ADA 2018 Summary

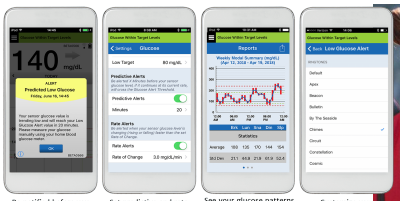
Plus Snippets of Science

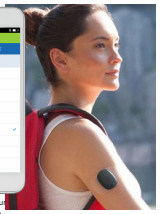
San Diego Pump Club
July 9, 2018
John Walsh, PA, CDTC

This presentation covers devices recently approved by the FDA, along with several abstracts from the 2018 ADA Convention related to Type 1 diabetes.

Sensionics Eversense XL

SQ-implanted CGM worn for 90 days with transmitter to phone attached to skin





Available now in Europe and soon in U.S.

Dexcom G6

- Slick applicator, 10 day wear, 2 yrs and older
- No fingersticks (But calibrate if it's off!)
- See BGs on display device, phone, or watch
- Sensible alarms
- Covered by Medicare
- First FDA approval as a fully interoperable CGM or iCGM
- Used for AP systems in Tandem, Omnipod, Sooil, OpenAPS

Available

Tandem t:slim X2 Basal.IQ

First half of an AP system.

Basal.IQ suspends basal delivery to prevent or reduce hypoglycemia.

Easy software updates from the web

Full TypeZero Control.IQ expected in early 2019.

Available in August

Medtronic 670 Data

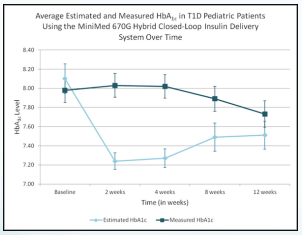
	24-hr			10:00PM-7:00AM			3:00AM-7:00AM		
	Baseline Run-in	Study	P	Baseline Run-in	Study	P	Baseline Run-in	Study	P
SG									
mg/dL	168.6±21.6	161.7±12.4	<0.001*	166.0±26.4	155.0±12.6	<0.001	157.4±29.0	141.4±12.5	<0.001
mmol/L	9.4±1.2	9.0±0.7	<0.001*	9.2±1.5	8.6±0.7		8.7±1.6	7.9±0.7	
Percentage of time in glucose range, mg/dL (mmol/L)									
<50 (≤2.8)	0.8±1.2	0.5±0.5	0.0012*	1.0±1.6	0.5±0.6	0.0125*	0.9±2.1	0.4±0.7	0.1305*
<70 (≤3.9)	4.7±3.8	3.0±1.6	<0.001*	4.9±5.2	2.4±1.6	<0.001*	5.0±6.9	2.0±1.9	<0.001*
>70-180 (3.9-10)	56.2±11.4	65.0±7.7	<0.001	56.6±15.3	70.9±9.4	<0.001*	62.1±18.4	81.5±9.8	<0.001
>180 (>10)	39.1±12.8	32.0±7.7	<0.001	38.5±16.7	26.7±9.0	<0.001	32.8±19.1	16.5±8.9	<0.001*
Total insulin delivered, units	35.7±14.6	38.5±15.5	<0.001*	8.3±3.5	8.8±3.5	<0.001*	3.7±1.8	3.5±1.6	0.2368*
No insulin delivery, minutes	23.5±38.6	395.7±97.5	<0.001	7.1±13.3	114.9±29.6	<0.001	1.9±5.1	50.8±18.5	<0.001
Within-period SG SD, mg/dL (mmol/L)	57.7±8.3 (3.2±0.5)	54.7±7.5 (3.0±0.4)	<0.001	42.1±7.9 (2.3±0.4)	39.6±6.3 (2.2±0.4)	<0.001*	20.7±5.1 (1.1±0.3)	19.4±3.5 (1.1±0.2)	0.0033
Median [IQR] Auto Mode use, %		80.6 [70.0-87.7]			81.3 [71.4-88.3]			80.7 [69.1-87.8]	

All data values are shown as mean±SD or median (IQR)
The run-in phase duration was 2 weeks and the study phase duration was 3 months
p-values were determined with paired t-test or Wilcoxon Signed Rank test*
SG = sensor glucose
SD = standard deviation

105 T1D children (10.8±1.8 yr) in 3 mo. study

Overnight to Early-Morning Glycemic Outcomes in Children Using the MiniMed™ 670G Hybrid Closed-Loop (HCL) System. 236-OR ADA 2018 Orlando; US study. This and the next slide cover data regarding use of the Medtronic 670 closed loop in children.

