EPIC DIABETES CONFERENCE

MAY 20, 2023 | SHERATON DENVER DOWNTOWN HOTEL

EMPOWERING PATIENTS FOR INDIVIDUALIZED CARE

Barbara Davis Center for Diabetes
Children's Diabetes Foundation

KEYNOTE ADDRESS

LONG-TERM STRATEGIES FOR HEALTHY LIVING WITH DIABETES:

Jennifer L. Sherr, MD, PhD
Professor of Pediatrics, Pediatric Endocrinology
Yale University School of Medicine

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LONG-TERM STRATEGIES FOR HEALTHY LIVING WITH DIABETES:
MOVING BEYOND INSULIN THERAPY

Jennifer L. Sherr, MD, PhD
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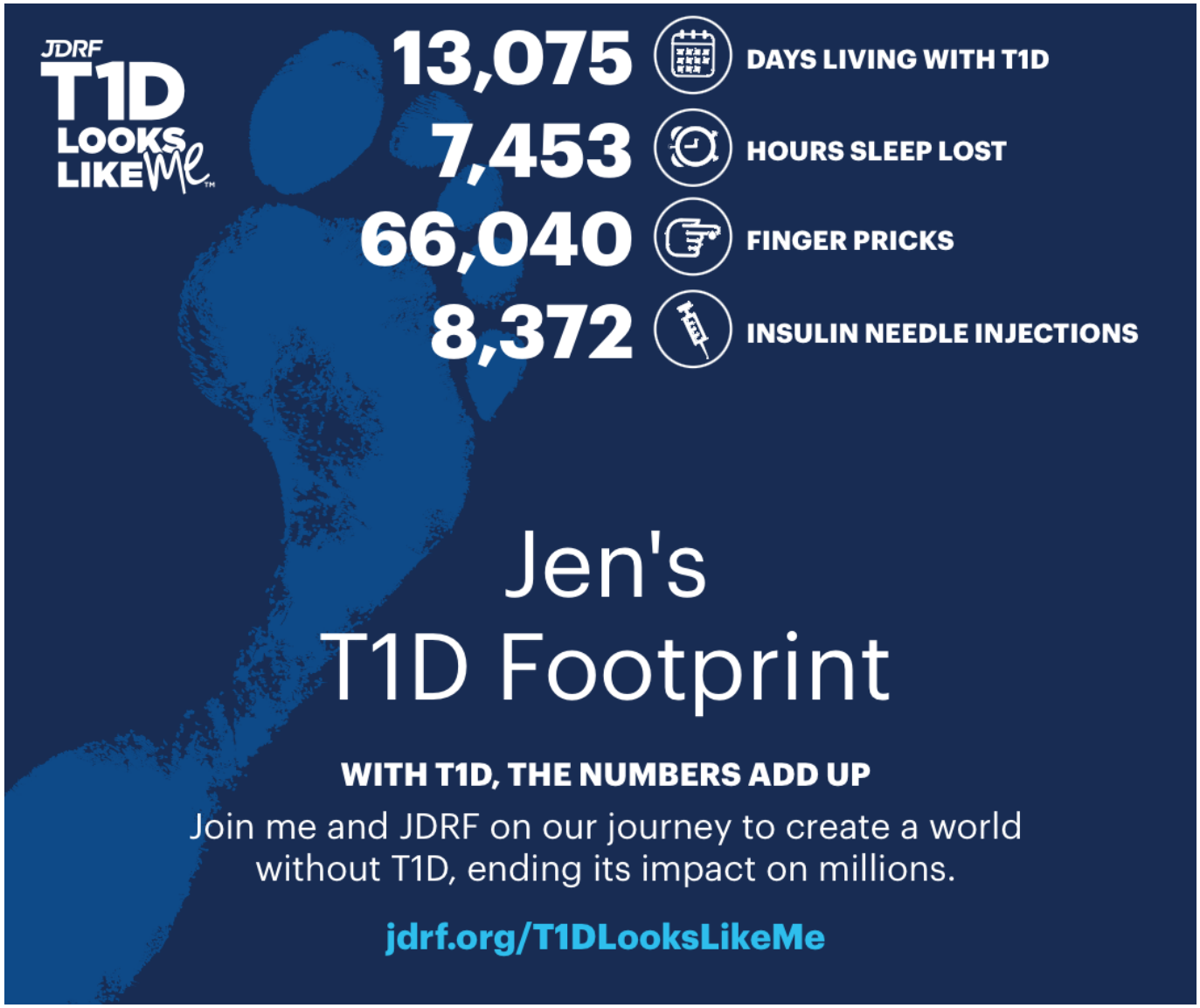
CONFLICT OF INTEREST DISCLOSURE

Research Contracts: Abott Diabetes, JDRF, Insulet, Medtronic, NIH, Provention Bio, Type 1 Diabetes Exchange

Consulting: Abott Diabetes, Bigfoot Biomedical, Insulet, Medtronic, Zealand

Advisory Boards: for Bigfoot Biomedical, Cecelia Health, Insulet Corporation, Medtronic Diabetes, Startup Health Diabetes Moonshot, and Vertex



Antihero by Taylor Swift
(a story about my
pancreas)

“It’s me, hi.
I’m the problem. it’s me.”

THE DISCOVERY OF INSULIN...

DIABETES SUFFERERS GIVEN MESSAGE OF HOPE

Discovery Made at University of Toronto Will Be Means of Prolonging Life Considerably—F. G. Banting and C. H. Best Pushed Experiments All Last Summer.

BANTING STAKES HIS ALL ON THE RESULT

A message of hope to sufferers from diabetes goes out authentically to-day from the medical research laboratories of the University of Toronto. The modesty of medical men and scientific investigators of the genuine brand attempts to minimize the results obtained. The harm of exaggeration and the injustice to both patients and research men in awakening false and premature hopes before the extracts can possibly be manufactured cannot be overemphasized. But the fact remains that one of the most important discoveries in modern medical research has been made at the university here. It is not a cure for diabetes, its authors state. Within six months, however, their discovery will be used on a large scale, they hope, to prolong life quite considerably at least. There will be no secrecy, as from the beginning. The medical profession will know all the facts.

Most significant of all the statements in the article issued by the experimenters to the medical profession to-day in the Canadan Medical Association Journal is the little sentence: "The effects observed in depancreatized animals have been paralleled in man." An active pancreatic extract discovered and prepared by two young doctors, F. G. Banting and C. H. Best, the principal experimenters, first prolonged the life of a diabetic dog fifty-six days beyond the records established before. A definite improvement in the condition of seven human pa-

Prof. J. J. R. Macleod, an investigator himself in this field of research for over 15 years, that every opportunity was given to the young doctor from London to push on his experiments. As the best man to assist Dr. Banting, Prof. Macleod chose Charles H. Best, a clever young graduate in the physiology and biochemistry course, who celebrated his twenty-third birthday a few days ago. Together they concentrated upon the problem in hand.

Work on the new hypothesis began in May. All through the heat of the summer the two young men, soon fast friends, pushed their experiments night and day. Both had served overseas. They had this in common too, and they often slept beside their work.

Everything that Banting possessed in the world he staked on the result. He had just been appointed to a junior position in surgery and an assistant in general physiology at the University in London, Ontario, when he got his idea while reading an article dealing with the Isles of Langerhans, a peculiar tissue of the pancreas to which no definite function had been proved up to that time. Banting had won his licentiate of the Royal College of Physicians and his membership in the Royal College of Surgeons overseas, and was not a "green" youth by any means.

Strangely slow in speech and unassuming, he might be, but also strangely he soon won the reputation of coming across with the punch at the critical moment. Going overseas with the C.A.M.C. in 1917, the year after graduation at Toronto

Pictures from University of Toronto website

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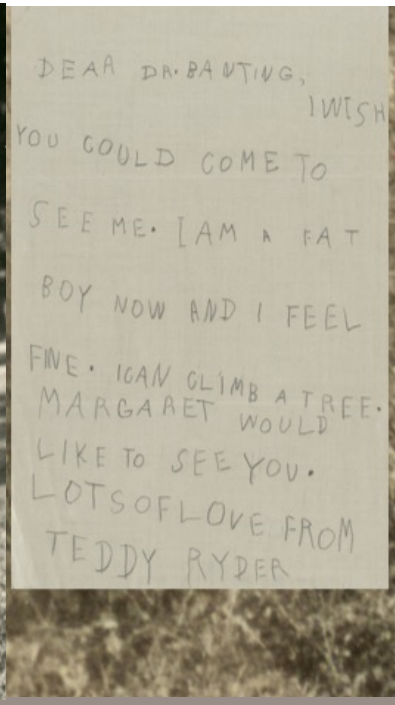
THE DISCOVERY OF INSULIN…

CHANGING A DEATH SENTENCE INTO A CHRONIC CONDITION



Pictures from University of Toronto website

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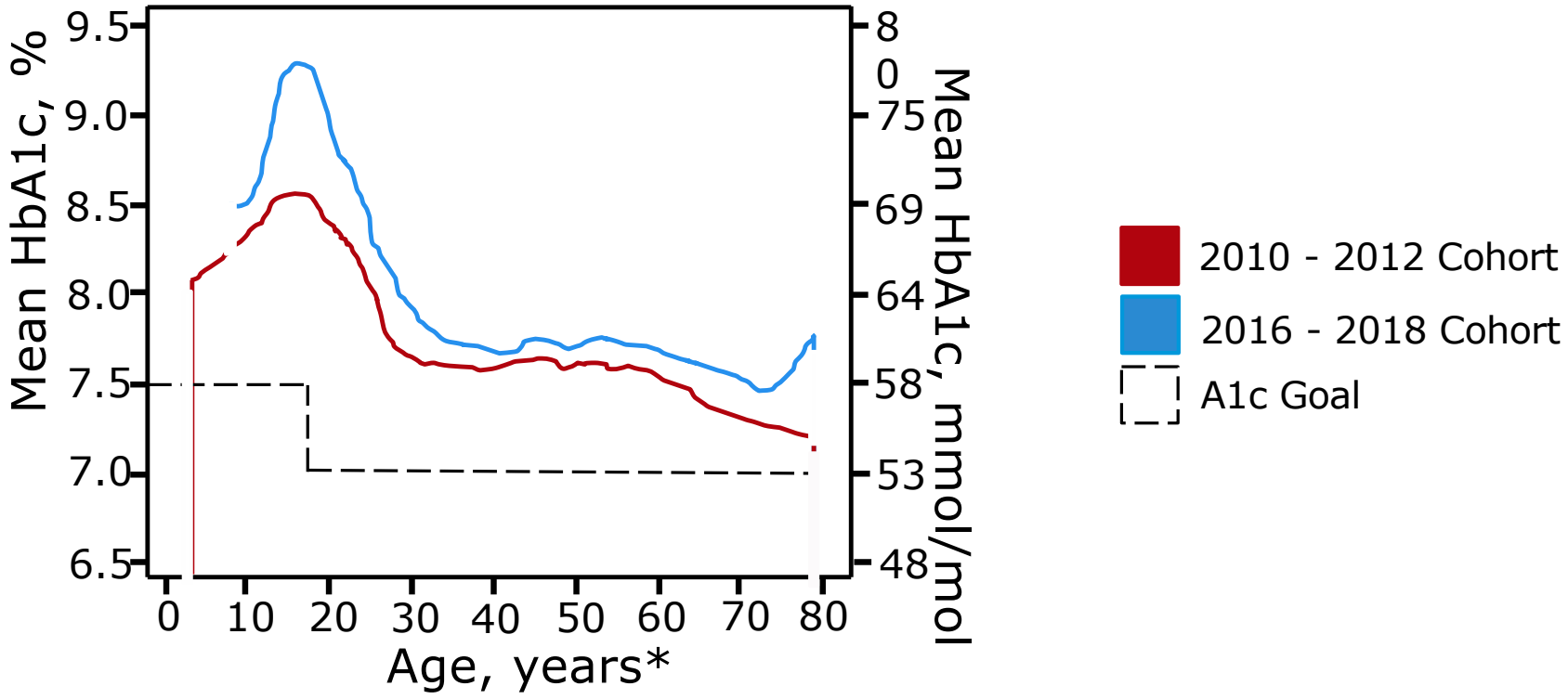
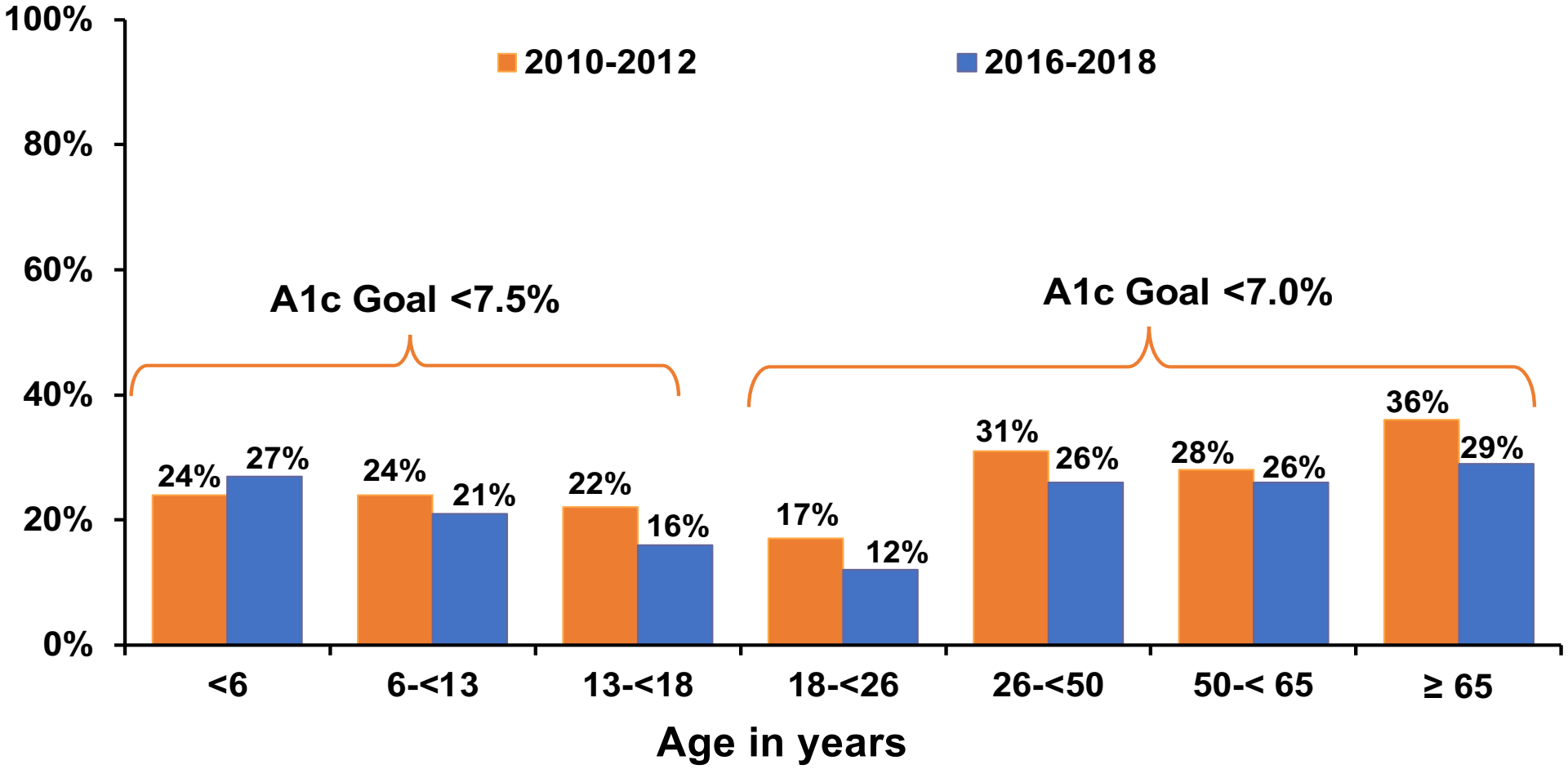
A Grim Picture - the State of Type 1 Diabetes



