Diabetes *Management in 2020: New Medications and New Technology*

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Disclosures: None

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Objectives

- To Review Noninsulin Pharmacotherapy for diabetes
  - Brief overview of medication classes
  - Important new indications, adverse effects and protective effects of newer medications
- To Review Emerging Diabetes Technologies, including:
  - Continuous Glucose Monitors (CGM)
  - Insulin pump basics
  - Insulin Pump and CGM Integration
  - Artificial Pancreas/Hybrid Closed Loop Technology
  - Other Diabetes Technology on the horizon

Insulin Pump Basics

What is Insulin Pump Therapy?

- Also called Continuous Subcutaneous Insulin Infusion (CSII)
- Allows for continuous administration of rapid-acting insulin analogs (i.e. aspart or lispro insulin) via a small subcutaneous plastic catheter that is changed every 2-3 days
- Insulin administration is based on insulin pump settings (basal rates, bolus dosing, corrective dosing) determined by the provider

Who is a candidate for insulin pump therapy?

- Insulin pump therapy may be considered as an option for all adults, children, and adolescents with type 1 diabetes who are able to safely manage the device.
- Certain patients with insulin deficiency.
  - those with long standing type 2 diabetes
  - those who have had a pancreatectomy
  - individuals with cystic fibrosis

  This is an individual decision and must be tailored to fit patient needs and preferences.

Diabetes Technology: *Standards of Medical Care in Diabetes—2020*
American Diabetes Association. Diabetes Care 2020 Jan; 43(Supplement 1): S77-S88.

Insulin Pump Guidelines: AACE

Type 1 Diabetes

- Not meeting glycemic control goals on MDI
- Especially those with:
  - High glycemic variability
  - Frequent severe hypoglycemia and/or unawareness
  - Significant "dawn phenomenon"
  - Extreme insulin sensitivity
- Consider for flexibility and QoL
- Special populations
  - Preconception, pregnancy
  - Children, adolescents
  - Competitive athletes

Type 2 Diabetes

- Select patients on insulin with any/all of the below:
  - C-peptide positive, but with suboptimal control on MDI
    - Note: CMS only covers insulin pump therapy for those who are c-peptide deficient
  - Substantial "dawn phenomenon"
  - Erratic lifestyle
  - Severe insulin resistance (candidate for U500 insulin by CSII)
  - Selected patients with other types of DM (e.g. post-pancreatectomy)

Grunberger G., et al. AACE/ACE 2018 Position Statement on Integration of Insulin Pumps and CGM in Patients with DM. Endocrin Pract. March 2018, Vol 24, No.3 pp 302-308

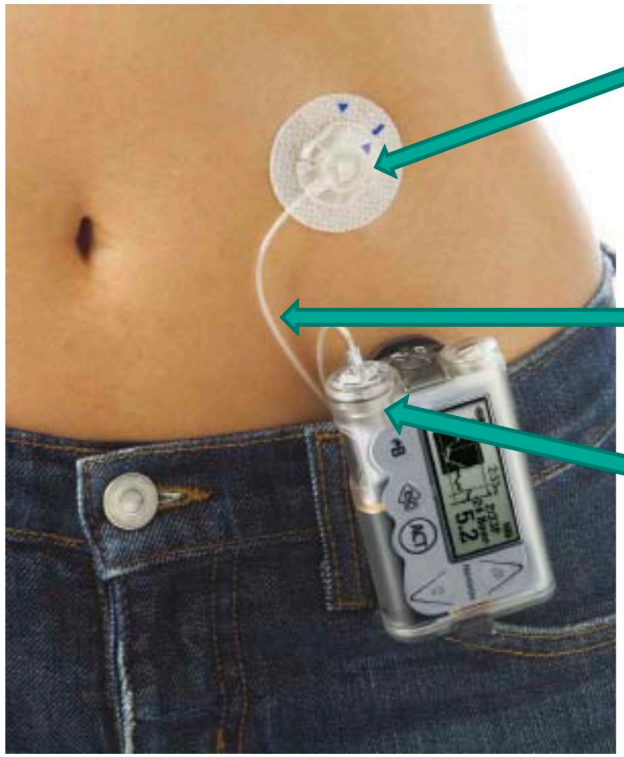
Insulin Pump Guidelines: Other Considerations

Characteristics suggesting patient may not be a good candidate for insulin pump therapy:

- Unable/unwilling to perform MDI, recommended glucose testing or carbohydrate counting
- Lack of motivation to achieve tighter glucose control, history of non-adherence
- Concerns about pump therapy interfering with lifestyle
- History of serious psychological or psychiatric condition
- Unable to recognize the limitations of insulin pump therapy
  - Unrealistic expectations (e.g. the insulin pump will eliminate patient responsibility for diabetes management)

Peters AL et al. J Clin Endocrinol Metab. 2016 Nov;101(11)
Grunberger G, et al. Endocrine Practice: May 2014, Vol. 20, No. 5, pp. 463-489.

