Insulin – Ultimate Hormone Replacement Therapy

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Disclosures

- Diana Isaacs, PharmD, BCPS, BCACP, CDCES, BC-ADM, FADCES, FCCP declares the following disclosures:
- Speaker: Abbott, Dexcom, Novo Nordisk, Insulet, Medtronic
- Consultant: Lilly, Sanofi
- CBDCES Credentialing Committee
- ADA Professional Practice Committe

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Objectives – Insulin –The Ultimate Hormone Replacement Therapy

Objectives:

- Discuss the actions of different insulins
- Describe how to use the ADA algorithm for insulin management
- Counsel a person with diabetes on safe and effective insulin use

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Learning Objectives

- Discuss strategies to determine and fine-tune basal and bolus insulin settings based on glucose pattern management
- Describe how insulin settings are used to program insulin pumps and connected insulin pens

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History of insulin

- Insulin is produced by beta cells in the pancreas
- Discovered in 1921 by Frederick Banting and his assistant Charles Best from a dog's pancreas
- First used in a dog with diabetes and kept him alive for 70 days until they ran out of extract
- With the help of JB Collip and John Macleod, insulin was derived from the pancreas of cattle and in January 1922, given to a 14-year-old dying from diabetes in a Toronto hospital
- In 1923, Banting and Macleod received the Nobel Price in Medicine which they shared with Best and Collip
- Soon after, Eli Lilly started large-scale production of insulin

ADA. The history of a wonderful thing we call insulin (accessed 2020 Aug 29).

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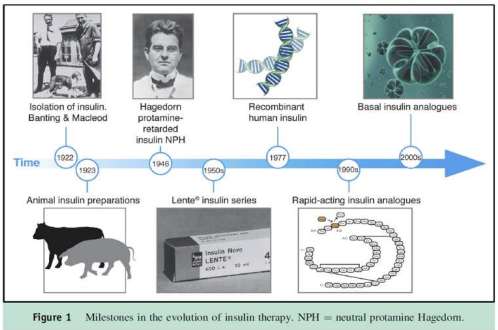

Figure 1 Milestones in the evolution of insulin therapy. NPH = neutral protamine Hagedorn.

Evolution of Insulin: From Human to Analog. Joseph M. Tibaldi, MD
American Journal of Medicine, 2014

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Evolution of Insulin

- Earlier insulins derived from bovine and porcine pancreas
- All human insulin now made from recombinant DNA technology
  - Modification of human insulin molecules
  - Overcame problems with human insulin
    - Onset of action
    - Duration of action
    - Absorption

Candido R, et al. Diabetes Ther. 2018; 9(3):927-949.

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Basal aka "Background" Insulin

- The liver plays a major role in maintaining glucose levels by regulating the process of gluconeogenesis and glycogenolysis in the liver
- Excessive hepatic glucose leads to hyperglycemia
- In a person without diabetes, there is a low level of insulin to keep glucose homeostasis from glucose produced by the liver (**basal insulin**)
- People with type 1 diabetes lack the ability to produce insulin to counteract the liver's effects
- In people with type 2 diabetes, there may not be enough insulin due to insulin resistance
- Long-acting insulins or intermediate-acting insulins serve as a basal or "background insulin"
- In an insulin pump, a regular or rapid-acting insulin can be given continuously to serve as the basal

Everyone with T1D need basal insulin and many with T2D may need it

Sharabi K et al. Mol Aspects Med. 2015; 46:21-22.

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Bolus Insulin

- Glucose rises in response to carbohydrates
- A regular or rapid-acting insulin is given as a bolus to prevent the glucose from rising too much
- A regular or rapid-acting insulin can also be given to "correct" a high glucose

Everyone with T1D needs bolus insulin, some people with T2D may need it to achieve glycemic targets

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Physiologic Insulin Release

- **1st phase:** peak 1-2 minutes, duration 10 minutes, suppresses hepatic glucose production
- **2nd phase:** duration 1-2 hours

The perfect insulin would be fast enough to match the absorption of carbohydrates

Freeman JS. J Am Osteopath Assoc. 2009;109:26-36.

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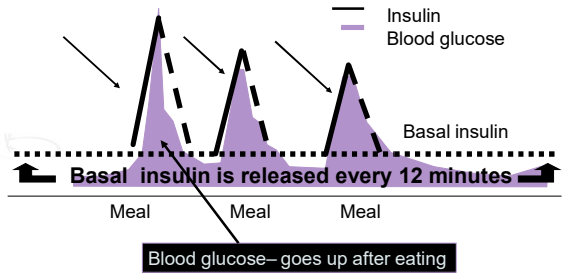
Normal Insulin Release:
Individuals without diabetes

Insulin bolus occurs in the first 10 minutes after eating



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Available Insulins

- None of the commercially available insulins are as fast as true physiologic insulin (as made from a person without diabetes)
- Almost all insulin is injected (SC or IV)
- Oral insulin is not available and degrades too quickly
- One inhaled insulin option (Afrezza®)

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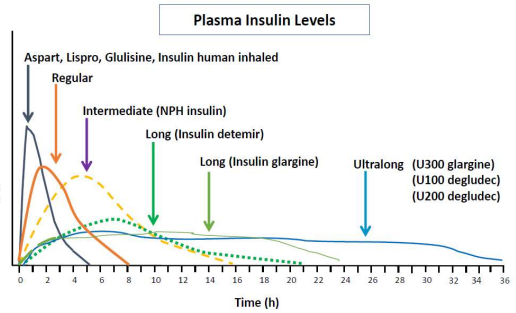
Insulin Profiles



Hirsch IB. NEJM 2005;352:174-183.
Lexicomp Online, Lexi-Drugs Online, Hudson, Ohio: UpToDate, Inc; 2020; August 21, 2020.

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Insulin PocketCard™

Diabetes Education Services

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Action		Insulin Name	Onset	Peak	Effective Duration	Considerations
Bolus	Very Rapid Acting Analogs	Aspart (Fiasp)	2.5 min	~60 min	3-5 hours	Bolus insulin lowers after-meal glucose. Post meal BG reflects efficacy. Basal insulin controls BG between meals and nighttime. Fasting BG reflects efficacy. Side effects: hypoglycemia, weight gain. Typical dosing range: 0.5-1.0 units/kg body wt/day. Discard most open vials after 28 days. For pen storage guidelines, see package insert.
		Lispro-aabc (Lyumjev)	1 min	~60 min	4-5 hours	
	Rapid Acting Analogs	Aspart (Novolog)	5 - 15 min	30 - 90 min	< 5 hrs	
		Lispro (Humalog*/ Admelog)				
		Glulisine (Apidra)				
	Short Acting	Regular*	30 - 60 min	2 - 4 hrs	5 - 8 hrs	
Basal	Intermediate	NPH	2 - 4 hrs	4 - 10 hrs	10 - 16 hrs	
	Long Acting	Detemir (Levemir)	3 - 8 hrs	No peak	6 - 24 hrs	
		Glargine	2 - 4 hrs		20 - 24 hrs	
		Degludec (Tresiba)*	~ 1 hr		< 42 hrs	
Basal + Bolus	Intermediate + short	Combo of NPH + Reg 70/30 = 70% NPH + 30% Reg 50/50 = 50% NPH + 50% Reg	30 - 60 min	Dual peaks	10 - 16 hrs	
	Intermediate + rapid	Novolog® Mix - 70/30 Humalog® Mix - 75/25 or 50/50	5 - 15 min		24 hrs	

Concentrated insulins available - see Concentrated Insulin Card for details. Insulin action times vary; time periods are general guidelines only. All PocketCard content is for educational purposes only. Please consult prescribing information for detailed guidelines. © 3/2022

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Insulin Concentration

- Most insulin is U100: 100 units/mL
- There is also concentrated insulin
  - U500 insulin, 500 units/mL, U300, 300 units/mL, and U200, 200 units/mL
- Insulin is available in a vial, pen, or cartridge
- U100 insulin:
  - 1 vial =10mL = 1000 units
  - 1 pen =3 mL = 300 units
  - 1 cartridge = 3 mL = 300 units
  - 1 box of pens = 5 pens = 1500 units
- Inhaled insulin
  - 4, 8, 12 units cartridges

Afrezza, Novolog, Humalog, Lantus, Levmir (package inserts) 2022
Image: :Blausen.com staff (2014). Medical gallery of Blausen Medical 2014. WikiJournal of Medicine 1 (2).

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Concentrated and Inhaled Insulin

Name/Concentration	Insulin/Action	Considerations
Humulin Regular U-500 • 500 units insulin/mL • KwikPen or Vial	Regular Bolus / Basal	Indicated for those taking 200+ units daily. 3 mL pen holds 1,500 units. Max dose 300 units. Once opened, good for 28 days. 20 mL vial holds 10,000 units. Max dose 250 units using U-500 syringe. Once opened, good for 40 days.
Humalog KwikPen U-200 200 units insulin/mL.	Lispro (Humalog) Bolus	3 mL pen holds 600 units. Max dose 60 units. Once opened good for 28 days.
Lyumjev KwikPen U-200 200 units insulin/mL.	Lispro (Lyumjev) Bolus	3 mL pen holds 600 units. Max dose 60 units. Once opened good for 28 days.
Toujeo Solostar U-300 Pen 300 units insulin/mL.	Glargine (Lantus) Basal	1.5 mL pen holds 450 units. Max dose 80 units. 3 mL Max Solostar pen holds 900 units. Max dose 160 units. Once opened good for 56 days.
Tresiba FlexTouch U-200 Pen 200 units insulin/mL.	Degludec (Tresiba) Ultra basal	3 mL pen holds 600 units. Max dose 160 units. Once opened good for 56 days.