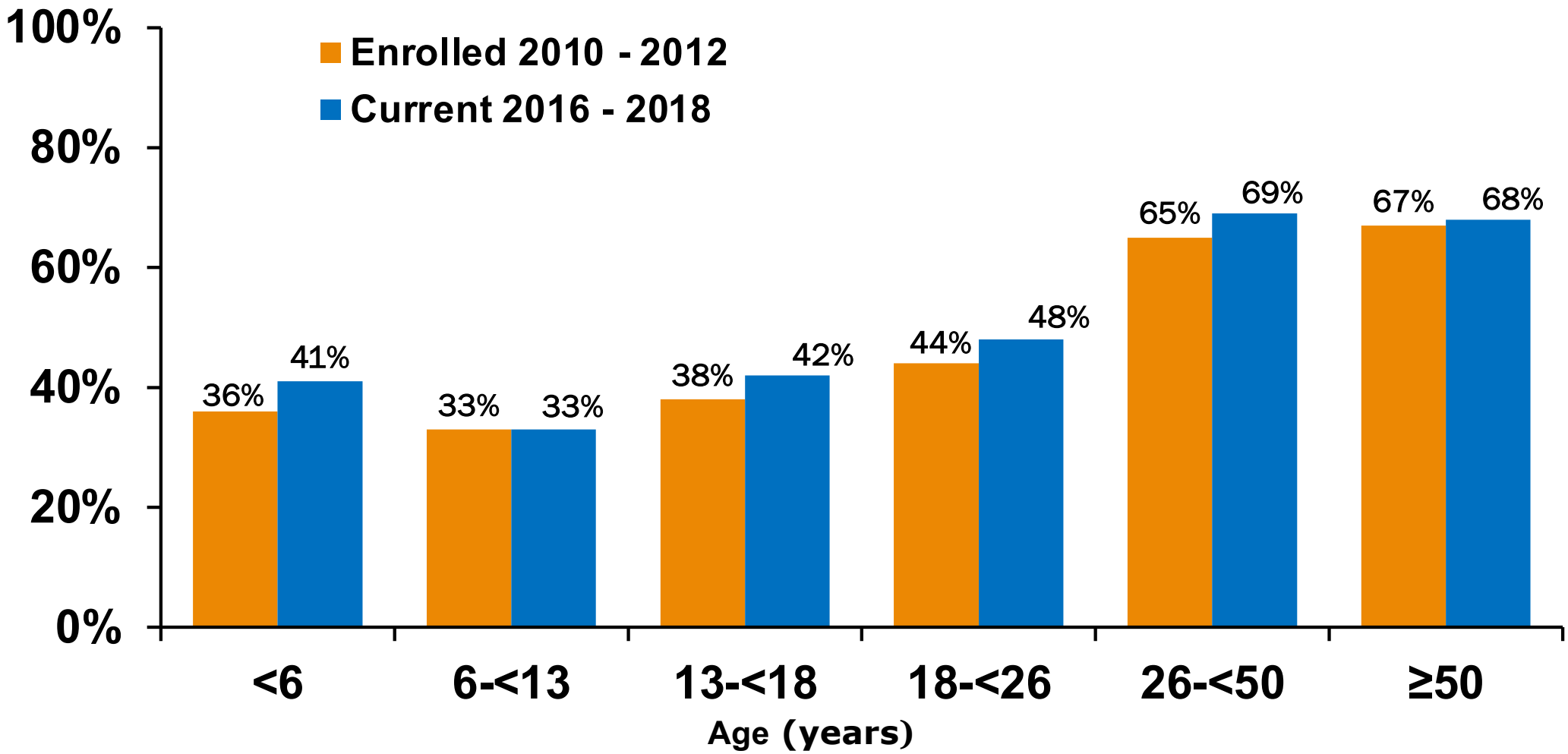
Foster NC, Roy W Beck RW, Miller KM1, et al. State of Type 1 Diabetes Management and Outcomes From the T1D Exchange in 2016-2018 Diabetes Technol Ther. 2019 Feb;21(2):66-72. doi: 10.1089/dia.2018.0384.

MOST INDIVIDUALS WITH T1D HAVE GLYCEMIA ABOVE TARGETS



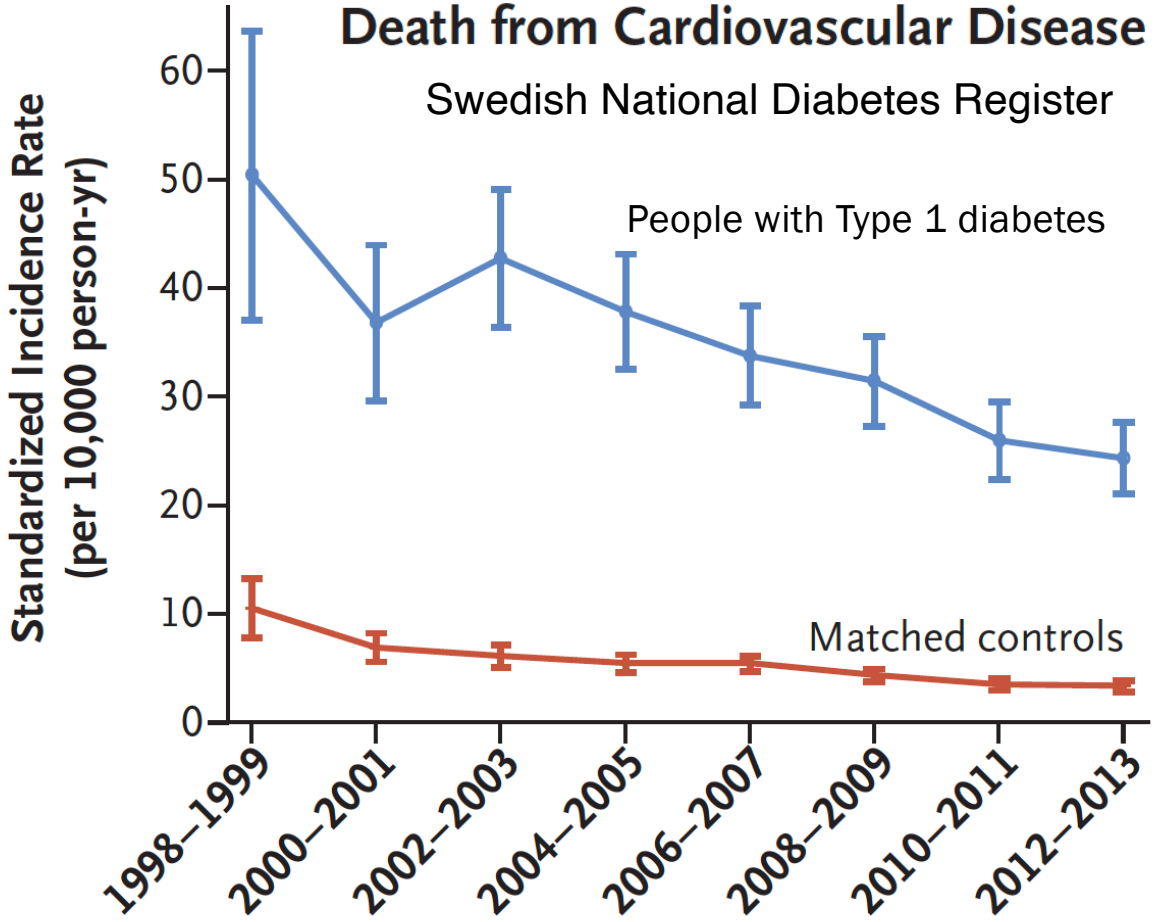
Foster et al. State of Type 1 Diabetes Management and Outcomes from the T1D Exchange in 2016-2018 DTT 2019; 21 (2):66-72

MANY WITH T1D HAVE OVERWEIGHT/OBESE BMI



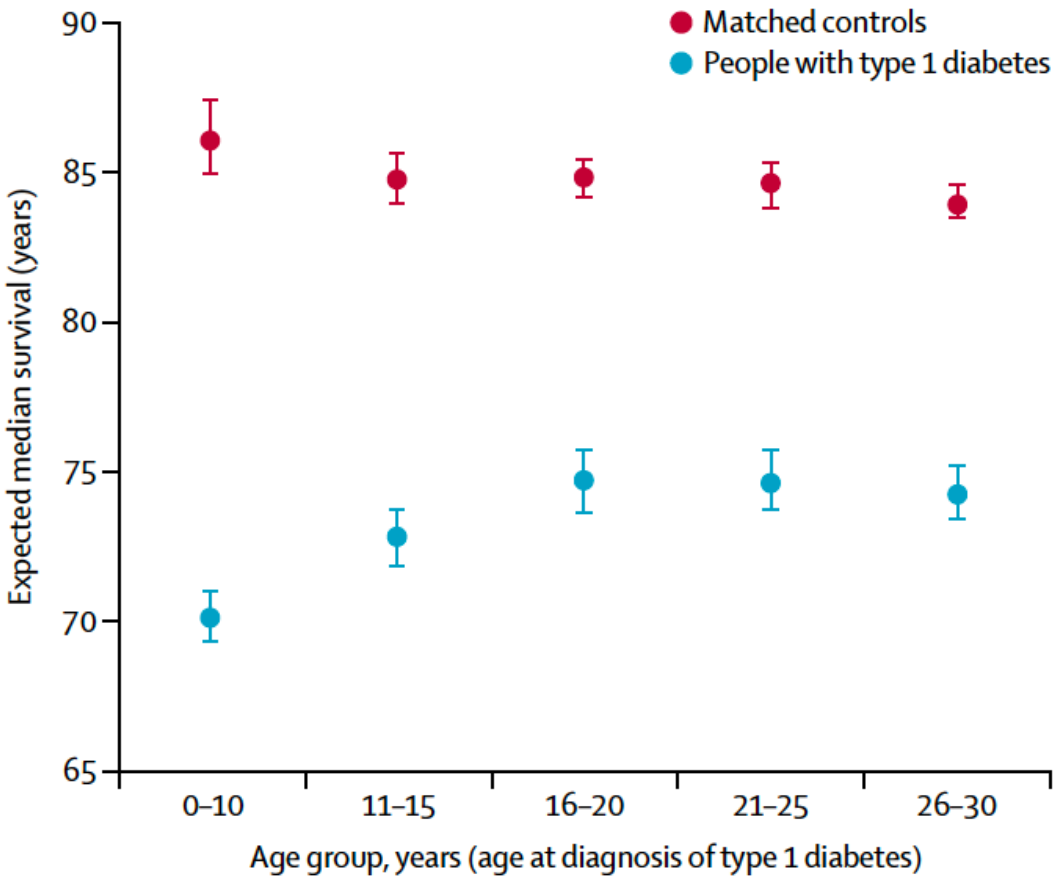
Foster et al. State of Type 1 Diabetes Management and Outcomes from the T1D Exchange in 2016-2018 DTT 2019; 21 (2):66-72

CARDIOVASCULAR DISEASE RISK IS HIGH IN T1D



Rawshani A, Rawshani A, Franzen S, Eliasson B, Svensson AM, Miftaraj M, McGuire D, Sattar N, Rosengren A, Gudbjornsdottir S. Mortality and Cardiovascular Disease in Type 1 and Type 2 Diabees. NEJM 2017; 376: 1407-18.

CVD RISK IS ASSOCIATED WITH AGE OF ONSET



Development of type 1 diabetes before age 10 resulted in a loss of **17.7 life-years for women and 14.2 life years for men.**

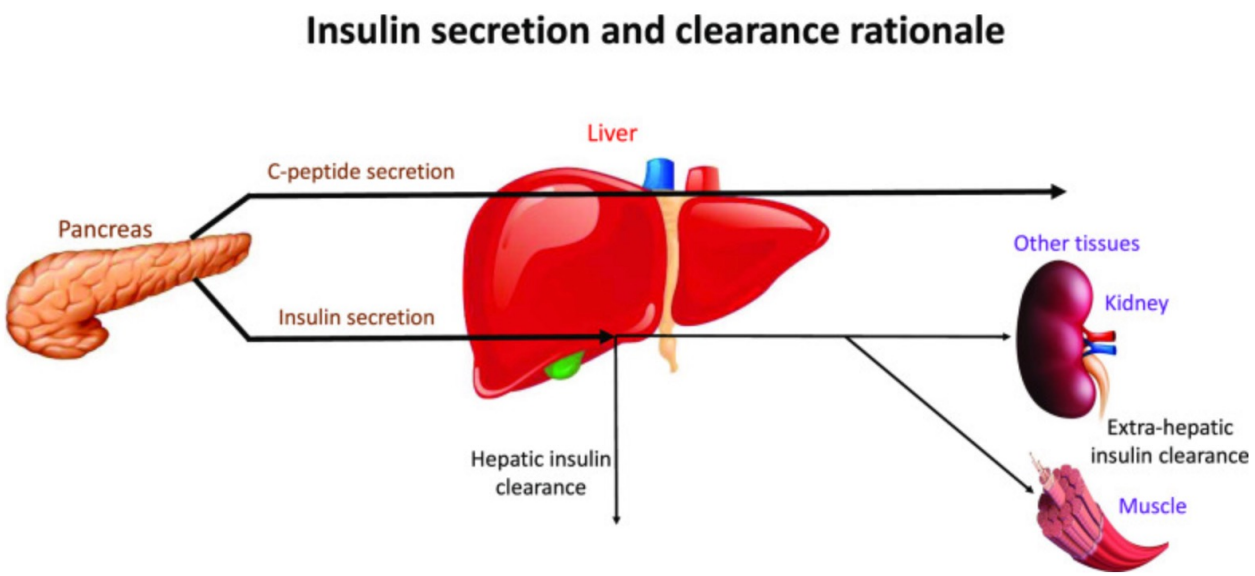
Life lost **was ~10 years** for those diagnosed later in life.

Rawashani A, Sattar N, Franzen S, Rawshani A, Hattersley AT, Svensson AM, Eliasson B, Gudbjornsdottir S. Excess mortality and cardiovascular disease in young adults with type 1 diabetes in relation to age at onset: a nationwide, register-based cohort study. Lancet 2018; 392:477-86.

IS TOO MUCH INSULIN A PROBLEM?