Anatomy of the Insulin Pump



Infusion site/cannula:

- Small flexible plastic cannula inserted into SC tissue by a small retractable needle

Tubing: component of each insulin pump (except Omnipod)

- Connects insulin reservoir to infusion site

Reservoir: insulin storage

- Between 200-300 units

Current Commercially Available Insulin Pumps

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Insulin Pump Settings

- **Basal Rate**
  - Continuous infusion of rapid-acting insulin to provide basal/long-acting coverage
  - Entered as units of insulin/hour and can be programmed to have different rates for different times of day
  - Temporary increases or decreases in basal rates can also be programmed
- **Insulin-to-Carb Ratio**
  - Used to calculate insulin bolus dose to cover carbohydrate/meal intake
- **Sensitivity Factor**
  - Used to calculate corrective insulin dosing for hyperglycemia
- **Target Glucose**
  - Entered as a single target glucose value or target glucose range (i.e. 90-150 mg/dL)
    - Corrects hyperglycemia using sensitivity factor at upper limit
    - Subtracts insulin from bolus dose if pre-meal blood sugar is under lower limit
- **Active Insulin Time**
  - Estimated duration of insulin action (usually 3-4 hours)

Advantages of Insulin Pump Therapy

- Ability to more closely approximate physiologic insulin secretion
- Ability to administer very small doses of insulin accurately
- Flexibility in insulin dosing to accommodate lifestyle needs (i.e. reduced basal rates for physical activity)
- Improved quality of life for many patients
- Improvement in glycemic control[1]
- Reduction in rates of severe hypoglycemia and DKA[2]

Possible Disadvantages of Insulin Pump Therapy

- High cost, need for insurance coverage
- Labor-intensive
  - Site changes every 2-3 days
  - Close monitoring for any device/site malfunction
  - Maintaining adequate supplies
  - May not improve quality of life for some patients
- Appearance/Device wear
- Adhesive allergy

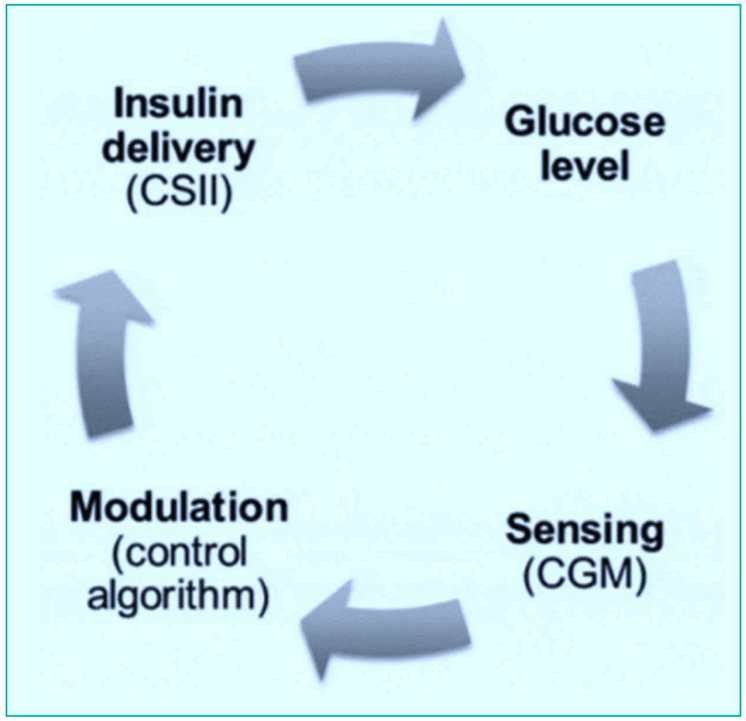
Integrating CGM and Insulin Pump Technology

- Insulin pump therapy can help improve glycemic control and reduce hypoglycemia, but it requires close monitoring and attention from the patient
- The use of insulin pump and CGM technology together has progressed towards automated insulin delivery, where infusion of insulin is automated and driven by CGM glucose values

Integrating CGM and Insulin Pump Technology

- **Sensor-augmented pump (SAP) therapy**
  - Use of insulin pump and CGM, but without cross-talk between them
- **Threshold or low glucose suspend**
  - Suspends insulin infusion at a predetermined glucose value
- **Predictive low glucose suspend (PLGS)**
  - Suspends insulin infusion prior to reaching threshold low glucose value
- **Automated insulin delivery (AID) or Hybrid Closed-Loop (HCL)**
  - Algorithm-based modulation of insulin infusion according to CGM glucose values and trends, including PLGS functions.