All concentrated insulin pens and the U-500 syringe automatically deliver correct dose (in less volume). No conversion, calculation or adjustments required. For example, if order reads 30 units, dial the concentrated pen to 30 units or draw up 30 units on the U-500 syringe. **Important – never withdraw concentrated insulin from the pen using a syringe.**

Inhaled Insulins

Action	Insulin Name	Dose Range	Onset	Peak	Duration	Considerations
Bolus – Rapid-acting	Afrezza inhaled regular human insulin	4, 8, and 12 unit cartridges before meals	~ 12 min	35 - 45 mins	1.5 - 3 hrs	Assess lung function. Avoid in lung disease — bronchospasm risk. Side effects: hypo, cough, throat irritation.

The information listed here are not guidelines. Please consult prescribing information for details. DiabetesEd.net ©2022

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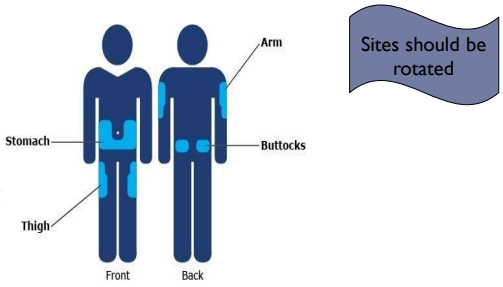
Insulin Injection Sites



Sites should be rotated

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Insulin Key Counseling Points

- Do not shake insulin
- Cloudy insulin (NPH or pre-mixed) should be rolled before use so suspension is uniform
- Pens should be primed before every use to get air bubbles out
- Skin thickness is usually 2mm regardless of person's size, so shortest needles (4mm) work well for most
- Take outer and inner covering off for pen needles
- Leave the needle/syringe in the body for 5-10 seconds
- Change needle or syringe with each injection
- Dispose of needles/syringes in a sharps container or per local regulations

Dang DK. Taking medication. In: Cornell S et al, eds. The art and science of diabetes self-management education desk reference. 5th ed.

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Priming insulin

- Hold vertically with needle at the top
- Turn dial to 2 units
- Push plunger
- Repeat until insulin comes out of the top
- May have to do multiple times for a new pen
- This will ensure all of the air is out and that pen needle works
- Do this every time an insulin pen injection is given

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Importance of Insulin Storage

- Insulin is a peptide hormone drug
- It is susceptible to changes in stability when exposed to environmental factors
- These factors accelerate physical and chemical degradation
- If unopened, insulin should be stored in a refrigerator at 2℃ to 8℃ (36℉ - 46F) to keep their quality until the expiration date
  - Max temperature 8℃ (46F)
- Once opened, Insulin can be stored at room temperature up to 25℃ or 30℃ (77℉ or 86F)
  - No need to keep in fridge
  - Injecting cold insulin may be uncomfortable

Heinemann, L et al. J Diabetes Sci Techno. 2020.

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Insulin & Expiration

Type		Expiration Once Open
Long Acting		
Toujeo	Glargine U-300	56 days
Lantus, Basaglar, Semglee	Glargine U-100	28 days
Tresiba	Degludec U-100, U-200	56 days
Rapid Acting		
Novolog, Fiasp	Aspart	28 days
Humalog, Admelog	Lispro U-100, U-200	28 days
Apidra	Glulisine	28 days
Lyumjev	Lispro-aabc	28 days

Package Inserts

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Insulin Teaching Keys

- Rotate
- Stay 1" away from previous site
- Don't re-use syringes/needles
- Look for:
  - Lipodystrophy
  - Lipohypertrophy
- Proper disposal
- Review patient's ability to withdraw and inject.

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Sharps Disposal: Product and Info

- Search for household hazardous waste listing for your city or county.
- Call 1-800-CLEANUP (1-800-253-2687)

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Side Effects of Insulin

- Weight Gain
- Lipodystrophy/ Lipohypertrophy
- Hypoglycemia

Dang DK. Taking medication. In: Cornell S et al, eds. The art and science of diabetes self-management education desk reference. 4th ed.

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Polling Question

- After how many days should an open vial of insulin degludec be discarded?

A. 28 days
B. 30 days
C. 42 days
D. 56 days

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How to Dose Insulin

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Type 1 Diabetes (T1D)

- Absolute deficiency in endogenous insulin
- Exogenous insulin is required
- The regimen should include:

Basal Insulin + Bolus Insulin

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How to Dose Insulin? T1D

- Newly diagnosed T1D
  - Total insulin dose: 0.5-1.0 units/kg/day
  - 50% basal
  - 50% bolus
- Bolus can initially start with set doses or calculations can be used to determine initial carbohydrate ratio and correction factor

Pamagluapatai LG et al. In: Cornell S et al., Pharmacolotherapy for Glucose Management. The art and science of diabetes self-management education desk reference. 5th ed.

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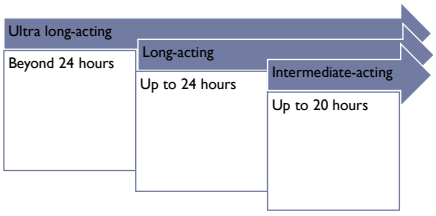
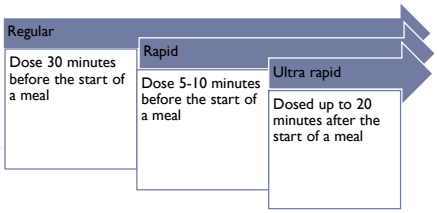
Types of Basal Insulin



Pamagluapatai LG et al. In: Cornell S et al., Pharmacolotherapy for Glucose Management. The art and science of diabetes self-management education desk reference. 5th ed.

29

Types of Bolus Insulin



Pamagluapatai LG et al. In: Cornell S et al., Pharmacolotherapy for Glucose Management. The art and science of diabetes self-management education desk reference. 5th ed.

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T1D: Insulin Dosing Regimens

Time of Insulin Administration	Before breakfast	Before lunch	Before dinner	Bedtime
Method 1	Intermediate: Regular (2/3 TDD) 2:1 ratio		Intermediate: Regular (1/3 TDD) 2:1 ratio	
Method 2	Regular/ analog (1/2 TDD ÷ by 3)	Regular/ analog (1/2 TDD ÷ by 3)	Regular/ analog (1/2 TDD ÷ by 3)	Long-acting (1/2 TDD)

***These are starting regimens and are adjusted based on ability to carbohydrate count and glycemic management as determined by A1C, BGM and/or CGM

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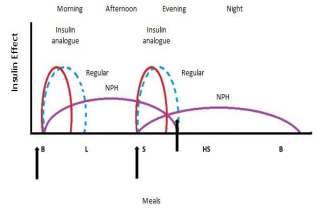
Intermediate-acting Insulin + Regular Insulin or Insulin Analog



Intermediate insulin serves as basal while regular or insulin analog serves as bolus

Regular insulin: Novolin R, Humulin R
Intermediate insulin: Novolin N, Humulin N
Insulin analogue: aspart, lispro, glulisine

Dipiro JT et al, eds. Pharmacotherapy: a pathophysiologic approach. 11th ed. 2020.

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Method 1 Example

- Lacy has T1D and prefers a simple regimen with less insulin injections. She also has difficulty paying for the more expensive insulin analogs. Lacy takes the following regimen:
  - Insulin NPH 27 units QAM and 13 units QPM (intermediate insulin)
  - Insulin regular 13 units QAM and 7 units QPM (regular insulin)
- She has the option of using a 70/30 formulation dosed twice daily or
- She can mix NPH and regular insulin if using vials (not commonly done anymore)

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Patient Education: Mixing Insulin

- NPH can be mixed with regular or rapid-acting insulins when using vials
- Inject air into NPH vial first (# of units for the NPH dose) and pull syringe out without NPH
- Then inject air into regular or rapid-acting insulin vial (# of units for the regular or rapid-acting dose) and this time draw out the exact amount of insulin
- Then put syringe filled with regular or rapid-acting insulin into NPH vial and draw out the full dose of NPH
- This is a way to reduce injections, but isn't commonly done anymore
- Other insulins should not be mixed!

ADCES. Insulin injection resources

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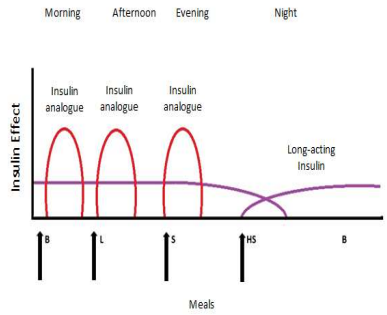
Long-acting Insulin with Insulin analog



Long-acting serves as basal insulin analog serves as bolus

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Method 2 Example

- Genie is 15 years old and newly diagnosed with T1D. She weighs 60kg and is started on 0.5 units/kg/day. (30 units total)
- She takes insulin glargine 15 units once daily (long-acting insulin)
- She takes insulin lispro 5 units TID a.c. (rapid-acting insulin)
- Question: Can these types of insulins be mixed?
- **NO**

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Carbohydrate Ratio

- Insulin to carbohydrate ratio (ICR)
  - 1 unit of insulin is expected to cover X grams of carbohydrates
- Rule of 450 (regular insulin) or 500 (rapid acting insulin) can be used
  - 500/TDD = estimated carbohydrate ratio

Trujillo J et al. Diabetes mellitus. In: Dipiro JT et al., eds. Pharmacotherapy: a pathophysiologic approach. 12th ed.

