



Just when you thought you knew everything about T1D...

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Conflicts of Interest/Disclosures

- I have no relevant financial relationships with commercial interests to disclose.
- Board member of the OR/SW Washington JDRF Board.
- I will be talking about off-label use of medication and diabetes technology.



Agenda

- Population Screening – new recommendations on population screening for type 1 diabetes (T1D)
- Immune Therapy – prolonging stage 3 T1D and prevention of progression of stage 1 and 2 T1D to stage 3.
- Diabetes technology – advancements and new options



Exemplary Cases



Patient 1

- Is an 11 yr old female with a family history of T1D in her mother.
- 1-2 week history of polys, fatigue, and weight loss.
- Last night she had new difficulty breathing and emesis x 1
- In the ED she is found to have a pH of 6.89 and a BG of 611.
- A1C is 14.8%.



Patient 2

- Is a 6 yr old male, Patient 1's youngest brother.
- Joined a research study called TrialNet Pathway to Prevention and is known to have 3 diabetes antibodies.
- The research site was unable to place an IV to do a GTT as follow-up to those antibodies.
- Mom follows her intuition one night and checks a BG. It's 274. Follow-up BGs the next day are mostly reassuring.
- A1C is 5.9%.



Screening



Stages of Type 1 Diabetes (T1D)

Stage 1

Normal blood sugar
2 or more autoantibodies

Stage 2

Abnormal blood sugar
2 or more autoantibodies

Stage 3

Insulin dependence
Some insulin secretion
**Clinical diagnosis of
T1D based on HbA1C**

Stage 4

Established T1D



Screening – Why is Screening Important

- Significantly reduces the risk of DKA at diagnosis from 60% to 3%
- Disease modifying therapy trials are launched and ready to recruit. Eligible participants are critical to immune therapy development.
- Current screening programs miss most people at-risk
 - 85% of those diagnosed with T1D do not have a family history and would not otherwise be screened.



Population Screening

- Current Screening Options: Positive family history
- TrialNet Pathway to Prevention Study
 - No cost screening of 5 diabetes autoantibodies
 - Qualifications:
 - Between the ages of 2.5 to 45 years with a parent, sibling, or child with T1D
 - Between the ages of 2.5 to 20 years with an aunt/uncle, cousin, grandparent, niece/nephew, or half-sibling with T1D
 - Between the ages of 2.5 to 45 years and have tested positive for at least one diabetes antibody outside of TrialNet.
 - In-home test kit or lab test kit or TrialNet location.



Population Screening

- Current Screening Options: No family history
- T1Detect ** NEW ** <https://www.jdrf.org/t1d-resources/t1detect/>
 - General population screening of 3 diabetes autoantibodies: GAD, Insulin, and IA-2A
 - Finger stick and blood spot filter paper
 - Currently \$55, with the option to order a subsidized kit
 - Goal to be able to bill insurance



Population Screening

- The JDRF now recommends universal screening of the general population for type 1 diabetes autoantibodies.
- Screening is not currently part of routine preventative services.
- Goal to receive positive rating by US Preventative Services Task Force which would encourage insurance coverage.



