protocol Limits in the Overall Results Table.

https://www.diabetestechnology.org/surveillance.shtml

Courtesy: UCSF mini med school

Thinking "Beyond A1c" – Glycemic Variability



Fifteen-day glucose traces of two subjects with identical A1c of 8.0% but different degrees of glycemic variability.

Boris Kovatchev, and Claudio Cobelli Dia Care 2016;39:502-510

Continuous Glucose Monitors (CGMs)

- Other than a venous glucose, they are the most precise way to measure a patient's glucometrics.
- Real-time observation allows patients to engage more in their lifestyle interventions
  - Can produce 0.5-1% reduction in a1c alone
- Important for safety in the setting of "brittle" patients or those who no longer retain hypoglycemia awareness.
- Allows those with visual/auditory disabilities various ways to understand what their glucose is doing.
- Helps ensure monitoring of sugar fits into the patient's life.
- Allows for the usage of **Time In Range metric**

Continuous Glucose Monitors (CGMs)

- Not all CGMs are created equal!
- Guidelines differentiate between Real Time and Intermittent Flash glucose sensing.
  - RT-CGM is endorsed for Type 1 Diabetes
  - IF-CGM OR RT-CGM can be appropriate for Type 2 Diabetes

CGMs: Abbott Freestyle Libre

- Manufacturer: Abbott
- Release dates:
  - 10d sensor in 2017 (12h warmup)
  - 14d sensor in 2018 (1h warmup)
- MARD averages 9.4% (8.5 - 10.8%)
- First **factory calibrated** sensor
- **FDA approved for insulin dosing**
- Medicare DME coverage if taking 4 shots/day and checks glucose 4x/d.
- Private coverage typically $75/month cap.
- Cost effective if pt checking ≥ 3x/d

CGMs: Abbott Freestyle Libre

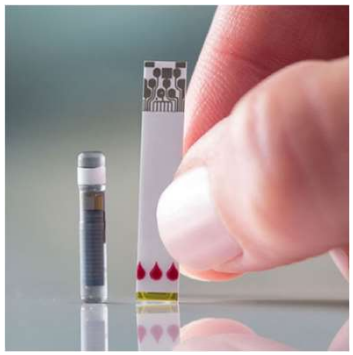
- Cash: typically each 14d sensor ~$60 and reader is $70-100 once.
- As of June 2019
  - Freestyle LibreLink app **replaces reader** for BOTH Android as well as iPhone 7 & higher.
- Imperfect alternative to consider:
  - Use of 1 sensor every 90 days instead of CBGs
  - Cash cost averages to $240/year or $20/month.

CGMs: Dexcom G6

- Manufacturer: Dexcom (CA)
- Release date: 2018
- Vastly simplified applicator
- 10 day wear
- 2 hour warm up time
- **Factory calibrated & FDA approved for insulin dosing**
- Measures interstitial glucose every 5 minutes
- Alerts can be shared with up to 5 people and connects to phone apps and smart devices.
- Sensor filament is the thickness of 2 human hairs
- Pharmacy benefit or DME

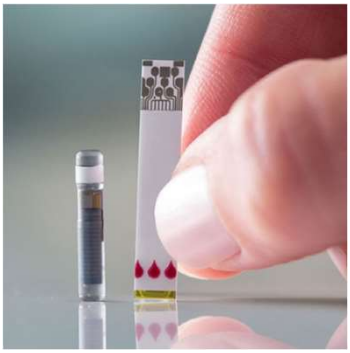
CGMs: Eversense

- Manufacturer: Senseonics (MD)
- US Release date: 2018
- The world's first **implantable CGM**
- MARD 8.5%
- Daily calibrations: 2
- **FDA approved for insulin dosing**
- First to use fluorescent glucose-polymer indicating technology.
- Currently approved for 90 day wear
- Transmitter is applied with new adhesive daily
- Implant safe for most MRIs
  - Transmitter must be removed



CGMs: Eversense

- Senseonics XL was approved in Europe for 180 day wear in 2017.
- Studies underway for 180 day approval in US.
- Cons:
  - Requires 2 calibrations/day
  - 24h warmup
- Next from Senseonics
  - Eventual Eversense 365 - 1 year wear
  - Factory calibration
  - Integration to other devices



CGMs: Guardian

- Manufacturer: Medtronic (CA)
- Release date: 2018
- Daily calibrations: 2-4
- MARD 8.7%
- 7 day wear
- 2 hour warm up time
- NOT FDA approved for insulin dosing

Who Has the Best Sensor?