Automated Insulin Delivery/Hybrid Closed-Loop (HCL) Technology



Majeed W, Thabit H. Closed-loop insulin delivery: current status of diabetes technologies and future prospects. Expert Review of Medical Devices. 2018;15(8):579-590.

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Hybrid Closed-Loop System: Medtronic 670G

- Approved US FDA September 2017 for patients with T1D ≥14 years old, then expanded to ages 7-13 years in June 2018[1]
- Auto mode
  - Preset glucose target 120 mg/dL
  - Temp target of 150 mg/dL up to 12 hours
  - Adjustment of basal rate every 5 minutes
  - Requires announcement of meals/carbohydrates for bolus calculation
- Predictive low-glucose suspend
  - Stops insulin infusion up to 30 minutes before reaching your preset low limit
- Manual mode
  - Standard insulin pump settings

[1]Knebel et al. Clin Diabetes. 2019 Jan;37(1):94-95.

Hybrid Closed -Loop System: Tandem t:slim X2 with Control-IQ

	Delivers	Delivers an automatic correction bolus if sensor glucose is predicted to be above 180 mg/dL
180		
	B Increases	Increases basal insulin delivery if sensor glucose is predicted to be above 160 mg/dL
160		
	B Maintains	Maintains active Personal Profile settings
112.5		
	B Decreases	Decreases basal insulin delivery if sensor glucose is predicted to be below 112.5 mg/dL
70 mg/dL		
	0 Stops	Stops basal insulin delivery if sensor glucose is predicted to be below 70 mg/dL

https://www.tandemdiabetes.com/products/t-slim-x2-insulin-pump/control-iq.
Accessed on September 11, 2020.

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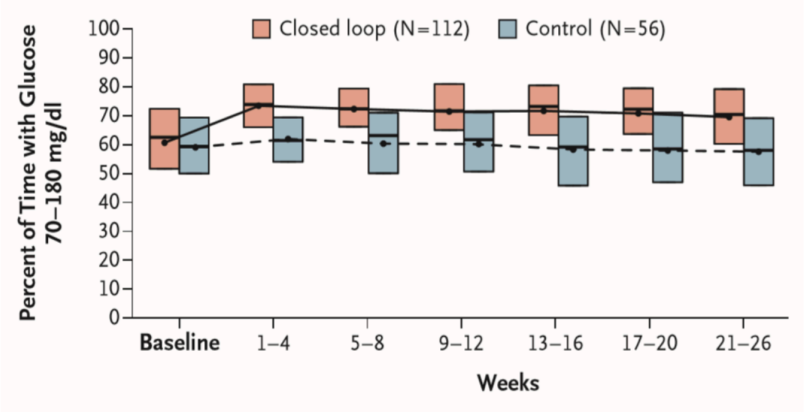
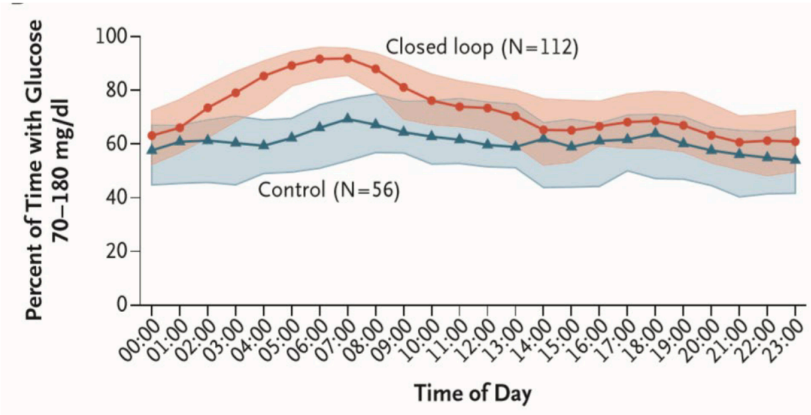
Tandem HCL algorithm

- **Multicenter RCT comparing SAP to closed-loop therapy with Control-IQ algorithm**
- 168 patients with T1D > 1 year on insulin therapy, age 14-71 years, A1C 5.4%-10.6%
- **Primary outcomes**: Percentage of time in target glucose range (70-180 mg/dL)
- **Results**: Use of the Control-IQ closed-loop algorithm resulted in a greater percentage of time spent in target glucose range compared to SAP (71±12% vs. 59±14%, P<0.001).