A1c Improvement on 670G



67 T1D patients aged 5-23

HbA_{1c} decreased from 7.98% ± 1.03% to 7.73% ± 1.03% (P=0.0008) Light blue line shows est. A1c from BG readings

Time in range (70-180) rose from 50% at baseline to 61% at 12 weeks (P<0.0001).

Time in Auto Mode declined from 75.1% at start to 68.4% at 12 weeks

Estimated A1c is derived from current BG readings. This drops rapidly at first, later climbing ner the actual A1c lab value above it. Time in range and time in auto mode are substantially lower in younger patients, partly due to the low time in auto mode.

Clinical Experience with the MiniMed 670G System in Children, Adolescents, and Young Adults with Type 1 Diabetes. 84-LB ADA 2018 Orlando; U.S. study

Sooil Dana RS Insulin Pump

- Bolus delivery from phone, pump, or meter via Bluetooth
- Open protocol, later appeal to FDA for OpenAPS (used now in Orient and EU)
- Bolus calculator subtracts IOB from carb and correction for improved safety
- More Chinese and Korean pumps and CGMs soon

FDA Submission Shortly

Omnipod Horizon Closed Loop

11 people, 1 week home CGM compared to 4 day hotel CGM with unrestricted meals **plus >30 min exercise per day** on closed loop.

Glycemic outcomes during hybrid closed-loop (HCL) and open-loop (OL) phases

Glycemic outcomes	HCL Overall	OL Overall	HCL Night (23:00 - 06:59)	OL Night (23:00 - 06:59)
Mean glucose (mg/dL)	149.7 ± 11.3	156.1 ± 28.6	151.9 ± 31.7	156.3 ± 38.5
Percent time <54 mg/dL (%)	0.2 ± 0.3	1.1 ± 1.6	0.2 ± 0.5	1.1 ± 2.1
Percent time <70 mg/dL (%)	1.9 ± 1.3	5.1 ± 4.8	0.7 ± 1.1	5.7 ± 7.4
Percent time 70-140 mg/dL (%)	49.4 ± 9.2	41.2 ± 17.6	52.7 ± 28.4	43.5 ± 20.9
Percent time 70-180 mg/dL (%)	73.7 ± 7.5	62.5 ± 16.0	73.9 ± 21.0	60.7 ± 21.8
Percent time >180 mg/dL (%)	24.5 ± 7.7	32.3 ± 18.1	25.3 ± 21.2	33.6 ± 23.5
Percent time ≥250 mg/dL (%)	4.5 ± 4.2	8.5 ± 9.1	6.1 ± 10.9	8.6 ± 14.1

This study added exercise with an unclear impact. Other Omnipod studies show significant improvements without an added exercise component.

Safety and Performance of the Omnipod® Hybrid Closed-Loop System in Adults with Type 1 Diabetes over Five Days Under Free-Living Conditions. 207-OR ADA 2018 Orlando; US study

Cell Novo Closed Loop

Cell Novo pump and Dexcom G5 sensor in 68 people, age 47.2 ±13.4 years, HbA1c 7.6 ±0.9%, diabetes 27.9 ±13.2 years. Randomized 12 weeks on and off of closed loop.

Time in 70-180 mg/dl range: 58.7% [45.2;64.9] in open loop versus 69.5% [62.4;75.6] in closed loop.

Time in hypoglycemia <70 mg/dl: 4.1% [1.9;6.1] in open loop versus 2.1% [1.2;2.6] in closed loop.