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Correction Factor

- Insulin correction factor (ICF)
  - Often returned to as insulin sensitivity
  - 1 unit of insulin is expected to lower glucose by Y points
- Rule of 1700 or 1800 can be used
  - 1700/TDD = estimated ICF
- For regular insulin, the rule of 1500 is typically used

Trujillo J et al. Diabetes mellitus. In: Dipiro JT et al., eds. Pharmacotherapy: a pathophysiologic approach. 12th ed.

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An Example: Meet Larry

- Larry is a 12-year-old newly diagnosed with T1D, he weighs 40kg
- He is started on 0.5 units/kg/day of total insulin
  - 40*0.5=20 units
  - 50% basal=10 units
  - 50% bolus=10 units
- Larry is prescribed 10 units of long-acting insulin and 3 units of rapid-acting insulin at meals
- The insulin doses will be adjusted based on glucose data

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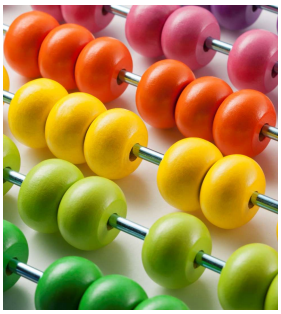
Larry Calculation cont'd

- Larry is ready for carbohydrate counting
- Based on the rule of 500 and rule of 1700, what should his ICR and ICF be?



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Poll Question

- Based on the rule of 500 and rule of 1700, what should Larry's ICR and ICF be? (TDD=20 units/day)

A. ICR=25, ISF=85
B. ICR=20, ISF=60
C. ICR=15, ISF=50
D. ICR=30, ISF=75
E. I am not sure

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Answer and Explanation

- ICR=500/20=25
  - This means that 1 unit of insulin covers 25 grams of carbohydrate
  - If Larry eats 50 grams of carbohydrate, he should inject 2 units
- ISF=1700/20=85
  - This means that 1 unit of insulin is expected to lower glucose by 85 mg/dL
  - Larry's glucose target is 100
  - If his current glucose is 185, he should take 1 extra unit of insulin

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Correction Bolus (Common Scale)

Rapid/Fast Acting Insulin (1 unit:50 mg/dl>150)

Less than 70	Subtract 1 unit
70-150 mg/dl	0 units
151-200 mg/dl	1 unit
201-250 mg/dl	2 units
251-300 mg/dl	3 units
301-350 mg/dl	4 units
351-400 mg/dl	5 units

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Correction Bolus (Common Scale)

Rapid/Fast Acting Insulin (2 units:50 mg/dl>150)

Less than 70	Subtract 1 unit
70-150 mg/dl	0 units
151-200 mg/dl	2 unit
201-250 mg/dl	4 units
251-300 mg/dl	6 units
301-350 mg/dl	8 units
351-400 mg/dl	10 units

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Poll Question

- How much insulin does a person with type 1 diabetes need a day?
  a. About 1 unit per pound per day
  b. No more than 0.5 units/kg per day
  c. Approximately 5 units/kg per day
  d. About 0.5 to 1.0 units/kg per day

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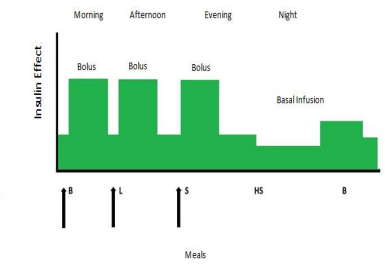
Insulin Pump Therapy



Regular or insulin analogs serve as both the basal and bolus

Dipiro JT et al, eds. Pharmacotherapy: a pathophysiologic approach. 11th ed. 2020.

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Pump Terminology

- Basal rate - a continuous 24-hour delivery of insulin, "background" insulin
- Bolus dose – used for carbohydrate and correction doses
- Insulin-to-carb ratio – how many grams of carbs will be covered by 1 unit of insulin
- Insulin sensitivity factor (aka correction bolus or ISF) – how much 1 unit of insulin is expected to lower glucose
- Target – the goal glucose level
- Insulin-on-board (aka active insulin time or IOB) – a pump feature that keeps track of a previous bolus

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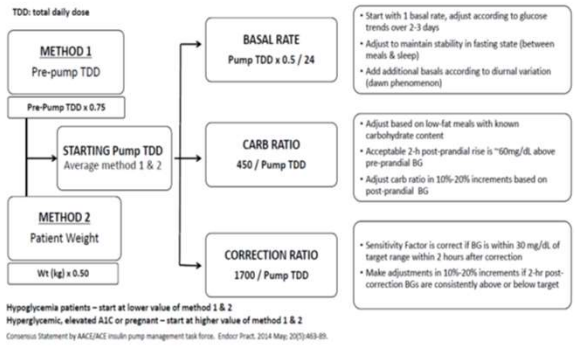
Initial Pump Calculations



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Nick is a 21 year old male about to start insulin therapy

- Weight: 72kg
- Weight based dosing
  - 72*0.5=36 units
- Basal=36/2=18 units
  - If using injections, plan for a basal of 18 units daily
  - If using a pump, start at 18/24=0.75 units/hour

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Nick's Bolus Settings

- Rule of 500 for insulin to carb ratio
  - 500/36=13.88
  - What does this mean?
    - 1 unit of insulin is expected to cover 14 grams of carbohydrate
- Rule of 1700 for sensitivity factor
  - 1700/36=47
  - What does this mean?
    - 1 unit of insulin is expected to lower glucose by 47 points

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In Depth: Types of Insulin

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So Much Insulin…

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Action		Insulin Name	Onset	Peak	Effective Duration	Considerations
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		Glulisine (Apidra)				
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Basal	Intermediate	NPH	2 - 4 hrs	4 - 10 hrs	10 - 16 hrs	
	Long Acting	Detemir (Levemir)	3 - 8 hrs	No peak	6 - 24 hrs	
		Glargine	2 - 4 hrs		20 - 24 hrs	
		Degludec (Tresiba)*	~ 1 hr		< 42 hrs	
Basal + Bolus	Intermediate + short	Combo of NPH + Reg 70/30 = 70% NPH + 30% Reg 50/50 = 50% NPH + 50% Reg	30 - 60 min	Dual peaks	10 - 16 hrs	
	Intermediate + rapid	Novolog® Mix - 70/30 Humalog® Mix - 75/25 or 50/50	5 - 15 min		24 hrs	

Concentrated insulins available - see Concentrated Insulin Card for details. Insulin action times vary; time periods are general guidelines only. All PocketCard content is for educational purposes only. Please consult prescribing information for detailed guidelines. © 3/2022

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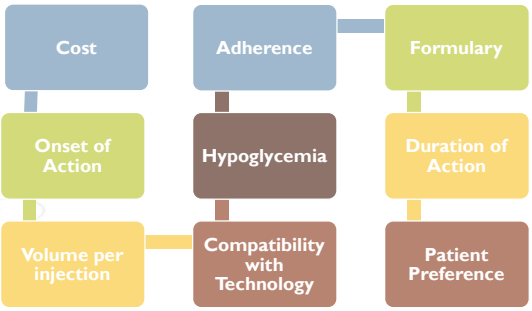
Insulin Selection



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Biosimilar and Follow-On Insulin

- The expiration of patents for brand name insulin opens up the insulin market worldwide to manufacturers of insulin copies or biosimilars
- Can't use the term generics for *large* molecule biologicals because they are manufactured in living organisms (bacteria and yeast)
- Terminology
  - **Biologic products**: large, complex molecules produced through biotechnology in a live system such a microorganism, plan cell or animal cell
  - **Biosimilar**: a biologic product highly similar and has no clinically meaningful difference from an FDA-approved reference product
  - **Follow-on product**: copies of biologic products approved under the Food, Drug, and Cosmetic Act 505b2 pathway

White J et al. J Pharm Technol. 2019; 35(1):25–35.

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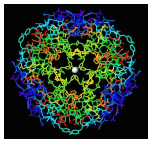
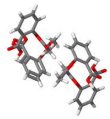
Follow-On Insulin

- Follow-on insulin products usually require a separate prescription (not directly interchangeable)
  - Examples:
    - Insulin glargine (Lantus), follow-on products (Semglee, Basaglar),
    - Insulin lispro (Humalog), follow-on product (Ademlog)
- Recently the FDA announced that Semglee can be interchangeable with Lantus



Insulin – Large Molecule



Aspirin – Small Molecule

55

Generic Insulins

- Insulin aspart
- Insulin lispro

- About half the cost of the brand name
- Exact same formulation, produced by same manufacturer

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Basal Insulin Summary

- Covers in between meals, through night
- Starts working slow (4 hours)
- Stays in long (12-42 hours)
- Fasting blood glucose and pre-meal glucose levels reflect effectiveness
- Fix fasting first but don't overbasalize

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Which Insulin is Interchangeable with Lantus (Insulin glargine U100)?