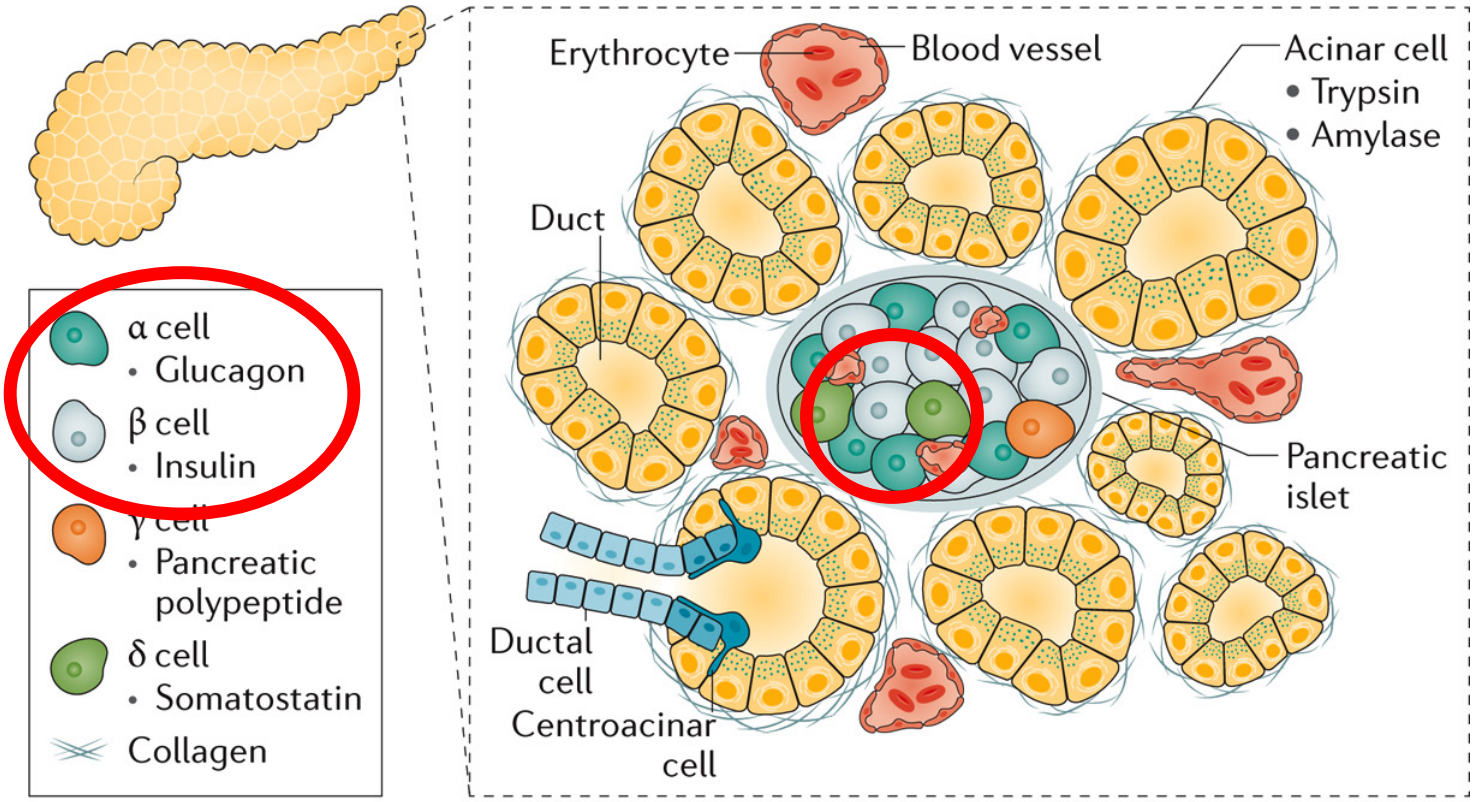
ISSUES WITH SUBCUTANEOUS INSULIN DELIVERY

- Insulin is released from the pancreas.
- More than 50% is cleared by the liver.
- Thus, injected insulin needs to be 2X higher than what the body would make.
- These high insulin levels make people more insulin resistant.



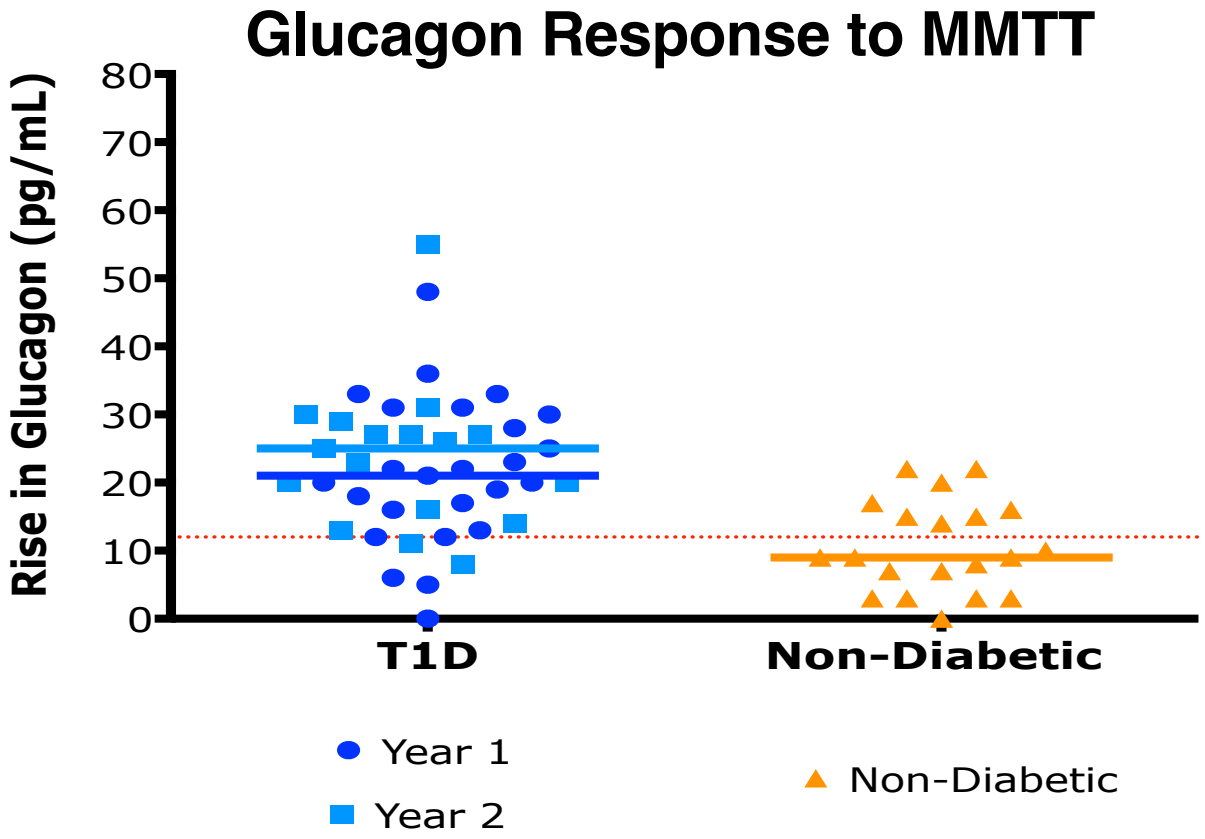
Gregory, J. M., et al. The Peripheral Peril: Injected Insulin Induces Insulin Insensitivity in Type 1 Diabetes. Diabetes 2020; **69**(5): 837-847. Gregory JM, Smith TJ, Slaughter JC, et al. Iatrogenic hyperinsulinemia, not hyperglycemia, drives insulin resistance in type 1 diabetes as revealed by comparison with GCK-MODY (MODY2). Diabetes 2019;68:1565–1576
Figure from: Piccini F, Bergman RN. The Measurement of Insulin Clearnace. Diabetes Care 2020; 43 (9):2296-2302.

INSULIN IS NOT THE ONLY PROBLEM , GLUCAGON ALSO LEADS TO ISSUES



Nature Reviews | Gastroenterology & Hepatology

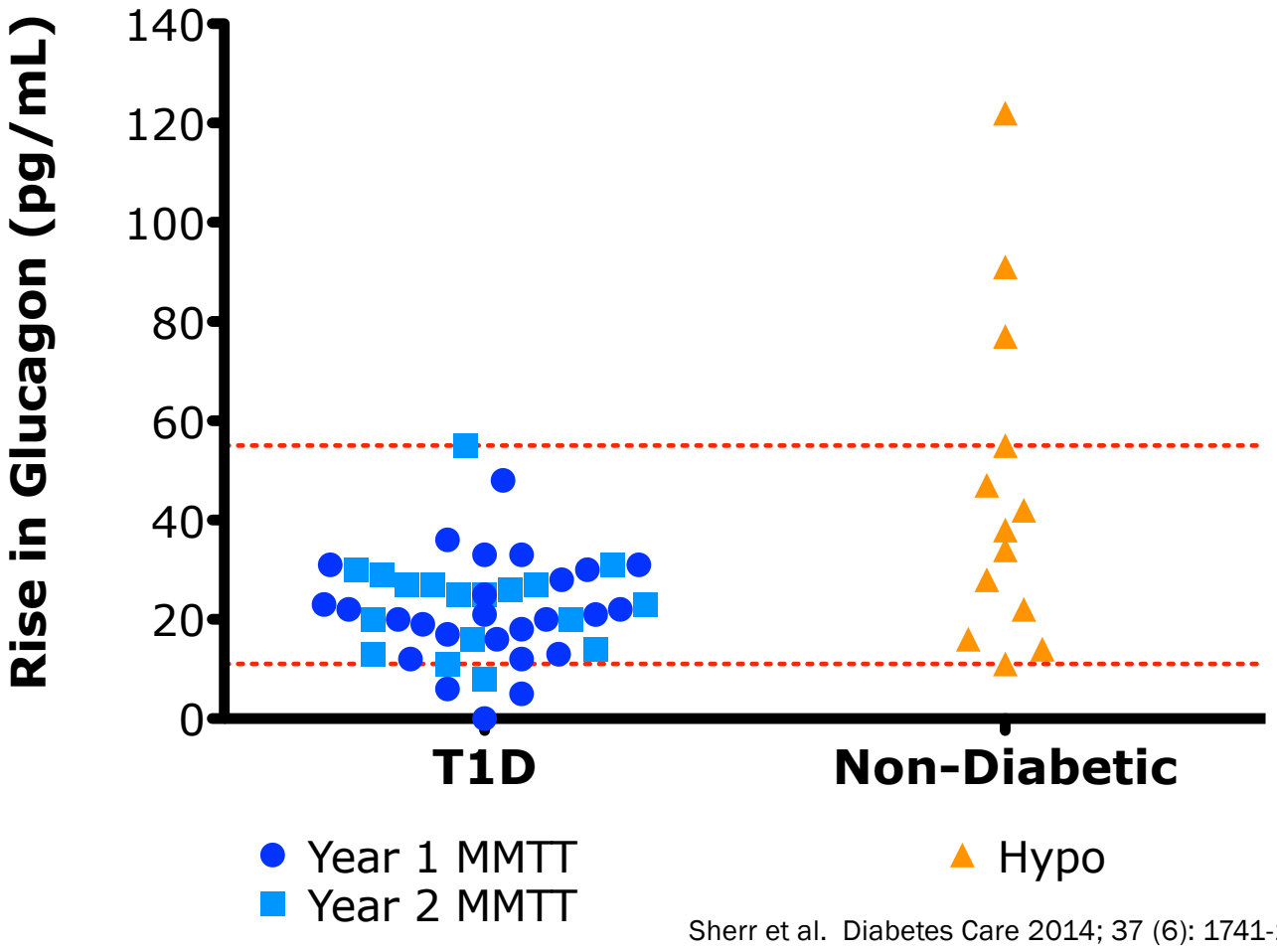
INAPPROPRIATE GLUCAGON RELEASE CONTRIBUTES TO HYPERGLYCEMIA



Mixed meal tolerance test=
Boost High Protein Shake

Sherr et al. Diabetes Care 2014; 37 (6): 1741-1744.

GLUCAGON RISE WAS SIMILAR TO HEALTHY CONTROL RESPONSE TO LOWS



Hypoglycemia (or a low) for healthy controls was induced with IV insulin

Sherr et al. Diabetes Care 2014; 37 (6): 1741-1744.

HOW DO WE THINK ABOUT GOALS FOR DIABETES MANAGMENT?

WHAT ARE SOME POTENTIAL GOALS FOR TREATMENT?

- To achieve glycemic targets
- To maintain healthy body weight
- To reduce risk of long-term complications of diabetes
- To tackle abnormal glucagon response
- To minimize the burden of disease

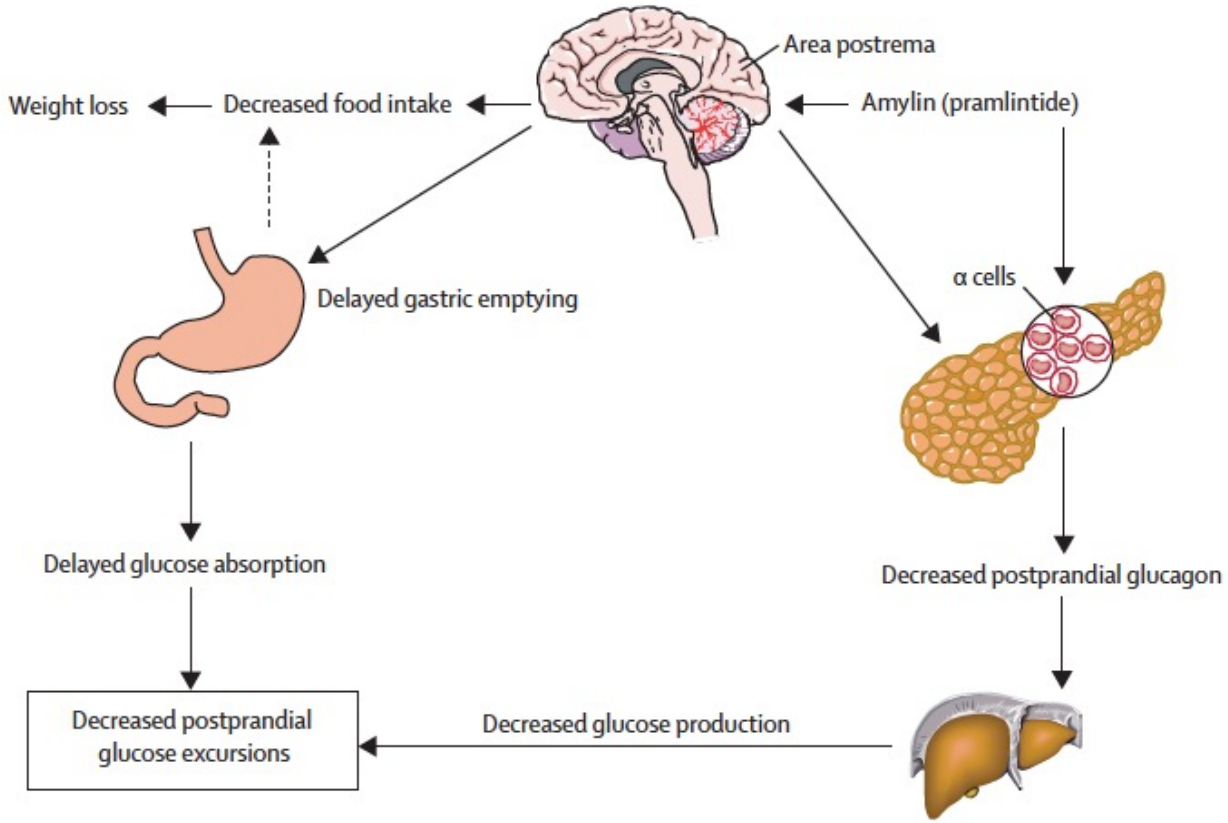
The Caveat: *Care plans need to be individualized with shared goal setting between people with diabetes and their providers*

WHAT IS IN OUR ARSENAL FOR MANAGEMENT OF TYPE 1 DIABETES?

WHAT MEDICATIONS ARE APPROVED FOR USE IN PEOPLE WITH T1D?