Twelve-Week Home Use of Hybrid Closed-Loop Insulin Delivery System vs. Sensor-Assisted Pump Therapy in Adults with Type 1 Diabetes—Intermediate Results of the Multicenter Randomised Crossover Diabeloop WP7 Trial. 208-OR ADA 2018 Orlando; France study

OpenAPS Closed Loop

Twenty T1D patients aged 11.9 ± 6.9 years used openAPS, Dexcom G4® CGM, and Sooil Dana R® insulin pump for an average openAPS duration of 180 days:

- Time in 70-180 mg/dl range increased from 70.1% (± 16.4) to 83.3% (± 10.1), p<0.001.
- A1C fell from 6.8% to 6.3%, p<0.001
- Time above 180 mg/dl fell from 24.7 ± 16.5% to 13.3 ± 9.4%, p<0.001
- Time below 70 mg/dl fell from 5.1 ± 3.3% to 3.4 ± 2.3%, p= 0.004.

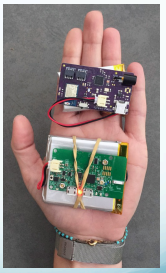
This OpenAPS study shows a significant improvement in time in range and in A1c values in patients who were already well controlled.

Open Artificial Pancreas System Reduced Hypoglycemia and Improved Glycemic Control in Patients with Type 1 Diabetes. 964-P ADA 2018 Orlando; South Korea study

OpenAPS Features

Open source developed by parents whose children have Type 1 diabetes.

- Fast adjustment when exercising or ill
- Carbs on board – fast, med, slow
- User selects own glucose target
- Always in AutoMode if CGM active
- Works on Medtronic 512-723 with firmware 2.4 or earlier, Sooil; Dexcom 4-6, Medtronic
- Cost: OpenAPS $200; Loop $135 plus $99 a year as Apple developer
- Options: Eating Soon, Autosensitivity (settings optimizer), OpenAPS Simulator (virtual testing of food/insulin options)



Loop on top
OpenAPS on bottom

http://seemycgm.com/2017/09/02/loop-vs-openaps-update/

Coefficient of Variation (CV) and Hypoglycemia

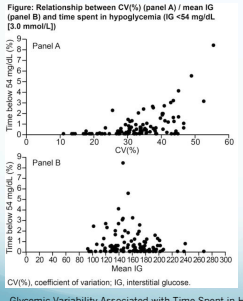


Figure: Relationship between CV(%) (panel A) / mean IG (panel B) and time spent in hypoglycemia (IG <54 mg/dL [3.0 mmol/L])

CV(%), coefficient of variation; IG, interstitial glucose.

CV = standard deviation/average BG

CV ranged from 11% to 56% in 112 Type 1s

Panel A: CV versus %time/day below 54 mg/dL (1% = ~15 min a day)

Risk of hypo greater when CV >33%

Panel B: mean BG versus %time per day below 54 mg/dL. Avg glucose has less impact on hypoglycemia

Less BG swing = less hypos!
Keep CV less than 33.

Glycemic Variability Associated with Time Spent in Hypoglycemia in Type 1 Diabetes—Explorative Data in Real-World, Real-Time Continuous Glucose Monitoring. 80-LB ADA 2018 Orlando; Denmark study

Insulin + Symlin in Closed Loop

Comparison of 1) rapid insulin-alone (AP), 2) rapid insulin & Symlin/ pramlintide (DAP), and iii), 3) regular insulin & amylin (R-DAP) in 12 adults with type 1 diabetes, all run in a closed loop system.

Table 1. Comparisons between AP, DAP, and R-DAP (mean±SD)

Outcome	AP	DAP	R-DAP	P-value DAP vs. AP	P-value R-DAP vs. AP
Time spent between 3.9 and 10.0 mmol/L during 24-hour study period (%)	71 ± 19	85 ± 10	72 ± 16	**0.03**	0.86
Mean glucose level during 24-hour study period (mmol/L)	8.2 ± 1.3	7.4 ± 1.1	7.7 ± 0.8	0.07	0.38
Coefficient of variance during 24-hour study period (%)	34 ± 11	25 ± 6	35 ± 8	**0.01**	0.65
Time spent between 3.9 and 10.0 mmol/L during daytime period (%)	58 ± 26	78 ± 16	66 ± 21	**0.02**	0.58
Mean glucose level during daytime period (mmol/L)	9.1 ± 1.9	7.8 ± 1.5	8.4 ± 1.5	**0.02**	0.34
Time spent between 3.9 and 7.8 mmol/L during overnight period (%)	77 ± 20	71 ± 29	65 ± 19	0.47	0.16
Mean glucose level during overnight period (mmol/L)	6.6 ± 0.9	6.8 ± 0.9	6.6 ± 1.2	0.51	0.87