A Three-Way Accuracy Comparison of the Dexcom G5, Abbott Freestyle Libre Pro, and Senseonics Eversense CGM Devices in an Outpatient Study of Subjects with Type 1 Diabetes

RABAB Z. JAFRI, COURTNEY A. BALLIRO, FIRAS EL-KHATIB, MICHELE MAHENO, MALLORY A. HILLARD, ALEXANDER J. O'DONOVAN, RAJENDRANATH SELAGAMSETTY, HUI ZHENG, EDWARD DAMIANO and STEVEN J. RUSSELL

- n=23, in vivo crossover trial over 6 weeks
- Each patient wore all 3 sensors and utilized Nova Biomedical Stat Strip Xpress meter for calibrations
- Nominal MARDS (2277 data sets)
  - Eversense 14.8%
  - Dexcom G5 16.3%
  - Libre Pro 18%
- The difference in MARD between Eversense and Dexcom G5 p = 0.008
- Point accuracy of Eversense was superior

Diabetes 2018 Jul; 67(Supplement 1): -.
https://doi.org/10.2337/db18-14-OR

Other Cutting Edge Resources

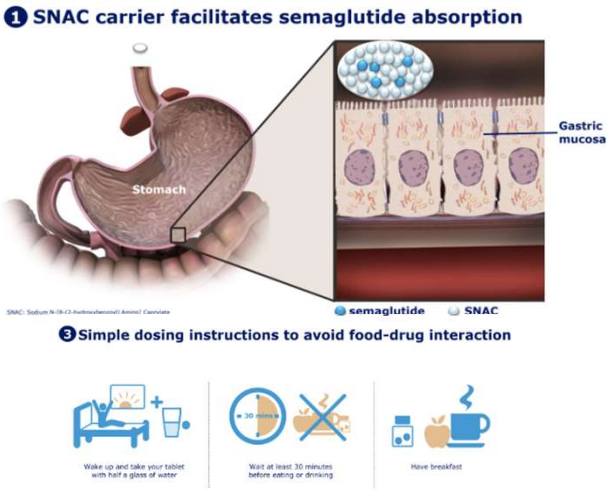
- Tidepool Loop - originated as an open source DIY project for "hacking" insulin pumps and producing algorithms for automated closed loop delivery.
  - Pending FDA approval for the Loop app now
  - Partnership with Omnipod underway
  - Plans to remain open source to partner with other devices
- Coaching
- Livongo

Novel Approaches to Medications

- SGLT2/SGLT1 combinations are now before the FDA for use in Type 1 Diabetes.
  - Timeline is undetermined
- Semaglutide (Ozempic) will be **the first GLP1a** available as **daily oral medication**
  - Anticipated in Q4 2019

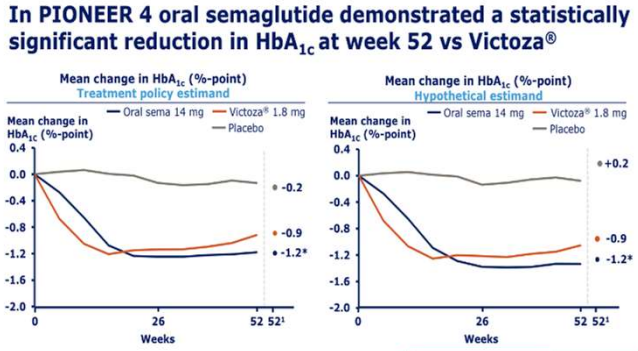
Oral GLP-1a: How'd They Do It?