Immune Therapy

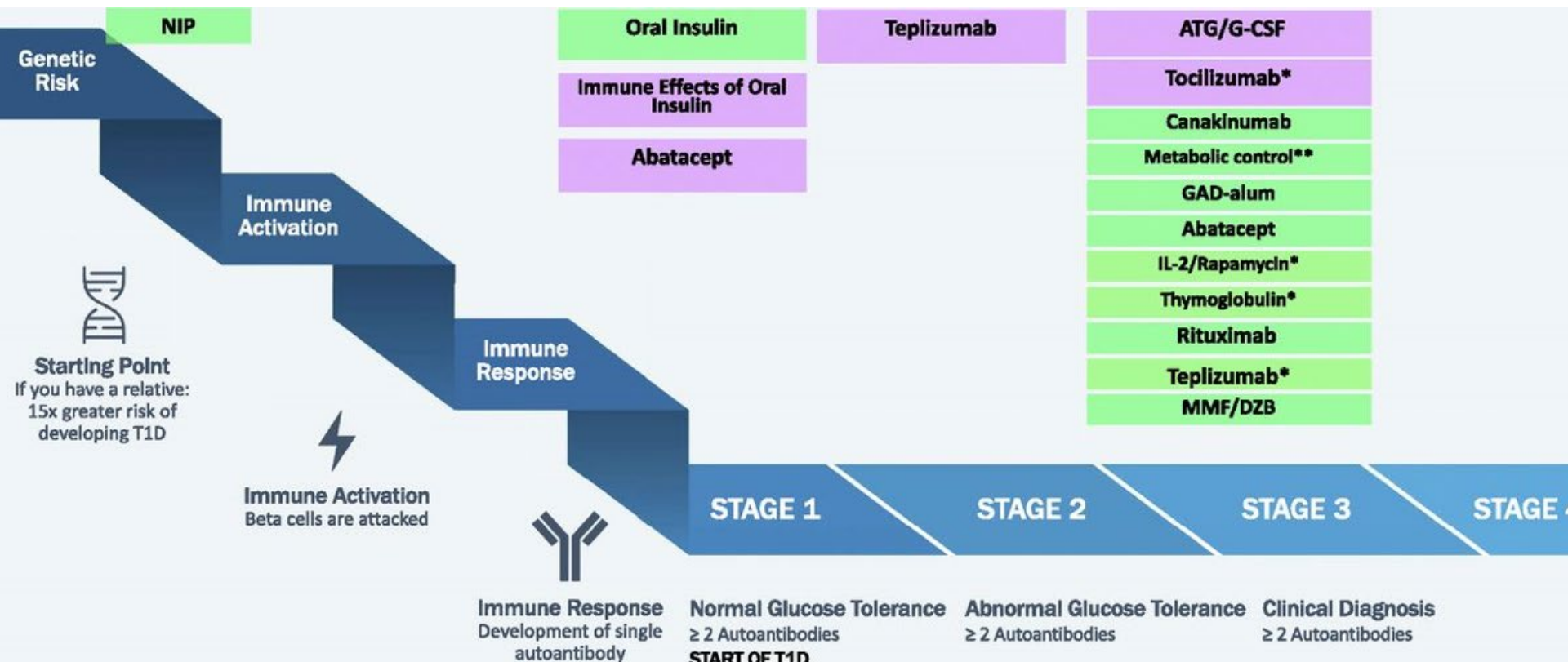


Immune Response in T1D

Cell types / Players	Function / Role in non-diabetes	Changes due to T1D	Desired Therapies
Beta Cells	Produce insulin	<ul style="list-style-type: none"> • Become stressed and more attractive to immune cell killing 	Increase their survival, number, and function
Teff Cells (Effector T Cells)	Fight threats and remove them	<ul style="list-style-type: none"> • Sees beta cells as threat and attacks • Too many; too active 	Disable Teff
Treg Cells (Regulatory T cells)	Reduce aggression from Teff and maintain immune regulation	<ul style="list-style-type: none"> • Unable to protect beta cells • Too few; too weak 	Enhance Treg
Immune Deviator Cells	Support Teff and Treg in their function	<ul style="list-style-type: none"> • Support Teff too much and Treg too little (imbalanced) 	Support Treg and hinder Teff



Immune therapy





Immune therapy

- Teplizumab – disables activated Teff cells
 - 2021 – one course prevents progression of stage 2 diabetes to stage 3 by at least 3 years. In FDA awaiting priority review for treatment in preventing T1D!
- Ustekinumab – blocks multiple harmful immune pathways
 - 2020 - Phase 2/3 study in pediatric stage 3 T1D
- ATG – inhibits activated immune cells
 - 2019 – prolongs “honeymoon” by 2 years in stage 3 T1D



Immune therapy

- JAK Inhibitors – stop the destruction of target organs in autoimmune disease and block immune cell activity
 - Case report: reversal of insulin dependence!
- Verapamil – cell stress reducer
 - 2018 – Verapamil could halt T1D disease progression in recently diagnosed adults
 - Pediatric study with pump therapies is starting (CLVer).



Immune therapy

- Local studies in pediatrics
 - Through the Benaroya Research Institute in Seattle, WA
- DREAMT Study: Identify markers to explain how Abatacept preserves insulin production
 - 6 – 55 years and diagnosed within the past 6 months
- PROTECT Study: Teplizumab in newly diagnosed children
 - 8 – 17 yrs old and diagnosed within the past 2-3 weeks
- Pathway to Prevention