The addition of Symlin creates a dramatic increase in time in range (delivered in a second pump?) Adding pramlintide or other amylin derivative into a fast insulin appears long overdue. The pancreas does it, why not us?

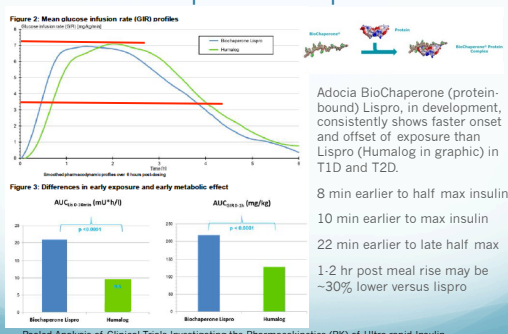
Insulin-plus-Pramlintide Artificial Pancreas in Type 1 Diabetes—Randomized Controlled Trial. 210-OR ADA 2018 Orlando; Canada study

Companion Medical InPen

- Easy to use
- Bluetooth to phone
- Excellent bolus calculator with IOB tracking
- View Dexcom data and history

Available

New BioChaperone Lispro Insulin



Adocia BioChaperone (protein-bound) Lispro, in development, consistently shows faster onset and offset of exposure than Lispro (Humalog in graphic) in T1D and T2D.

8 min earlier to half max insulin

10 min earlier to max insulin

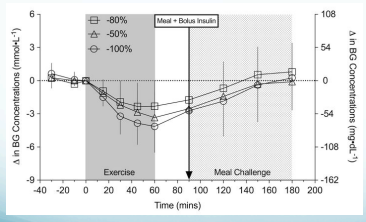
22 min earlier to late half max

1-2 hr post meal rise may be ~30% lower versus lispro

Pooled Analysis of Clinical Trials Investigating the Pharmacokinetics (PK) of Ultra-rapid Insulin BioChaperone Lispro (BCLIS) vs. Lispro (LIS) in Subjects with Type 1 (T1D) and Type 2 (T2D) Diabetes. 998-P ADA 2018 Orlando; EU and US study

When to Lower Basal for Exercise

13 Type 1s on Omnipods. Basal reduced by; a) 80%, 90 min pre-exercise; b) 50%, 90 min pre-exercise or; c) 100% at exercise onset. Full basal resumed at end of exercise with 75% of normal meal bolus after.

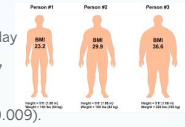


Nice glucose control with 1 hour aerobic exercise from 80% basal reduction 90 min before exercise until end of exercise, followed by 25% reduction in meal bolus afterward.

Lower basal early!

Reducing Basal Insulin 90 Minutes before Exercise Protects Against Hypoglycemia Better than Insulin Suspension at Exercise Onset in T1D—The OmniTIME Results. Abstract 65-OR ADA 2018 Orlando; Canada

Victoza in Type 1 Diabetes



Year-long study of 26 people on 1.8 mg Victoza/day vs 20 on placebo. Mean HbA1c 7.82%, mean age 46.7 ±1.9 years, age of T1D diagnosis: 22.3 ±1.7 years, BMI: 28.9±1.4kg/m^2

- HbA1c fell by 0.57% from 7.92 to 7.45% (p=0.009).
- Weekly average glucose fell by 15 mg/dl from 174 to 156 mg/dl (p=0.021). Total insulin dose did not change.
- Systolic BP fell from 128 ±3 to 122 ±3 mmHg; diastolic BP fell from 79 ±2 to 75 ±2mmHg.
- Weight loss: 2.5 ±0.9 kg (5.5 lbs, p=0.041) from 83.6 ±4.1 (184 lbs) to 80.5 ±4.0 kg (p=0.01)
- No change in hypoglycemia or time spent below 70mg/dl on CGM.