A. Toujeo (Insulin glargine U300)
B. Basaglar (Insulin glargine U100)
C. Semglee (Insulin glargine U100)
D. Insulin degludec U100
E. All of the above

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Bolus Insulins
(½ of total daily dose ÷ meals)

Action		Insulin Name	Onset	Peak	Effective Duration
Bolus	Very Rapid Acting Analogs	Aspart (Fiasp)	2.5 min	~60 min	3-5 hours
		Lispro-aabc (Lyumjev)	1 min	~60 min	4-5 hours
	Rapid Acting Analogs	Aspart (Novolog)	5 - 15 min	30 - 90 min	< 5 hrs
		Lispro (Humalog*/ Admelog)			
		Glulisine (Apidra)			
	Short Acting	Regular*	30 - 60 min	2 - 4 hrs	5 - 8 hrs

Inhaled Insulins

Action	Insulin Name	Dose Range	Onset	Peak	Duration	Considerations
Bolus – Rapid-acting	Afrezza Inhaled regular human insulin	4, 8, and 12 unit cartridges before meals	~ 12 min	35 - 45 mins	1.5 - 3 hrs	Assess lung function. Avoid in lung disease — bronchospasm risk. Side effects: hypo, cough, throat irritation.

The information listed here are not guidelines. Please consult prescribing information for details. DiabetesEd.net © 2022

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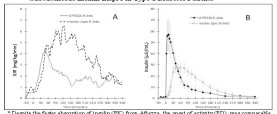
Afrezza – Inhaled Insulin

Injected Meal Time Dose	Inhaled Insulin Dose
Up to 4 units	4 units
5-8 units	8 units
9-12 units	12 units
12-16 units	16 units
17-20 units	20 units
21-24 units	24 units

- **FDA approved for adults over 18yo**
- **Not indicated for pregnancy, while breastfeeding**

Figure 3. Baseline-Corrected Glucose Infusion Rate (A) and Baseline-Corrected Serum Insulin Concentrations (B) after Administration of AFREZZA or Subcutaneous Insulin Lispro in Type 1 Diabetes Patients*



* Despite the faster absorption of insulin (PK) from Afrezza, the onset of activity (PD) was comparable to insulin lispro.

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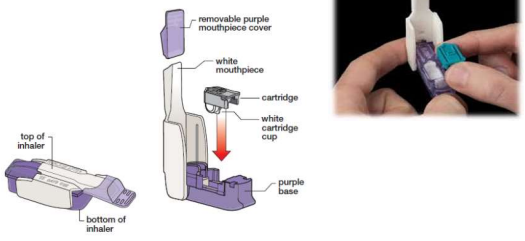
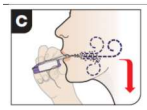
Afrezza Inhaler

Know your AFREZZA® inhaler:





Inhale Deeply and Hold Breath

With your mouth closed around the mouthpiece, **inhale deeply through the inhaler**.

Hold your breath for as long as comfortable and at the same time remove the inhaler from your mouth. After holding your breath, exhale and continue to breathe normally.

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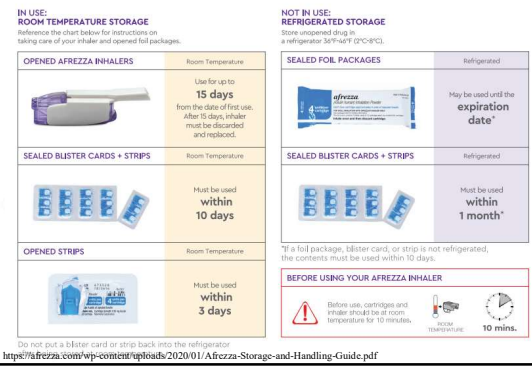
Afrezza Storage



https://afrezza.com/wp-content/uploads/2020/01/Afrezza-Storage-and-Handling-Guide.pdf

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Afrezza Dosing and Considerations

- Bolus regular insulin – inhaled before meals
- Dosing: 4, 8 and 12 unit cartridges
- Lung function test before start (FEV1)
  - Not for pts w/ chronic lung issues
    - Asthma, COPD, history of lung cancer, smokers
    - Can cause acute bronchospasm – Black box warning
- Side effects:
  - Hypoglycemia, sore throat, cough
  - Less hypoglycemia than injected insulin

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Bolus Insulin Timing

- How is the effectiveness of bolus insulin determined?
  - 1-2 hours post meal (if you can get it)
  - Before next meal blood glucose
- Glucose goals may be modified by provider/pt
  - 1-2 hours peak post meal <180 (ADA)
  - 2 hour post meal <140 (AACE)
  - Before next meal 80 - 130

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Poll Question

- Mary takes 4 units lispro (Humalog) before breakfast. Which BG result reflects that the dose was the right dose?

1. Before breakfast BG of 97
2. 1 hour post breakfast BG of 190
3. Before lunch BG of 69
4. 2-hour post breakfast BG of 154

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Bolus Insulin Summary

- Starts working fast (5-30 mins)
- Gets out fast (3-6 hours)
- Post meal BG reflects effectiveness
- Should comprise about ½ total daily dose in T1D
- Covers food or corrects for hyperglycemia
- In many people: 1 unit
  - Covers ≈ 10 -15 gms of carb
  - Lowers BG ≈ 30 – 50 points
  - Tons of exceptions to this though!

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Concentrated Insulin

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More than 200 units a day?

DRUG NAME	AVAILABILITY	PEN UNITS	EXPIRATION	ONSET	PEAK EFFECT	DURATION OF ACTION	CLINICAL PEARLS
INSULIN HUMAN REGULAR (HUMULIN R U500)	Pen, Vial	5 unit	Vial: 40 days Pen: 28 days	0.25-0.5 hours	4-8 hr	13-24 hr	This insulin is 5 time as concentrated. If using a vial, use the special U500 syringe.

DailyMed: https://dailymed.nlm.nih.gov/dailymed/index.cfm

Stahnke AM et al. ADCES in Practice. March, 2020. https://doi.org/10.1177/2633559X20896414

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Switching to u500 insulin

- Typically reserved for people requiring insulin >200 units/day
- U500 acts like an intermediate acting insulin but replaces both the basal and bolus doses
  - If A1C< 8%, recommend to reduce TDD by 10-20%
  - If A1C≥ 8%, consider 1:1 conversion
- Typically dosed 2-3 times daily
- It should be taken 30 minutes prior to meals
- Often initiated as a 60/40 or 40/30/30 split

Reid TS, et al. Postgrad Med. 2017;129(5):554-562.

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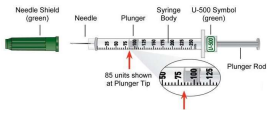
U500 example

- A woman with obesity, T2D, and insulin resistance takes insulin detemir 120 units BID and insulin aspart 60 units TID a.c. Her most recent A1C=9%. How would she switch to U500?
  - 1:1 conversion since A1C > 8%
  - TDD=180+240=420 units split as 40/30/30
- New Dose:
  - U500 165 units QAM, 125 units at lunch, 125 units at dinner
  - Must round to nearest 5 unit increment
  - Inject 30 minutes before each meal
  - Use U500 syringe or U500 pen
  - Do not use U100 syringes!



Reid TS, et al. Postgrad Med. 2017;129(5):554-562.

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Concentrated Insulin

Name/Concentration	Insulin/Action	Considerations
Humulin Regular U-500 • 500 units insulin/mL • KwikPen or Vial	Regular Bolus / Basal	Indicated for those taking 200+ units daily. 3 mL pen holds 1,500 units. Max dose 300 units. Once opened, good for 28 days. 20 mL vial holds 10,000 units. Max dose 250 units using U-500 syringe. Once opened, good for 40 days.
Humalog KwikPen U-200 200 units insulin/mL.	Lispro (Humalog) Bolus	3 mL pen holds 600 units. Max dose 60 units. Once opened good for 28 days.
Lyumjev KwikPen U-200 200 units insulin/mL.	Lispro (Lyumjev) Bolus	3 mL pen holds 600 units. Max dose 60 units. Once opened good for 28 days.
Toujeo Solostar U-300 Pen 300 units insulin/mL.	Glargine (Lantus) Basal	1.5 mL pen holds 450 units. Max dose 80 units. 3 mL Max Solostar pen holds 900 units. Max dose 160 units. Once opened good for 56 days.
Tresiba FlexTouch U-200 Pen 200 units insulin/mL.	Degludec (Tresiba) Ultra basal	3 mL pen holds 600 units. Max dose 160 units. Once opened good for 56 days.
All concentrated insulin pens and the U-500 syringe automatically deliver correct dose (in less volume). No conversion, calculation or adjustments required. For example, if order reads 30 units, dial the concentrated pen to 30 units or draw up 30 units on the U-500 syringe. **Important – never withdraw concentrated insulin from the pen using a syringe.**		

- Advantages of Tresiba U200 and Toujeo U300 is that the pens go up to 160 units/injection
- Humalog and Lyumjev U200 have less volume per injection and more units in pen (600 vs. 300)

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Barriers to Insulin Use

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Quick Question

- AJ tells you she doesn't want to start on insulin. What is your best response?

a. The needles are so small, you won't even feel it.
b. Lots of people are afraid of insulin.
c. It sounds like you are refusing to take insulin?
d. I'm sorry, but there is a doctors' order to start insulin.
e. What concerns do ou have about taking insulin?