- Engineer: Emisphere Technologies
- Famous for oral B12
- Molecule: SNAC
  - Carrier molecule facilitates peptides through the GI layers.
  - Does not interact with therapeutic rider.
  - Improves bioavailability of drug.
- Technology could facilitate oral options for many agents
  - Insulin
  - Heparin/LMWH
  - calcitonin/PTH



Oral GLP-1a: What Can We Expect?

- PIONEER trials demonstrated equivalent lowering a1c.
  - n = 711 randomized placebo controlled crossover trial
  - PO semaglutide vs. liraglutide
  - Primary endpoint: change a1c
- Secondary endpoints:
  - weight loss, adverse events, hypoglycemia, a1c < 7%
- Injectable semaglutide still superior for weight loss.

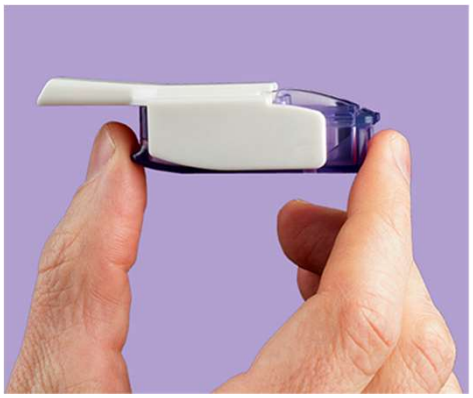


Insulins

- Still the most powerful way to control a1c
  - Pros: quick reduction in a1c and alleviates glucose toxicity
  - Cons: patients hate the concept of insulin, **it's not "smart"**, and it is tricky to navigate.
- Newest agents are novel molecules → improved stability & duration of action
  - Available in concentrated forms for smaller depot and better absorption
- There is a growing movement to make insulin analogues affordable for more patients.
  - Sanofi $99 - $120 offer
- NPH insulin from walmart is $25/vial
  - Equally effective, but with hypoglycemic costs
  - Everyone should have NPH as an **emergency back up plan**

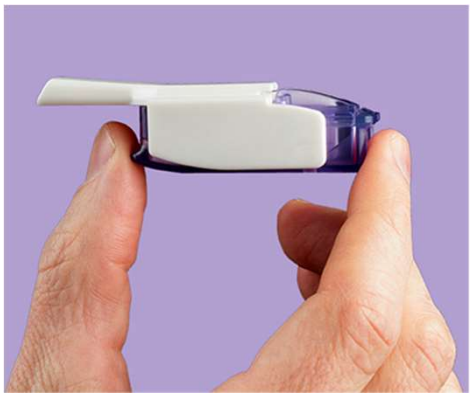
Insulins: Afrezza

- Manufacturer: Mannkind (CT)
- Release date: 2015
- Easy-to-use “whistle” for administering inhaled insulin.
  - Cartridges available in 4u, 8u and 12u
- Rapid onset - take it with the first bite of a meal
- Great for patients who don’t want to use a needle in public
- Flexible dosing & minimal concern for stacking:
  - multiple corrections if consuming a high fat or high protein meal.



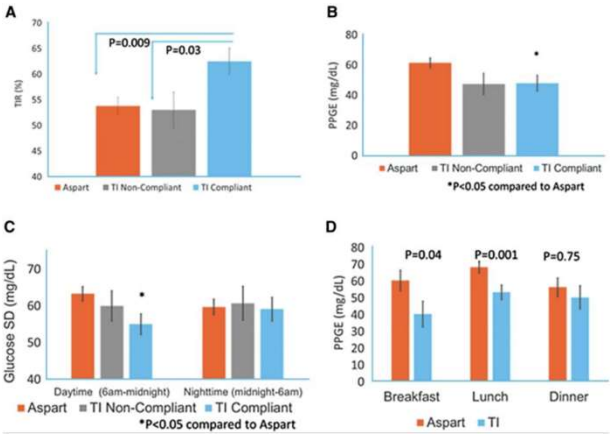
Insulins: Afrezza

- NOT appropriate for patients with underlying lung disease.
- Requires peak flow on the chart.
- Frequently requires specialty pharmacy to facilitate approval.
  - Cedra - Dallas & Houston