Liraglutide [Victoza] as an Additional Treatment to Insulin in Patients with Type 1 Diabetes Mellitus—A 52-Week Randomized Double-Blinded Placebo-Controlled Clinical Trial. 3-LB ADA 2018 Orlando; U.S. study

Victoza in Adult-Onset Type 1

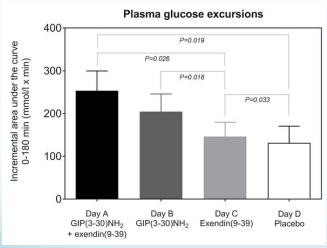
Victoza 1.8 mg a day was combined with insulin doses for 11 people with **Type 1??? diabetes** over 12 weeks.

- Mean age of diabetes diagnosis: **37 ±5 years; mean duration of diabetes: 6 ±2 years**.
- C-peptide concentrations increased significantly from 0.43 ±0.09 to 1.42 ±0.42ng/ml (p=0.01).
- HbA1c fell from 10.63 ±0.87% to 7.45 ±0.52%(p<0.01) .
- Weight fell from 71 ±2.0kg to 69 ±2kg (p=0.06).
- Total insulin dose fell by 64% from 34.45 ±5.73 to 12.27 ±4.01 units (p<0.01).
- **5 out of 11 patients no longer required insulin.**

Odd study. BMI not given, but weights do not suggest obesity. Victoza (along with metformin and Actos) has been shown to reverse and stabilize pre-diabetes. Can Victoza benefit adult onset Type 1s?

Addition of GLP-1 Therapy to Insulin in C-Peptide-Positive Patients with Type 1 Diabetes. 110-LB ADA 2018 Orlando; U.S. study

Are GLP-1 or GIP Agonists Better for BG?



Antagonists were given to 12 healthy men for gut-derived glucose-dependent insulinotropic polypeptide (GIP) and for glucagon-like peptide 1 (GLP-1) to find which is stronger at lowering glucose. More infusion of glucose was needed when GIP was blocked,

GIP appears stronger at lowering BG. Incretin therapy gets interesting.

Postprandial Effects of Individual and Combined GIP and GLP-1 Receptor Antagonization in Healthy Subjects. 145-OR ADA 2018 Orlando; Denmark study

New Therapy: SGLT-2 Inhibitors in Type 1

A meta-analysis of SGLT-2i treatments in Type 1 diabetes: 14 studies with 4,591 subjects:

- A1c reduced by 0.4%
- FBG lowered by 20 mg/dL
- Weight down 5.9 lbs (2.68 kg), systolic BP lowered 3.37 mmHg
- Approx. 2 more hours a day (8.3%) in time in range
- Total daily dose decreased 6.0 u/day, about 50% basal and bolus
- SGLT2s protect against heart failure with the metabolic syndrome
- SGLT2s increase DKA and genital infection by 3.4 fold. Avg. cost of DKA is $7,142 per episode plus some increased risk of death.

Sodium-Glucose Cotransporter 2 Inhibitors for Type 1 Diabetes Mellitus—Systematic Review and Meta-analysis. 1128-P ADA 2018 Orlando; Multiple country study

Cautions with SGLT-2 Inhibitors

Preventing DKA is critical when taking an SGLT-2 inhibitor. DKA begins at lower glucose levels when insufficient insulin levels are hidden by excess glucose passage into the urine. Dehydration may also cause a rapid rise in the glucose.

- Drink plenty of water each day.
- Test the urine periodically with Diastix of Ketodiastix strips for large glucose – a sign that insulin doses need to be increased.
- Check the blood with a blood ketone meter.
- More Type 2s are admitted to hospitals for DKA than Type 1s.
- Exercise caution on an SGLT-2 inhibitor, as well as the upcoming SGLT-1 and SGLT-2 combination drugs.