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Psychological Insulin Resistance (PIR)

- 50% of providers in study threatened pts "with the needle".
- Less than 50% of providers realized insulins' positive effect on type 2 DM
- Most pts don't believe that insulin would "better help them manage their diabetes".
- Solutions: Find the root of PIR and address it

Diabetes Attitudes, Wishes, Needs Study - Rubin

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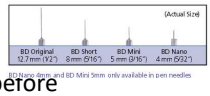
Needle Size often a Barrier: Size Matters

- Use shortest needles – 4 mm
- Effective for almost ALL patients
- Keeps it subq
- If thin, inject at angle
- To avoid leakage, count to 10 before withdrawing needle
- ½ the patients who could benefit from insulin are not using it due to needle phobias
- Also consider insulin pumps, patches, iport, and inhaled insulin



BD Nano 4mm and BD Mini 5mm only available in pen needles

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Intensifying Injectable Therapy in Type 2 DM

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Intensifying Injectable Therapy – Type 2

- Consider GLP-1 RA first
- Start basal insulin 10 units or 0.1 to 0.2 units/kg day
- Titrate up 2 units every 3 days, until FBG at goal
- If hypo, decrease insulin 20% or 4 units
- If basal insulin is >0.5 unit/kg day, add bolus insulin (avoid overbasalization)
- Adding bolus
  - Start with 4 units bolus at largest meal or
  - Start 1-2 injections with 10% of basal or
  - Switch to 70/30 twice or three times daily.

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Intensifying Injectable Footnotes 9.2

- Consider insulin as the first injectable if evidence of ongoing catabolism A1C levels (>10%) or BG levels ≥300mg/dL or a diagnosis of type 1 diabetes is a possibility.
- For those on GLP-1RA and basal insulin combination, consider using a fixed-ratio combination product (iDegLira or iGlarLixi).
- Consider switching from evening NPH to a basal analog if there is hypoglycemia and/or the individual frequently forgets to administer NPH in the evening. In this case, an AM dose of a long-acting basal insulin could be a better choice.
- If adding prandial insulin to NPH, consider initiation of a self-mixed or premixed insulin regimen to decrease the number of injections required.

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Insulin/Injectable Combos

PocketCards updated annually. Download FREE CDCES Coach App for latest updates and notifications.

Name	Combines	Considerations
IDegLira* Xultophy 100/3.6	Insulin degludec (IDeg or Tresiba) Ultra long insulin + Liraglutide (Victoza) GLP-1 Receptor Agonist (GLP-1 RA)	**Xultophy 100/3.6 pre-filled pen** = 100 units IDeg / 3.6 mg liraglutide per mL Once daily injection – Dose range 10 to 50 = 10 – 50 units IDeg + 0.36 -1.8 mg liraglutide **Recommended starting dose:** • 16 IDegLira (= 16 units IDeg + 0.58 mg liraglutide) Titrate dose up or down by 2 units every 3-4 days to reach target. Supplied in package of five single-use 3mL pens. Once opened, good for 21 days.
iGlarLixi* Soliqua 100/33	Insulin glargine (Lantus) Basal Insulin + Lixisenatide (Adlyxin) GLP-1 Receptor Agonist	**Soliqua 100/33 Solostar Pen** = 100 units glargine / 33 µg lixisenatide per mL Once daily injection an hour prior to first meal of day. Dose range 15 – 60 = 15-60 units glargine + 5 – 20µg lixisenatide **Recommended starting dose:** • 15 units if not meeting glucose target on 30 units basal insulin or GLP-1 RA • 30 units if not meeting glucose target on 30-60 units basal insulin or GLP-1 RA Titrate dose up or down by 2-4 units every week to reach target. Supplied in package of five single-use 3mL pens. Once opened, good for 14 days.

*Discontinue basal insulin /GLP-1 RA therapy before starting. If dose missed, resume with next usual scheduled dose.

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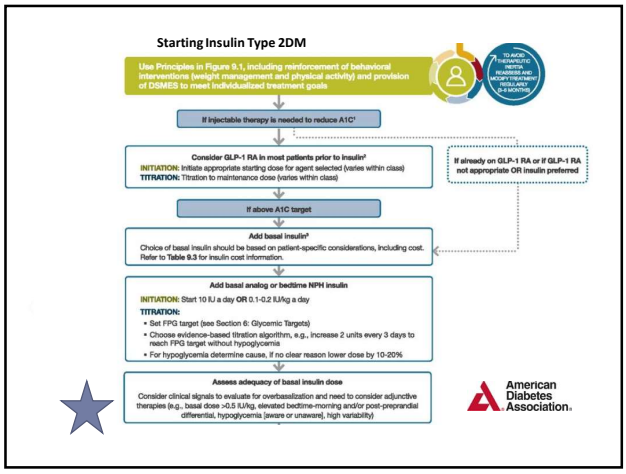

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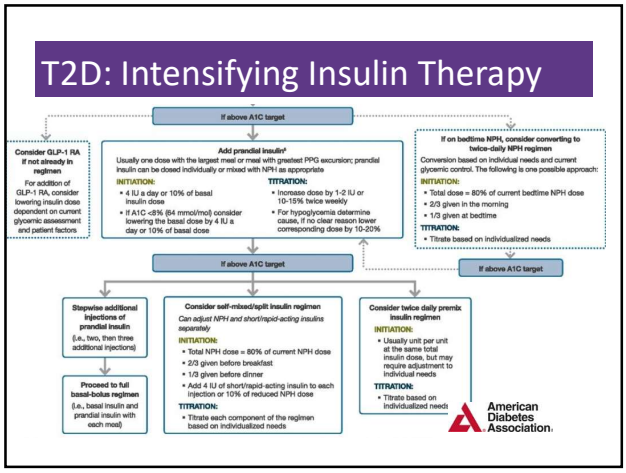

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Case Study: Jenny

Jenny is a 50-year-old woman that takes insulin glargine 100 units daily, glipizide 10mg BID, metformin 1000mg BID, and linagliptin 5mg daily. A1C is 9.3%. She weighs 110kg. She checks glucose in the AM only and reports it's 90-130mg/dL. Her eGFR is 70. She previously had UTI's with empagliflozin.

What is the best recommendation to adjust this regimen?

82

Thinking about the choices

- Continue glargine?
- Continue glipizide?
- Continue linagliptin?
- Switch to combination GLP1 receptor agonist /insulin injectable?
- Add GLP-1 agonist?
- Add prandial insulin?
- Add SGLT-2 inhibitor?

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Piecing it Together

- New Regimen:
  - Insulin glargine 80 units once daily (20% reduction)
- Semaglutide 0.25mg weekly, titrated up to 1.0mg weekly
- Stop linagliptin
- Continue glipizide (for now)
- Next step could be to retry SGLT2i with counseling on how to avoid UTIs
- Or replacing glipizide with prandial insulin with largest meal

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Switching Insulin

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How to Switch Basal Insulin

- When going from twice daily basal insulin to once daily, reduce dose by 20%
  - Examples:
    - Insulin NPH BID to insulin glargine daily
    - Insulin detemir BID to insulin degludec daily
- When switching between once daily, a unit per unit conversion is okay
- Long-acting to glargine U300 often requires higher doses (10 to 18%) but start with a unit to unit conversion
- When switching from glargine U300 to another long-acting insulin, reduce dose by 20%
- Need to use clinical judgement
  - For example, if A1C, FBG, and pre-meal BG are all above target, then may not be necessary to reduce basal insulin dose

Clinical Resource. Pharmacist's Letter/Prescriber's Letter. August 2019.

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Making the switch: Meet Joan

Joan is taking insulin glargine 30 units twice daily. Her insurance formulary wants her to switch to insulin degludec. Her current A1C is 6.9%. What is the best dose recommendation?

A. Insulin degludec 30 units twice daily
B. Insulin degludec 60 units once daily
C. Do not switch since her A1C is well-controlled and get a prior authorization to continue with insulin glargine
D. Insulin degludec 48 units once daily

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Switching Meal time Insulin

- This is a 1:1 conversion when switching between regular insulin, aspart, lispro, and glulisine including Fiasp® and Lyumjev™.
- The exception is when switching to Afrezza

Injected Meal Time Dose	Inhaled Insulin Dose
Up to 4 units	4 units
5-8 units	8 units
9-12 units	12 units
12-16 units	16 units
17-20 units	20 units
21-24 units	24 units

Clinical Resource. Pharmacist's Letter/Prescriber's Letter. August 2019.
Afrezza (package insert) 2019.

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5. Patient Case: Lumy

- Lumy's insurance formulary changed from insulin lispro to insulin aspart.
- She was following an insulin to carbohydrate ratio of 1:12 and a correction factor of 1:50.
- How should she dose insulin aspart when she switches?