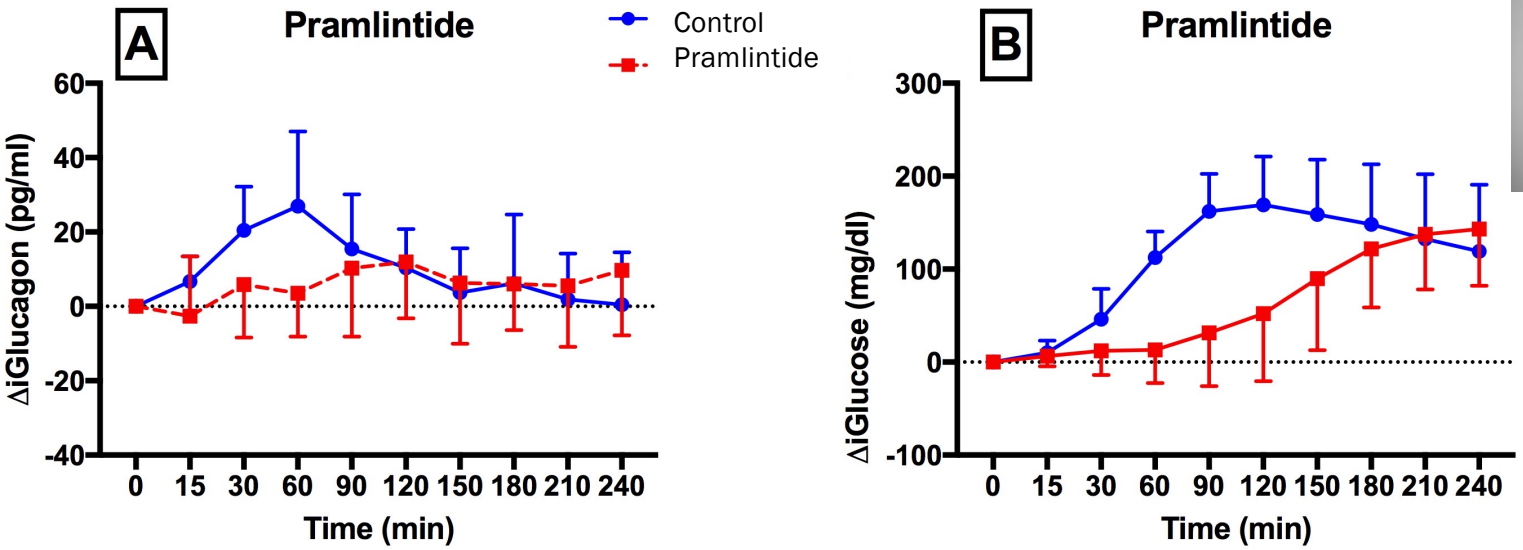
Insulin

Pramlintide



Seerup Frandsen Lancet Diabetes and Endocrinology 4(9):766-780. doi:10.1016/S2213-8587 (16)000395

HOW DOES IT WORK?



Dr. Alfonso Galderisi
Assistant Professor

There was a 39% reduction in both glucose and glucagon in the 4-hours after a mixed meal with pramlintide

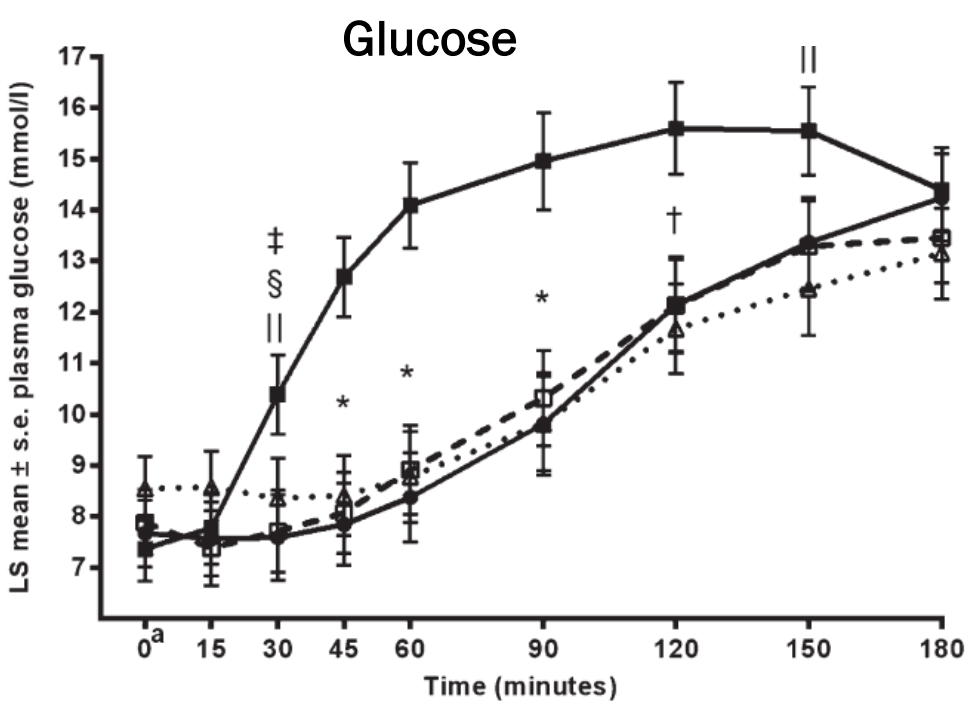
Galderisi, Sherr et al. JCEM 2018; 103 (3):1088-1094. doi10.1210/jc.2017-02265

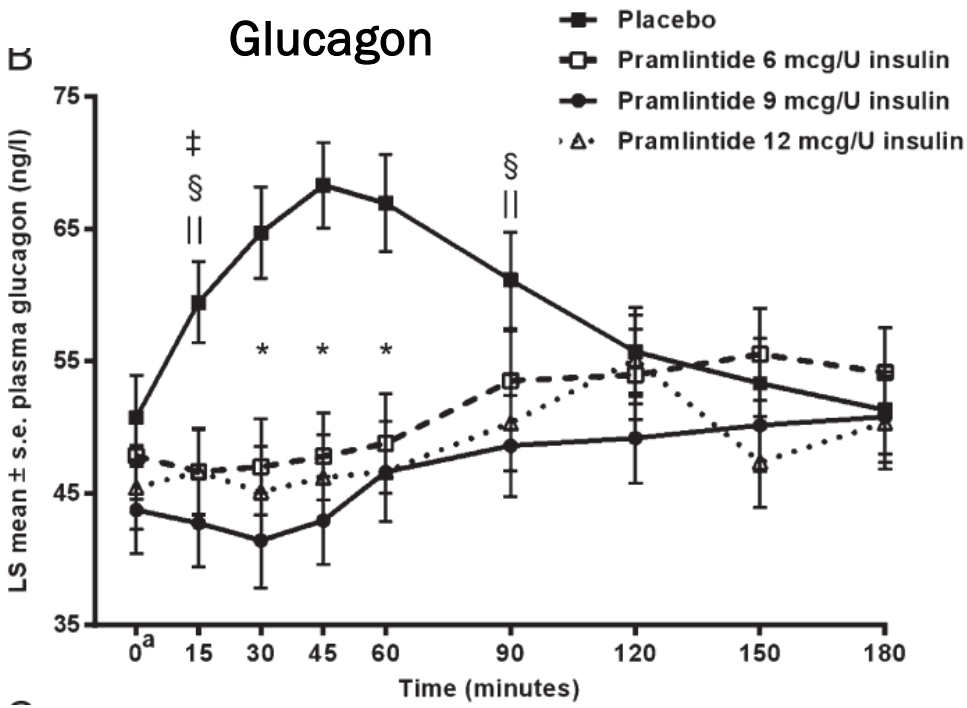
DATA ON PRAMLINTIDE USE IN PEOPLE WITH T1D

- Reductions in Hemoglobin A1c found with pramlintide[1,2]
- All 3 trials showed used of pramlintide led to weight loss[1-3]
- Side effects from the medication included mild nausea and decreased appetite[1-3]
- Severe hypoglycemia increased in the first 4-weeks of treatment with pramlintide[2]
- **The problem: injections prior to each meal!**

1- Whitehouse F,. Diabetes Care 2002; 25 (4):724-730, , 2- Ratner R et. al. Diabet Med 2004; 21 (11):1204-12. 3- Edeleman et al. Diabetes Care 2006; 28 (10):2189-95.

COULD CO-FORMULATION OF INSULIN AND PRAMLINTIDE WORK?



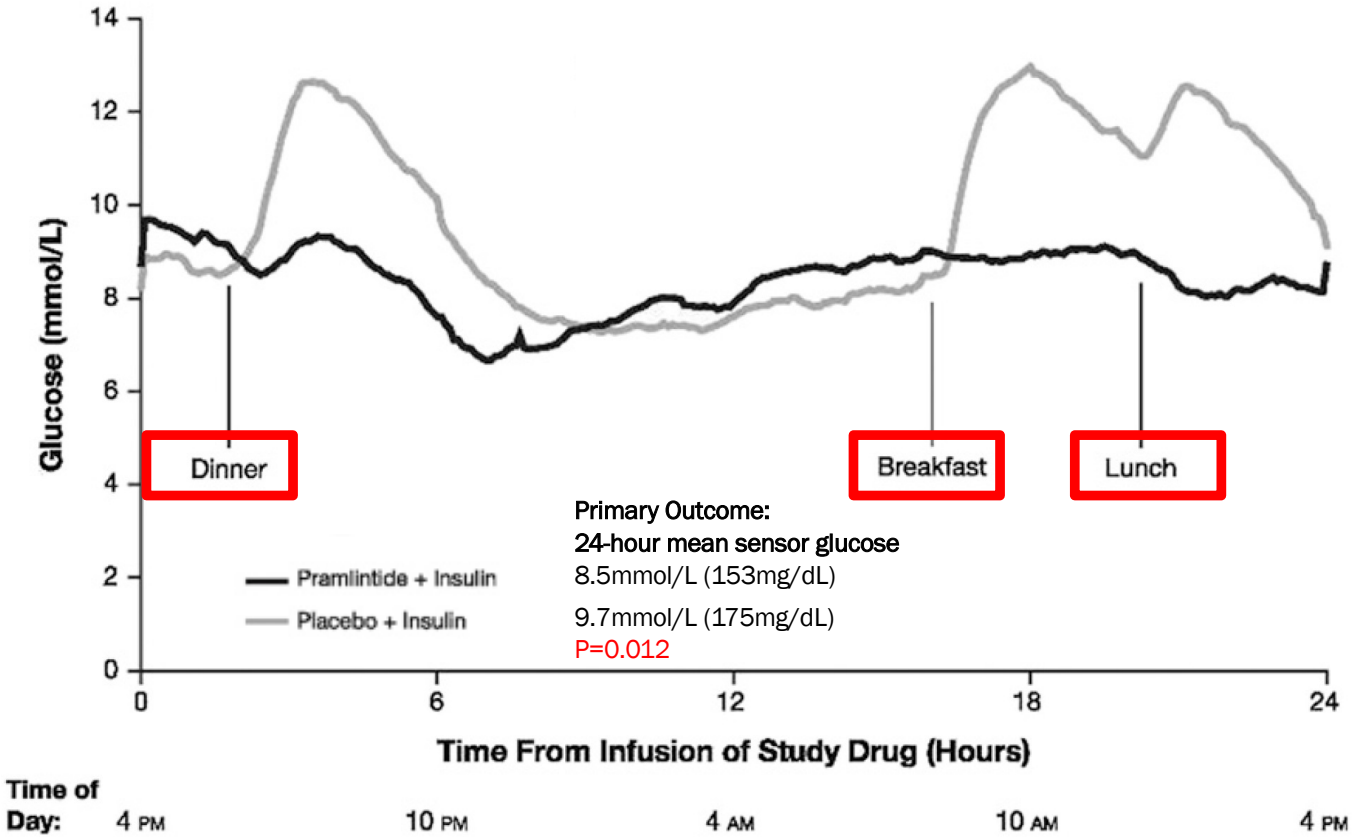


Riddle MC et. al.. Diabetes, Obesity, and Metabolism 2015; 17 (9):904-907.

LOWER MEAN SENSOR GLUCOSE WITH COADMINISTRATION

Study design: Feasibility trials to assess coadministration of pramlintide with regular insulin using two pumps

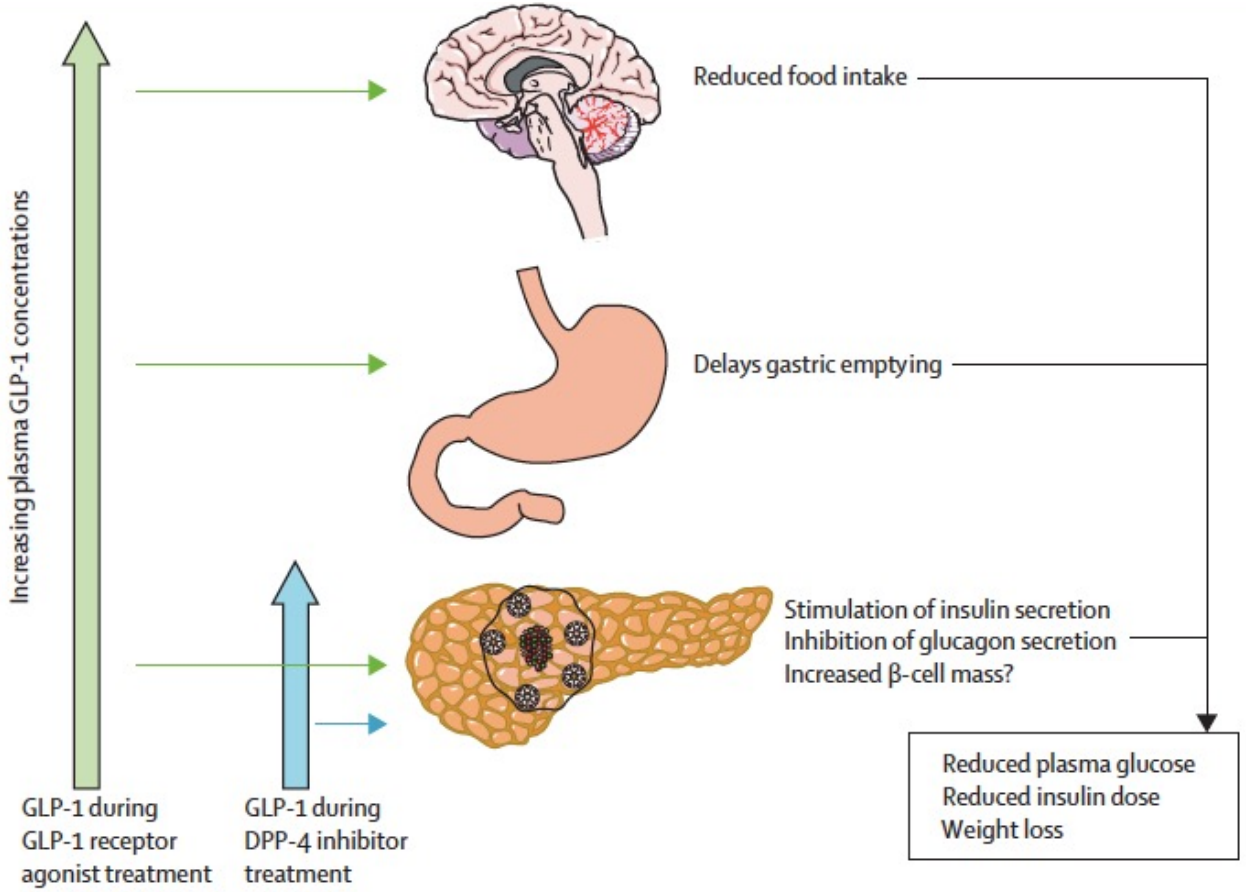
Safety: GI side effects noted in nearly half of the pramlintide admissions and in only 7% of the placebo admissions.



Riddle MC. Et al. Control of Postprandial Hyperglycemia in Type 1 Diabetes by 24-Hjour Fixed Dose Coadministration of Pramlintide and Regular Human Insulin: A Randomized Two-Way Crossover Study. Diabetes Care 2016; 41 (11):2346-2352.

DO WE NEED ADDITIONAL THERAPIES TO ACHIEVE OUR MANAGEMENT GOALS FOR PEOPLE WITH T1D?