Sodium-Glucose Cotransporter 2 Inhibitors for Type 1 Diabetes Mellitus—Systematic Review and Meta-analysis. 1128-P ADA 2018 Orlando; Multiple country study

AGEs Predict Kidney Disease in DCCT

109 people with diabetic kidney disease (>40% eGFR decline from baseline on 2 consecutive visits) compared to 350 controls.

GFR decline was predicted by 3 **Advanced Glycated Endproducts**:

- Carboxymethyllysine (CML, p=0.003)
- Carboxyethyllysine (CEL, p=0.021), and,
- 3-deoxyglucosone hydroimidazolone (3DG-H, p=0.0007).

- 3DG-H significantly increased predictive value for progression of kidney disease (and atherosclerosis) above traditional risk factors.

Take home: Not yet available as a routine lab test. Oxidation by free radicals trigger the reactions that form AGEs. Block AGEs with AGE inhibitors and antioxidants.

Advanced Glycation End Products (AGEs)—Role in Development and Progression of Kidney Disease in Type 1 Diabetes in DCCT/EDIC. 521-P ADA 2018 Orlando; Denmark study

Lysulin as AGE Blocker

Company formed by CEO John Burd PhD, former CEO of Dexcom.

Lysulin is composed of:

- **Lysine** as an amino acid may reversibly bind to glucose and may prevent formation of irreversible AGEs. Lysine and valine in proteins and enzymes are primary targets for AGE formation.
- Plus **vitamin C and zinc**

Minimal research other than for cold sores. Early treatment of rats with lysine prevented rise in HbA(1) (normal 6.98 +/- 0.71% vs. diabetic 7.78 +/- 1.50%; p = NS), reduced glycosylation of glomerular basement membrane collagen in kidney by 86%, and significantly reduced albuminuria.

Advanced Glycation End Products (AGEs)—Role in Development and Progression of Kidney Disease in Type 1 Diabetes in DCCT/EDIC. 521-P ADA 2018 Orlando; Denmark study

Alternative AGE Inhibitors

SuperLysine

- 1,500 mg lysine a day, vit C, propolis, echinacea, licorice root, and garlic bulb for 60 days: $10.72.

Carnosine or beta alanine or L-histadine

- Composed of amino acids beta-alanine and L-histidine, now being analyzed in a study in **Obesity**.
- Extensive animal and some human research shows reduced oxidation, glycation, protein cross-linking, mitochondrial dysfunction, telomere shortening, and transition metal accumulation.

http://www.lifeextension.com/Magazine/2016/12/Carnosine/Page-01
Diabetes 54:2320 –2327, 2005
Obesity (Silver Spring). 2016 May;24(5):1027-34.

N-Acetyl Cysteine Lowers REDD1

- High glucose levels in diabetic mice raises stress response protein REDD1 in retina. REDD1 forms an oxidation complex that creates excess free radicals.
- This causes nerve cells to die in early retinopathy, first recognized as a loss of contrast sensitivity.
- In mice, the antioxidant N-acetyl-L-cysteine (NAC) prevents the rise in free radicals, nerve cell death, and loss of contrast sensitivity.
- NAC increases the major cell antioxidant glutathione

Deletion of REDD1 Prevents Hyperglycemia-Induced Reactive Oxygen Species Accumulation and Retinal Cell Death. 242-OR ADA 2018 Orlando; US study

An Anti-AGE Regimen

- Alpha lipoic acid (strong antioxidant), 240 mg BID
- Alternate 2 flax with 2 borage oil capsules a day
- N-acetyl-cysteine (strong antioxidant), 600 mg BID
- Lysine or L-carnitine
- Jarrow B-Rite (methylated vit B complex), one a day
- Mitochondrial Energy Optimizer with PQQ, 1 a day

More food/nutrient research is needed!!!

Risks for CVD from Type 1 Exchange

4,463 T1s (55% female, 91% non-Hispanic white, avg age 41 years, T1D duration 21 years). At enrollment, avg HbA1c was 7.7%, 43% used statins, and 45% used BP meds. Incident CVD was reported by 419 (9.4%) participants during the 5-year follow-up.