HCL, hybrid closed-loop; MDI, multiple daily injections; A1C, hemoglobin A1C; AUC, area under the curve; RCT, randomized controlled trial; SAP, sensor-augmented pump; T1D, type 1 diabetes;

Brown SA et al. *N Engl J Med.* 2019 Oct 31;381(18)

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HCL Systems in Development: Omnipod5/Horizon

GLYCEMIC OUTCOMES OVER THE 36-H HYBRID CLOSED-LOOP PHASE

Parameter	*Adults*[a] *(n = 24)*	*Adults (n = 10)*	*Adolescents (n = 12)*	*Pediatrics (n = 12)*
Mean sensor glucose, mg/dL	161.5 (20.1)	155.0 (14.8)	153.4 (21.6)	156.9 (20.4)
Standard deviation, mg/dL	54.0	46.2	48.6	53.3
Coefficient of variation, %	33.4	29.8	31.8	34.0
Percentage time in glucose range				
<54 mg/dL	0.1 (0.3)	0.1 (0.3)	0.2 (0.3)	0.2 (0.7)
<60 mg/dL	0.2 (0.6)	0.2 (0.6)	0.7 (0.9)	0.6 (1.2)
<70 mg/dL	0.7 (1.7)	0.7 (1.2)	2.0 (2.4)	2.0 (2.6)
70 to 140 mg/dL	41.5 (18.1)	41.9 (16.3)	40.2 (15.5)	39.4 (16.1)
70 to 180 mg/dL	69.5 (14.4)	73.0 (15.0)	72.6 (15.5)	70.1 (12.3)
>180 mg/dL	29.7 (14.4)	26.3 (14.4)	25.4 (16.1)	27.9 (13.2)
≥250 mg/dL	8.0 (7.5)	3.6 (3.7)	4.9 (6.3)	6.7 (5.6)
≥300 mg/dL	2.0 (2.9)	0.5 (1.1)	0.1 (0.5)	1.0 (2.2)

- **Single-arm, multicenter observational trial evaluating safety and feasibility of OmniPod MPC algorithm in pediatric, adolescent, and adult patients with T1D**
- Population: 6-65 years, T1D ≥1 year, A1C 6%-10% in past 6 months, insulin pump use ≥6 months, and total daily insulin dose >0.4U/ kg
- **Primary outcomes:** % time sensor glucose was <70 mg/dL and % time in ≥ 250 mg/dL during HCL phase
  - Secondary endpoints: Sensor mean glucose, % time ≤50, ≤60, 70-140, 70-180, ≥180, ≥300 mg/dL, SD, CV of CGM values
- Omnipod MPC algorithm was safe during day and night for all three populations; longer term studies will assess safety and performance under independent living situations in all ages

Buckingham et al. *Diabetes Technol Ther*. 2018. 20(4). Republished by Pubmed 29431513

Do-It-Yourself Hybrid Closed-Loop Systems

- Medtronic 670G is the only first generation artificial pancreas system available
  - Several other systems are under evaluation in clinical trials[1]
- Frustration with the slow pace of such trials has led to ”looping” with DIY HCL systems, thus creating momentum for patient-led healthcare innovation[1]
- An online community of “loopers” exists for support and can be found via the hashtag #WeAreNotWaiting[1]
- DIY systems are not FDA approved, and in May 2019 the FDA issued its first-ever warning statement about their use[2]
  - This warning was based on a non-fatal accidental insulin overdose in a patient with T1D who used a DIY system
  - A joint statement from 3 online DIY system developers highlighted the fact that the warning was based on outcomes from a single patient who was outside of the US, and that the patient has since recovered

1. Marshall et al. *Diabetes Ther.* 2019 Aug 22. [Epub ahead of print]
2. Caffrey. https://www.ajmc.com/newsroom/fda-issues-warning-on-do-it-yourself-artificial-pancreas. 2019.

New Diabetes Technology On the Horizon…

- **Tandem t:sport mini-pump**: half the size of t:slim X2, patch style pump with no display screen with a side button for quick insulin dose from the device
- **Insulet's Omnipod Horizon**: closed loop system with a patch pump
- **Medtronic Minimed 780G**: advanced hybrid closed loop system, has SmartGuard technology and DreaMed Diabetes algorithm, provides automatic correction bolusing and basal dosing, adjusting for missed meals, built-in Bluetooth technology (this was cleared in EU June 2020)
- **Dexcom G7**: sensor duration 14-15 days, fully integrated sensor and transmitter, thinner, updated software, accelerometer
- **Senseonics**: 180-day sensor
- **MannKind Corp BluHalePro**: updated version of Afrezza inhaled insulin with connectivity capability and monitoring of inhalation technique
- **Lilly**: new connected insulin pen that communicates with Dexcom CGM
- **AerBetic**: noninvasive wristband CGM that uses nanotechnology

Hoskins M, Tenderich A. New diabetes technology to watch for in 2020, January 2020. Tenderich A. new diabetes wearables and more at CES and JP Morgan 2020, January 2020.

Diabetes Management in 2020: New Medications and New Technology

Summary

- Reviewed diabetes pharmacotherapy
- Overview of new data regarding CV and renal impact of several newer classes of diabetic medications

- Reviewed currently available diabetes technology
  - continuous glucose sensors
  - Insulin pumps
  - Hybrid closed loop systems
  - Upcoming diabetes technology

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Questions?