A. Reduce all doses by 10%
B. Increase all doses by 10%
C. Same dosing
D. Submit prior authorization so she doesn't change insulin

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Insulin Pattern Management

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Pattern Management –AKA

How to think like a pancreas

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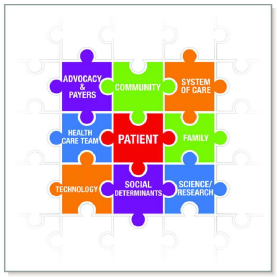
What do the numbers mean?

It's like a BIG puzzle!



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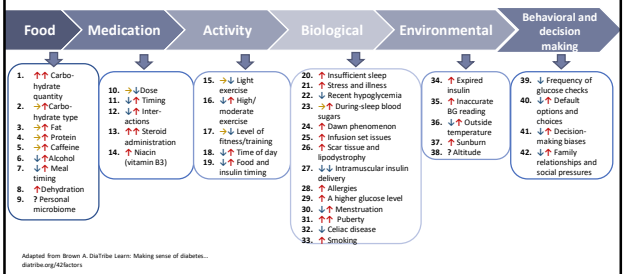
At Least 42 Factors Affect Glucose!



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Poll Question

- When looking at glucose patterns, which problem do you fix first?
  - a. Hyperglycemia
  - b. Hypoglycemia
  - c. Non-compliance
  - d. Legible writing

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Pattern Management

- Safety 1st!! - Evaluate 3 day patterns
- **Hypo:** eval 1st and fix:
  - If possible, decrease medication dose
  - Timing of meals, exercise, medications
- **Hyperglycemia:** evaluate 2nd
  - Identify patterns
  - Before increase insulin, make sure not missing something (carbs, exercise, omission)

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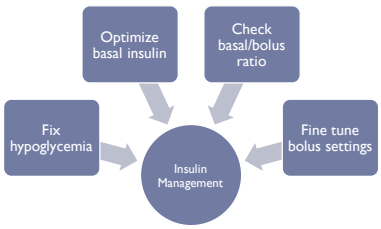
General Rules in T1DM

- Optimize basal dose (stay within 30mg/dL when not eating)



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Adjusting Insulin doses in a Basal/Bolus regimen

Out of Range Glucose	Insulin to Adjust
Fasting	Long acting insulin or evening NPH
Post-breakfast/pre-lunch	Pre-breakfast rapid/regular insulin
Post lunch/pre-dinner	Pre-lunch rapid/regular insulin or morning NPH
Post-dinner/before bedtime	Pre-dinner rapid/regular insulin

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Insulin to Carb Ratio Adjustments

- Compare pre-meal BG to 2 hour post-meal BG
- Goal post-meal BG should be 30-60mg/dL higher than pre-meal BG
- If the 2 hour PPG is >60mg/dL above pre-meal
  - Decrease carb ratio by 10-20%
- If the 2 hour PPG is <30mg/dL above pre-meal
  - Increase the carb ratio by 10-20%

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Insulin Sensitivity Adjustments

- When BG is above target and correction dose is taken (without food), does glucose return to target within 3-4 hours?
- If BG is low at 3-4 hours, the ISF is likely too strong
  - Increase by 10-20%
  - Example: 50→55 or 60
- If BG is high after 3-4 hours, the ISF is too weak
  - Decrease by 10-20%
  - Example: 50→45 or 40

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Bolus Pattern Management

- Does glucose go low after a correction dose?
  - May need a higher sensitivity
  - Ex. 1:60 instead of 1:50
- Does glucose remain high after a correction dose?
  - May need a lower sensitivity
  - Ex. 1:40 instead of 1:50
- Often people are more sensitive overnight (less insulin needed)
- Does the person spike high after eating?
  - Is the person bolusing BEFORE the meal
  - Counting carbs correctly?
  - May need a more intensive carb ratio
  - Ex. 1:6 instead of 1:8
- Does the person go low after eating?
  - Counting carbs correctly?
  - May need a less intensive carb ratio
  - Ex. 1:10 instead of 1:8

Adjustments typically made 10-20% at a time

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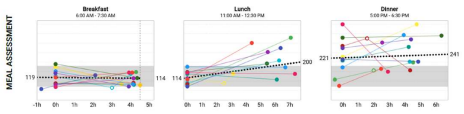
Meal Time Data Review

- Glucose data before and after breakfast, lunch and dinner
- Ideally, 2 hour post-meal should not rise above 180mg/dL or 50mg/dL from the pre-meal start
- By 4-5 hours, glucose should return to pre-meal level



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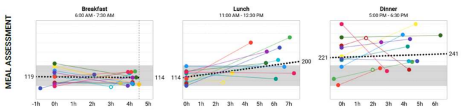
Meal Time Assessment

- Glucose is steady after breakfast
- Glucose is higher after lunch-may need more intensive medication adjustment or decrease carbohydrate intake
- Dinner is variable, often starting dinner high but also times where there is an elevation or a drop, likely needs more consistency with food and/or medications



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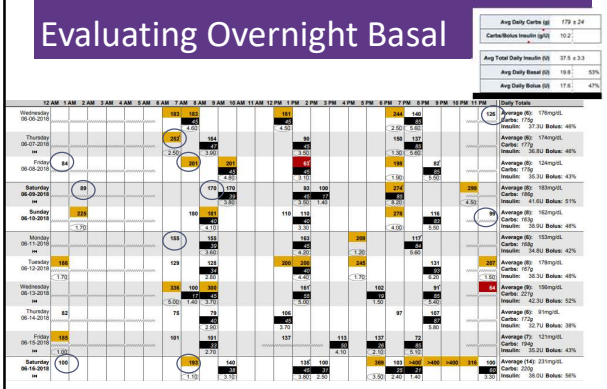
Evaluating Overnight Basal



Do you see any problems?

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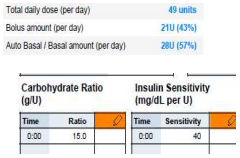
Checking the Sensitivity

- TDD=49 units
- Rule of 1700
  - 1700/49=35
- Current sensitivity is 40



The calculation is slightly different from the current sensitivity. Look at the glucose data to determine if the sensitivity should be decreased.

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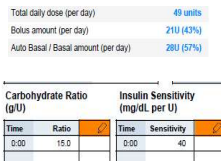
Checking the Carb Ratio

- TDD=49 units
- Rule of 450
  - 450/49=12.9
- Current carb ratio is 15



The calculation is different from the current carb ratio. Look at the glucose data to determine if the carb ratio should be decreased.

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Insulin Pump adjustments

- Use calculations as a starting point

- Fix fasting first
  - Begin with basal rate testing
- Multiple patterns can be set throughout the day
- Alternative basal patterns can be set for sick days, menstruation, etc
- Once basal at goal, focus on bolus settings

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Basal Rate Testing

- Start with glucose 80-180mg/dL with last bolus > 4 hours
- Wear CGM or check glucose every 2 hours
- Glucose should not change by more than 30mg/dL if basal is effective
- Avoid physical activity, stress, and high fat meals before test
- Start with overnight, and then work on the rest of the day in smaller segments
- If >30mg/dL rise or fall, make basal rate adjustment, 10-20% increments

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Case Study

- 70 yr old, weighs 100kg, eGFR=58
- History of CABG, foot ulcers, smokes
- A1c – 11.3%, BG 400-500mg/dL for weeks
- Insulin – 120 units insulin glargine qpm
- Oral Meds: Metformin 1000mg BID & canagliflozin 100mg daily

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Case Study

- 70 yr old, weighs 100kg, eGFR 58
- History of CABG, foot ulcer, smokes
- A1c – 11.3%, BG 400-500 for past weeks
- Insulin – 120 units Lantus at hs (solostar).
- Metformin 1000mg BID & canagliflozin
- What is max basal insulin he should be taking without a prandial dose?
- Given his history, what diabetes meds would benefit him?
- Which of his meds may have adverse effects?

109

Case Study

- 70 yr old, weighs 100kg, GFR 58
- History of CABG, foot ulcer, smokes
- A1c – 11.3%, BG 400-500 for weeks
- Insulin glargine 120 units qpm
- Metformin 1000mg BID, canagliflozin 100mg daily
- What is max basal insulin should he be taking before considering prandial insulin?
  - 100kg x 0.5 = 50 units a day
- Given his history, what diabetes meds would benefit him?

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Case Study

- What can we do next to improve BG?
  - Ask about medication taking behaviors
  - Consider CGM
  - Add GLP-1
    - What about GLP-1/insulin combination?
  - Add bolus insulin:
    - 4 units bolus insulin to largest meal (or 10% of basal = 12 units)
  - Switch to 70/30 insulin ac breakfast and dinner
    - Total previous basal dose – 120 units
    - 70% in am – 84 units am
    - 30% pre dinner – 36 units pm

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Dosing Will Not Work for This Patient

Insulin/Injectable Combos *PocketCards updated annually. Download FREE CDCES Coach App for latest updates and notifications.*

Name	Combines	Considerations
IDegLira* Xultophy 100/3.6	Insulin degludec (IDeg or Tresiba) Ultra long insulin + Liraglutide (Victoza) GLP-1 Receptor Agonist (GLP-1 RA)	**Xultophy 100/3.6 pre-filled pen** = 100 units IDeg / 3.6 mg liraglutide per mL Once daily injection – Dose range 10 to 50 = 10 – 50 units IDeg + 0.36 -1.8 mg liraglutide **Recommended starting dose:** • 16 IDegLira (= 16 units IDeg + 0.58 mg liraglutide) Titrate dose up or down by 2 units every 3-4 days to reach target. Supplied in package of five single-use 3mL pens. Once opened, good for 21 days.
iGlarLixi* Soliqua 100/33	Insulin glargine (Lantus) Basal Insulin + Lixisenatide (Adlyxin) GLP-1 Receptor Agonist	**Soliqua 100/33 Solostar Pen** = 100 units glargine / 33 µg lixisenatide per mL Once daily injection an hour prior to first meal of day. Dose range 15 – 60 = 15-60 units glargine + 5 – 20µg lixisenatide **Recommended starting dose:** • 15 units for pts not controlled on 30 units basal insulin or GLP-1 RA • 30 units for pts not controlled on 30 -60 units basal insulin or GLP-1 RA Titrate dose up or down by 2-4 units every week to reach target. Supplied in package of five single-use 3mL pens. Once opened, good for 14 days.