Technology Advancements



Continuous Glucose Monitors

Freestyle Libre 2



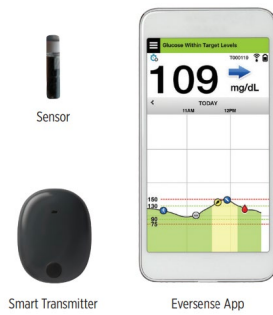
Medtronic Guardian3



Dexcom G6



Eversense





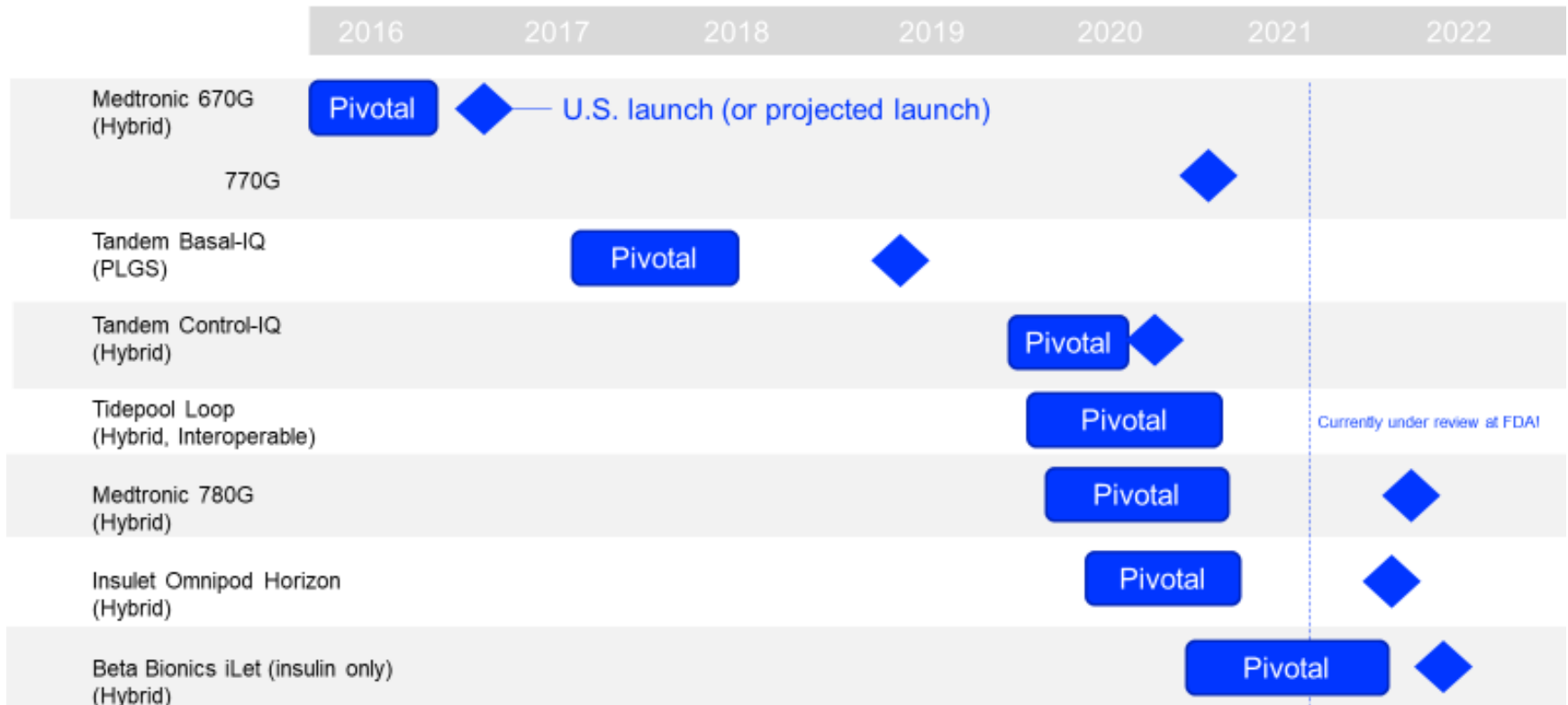
Continuous Glucose Monitoring

CGM	Dexcom G6	Freestyle Libre 2	Medtronic Guardian 3
Calibration	No	No	Yes, minimum 2 times/day
Length of wear	10 days	14 days	7 days
Linked Pump	Tandem, Omnipod5, Tidepool	No, not FDA approved for pumping	Medtronic 670G and 770G/780G
Alerts	Predictive, Customizable	Customizable	Predictive, Customizable
Remote Monitoring	Yes	No*	Yes*
Age (years)	2+	4+	2+
FDA Approval	iCGM, approved for bolusing	iCGM	Not for bolusing



Past 5 years of Pump Development

AP systems in development: current status in the U.S.