GLUCAGON LIKE PEPTIDE-1 RECEPTOR AGONISTS



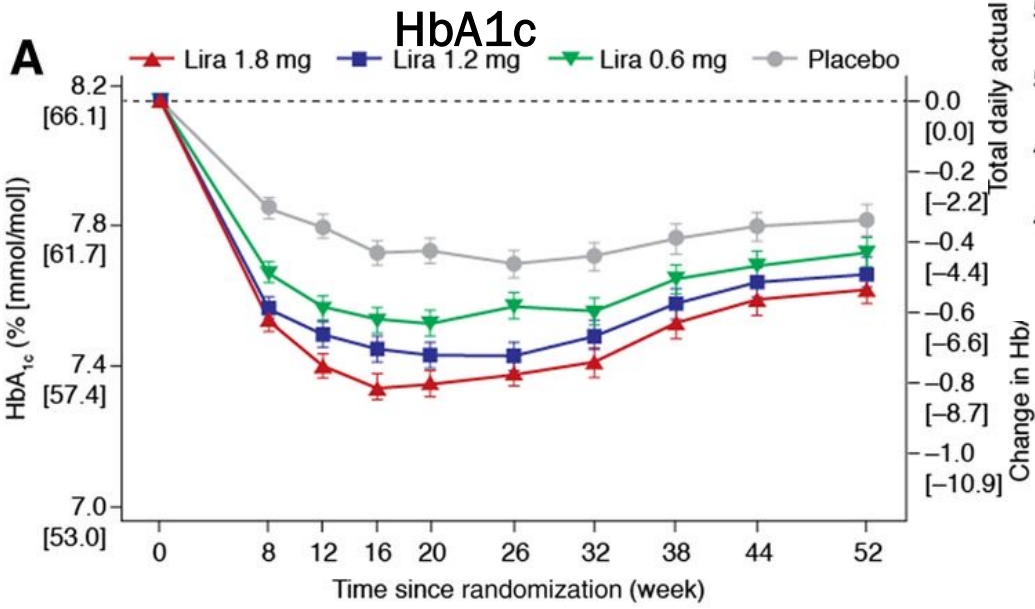
Seerup Frandsen Lancet Diabetes and Endocrinology 4(9):766-780. doi:10.1016/S2213-8587 (16)000395

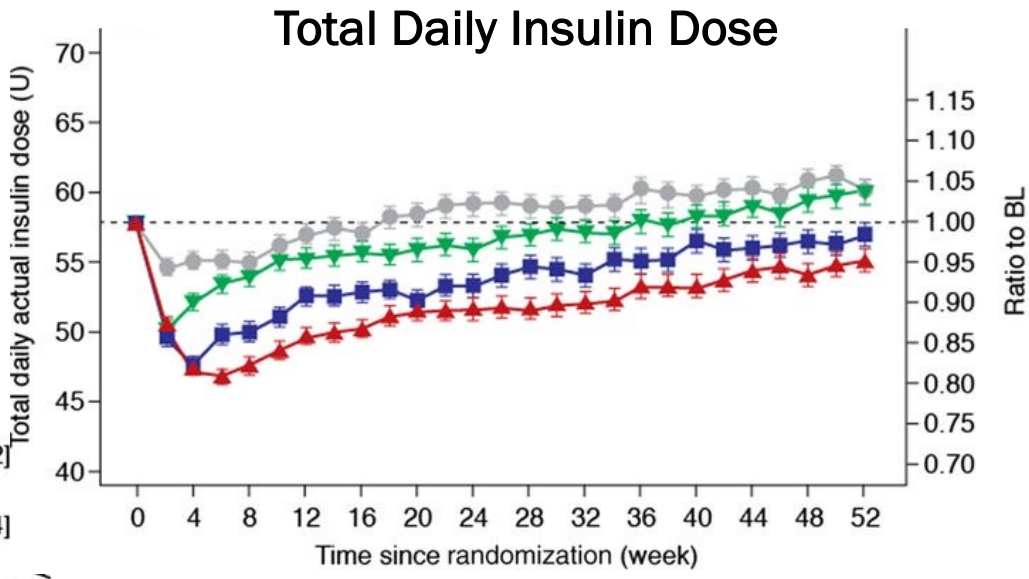
ADJUNCT ONE: LOWER HEMOGLOBIN A1C AND INSULIN DOSES

1398 adults randomized 3:1

52-week double blind study

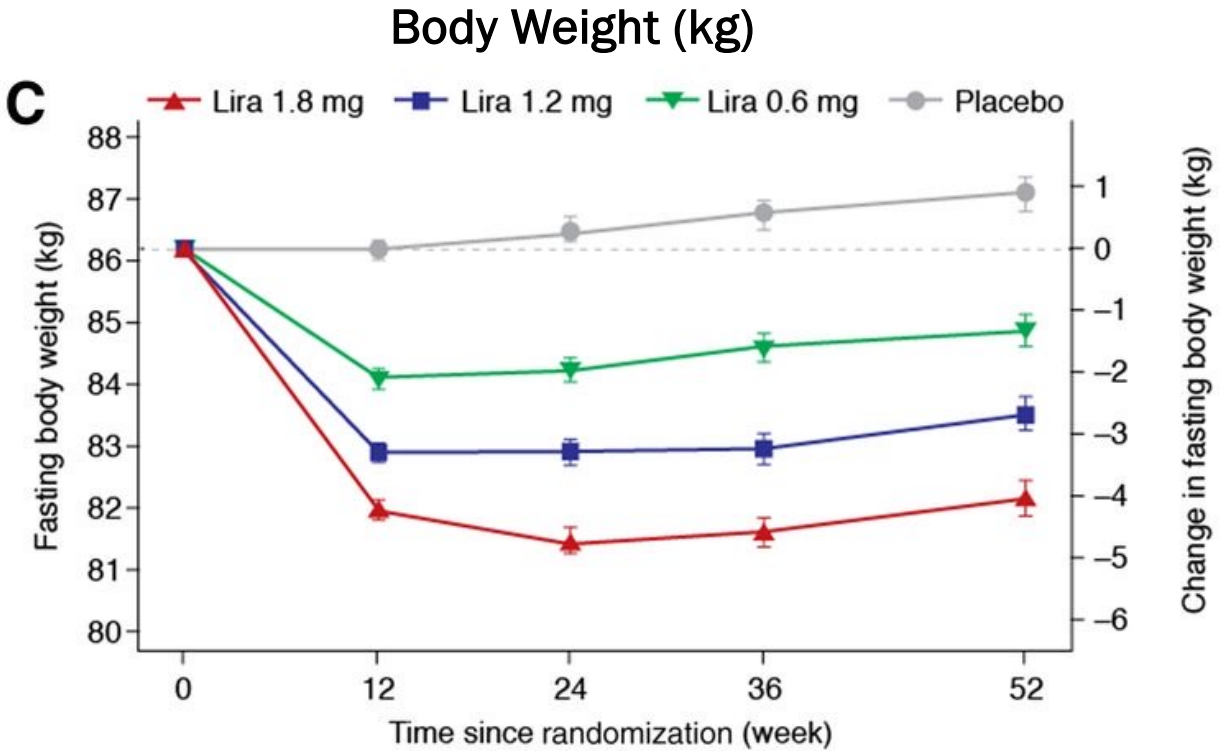
Primary Outcome: HcA1c





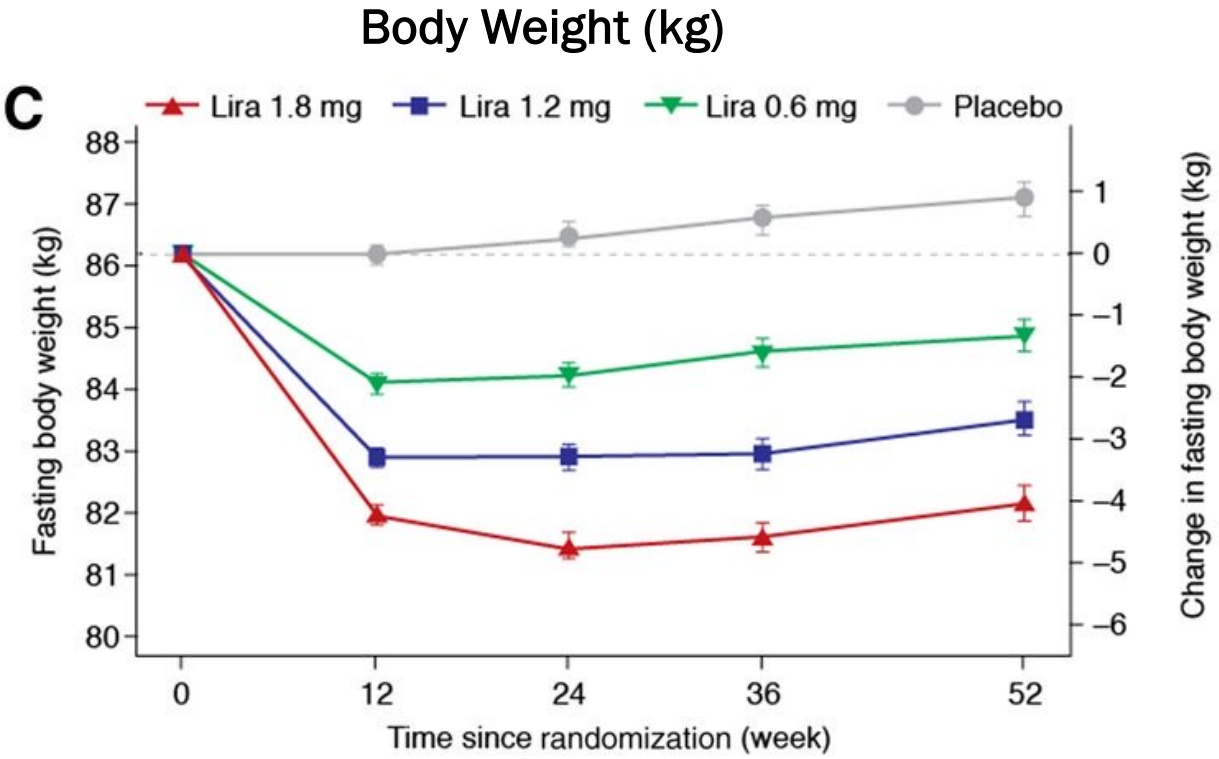
Mathieu C, et al. Diabetes Care. 2016;39(10):1702-1710. doi:10.2337/dc16-0691

ADJUNCT ONE: BENEFICIAL IMPACT ON BODY WEIGHT



Mathieu C, et al. Diabetes Care. 2016;39(10):1702-1710. doi:10.2337/dc16-0691

ADJUNCT ONE: THE DRAW BACKS



Side effects:

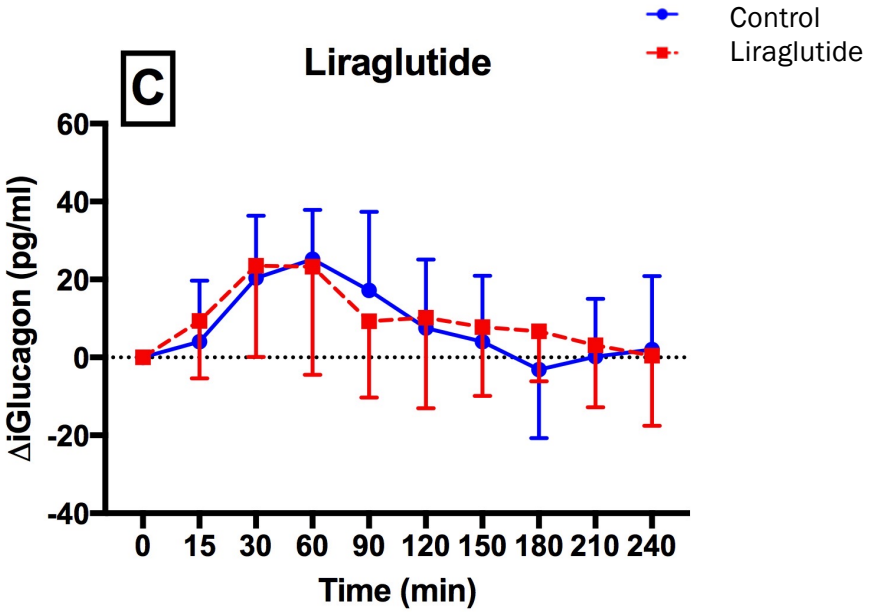
- Higher rates of hypoglycemia in all groups receiving liraglutide
- The liraglutide 1.8 mg group had a higher rate of hyperglycemia with ketosis

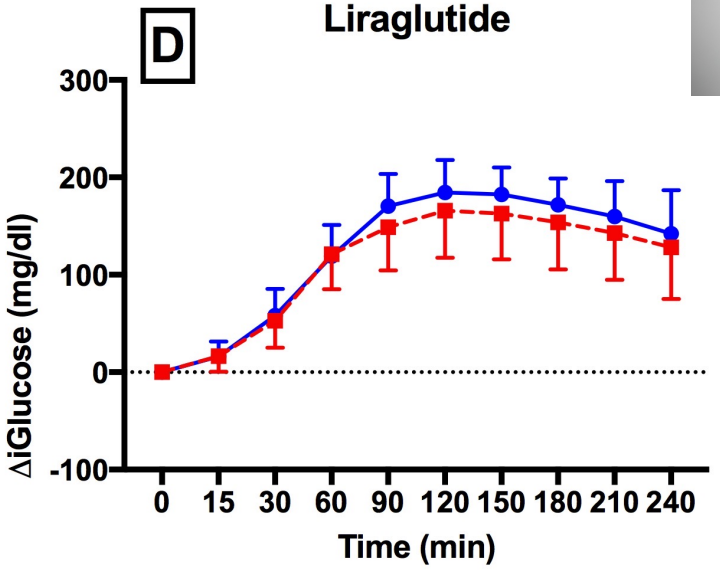
Mathieu C, et al. Diabetes Care. 2016;39(10):1702-1710. doi:10.2337/dc16-0691

INSULIN DOSES REDUCED WITH GLP-1, BUT NO CHANGE IN GLUCAGON

Liraglutide led to a 5% reduction in weight and a 26% reduction in total daily insulin dose.

Dr. Alfonso Galderisi
Assistant Professor





Galderisi, Sherr et al. JCEM 2018; 103 (3):1088-1094. doi10.1210/jc.2017-02265

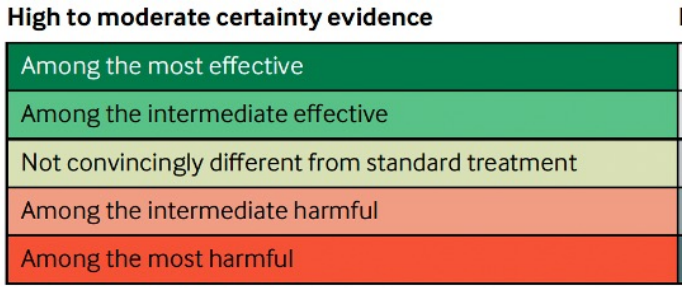
WHAT CAN WE LEARN FROM STUDIES OF GLP-1 AND TYPE 2 DIABETES

Interventions	All cause death (OR, 95%CI)	Cardiovascular death (OR, 95%CI)	Admission to hospital for heart failure (OR, 95%CI)	End stage kidney disease* (OR, 95%CI)	Health related quality of life score (OR, 95%CI)	Severe hypoglycaemia (OR, 95%CI)	Drug specific adverse events (OR, 95%CI)
GLP-1 receptor agonists	0.88 (0.82 to 0.93)	0.87 (0.81 to 0.94)	0.91 (0.83 to 0.99)	0.83 (0.75 to 0.92)	0.17 (0.07 to 0.27)	0.98 (0.90 to 1.06)	Severe gastrointestinal events 1.97 (1.39 to 2.80)
Standard treatments	Reference group						

↓ Cardiovascular Disease

↓ Kidney Disease

↑ Improving Quality of Life



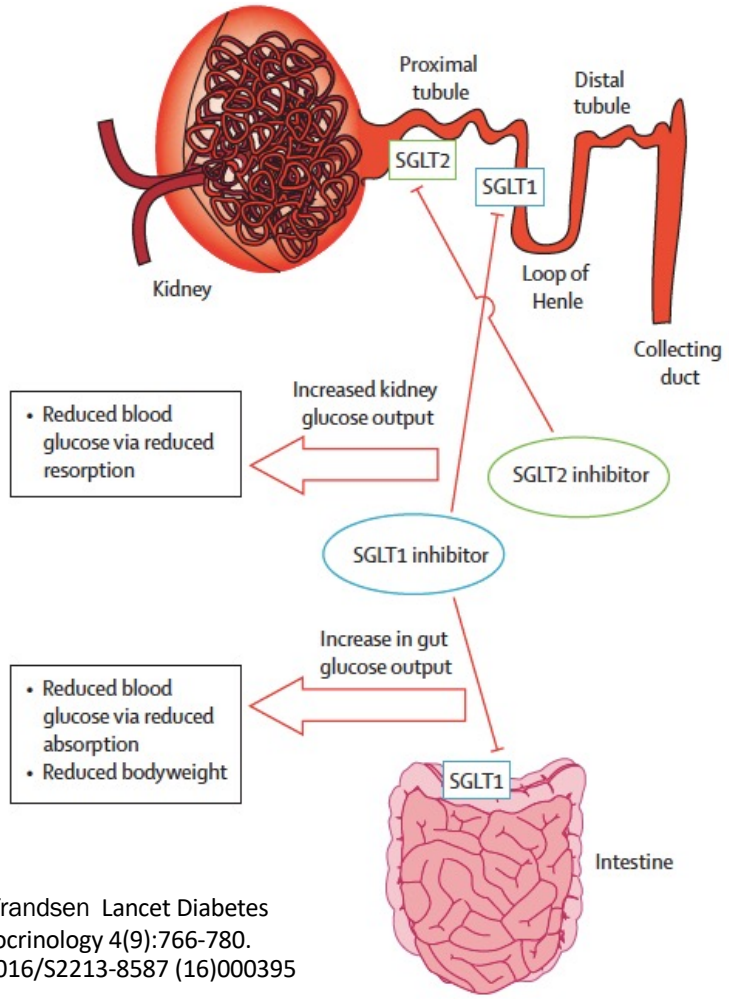
Moving beyond glucose targets and seeing benefits for the whole body

Shi Q et al. Benefits and harms of drug treatment for type 2 diabetes: a systematic review and network meta-analysis of randomized controlled trials. BMJ 2023; 381:e0704068

ONGOING INVESTIGATION OF GLP-1 AT BDC

- Led by Dr. Viral Shah
- Recruiting adults (>18 years old) with Type 1 diabetes on automated insulin delivery.
- Exploring once weekly semaglutide
- For more information, please go to the BDC table outside.