Sex, mean HbA1c (0.97), HbA1c variability (0.95), pulse pressure (1.03), LDL (0.99), and hypertension (1.16) were not associated with CVD.

Age at baseline (1.59) and diabetes duration (1.36) carry greater odds of CVD. Markers of insulin resistance (elevated BMI (1.02) and triglycerides (1.03)) and diabetic nephropathy, microalbumin (1.89), macroalbumin (2.29), and low eGFR (1.29), are important modifiable risk factors for CVD. Higher HDL (0.83) was protective.

Insulin resistance (abdominal obesity, low HDL, high TGs, high BP, PCOS, gout) **and especially kidney disease are risk factors for CVD with Type 1.**

Impact of cholesterol is lessened in this study due to frequent (43%) use of statins. Women (48% of CVD cases) have similar risk as men.

Risk Factors for Cardiovascular Disease (CVD) in Adults with Type 1 Diabetes (T1D). 15-LB ADA 2018 Orlando; U.S. study

CVD Risks: DCCT/EDIC vs Pitt. EDC

DCCT/EDIC; 27 yo & 12 yr DM duration at start; #726; 27 yr FU; **high BP & chol pts excluded**:

- A1c major predictor
- T1D duration, SBP, LDLc, & smoking have similar impacts
- ACE inhibitors and lower heart rate are protective
- Renal status not a factor

Pittsburg Epid of DM Study; 27 yo with 18 yr DM duration at start; #658; 25 yr FU; **high BP & chol pts included**:

- BL smoking (HR 1.9),
- MA/creat (HR 1.3))
- Avg. A1c (HR 1.2)
- BL T1D duration (HR 1.1)
- Avg.Syst. BP (HR 1.03)
- Avg. LDLc (HR 1.01)

Over time, smoking, insulin resistance, kidney disease, and high A1c carry the greatest risks for CVD. All are clearly or potentially modifiable.

Risk Factors for Major Atherosclerotic Cardiovascular Events (MACE) in Type 1 Diabetes (T1D)—The Pittsburgh Epidemiology of Diabetes Complications (EDC) Study. 183-OR ADA 2018 Orlando; U.S. study

Risks for 2 or More Diab. Complications

Selected characteristics and prevalence of 2+ complications at follow-up by risk factor clusters

	Cluster 1 (n=261)	Cluster 2 (n=509)	Cluster 3 (n=348)	Cluster 4 (n=24)	p-value
NHW (n, %)	217 (83.1)	395 (77.6)	257 (73.9)	15 (62.5)	0.002
Private insurance (n, %)	211 (80.8)	386 (76.1)	222 (64.2)	9 (37.5)	<0.001
A1c (%)	8.5 ± 1.5	9.0 ± 1.7	9.7 ± 1.9	11.8 ± 2.0	<0.001
Non-HDLc (mg/dl)	79.0 ± 12.9	105.7 ± 12.2	147.9 ± 21.5	245.5 ± 33.5	<0.001
Waist to height ratio	0.44 ± 0.05	0.46 ± 0.06	0.49 ± 0.07	0.50 ± 0.05	<0.001
Mean arterial pressure (mmHg)	80.0 ± 8.0	82.6 ± 8.6	82.4 ± 8.4	84.4 ± 10.1	<0.001
≥2 complications (n, %)	6 (2.3)	32 (6.3)	28 (8.0)	5 (20.8)	<0.001

Risk factors for having 2 or more early diabetes complications were evaluated among 1327 SEARCH T1DM participants aged 10-30 years followed up for 18 years. Retinopathy, kidney disease, peripheral neuropathy, cardiovascular autonomic neuropathy, and arterial stiffness were assessed at follow-up.

Lack of insurance, higher A1c and cholesterol, abdominal obesity, and high BP all carry a significantly higher risk for developing complications.

Co-occurrence of 2+ Early Complications in Type 1 Diabetes—SEARCH for Diabetes in Youth. 1366-P ADA 2018 Orlando; U.S. study

New Therapy? BCG Tuberculosis Vaccine

Denise Faustman, MD, Massachusetts Gen. Hospital has followed 6 T1s, 3 of whom who received two Connaught BCG vaccines a month apart 8 yrs earlier.