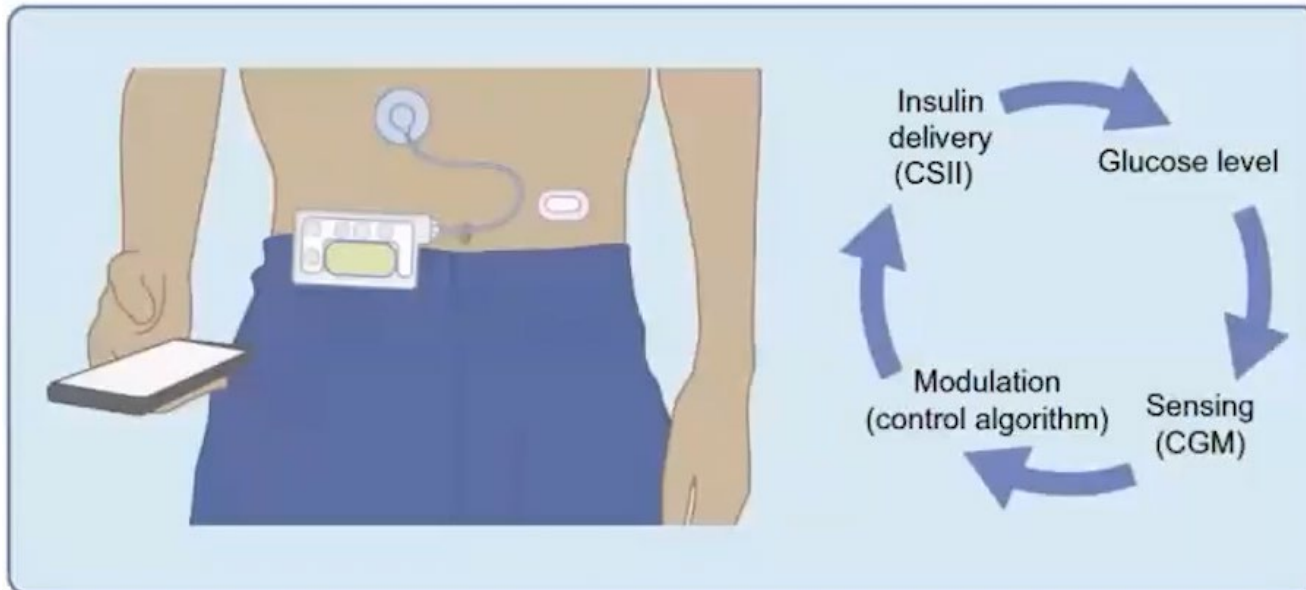




Hybrid Closed Loop Pumping

A hybrid closed loop system is made up of three parts:

1. A continuous glucose monitor
2. An insulin pump
3. A computer program (called an "algorithm") that takes data from both the pump and CGM and adjusts the pump's insulin delivery automatically





Hybrid Closed Loop Pumps



Medtronic 770G



Omnipod 5

Tandem X2 w/Control IQ



Tidepool Loop



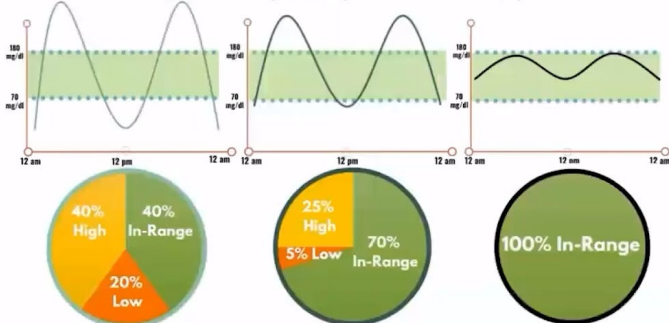
Tidepool Loop is not cleared for use in the US or outside of the US. Displayed is a conceptual rendering of a product in development.



Current Targets – A1C and Time in Range

- Time in Range: The amount of time the blood sugar is between 70 – 180.