SODIUM GLUCOSE CO-TRANSPORTERS



Seerup Frandsen Lancet Diabetes and Endocrinology 4(9):766-780. doi:10.1016/S2213-8587 (16)000395

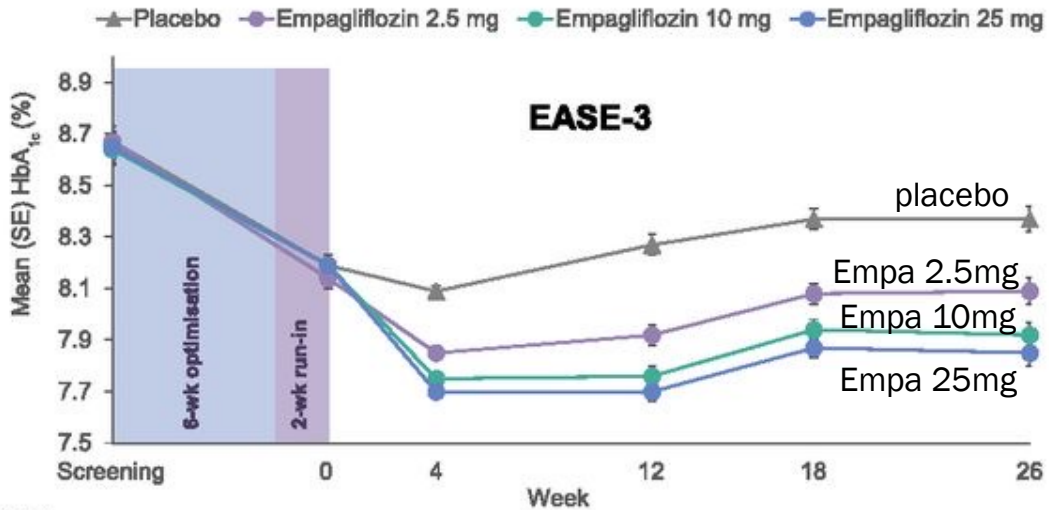
- Initial studies demonstrated the efficacy of SGLT-2 inhibitors in those with T1D.
- Yet, use of these agents has been associated with an increased risk of near euglycemic DKA.

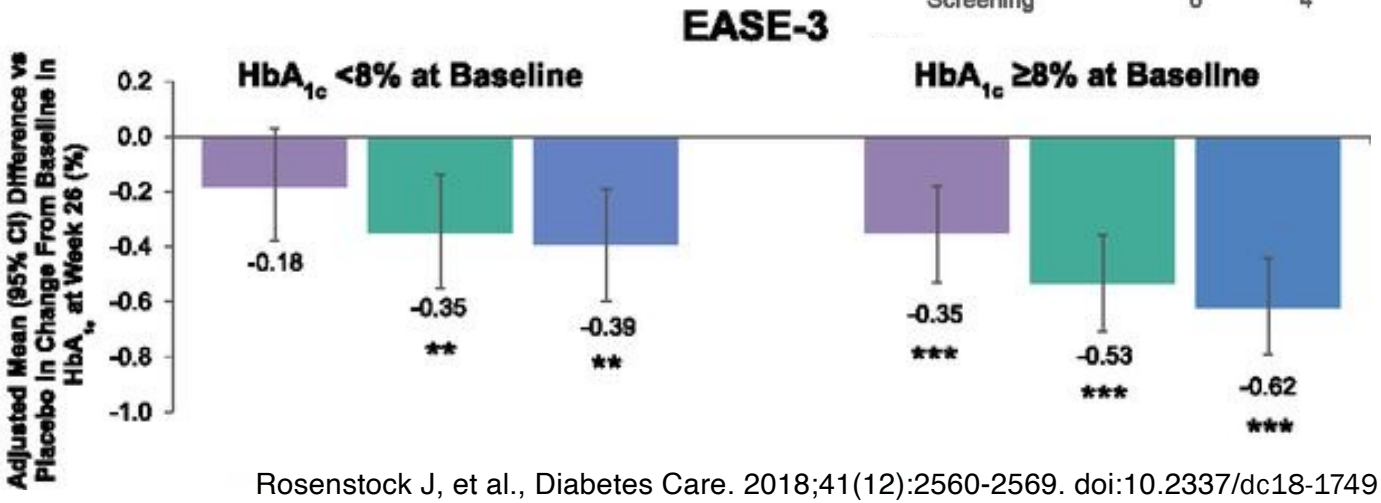
Perkins Diabetes Care 2014; 37(5):1480-3. doi:10.2337/ dc13-2338.Henry Diabetes Care 2105; 38 (3):412-9. doi10.2337/dc-2955. Pieber Diabetes Obes Metab 2015; 17 (10):928-35. doi:10.111/dom.12494. Peters Diabetes Care 2015 38 (9):1687-93. doi:10.2337/dc15-0843.

EASE 3: SGLT2s IN PEOPLE WITH T1D LEADS TO LOWER HbA1c

977 adults randomized 3:1
Inclusion Criteria: A1c 7.5-10%
Primary Outcome: Δ A1c at 26 weeks

Results: There was a significant difference vs placebo
2.5mg: -0.28
10mg: -0.45
25mg: -0.52

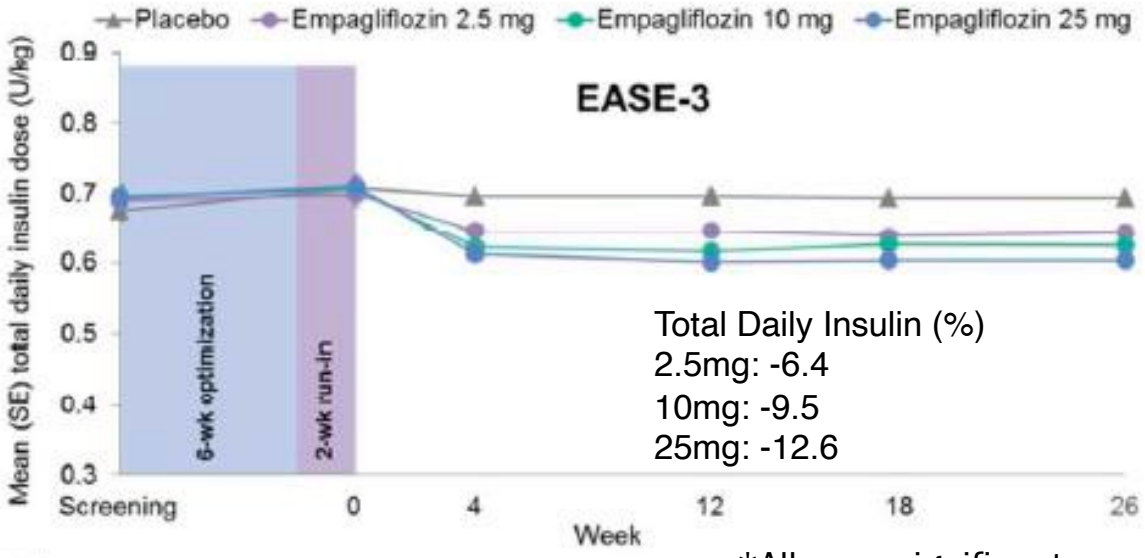




Rosenstock J, et al., Diabetes Care. 2018;41(12):2560-2569. doi:10.2337/dc18-1749

EASE 3: LOWER HbA1c ACHIEVED WITH LOWER INSULIN DOSES AND WEIGHT LOSS

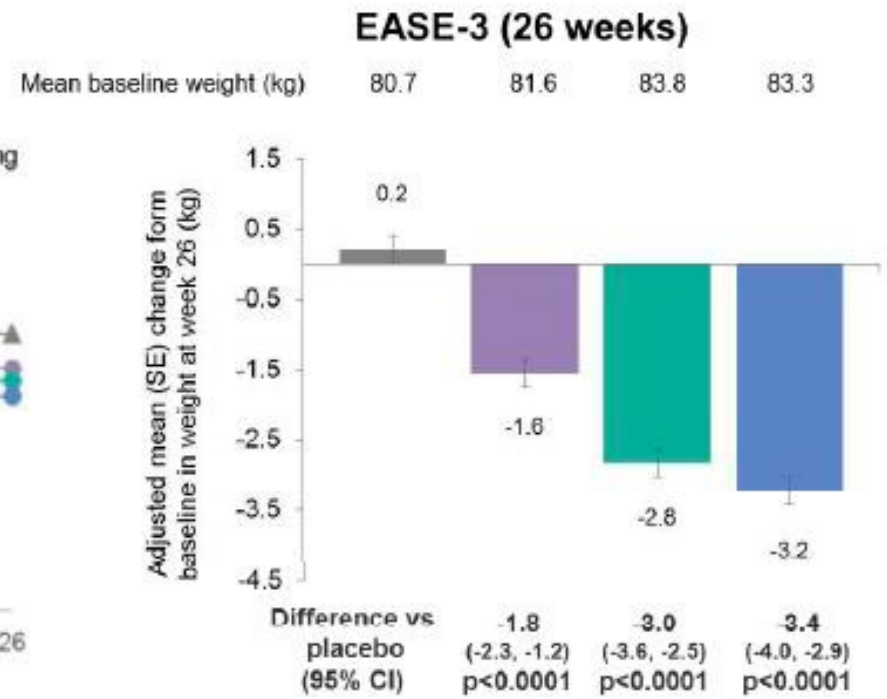
Insulin Dose Change (units/kg)



Total Daily Insulin (%)
2.5mg: -6.4
10mg: -9.5
25mg: -12.6

*All were significant

Weight Change (kg)



*All were significant

Rosenstock J, et al., Diabetes Care. 2018;41(12):2560-2569. doi:10.2337/dc18-1749

ARE RATES OF DKA HIGHER WITH SGLT2 inhibitors?

SUPPLEMENTARY TABLE S1. FREQUENCY OF DKA AND ITS CAUSES DURING CLINICAL TRIALS ADOPTING SGLT2I AND SGLT1/2I IN TYPE 1 DIABETES

	DEPICT1[S1]			*DEPICT2*[a,S2]			*EASE-2 and EASE-3*[b,S3]			*EASE-3*[S3]		*Tandem3*[c,S4]		*Canagliflozin trial*[S5]		
Drug	*Dapagliflozin*			*Dapagliflozin*			*Empagliflozin*			*Empagliflozin*		*Sotagliflozin*		*Canagliflozin*		
Dose (mg/day)	5	10	Placebo	5	10	Placebo	10	25	Placebo	2.5	Placebo	400	Placebo	100	300	Placebo
N	277	296	260	271	270	272	491	489	484	241	241	699	703	117	117	117
Pump users, *n* (%)	97 (37)	94 (36)	95 (37)	92 (34)	92 (34)	92 (34)	99 (41)	98 (41)	97 (41)	82 (34)	81 (34)	275 (39.3)	280 (39.8)	74 (61.5)	73 (62.4)	72 (61.5)
Basal insulin dose reduction (%)	−11.6	−13.7	−0.6	−11	−17	−1.4	−13.3[d]	−12.7 [d]	—	−7.9[c]	—	−9.9	—	−19	−22.4	—
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Frequency of DKA																
Number of patients with definite DKA, *n* (%)	11 (4)	10 (3.4)	5 (1.9)	7 (2.6)	6 (2.2)	0 (0)	32[e] (4.3)	31[e] (3.3)	8[e] (1.2)	3 (0.8)	5 (1.2)	21 (3)[f]	4 (0.6)[f]	6 (5.1)	11 (9.4)	0 (0)
Cause of DKA documented																
Insulin pump failure, *n* (%)	3 (25)	2 (20)	2 (40)	1 (14)	2 (33)	0 (0)	7 (22)	2 (6)	0 (0)	0 (0)	0 (0)	—	—	—	—	—
Missed insulin dose, *n* (%)	4 (33)	4 (40)	1 (20)	2 (28)	1 (17)	0 (0)	1 (3)	2 (6)	1 (13)	0 (0)	0 (0)	—	—	—	—	—
Severe illness, *n* (%)	0 (0)	0 (0)	0 (0)	—	—	—	7 (22)	12 (39)	2 (25)	0 (0)	2 (40)	—	—	—	—	—
Other/not identified, *n* (%)	5 (41)	4 (40)	2 (40)	4 (57)	3 (50)	0 (0)	17 (53)	15 (48)	5 (62)	3 (100)	3 (60)	—	—	—	—	—

[a]The trial included subjects with HbA_{1c} 7.5%–10% at baseline, whereas in DEPICT1 HbA_{1c} was between ≥7.7% and ≤11.0%.
[b]Data for EASE-2 and EASE-3 are pooled for analysis of DKA events.
[c]Sotagliflozin is an inhibitor of sodium–glucose cotransporters 1 and 2 (SGLT1 and 2), whereas dapagliflozin and empagliflozin are selective inhibitors for SGLT2 channel.
[d]Percentage reduction is referred to total daily dose adjusted for change in placebo group.
[e]Data are reported as number of patient-event (percentage of patients).
[f]The events in pump users were 12 (4.4%) and 2 (0.7%) for sotagliflozin and placebo group, respectively.

Siebel Diabetes Technol Ther. 2019; 21 (3):101-104. doi:10.1089/dia.2018.0356

ARE RATES OF DKA HIGHER WITH SGLT2 inhibitors?