Insulins: Afrezza

- Randomized Controlled Clinical CGM Trial, n = 60 DM1 patients
  - Control arm: MDI with aspart
  - Treatment arm
    - Aspart conversion ratio, AC
    - Post-prandial correction protocol
  - Dexcom G5 real time CGM
- Primary endpoint: Time in Range
- Secondary endpoints: change a1c, hypoglycemia, hyperglycemia and variability



Improved Time-in-Range (TIR) on Continuous Glucose Monitor (CGM) with Technosphere Inhaled Insulin (TI) Compared with Insulin Aspart in T1D Patients—STAT Study JANET K. SNELL-BERGEON, HALIS K. AKTURK, AMANDA REWERS, BRUCE W. BODE,LESLIE J. KLAFF, ANNE PETERS, TIMOTHY S. BAILEY, SATISH K. GARG Diabetes Jul 2018, 67 (Supplement 1) 1017-P; **DOI:** 10.2337/db18-1017-P

Insulin Smart Pen: The New Standard

- Manufacturer: Companion Medical
- Release date: 2019
- Team from Tandem, Dexcom & Medtronic
- Acts as an “intermediate” insulin pump
- ½ unit dosing
- Patient uses a normal basal pen injection once or twice daily
- The smart pen is loaded with insulin and the app tracks the same data that a pump would:
  - Time and volume of last dose
  - Insulin on board
  - Total daily dose
  - Carb and correction ratios
  - Dose calculator

Insulin Smart Pen: The New Standard

- Order a Novo-style or a Huma-style pen.
- Patients can choose blue, grey or pink colors.
- Order the Novolog or Humalog in **cartridges**--these are not interchangeable.
- Copay for 1 pen is $18 on average.
- Each pen lasts 1 year.
- Reminds patients when insulin is expiring.
- Alerts patients to insulin temperature changes.
- Be on the lookout for other Smart Pens to enter the market
  - NovoPen6 & NovoPen Echo in Europe

Insulin Pumps

- Unequivocally the standard of care among type 1 diabetes patients
- Growing number of type 2 diabetes patients are utilizing pump technology
- Hybrid closed loop “artificial pancreas” was released by Medtronic in 2017 and more are on the way
- Expect new names to enter the market
  - Bigfoot
  - Tidepool
  - BetaBionic

Insulin Pumps: Medtronic 670G

- Release date: 2017
- Basal rates adjust to accumulating data from Guardian sensor for 6 days.
- NO automated changes to I/C or SF ratios
- **NOTE:** if a Medicare patient is wearing a Guardian and tries to get approval for another CGM, CMS will NOT accept any data from the Guardian sensor.

Insulin Pumps: T-slim X2

- Manufacturer: Tandem (CA)
- Release date: 2018
- **First updateable insulin pump**
- Coordinates with Dexcom G5 & G6 for basal-IQ suspend feature.
- Coming soon: Closed Loop system, Q4 of 2019 will feature Control IQ algorithms
  - **All X2 pumps can receive the update**
  - New Rx and online training required to unlock the auto features.
  - Algorithm will automate both basal rates and correction boluses.
  - Carb boluses will remain manual.

Insulin Pumps: What's Next From Tandem?

- T-slim X2 mobile app: 2019-2020
  - Allow user to review data without handling pump
  - Allow for remote caregiving
  - Integration to other smart devices is expected.
- T-sport Pump: 2020-2021
  - Half the size of the current T-slim
  - NO device screen, all controls handled through app
  - Can choose short (patch pump) or long tubing.