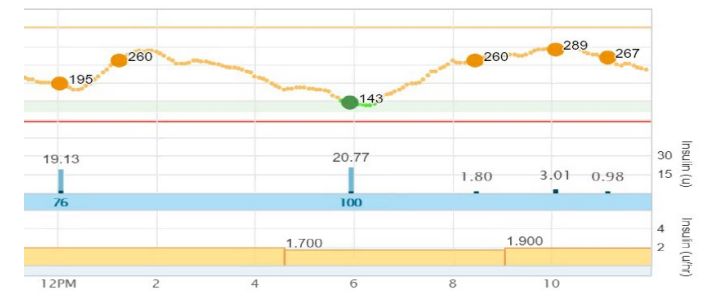
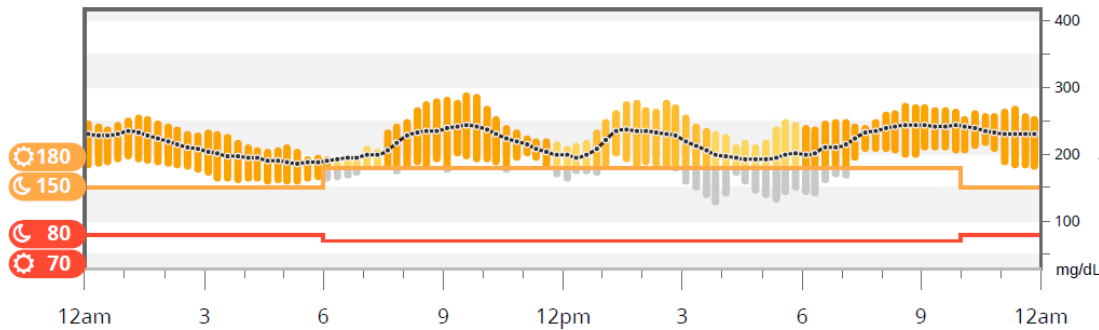
THE MANY FACES OF A 7% A1C
(and an average blood glucose of 8.6mmol/L)



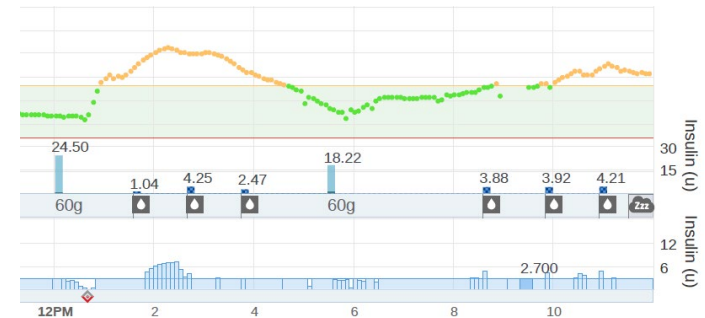
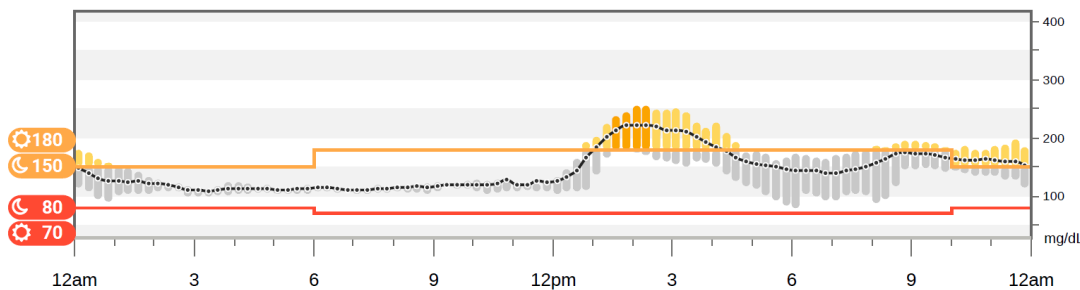


Pre and Post Hybrid Closed Loop Pumping

Pre



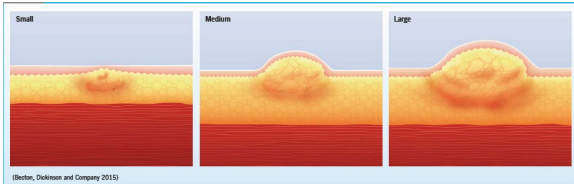
Post





Skin issues with pumps and CGMs

- Lipohypertrophy



- Lipoatrophy

- Reactions to adhesive

- Pump site infections





Future therapies

- Fully closed loop pumps
- Co-formulation of insulin and amylin
- Continuous ketone monitoring
- GLP-1 agonists for T1Ds
- Smart Insulin



When to Refer

- Epic code for internal referrals: Ref70I
- Fax number for external referrals: 971-282-0102
- Most T1D diabetes referrals are urgent and we prefer to discuss with you to triage the patient appropriately. We can provide out-patient education when clinically appropriate. Please call and ask to speak to the pediatric endocrinologist on call urgently so we are pulled immediately. Thank you!
- Phone: 503-216-6050, option 6 to reach the provider line.



Questions?

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 - Our Team:
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 - Rachel Marsh, CDCES
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PPSV23 Vaccine and Diabetes

- CDC Recommendations:
- Children 2 – 5 yrs old with diabetes
 - Give 1 dose of PPSV23 at least 8 weeks after completing the PCV13 series
- Children 6 – 18 yrs old with diabetes
 - Give 1 dose of PPSV23 if not already given earlier in childhood.