	DEPICT1[S1]			*DEPICT2*[a,S2]			*EASE-2 and EASE-3*[b,S3]			*EASE-3*[S3]		*Tandem3*[c,S4]		*Canagliflozin trial*[S5]		
Drug	*Dapagliflozin*			*Dapagliflozin*			*Empagliflozin*			*Empagliflozin*		*Sotagliflozin*		*Canagliflozin*		
Dose (mg/day)	5	10	Placebo	5	10	Placebo	10	25	Placebo	2.5	Placebo	400	Placebo	100	300	Placebo
N	277	296	206	271	270	272	491	489	484	241	241	699	703	117	117	117
Frequency of DKA																
Number of patients with definite DKA, *n* (%)	11 (4)	10 (3.4)	5 (1.9)	7 (2.6)	6 (2.2)	0 (0)	21[e] (4.3)	31[e] (3.3)	6[e] (1.2)	3 (0.8)	5 (1.2)	21 (3)[f]	4 (0.6)[f]	6 (5.1)	11 (9.4)	0 (0)

Placebo rate of DKA ranges from 0-1.9% of those studied

Higher dose SGLT2 inhibitors rate of DKA ranges from 2.2-9.4% of those studied

Lower dose SGLT2 inhibitors rate of DKA is 0.8%

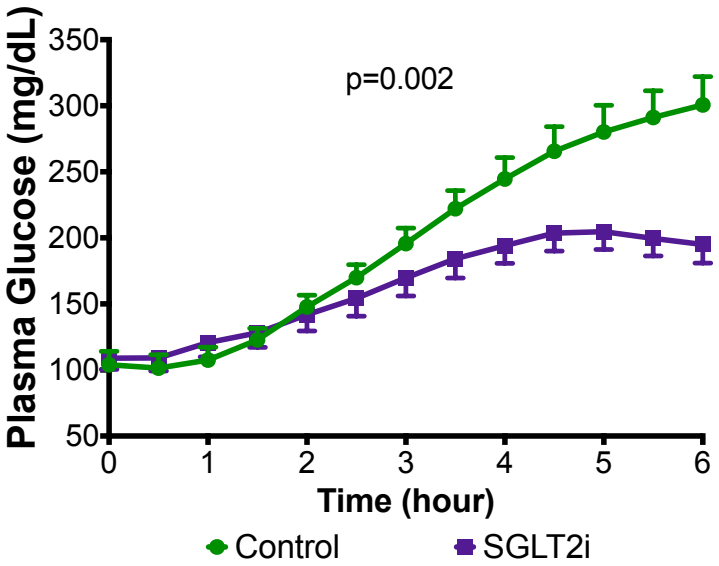
Maybe use of lower doses can provide a path forward.
But can we do anything else?

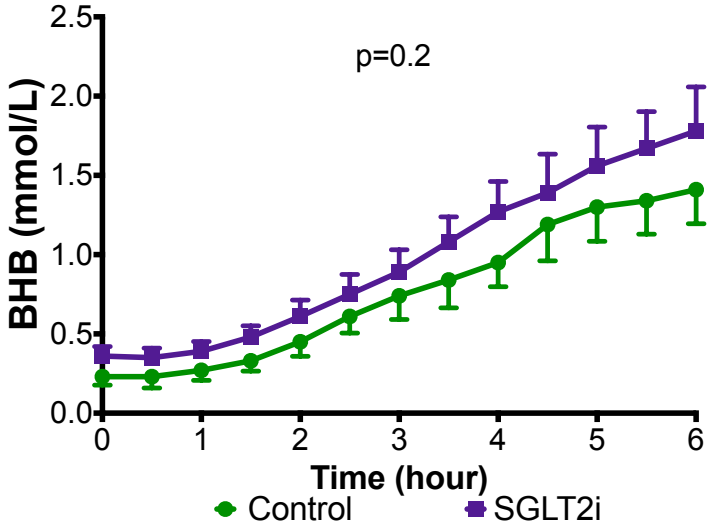
Siebel Diabetes Technol Ther. 2019; 21 (3):101-104. doi:10.1089/dia.2018.0356

MIMICKING THE TIME OF GREATEST RISK

- Insulin infusion sets are the Achilles heel of pump (and AID) therapy.
- With an infusion set failure, hyperglycemia ensues with subsequent development of ketosis.
- The time such issues are most likely to go unnoticed is overnight.
- Can we create an experimental condition to see how SGLT2i impact ketosis development?

RISE IN GLUCOSE WAS BLUNTED, BUT KETONE LEVEL WAS SIMILAR



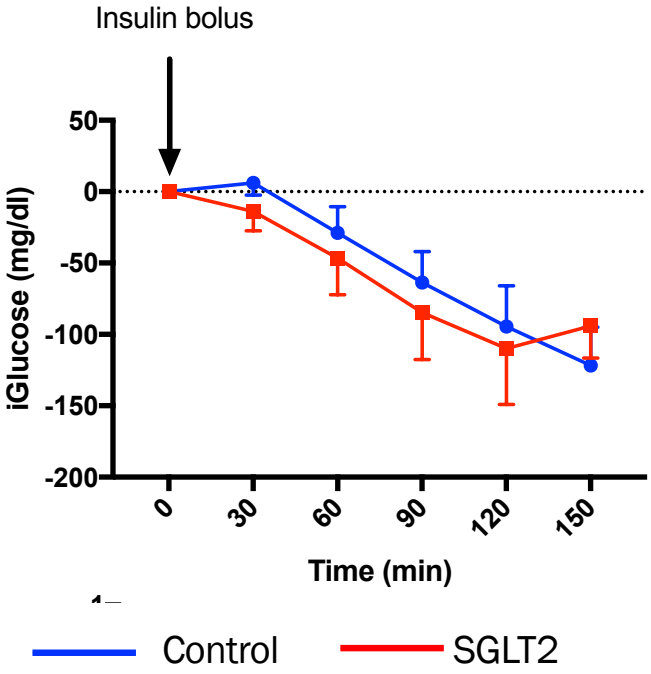


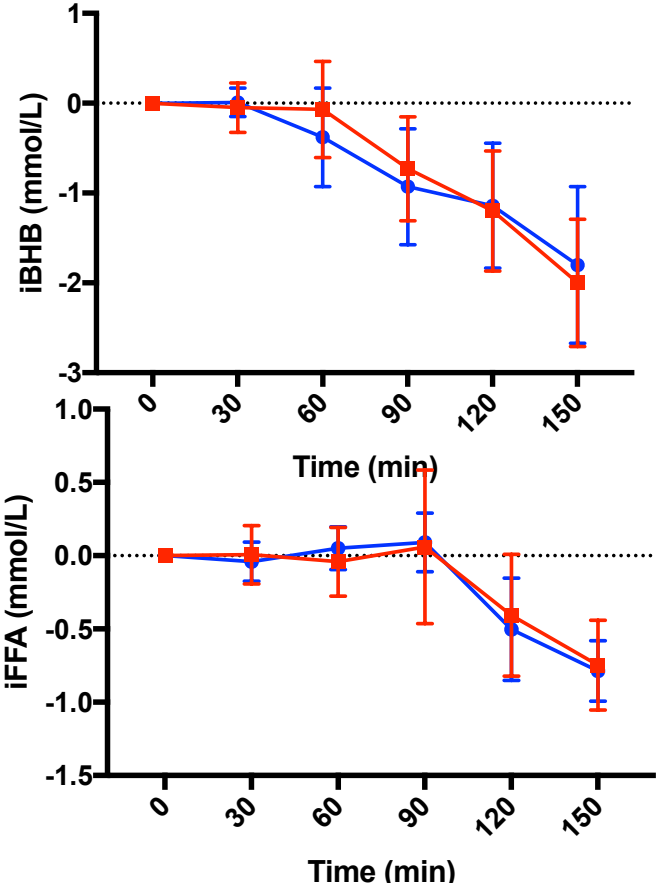
Dr. Neha Patel

Patel Diabetes Technol Ther. 2017; 19(11):618-622. doi:10.1089/dia.2017.0267

REVERSAL OF KETOSIS IS NOT AFFECTED BY SGLT2I

- Following the insulin suspension period, a standardized dose of 0.2units/kg of aspart was given to study participants.





Dr. Stephan Siebel
Associate Research Scientist

Siebel Diabetes Technol Ther. 2019; 21 (3):101-104. doi:10.1089/dia.2018.0356

ALTERED SIGNAL TO ASSESS FOR KETOSIS

- The use of SGLT2i does not affect rate of ketone development after the interruption of basal insulin delivery.
- SGLT2i use does NOT affect the recovery from ketosis after insulin suspension in pump users
- The key is altering the threshold to check for ketones.
- But other methods of ketone monitoring may be of benefit.

COULD CONTINUOUS KETONE MONITORS BE THE KEY TO SAFE SGLT2 USE

Initial feasibility trials of these monitors have been conducted.

Each participant wore 3 continuous ketone monitors and data was compared to fingerstick ketone measurements.

Study Outcome:

- The continuous ketone meter results were similar to the blood ketone measures.
- Further assessments needed

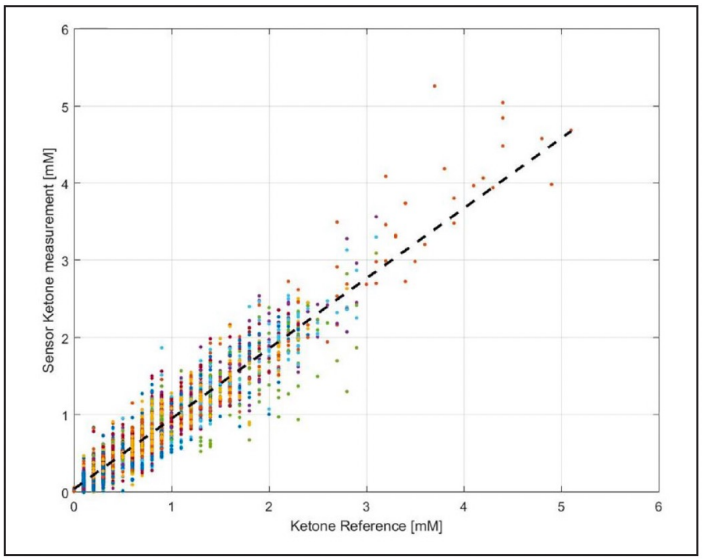


Figure 5. Plot of ISF ketone values measured by the sensors against capillary ketone strip reference measurements. Number of Paired data points is 3132.

Alva et al. Journal of Diabetes Sci Technol 2021; 15 (4) 768-774.

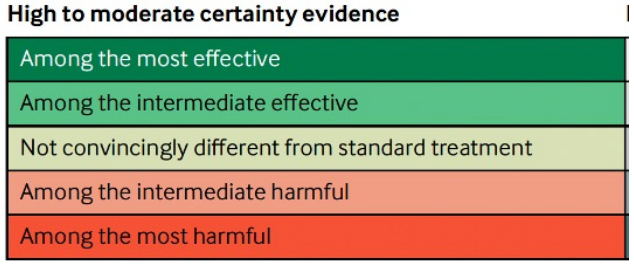
WHOLE BODY BENEFITS OF SGLT2 IN PEOPLE WITH TYPE 2 DIABETES

Interventions	All cause death (OR, 95%CI)	Cardiovascular death (OR, 95%CI)	Admission to hospital for heart failure (OR, 95%CI)	End stage kidney disease* (OR, 95%CI)	Health related quality of life score (OR, 95%CI)	Severe hypoglycaemia (OR, 95%CI)	Drug specific adverse events (OR, 95%CI)
SGLT-2 inhibitors	0.88 (0.83 to 0.94)	0.86 (0.80 to 0.94)	0.66 (0.60 to 0.73)	0.61 (0.55 to 0.67)	0.30 (0.10 to 0.49)	0.90 (0.79 to 1.02)	Genital infection 3.30 (2.88 to 3.78) Amputation 1.27 (1.01 to 1.61) Ketoacidosis 2.07 (1.44 to 2.98)
Standard treatments	Reference group						

↓ Cardiovascular Disease

↓ Kidney Disease

↑ Improved Quality of Life



Moving beyond glucose targets and seeing benefits for the whole body

Shi Q et al. Benefits and harms of drug treatment for type 2 diabetes: a systematic review and network meta-analysis of randomized controlled trials. BMJ 2023; 381:e0704068

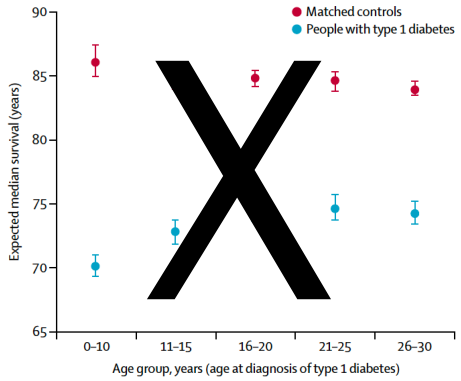
SUMMARY

- Adjunctive to insulin agents help
  - Lower hemoglobin A1c
  - Reduce insulin doses
  - Reduce weight, or maintain healthy body weight

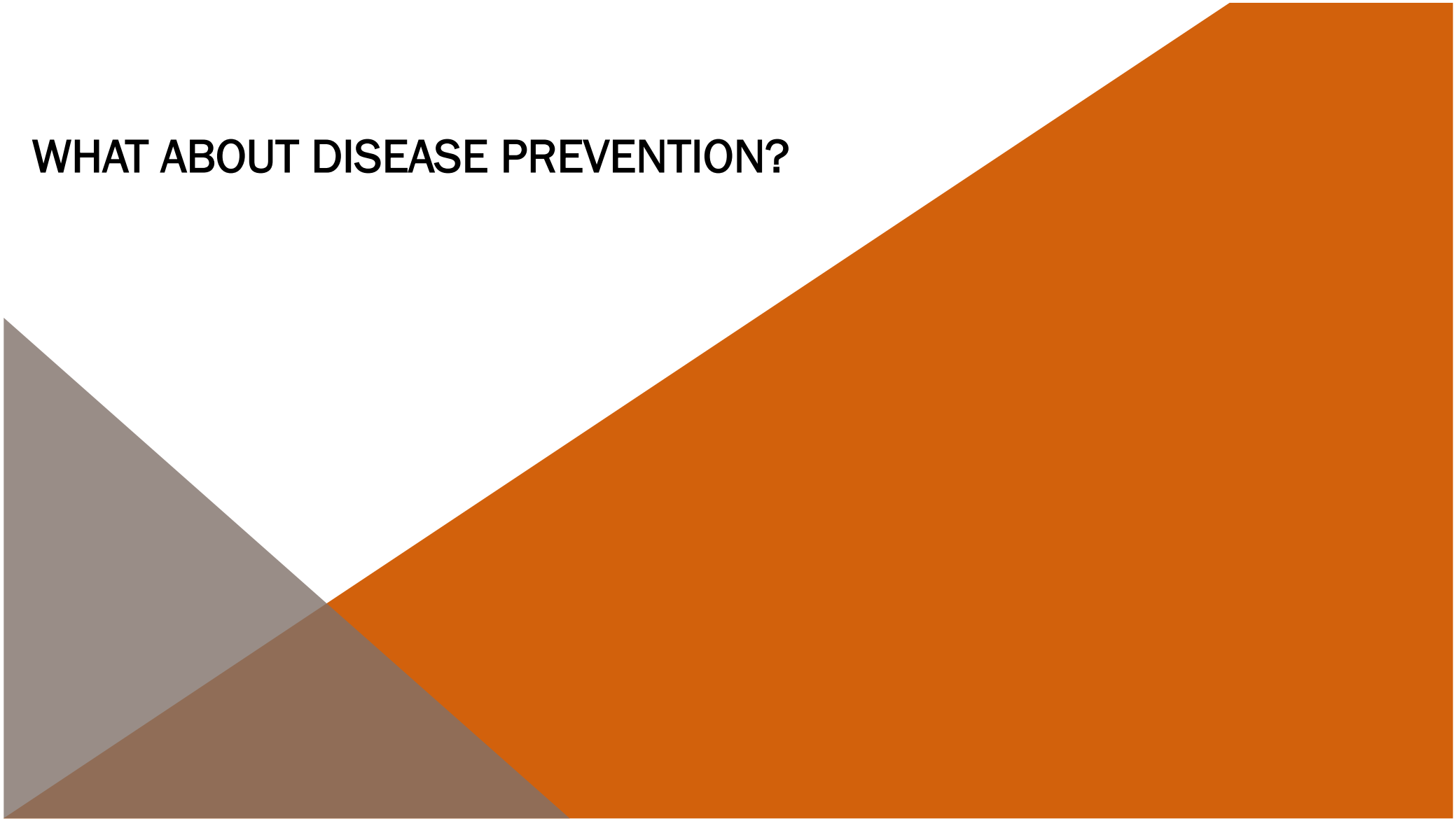
- Benefits extend to our whole body:
  - Reducing risk of cardiovascular disease
  - Reducing risk of kidney disease
  - Improving quality of life

- Methods for safe adoption of some therapies may require new technologies, like continuous ketone monitors.