*Discontinue basal insulin /GLP-1 RA therapy before starting. If dose missed, resume with next usual scheduled dose.

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Case Study

- 70 yr old, weighs 100kg, GFR 58
- History of CABG, foot ulcer, smokes
- A1c – 11.3%, BG 400-500 for weeks
- Insulin glargine 120 units qpm
- Metformin 1000mg BID, canagliflozin 100mg daily
- What will inform you of how to proceed?
  - Insurance coverage
  - His willingness to stick to a complex regimen
  - His ability to self-monitor
  - His social support and connection to his medical team

My Plan:
- Professional CGM
- Add GLP1-RA
- Stop SGLT2i (for now)
- Referral to diabetes care & education specialist
- Build rapport-discussion on medication taking behaviors

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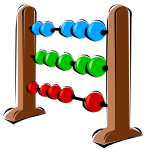
Quick Calculation

- If a person takes:
- 20 units of Humalog at breakfast, lunch and dinner
- Also has correction factor: 2 units for every 50 over 150 (up to 10 extra units/meal)
- A1c 8.7%
- How many vial(s) of insulin or boxes of pens should be prescribed per month?



114

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Quick Calculation

- If a person takes:
- 20 units of Humalog at breakfast, lunch and dinner
- Also has correction factor: 2 units for every 50 over 150 (up to 10 extra units/meal)
- A1c 8.7%

Tip: Always round up!

- How many vial(s) of insulin or boxes of pen would he use a month?
- Vial:
  - Takes up to 90 units/day
  - 1000 units in a vial
  - 1000 / 90 = 11
  - 1 vial lasts 11 days
  - ~3 vials a month
- Box of pens
  - 1 box of pens=1500 units
  - 1500/90-16.67=17
  - 1 box lasts 17 days
  - ~2 boxes needed per month

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Poll Question

- Mary takes 6 units lispro (Humalog) before dinner. Which BG result reflects that it was the right dose?

a. Before breakfast BG of 97
b. 1 hr post dinner BG of 189
c. Before dinner blood glucose of 102
d. 2 hour post dinner BG of 178

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Adjusting Bolus and Correction Doses Carbohydrate-to-Insulin Ratio

Based on four questions before meals:

1. How much carbohydrate am I going to eat?
2. What is my insulin dose for this amount of carbohydrate?
3. Should I lower the dose because I plan to be very active or have recently been active?
4. Should I lower dose because my blood sugar is low?

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Poll Question 7

- Erick uses an insulin pump with a carbohydrate ratio of 12 and correction factor of 50
- He plans to eat the following: 1 cup rice, steak, 1 c. skim milk, 1/2 banana, SF ice tea. BG 118. How much insulin should he take?
- How much insulin should he take?

a. 4.8 units
b. 6.0 units
c. 5.2 units
d. 5.0 units

What if he planned to cut the grass right after lunch which usually drops his blood sugar by 75 points?

118

Meet Erin

- Erin is a 62 year old woman with type 2 diabetes x 30 years. She recently underwent a kidney transplant 6 weeks ago. Her current DM2 medications now include: insulin glargine 40 units every morning and insulin lispro 14 units TID a.c. + ss#2 (2 units for every 50 over 150). She also takes prednisone 10 mg every morning. This is her last 7 days of glucose logs.

Day	FBG	Pre-lunch	Pre-dinner	Pre-bedtime
1	123	210	210	278
2	132	194	298	187
3	141	198	210	220
4	98	199	232	218
5	103	210	209	197
6	114	205	207	178
7	109	212	205	301

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Key Questions to Ask Erin

- Any hypoglycemia?
- Timing and consistency of meals
- Types of meals and snacks and drinks
- Timing of insulin in regards to the meals
- Missed doses
- Changes in other medications (ex. Prednisone)

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Erin's Plan

- What is the best plan for Erin?

A. Increase insulin glargine to 44 units daily
B. Increase insulin lispro to 16 units TID a.c.
C. Increase insulin glargine to 48 units daily
D. Increase insulin lispro to 16 units at lunch and dinner, continue 14 units at breakfast

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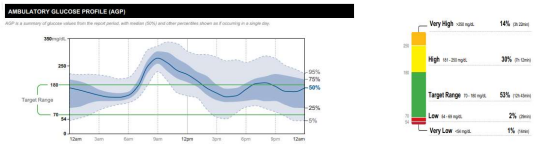
Meet Sandra

- Sandra is a 66 year old woman with T2DM. She uses CGM for glucose monitoring. She takes metformin 1000mg twice daily, insulin degludec 70 units daily and insulin lispro 15 units TID a.c. She also has HF and osteoarthritis. eGFR=80. A1C=7.5%, 53% time in range 70-180mg/dL. CV=36.3, 3% glucose <70mg/dL



122

Questions for Sandra

- Medication taking behaviors
- What's for breakfast?
- Does she feel symptoms with hypoglycemia events, has she noticed any patterns leading up to them?

- In the discussion, we learn
  - Sandra goes low often
  - She tries to eat at night to prevent going low (a cookie)
  - She takes her insulin 1 hour after breakfast, out of fear of hypoglycemia

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Changes to the Regimen

- Insulin degludec is too high, contributing to hypoglycemia
- Counseling on when to take meal time insulin to prevent post-prandial spike after breakfast
- New regimen:
  - Insulin degludec 60 units daily
  - Insulin lispro 15 units TID a.c.
  - Counseling on taking lispro BEFORE the meal
  - Reassess in 2 weeks

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Case Study: Larry

Larry takes metformin 1000mg BID, insulin glargine 50 units once daily, empagliflozin 10mg daily. His A1C is 7.8%. He weighs 90kg. FBG averages 100mg/dL. PP breakfast=190mg/dL, PP lunch=210mg/dL, and PP dinner is 240mg/dL. What is the best recommendation for an agent to add to the regimen to achieve A1C target?

A. Initiate insulin aspart 5 units at dinner, decrease insulin glargine to 45 units daily
B. Initiate insulin aspart 5 units with all meals, decrease insulin glargine to 35 units daily
C. Initiate insulin aspart 5 units at dinner, continue insulin glargine 50 units daily
D. Initiate dulaglutide 0.75mg weekly, decrease insulin glargine to 45 units daily

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Summary

- Many different types of insulin
- Basal + bolus needed for T1DM
- Weight based dosing and rules of 1700 and 500 can be used to calculate correction factor and carb ratio
- GLP1 agonist preferred 1st injectable in T2DM
- Avoid overbasalization, if taking more than 0.5unit/kg/day, think about prandial insulin
- Counsel patients on injection site technique, administration and storage
- Fine tune insulin settings based on BGM and CGM data

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Extra Practice

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Types of Insulin

Activity: Match the type to the definition

1. Basal insulin
2. Bolus insulin
3. Rapid-acting insulin
4. Regular insulin
5. Intermediate-acting insulin
6. Concentrated insulin
7. Biosimilar insulin

A. Insulin for meals and correction doses (prandial)
B. Background insulin
C. Made with different excipients
D. A faster type of bolus insulin
E. More than 100 units/mL
F. A slower form of bolus insulin
G. A basal insulin that has a peak and is typically dosed twice daily in T1D

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Types of Insulin

Activity: Match the type to the definition

1. Basal insulin **B**
2. Bolus insulin **A**
3. Rapid-acting insulin **D**
4. Regular insulin **F**
5. Intermediate-acting insulin **G**
6. Concentrated insulin **E**
7. Biosimilar insulin **C**

A. Insulin for meals and correction doses (prandial)
B. Background insulin
C. Made with different excipients
D. A faster type of bolus insulin
E. More than 100 units/mL
F. A slower form of bolus insulin
G. A basal insulin that has a peak and is typically dosed twice daily in T1D

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Meet Tori

- Tori is a 43 year old woman with T2DM for 4 years. She takes the following medications:
  - metformin 1000mg twice daily
  - glimepiride 4mg daily
  - saxagliptin 5mg daily
  - pioglitazone 15mg daily
- A1C is 10.1%. Weight is 167lbs and height is 61 inches. BMI=31.6.
- She rarely checks glucose and denies hypoglycemia

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Meet Tori

What is the best recommendation for drug therapy intensification?