Insulin Pumps: Omnipod

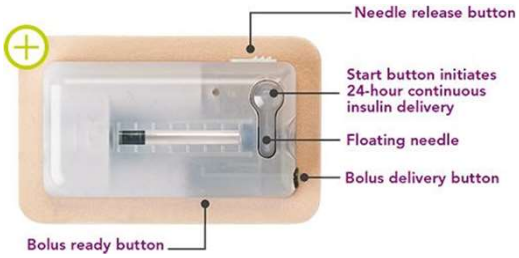
- Manufacturer: Insulet (MA)
- Release date: 2010
- DASH system released 2019
  - Smartphone style interface
  - Allows for data to be sent to other caregivers
- To-date the **only "tubeless" insulin pump**
- Coming in 2020: Omnipod Horizon hybrid closed loop system.
  - Partnered with Tidepool Loop for an on-pod algorithm
  - All controls through DASH or phone app
  - Will remain on automatic delivery even if apps are out of range.
  - Expected Q2-Q3 2020

Insulin Pumps: Next From Omnipod

- ETA: 2020+
- Expanding the use of the DASH system
- The pod itself will be redesigned for on-body analytics.
- Plans to expand the Type 2 market with a concentrated insulin delivery system.
- Stay tuned...

Insulin Pumps: Vgo “Patch” Pump

- Manufacturer: Valeritas (CA)
- Release date: 2010
- Fill with rapid acting analogue
- Uses clockspring for 1 basal rate
- Bolus button delivers 2 u per “click”
- Comes in 3 basal rates
  - 20 u basal + up to 36 u prandial
  - 30 u basal + up to 36 u prandial
  - 40 u basal + up to 36 u prandial
- Price: usually the same or less than MDI with insulin analogues



Insulin Pumps: Vgo “Patch” Pump

- VGO -1.82% & -1.98%
- MDI -0.98% & -1.34%
- Tx Difference -0.84%

P < 0.001 compared to baseline

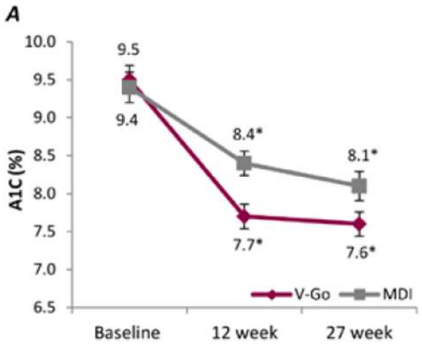
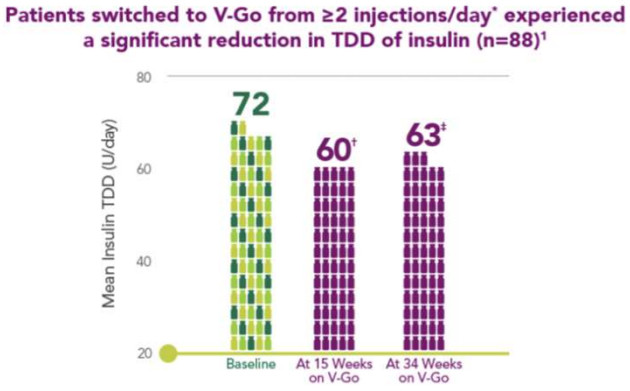


Fig. 1. Outcomes for clinical parameters from baseline. Data reported are mean (SE). (*A*) Glycated hemoglobin (A1C). (*B*) Fasting plasma glucose from baseline in subset of patients (43 V-Go, 37 multiple daily injections [MDI]) with baseline fasting levels. (*C*, *D*) Total daily dose (TDD) units/day and units/kg. (*E*, *F*) Daily basal insulin dose units/day and units/kg. *P<.001 compared to baseline; †P<.005 compared to baseline.

Lajara,R. et al. Endocrine Practice. 2016; 22(6) 726-735.