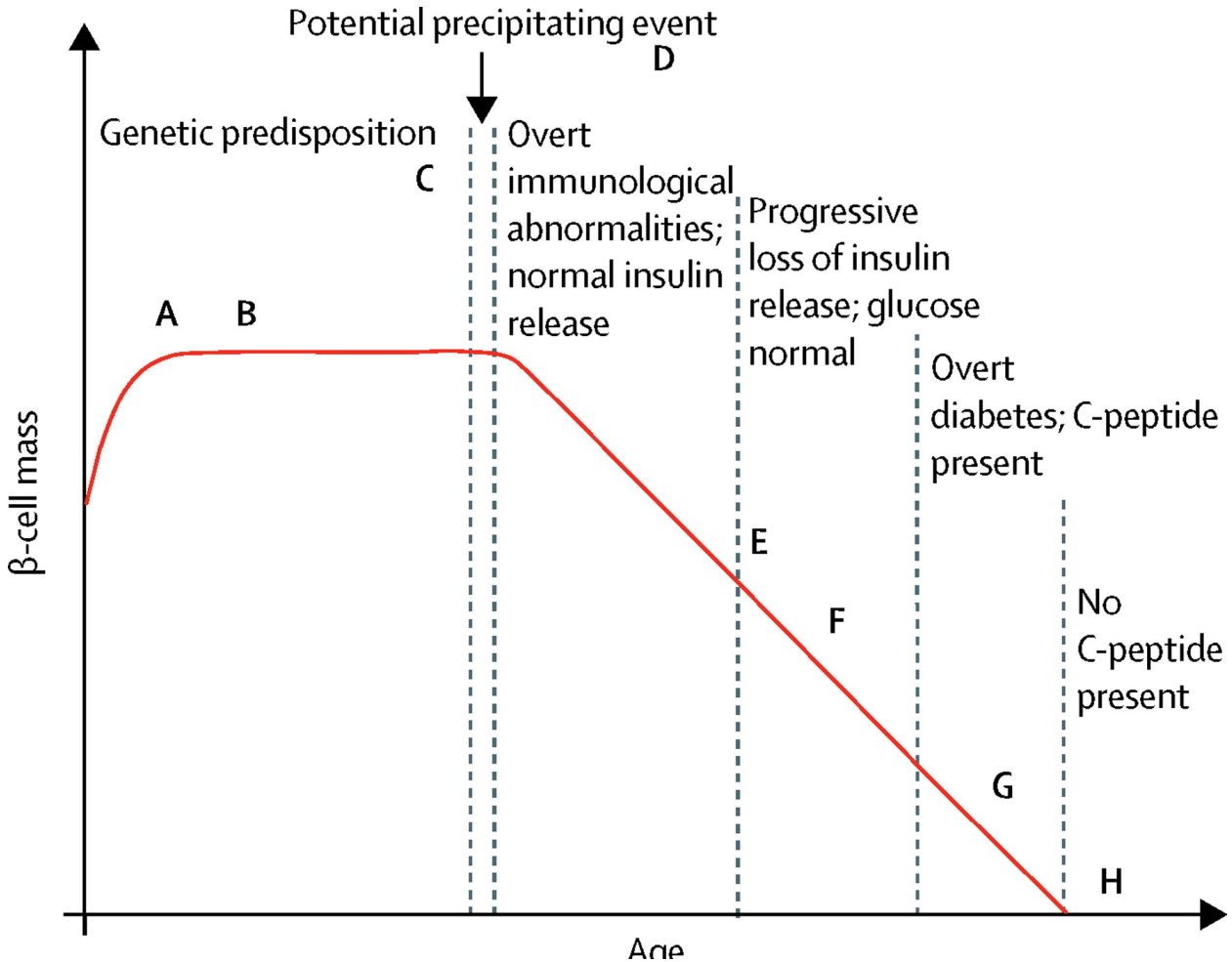
We are re-writing the story of Cardiovascular disease



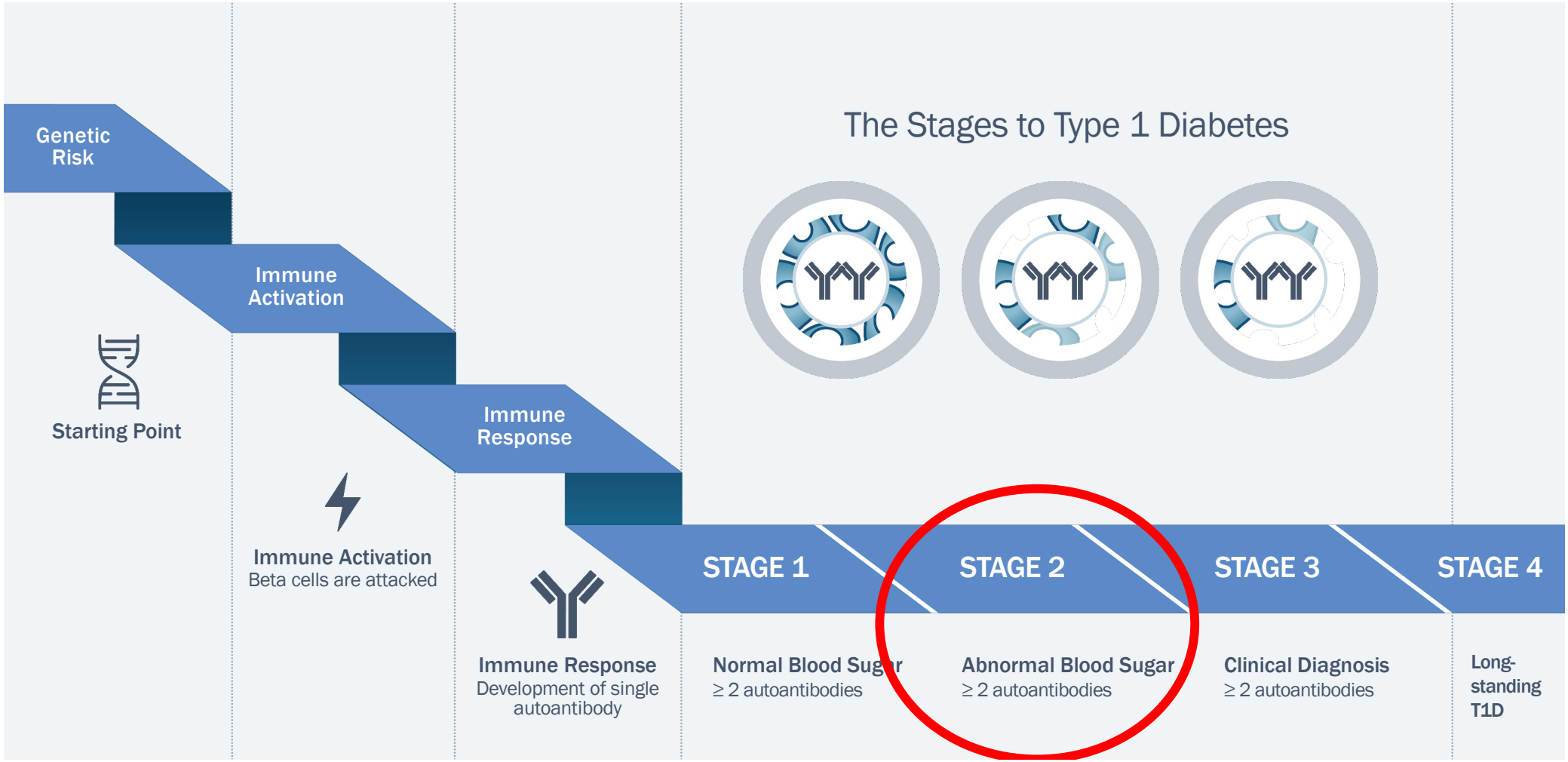
WHAT ABOUT DISEASE PREVENTION?



CLASSIC MODEL OF TYPE 1 DIABETES DEVELOPMENT



USING STAGES TO DEFINE PROGRESSION



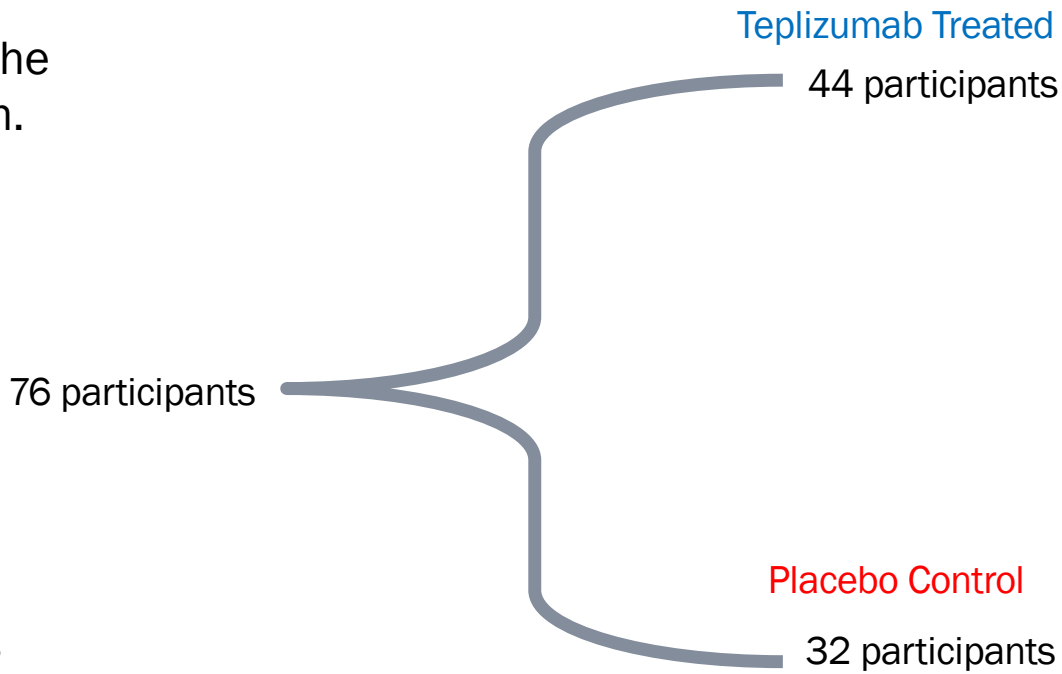
TRYING TO PREVENT PROGRESSION IN RELATIVES AT RISK

Anti-CD3: binds to t-cells that are causing the autoimmune response and inactivates them. Therefore, the beta cells are not destroyed.

Delivered as a 14-day IV infusion

Study population:

- Relatives of people with Type 1 Diabetes
- >8 years old at enrollment
- High risk for progression to clinical diabetes (stage 2 disease)



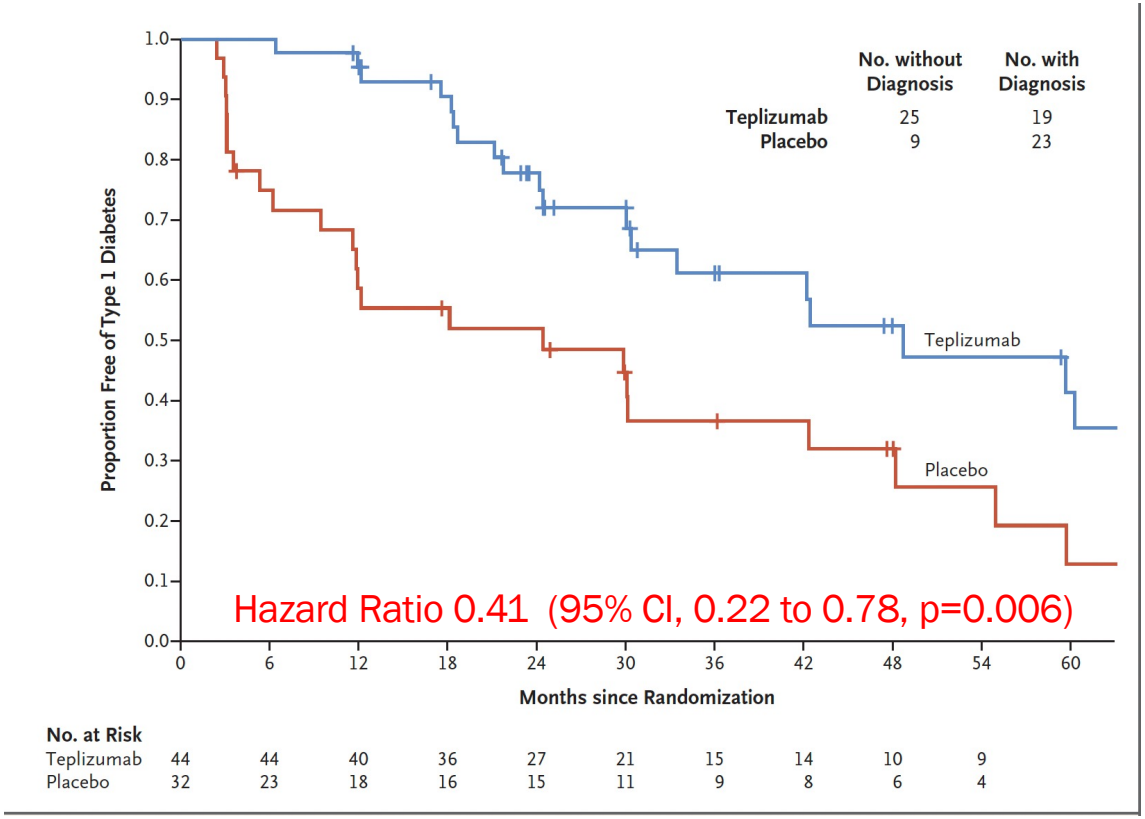
Herold KC, Bundy BN, Long, A, Bluestone JA, DiMeglio LA, Dufort MJ, Gitelman SE, Gottlieb PA, Krischer JP, Linsley PS, Marks JB, Moore W, Moran A, Rodriguez H, Russell WE, Schatz D, Skyler JS, Tsalikian E, Wherrett DK, Ziegler AG, Greenbaum CJ for the Type 1 Diabetes TrialNet Study Group. An Antic-CD3 Antibody, Teplizumab, in Relatives at Risk for Type 1 Diabetes. NEJM 2019; 381: 603-13

TEPLUZIMAB DELAYS DIAGNOSIS OF STAGE 3 DISEASE

Median time to diagnosis:

Treated Group = 48.4 months

Placebo= 24.4 months



Disease diagnosis at trial conclusion:

Treated Group 43%

Placebo 72%

Herold KC, Bundy BN, Long, A, Bluestone JA, DiMeglio LA, Dufort MJ, Gitelman SE, Gottlieb PA, Krischer JP, Linsley PS, Marks JB, Moore W, Moran A, Rodriguez H, Russell WE, Schatz D, Skyler JS, Tsalikian E, Wherrett DK, Ziegler AG, Greenbaum CJ for the Type 1 Diabetes TrialNet Study Group. An Antic-CD3 Antibody, Teplizumab, in Relatives at Risk for Type 1 Diabetes. NEJM 2019; 381: 603-13

- Those with stage 2 diabetes who are over age 8 are eligible for treatment.
- Clinical infusion protocols have been created.

SUMMARY

- With screening, a method to delay clinical diagnosis is feasible.
- Just as insulin transformed life for people with diabetes over a century ago, Tzield has opened the door to a new age of diabetes management.

- This is not the end, but the end of the beginning.

THANK YOU!


Laughter is the best medicine....
Unless you have
diabetes, then
insulin,
insulin is the
best
medicine.

EPIC DIABETES CONFERENCE

MAY 20, 2023 | SHERATON DENVER DOWNTOWN HOTEL

EMPOWERING PATIENTS FOR INDIVIDUALIZED CAREEARLY

Barbara Davis Center for Diabetes
Children's Diabetes Foundation