- A1cs lower: 6.18% vs 7.07% at 5 yrs, and 6.65% vs 7.22% at 8 yrs ($p<0.0002$), with no additional hypoglycemia. On insulin pumps, no CGMs.
- Increases aerobic glycolysis for faster cell glucose utilization.
- Stimulates production of tumor necrosis factor (TNF) that in turn triggers cell death in abnormal, disease-causing T cells. Clinical trials are underway in multiple sclerosis and Type 1 diabetes.
- Resets T-regulatory genes for improved immune tolerance with short-term increase in insulin production.
- Benefit start 2-3 years after vaccination; cost <$20; various BCG strains differ – Connaught and Moreau strains may be more protective.
- **Small but very interesting study with good outcome data in MS. Testing of various BCG strains and vaccination number/interval seems warranted.**

Repeat BCG Vaccination Creates Lasting Reductions of HbA1c in Subjects with Long-Term Type 1 Diabetes—Long-Term Clinical Trial Follow-up. 109-LB ADA 2018 Orlando; U.S. study

Future Technology
ConvaTec Lantern 7-Day Infusion Set

Study of 16 C-peptide negative T1s (44.2 ± 15.4 years, BMI 24.5 ± 2.3, A1c 7.2%, diab. duration 20 ± 9 years)

GIR curve over 8 hours (874.2 ± 1.4 vs. 744.5 ± 1.7 vs. 509.2 ± 2.0 on days 1, 4 and 7, respectively; p<0.05). That is, insulin action **declines** over 7 days.

The novel Lantern catheter can be worn for 7 days but further testing is needed to find why insulin action is lost.

Other companies also working on longer infusion set wear.

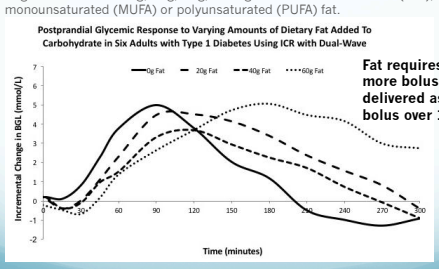
Assessment of Infusion Set Survival of the Newly Developed Lantern Catheter in Type 1 Diabetes by Glucose CLA Technique, 89-LB ADA 2018 Orlando; U.S. study

Better Bolus Calculator Apps

- **mySugr** https://mysugr.com/mysugr-bolus-calculator-2-1/
- **AccuChek Connect** https://www.accu-chek.com/data-management/connect-app
- **Companion Medical** for iPhone https://itunes.apple.com/us/app/companion-inpen-app/id1236236656?mt=8
- **Sugar.IQ** for Medtronic Guardian Connect https://www.medtronicdiabetes.com/products/sugar.iq-diabetes-assistant

Glucose Impact of Dietary Fat

Six adults with T1D using insulin pump therapy attended the research clinic on 9 to 12 occasions. On the first 6 visits, participants consumed meals containing 45g CHO with either 0g, 20g, 40g, or 60g fat and either saturated (SFA), monounsaturated (MUFA) or polyunsaturated (PUFA) fat.



Fat requires 20-60% more bolus insulin, delivered as a combo bolus over 1.25-2 hrs.

Relationship between Amount and Type of Dietary Fat, Postprandial Glycemia, and Insulin Requirements in Type 1 Diabetes. 290-OR ADA 2018 Orlando; Australia and US study

Seasonal Trends in Type 1

The average A1c was shown to vary by season in 453 Polish Type 1s over a 9 year period:

- July – 6.8%
- February – 7.3%

The Good: insulin doses will go farther with global warming.

The Bad: Type 1 diabetes will increase as enterovirus and dust levels rise.

The Ugly: its already well underway.

Take home: more insulin in winter, no change in summer?

And what the hell is Poland doing to get these A1cs?

Seasonal Trends in HbA1c Level in Adult Patients with Type 1 Diabetes Treated with Personal Insulin Pumps. 1677-P ADA 2018 Orlando; Poland study

Thank You