Insulin Pumps: Vgo “Patch” Pump

- Achieve reduction of TDD by:
  - Reducing the number of injections per day
  - Optimizing consistency of dosing
  - Minimizing human error
- This phenomenon was consistently clinically beneficial across strata by the 7 month mark.
  - Statistically significant among the 5-15y duration of diabetes strata.



Harrison HC, Everitt B, Nikkel C. Poster: The Impact of utilizing a novel insulin delivery device in patients with type 2 diabetes. AACE 2017.

Insulin Pumps: Paq Meal & Paq Total "Patch" Pumps

- Manufacturer: CeQur (Switzerland/MA)
- ETA: ??
- Same concept as the Vgo, with some improvements
- Wearable patch for 3 days
- 7 different basal rates
- Maximum daily dose: 110 units

Insulin Reservoir

- Delivers 3 days of steady basal insulin
- Provides injection-free bolus with a push of the button

Messenger

- Notifies wearer when to replace the insulin reservoir
- It is a reusable unit that is transferred to each new insulin reservoir

Mader JK, Lilly L, Aberer F, Poettler T, Johns D, Trautmann M, Warner J, Pieber T. 2018. Improved glycaemic control and treatment satisfaction with a simple wearable 3-day insulin delivery device among people with Type 2 diabetes. Diabetic Medicine. 35(10):1448–1456.

Insulin Pumps: Paq Meal & Paq Total "Patch" Pumps

- Crossover clinical trial, n = 24
- Baseline assessments
- Transition phase of at least 6 days
- 12 weeks treatment
- Significant changes in a1c realized at weeks 8 (p = 0.0001) & week 12 (p < 0.0001)

- NOTE: study funded, overseen and analyzed by CeQur

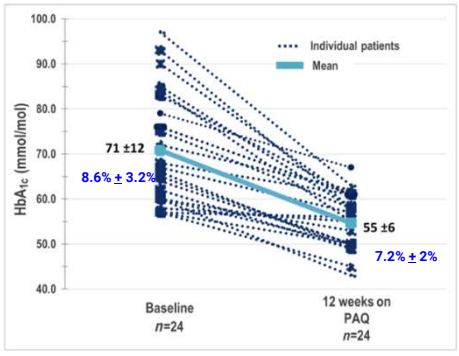


Figure 4 Open in figure viewer | PowerPoint

Change from baseline in HbA_{1c} values after 12 weeks of continuous subcutaneous insulin infusion with the PAQ. Per protocol population.

Mader JK, Lilly L, Aberer F, Poettler T, Johns D, Trautmann M, Warner J, Pieber T. 2018. Improved glycaemic control and treatment satisfaction with a simple wearable 3-day insulin delivery device among people with Type 2 diabetes. Diabetic Medicine. 35(10):1448–1456.

Insulin Pumps & More: Bigfoot Biomedical

- ETA: ?? (overdue)
- They ask the same question: “how to reduce the burden of diabetes care?”
- Developing subscription based support and bundled supplies
- Connected pens
- Closed loop system with [disposable] pump and CGM
- All overseen by developing artificial intelligence

Courtesy: Park Nicollet International Diabetes Center

Insulin Pumps & More: Beta Bionics

- Originated at Boston University
- ETA: ??
- Integrated insulin-dasiglucagon analogue pump
- Randomized in vivo crossover trial underway
- A 3-in-1 device with life long, machine-learning for individualized glucose control
- Claim fully autonomous control--no carb counting, adjusting rates or manual boluses

courtesy : Beta Bionics


American Association of Clinical Endocrinologists
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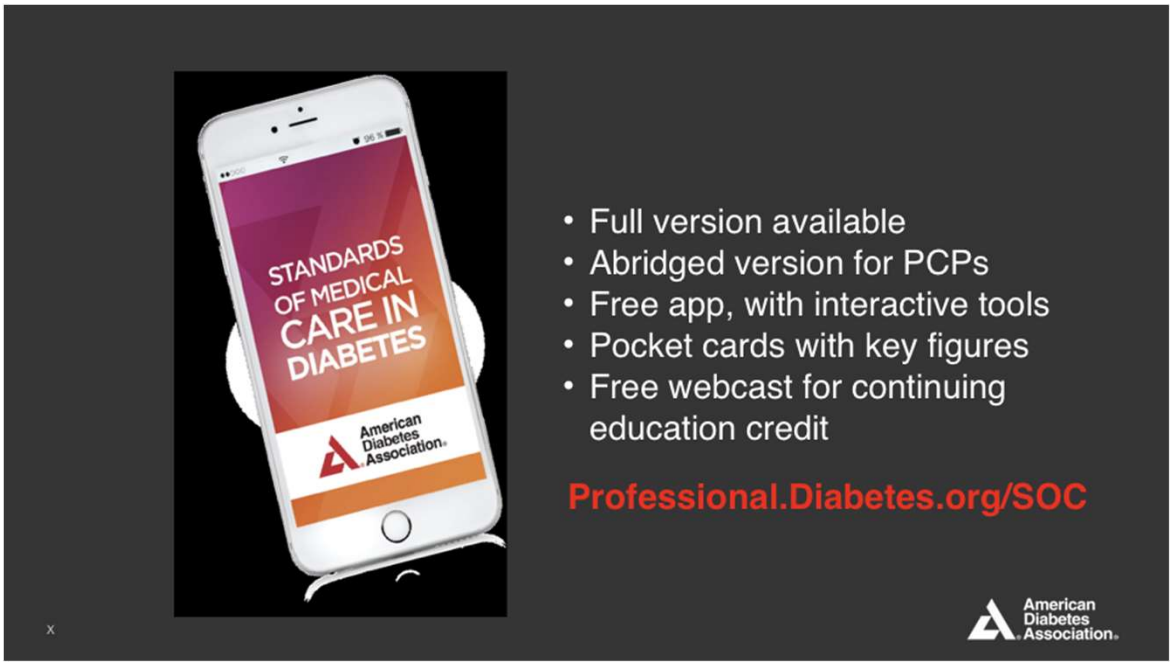
UPDATED INPATIENT RESOURCE CENTER SLIDES
In The News
randomized trial compared the efficacy and safety of the glucagon-like peptide-1 receptor agonist dulaglutide (1.5 mg and 0.75 mg) vs insulin glargine, both in combination with insulin lispro. Patients (N=577) had type 2 diabetes and moderate-to-severe chronic kidney disease.
Read more
FDA Approves First Long-Term Implantable Continuous Glucose Monitor
June 21, 2018. The US Food and Drug Administration has approved the Eversense Continuous Glucose Monitor (CGM) System by Senseonics, which is the first long-term (up to 90 days) implantable CGM. The device is implanted subcutaneously in the patient's upper arm under local anesthesia. Glucose data, stored in a HIPAA-compliant cloud, are transmitted to the user's mobile phone via Bluetooth. The device is approved for patients aged 18 years and older with type 1 or type 2 diabetes and should be used in addition to fingerstick blood

www.aace.com


STANDARDS OF MEDICAL CARE IN DIABETES
American Diabetes Association.
• Full version available
• Abridged version for PCPs
• Free app, with interactive tools
• Pocket cards with key figures
• Free webcast for continuing education credit
Professional.Diabetes.org/SOC
American Diabetes Association.

Additional Resources

For you:

Lindsey M. VanDyke

O: 817 - 453 - 7707

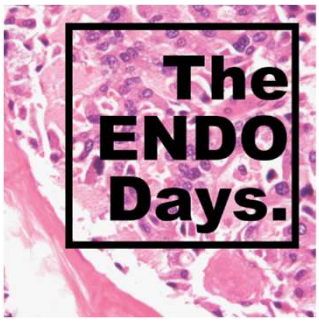
lindseyvandyke@mhd.com

Diabetes Technology Night - November 2019

For the Patients:

Podcast: The Endo Days

YouTube Channel: Mansfield Endocrine



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