A. Increase metformin
B. Increase glimepiride
C. Increase pioglitazone
D. Start basal insulin
E. Start basal + GLP-1 agonist

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Basal + GLP-1 Agonist

- Remember, GLP-1 agonist should be 1st injectable
- However, with high A1C, Tori is likely going to also need insulin
- A combined product would mean just 1 co-pay and allow her to start both with 1 injection
- Another option would be a weekly GLP-1 agonist and a daily insulin
- Do any of her medications need to be stopped when adding this combination?

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Tori Worries about Weight Gain

- Tori heard that insulin will cause her to gain weight. She is concerned about weight gain. How could her regimen be adjusted to reduce weight gain?
- Which drugs on her list contribute to weight gain?

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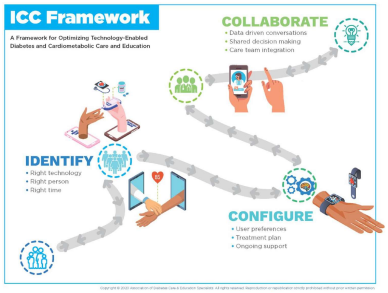
Integrating Technology: CGM Connected Pens and Insulin Pumps DiabetesEd Virtual Course – Day 2

Diana Isaacs, PharmD, BCPS, BC-ADM, BCACP CDCES
CGM and Remote Monitoring Program Coordinator
Cleveland Clinic Diabetes Center

Learning Objectives

- Describe critical teaching content for insulin pump and CGM use
- Discuss continuous glucose monitoring (CGM) and the clinical benefits for managing diabetes
- Compare and contrast the CGM, connected pen and insulin pump devices
- Describe appropriate candidates for insulin pump therapy
- List inpatient considerations for insulin pump therapy and CGMs

ICC Framework – Identify-Configure-Collaborate



Greenwood DA, Howell F, Scher L, et al. A Framework for Optimizing Technology-Enabled Diabetes and Cardiometabolic Care and Education: The Role of the Diabetes Care and Education Specialist. The Diabetes Educator. 2020;46(4):315-322. doi:10.1177/0145721720935125

Technology is Here


CONTINUOUS GLUCOSE MONITORS (CGM)


INSULIN PUMPS


CONNECTED PENS AND CAPS


MOBILE APPS

Continuous Glucose Monitors

Continuous Glucose Monitors (CGM)

- Measures glucose (sugar) every 1-5 mins and records it every 5-15 mins (up to 288 readings/day)
- Includes 3 components: transmitter, sensor, receiver/reader

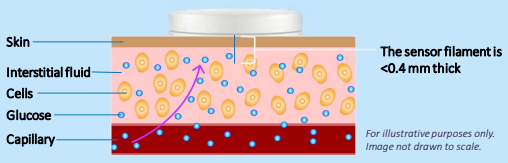
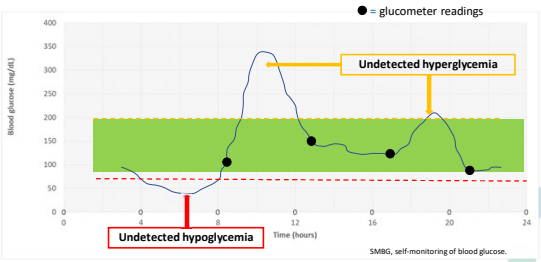
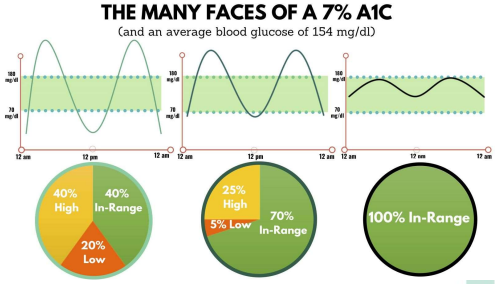


Illustration adapted from: Association of Diabetes Care & Education Specialists. ADCES Practice Paper. Accessed 11/9/21. https://www.diabeteseducator.org/docs/default-source/practice/practice-documents/practice-papers/the-diabetes-educator-role-in-continuous-glucose-monitoring.pdf?sfvrsn=4

BGM vs CGM



A1C Alone is Just Not Enough



CGM: Real-Time Data

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Types of CGM

Professional	Personal
Owned by the clinic	Owned by the person with diabetes
Blinded and unblinded (real-time feedback) options	Real-time feedback or scan for feedback (flash device)
Short-term use (3-14 days)	Long-term use
Insurance coverage for most people with type 1 or type 2 diabetes	Insurance coverage more focused on type 1 diabetes or those on intensive insulin regimens
Not compatible with insulin pumps or connected pens	Compatible with smartphones, connected pens and insulin pumps with select devices

Wright LA, Hirsch IB. *Diabetes Technol Ther.* 2017;19(suppl 2):S16-S26; Kruger DF, et al. *Diab Educ.* 2019;45(suppl 1):S3-S20.

Professional CGM Options

Abbott FreeStyle Libre Pro

Dexcom G6 Pro

Professional CGM Comparison

	Dexcom G6 Pro	LibrePro
Blinded vs unblinded	Both	Blinded
Maximum wear time of sensor	10 days	14 days
Calibration	None	None
Downloading reports	Clarity	LibreView
Care between transmitter use	Disposable-1 time use, must attached transmitter	Disposable 1-time use, combined sensors/transmitter
Alarms for high/low glucose alerts	Yes	No
Interfering substances	Hydroxyurea	Salicylic acid and high-dose vitamin C

ADCES Practice Paper. The diabetes care and education specialist role in CGM.

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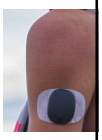
Personal CGM Options

Libre 2

Guardian Connect or
Guardian 3



Eversense

G6

Dexcom G6

- 10 day wear
- 2 hour warm-up
- FDA approved ages 2 and over
- No calibrations required-optional
- 1 press inserter, must attach transmitter
- Reusable transmitter-3 months
- FDA approved for dosing decisions
- Choice of receiver or smart phone
- High, low, predictive low alert
- Hydroxyurea drug interference
- Dexcom G6, Clarity, and Dexcom follow apps (up to 10 follow
- iCGM Status

https://www.dexcom.com/g6-cgm-system

Inserting the G6 Sensor

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Guardian Connect and Guardian 3

- 7 day wear
- Up to 2 hour warm-up
- Not FDA approved for dosing decisions
- Calibrations required 2-4 times/day
- Acetaminophen and Hydroxyurea interference
- Guardian 3 sensor –compatible with 670G and 770G inulin pumps
- Guardian Connect- compatible with smart phone (no separate receiver)
- Reusable transmitter
  - Charge every 7 days, transmitter lasts for ~1 year
- Guardian Connect, Sugar IQ apps
  - Sugar IQ provides predictive glycemic patterns based on user input
- Ability to have followers through carelink website
- Carelink Connect Mobile app for 770G users

https://www.medtronicdiabetes.com/products/guardian-connect-continuous-glucose-monitoring-system

Inserting the Guardian Sensor

Freestyle Libre 2

- 14 day wear
- 1 hour warm-up
- FDA approved ages ≥ 4 years
- Real time alerts (hypo, hyper, out of range) - must scan for actual number
- FDA approved for insulin dosing except for the first 12 hours after insertion
- Must scan every 8 hours to avoid data gaps
- Vitamin C interference (>500mg)
- 1 press inserter, disposable transmitter included with sensor
- Libre2 mobile app, required alert when glucose is urgent low (55mg/dL)
- LibreLinkUp allows up to 20 followers
- iCGM status

https://www.freestylelibre.us/safety-information.html

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Inserting the Libre



Eversense

- Implantable CGM sensor – lasts 90 days
  - Sensor is MRI safe
  - 180 version was just FDA approved
- Removable, rechargeable transmitter
  - Taped above sensor
  - Communicates to smartphone (no separate receiver)
  - On-body vibe high and low glucose alerts
- FDA-approved for insulin dosing
- 24-hour warm-up (dressing for 2 days after insert)
- Requires calibrations every 12 hours
- 180 day version only requires 1 calibration/day after 21 days
- Eversense CGM Mobile app with predictive alerts
- Eversense Now app allows 5 followers

https://www.eversensediabetes.com/


Personal CGM Comparison

	G6	Libre 2	Guardian Connect or Guardian 3	Eversense
Integration	T:Slim X2, Omnipod 5, InPen	Bigfoot Unity	Medtronic 770G, InPen	No
Receiver	Smartphone or receiver	Smart phone or reader	Smartphone only	Smartphone only
Maximum wear time	10 days	14 days	7 days	180 days
Warm-up time	2 hours	1 hour	Up to 2 hours	24 hours
Calibrations required	0	0	At least 2/day	2/day for 21 days, then 1/day
FDA approved sites	Abdomen (ages 2+) Upper buttocks (ages 2-17)	Upper arm	Upper arm, abdomen	Upper arm
FDA Approved for dosing (non-adjunctive indication)	Yes	Yes	No	Yes
FDA Approved ages (years)	≥2	≥4	≥2 Guardian 3 ≥14 Guardian Connect	≥18
Drug Interactions	Hydroxyurea	Vitamin C	Acetaminophen, Hydroxyurea	Tetracycline antibiotics
MARD	9%	9.2%	9.64%	8.5%
Alarms	Yes	Yes	Yes	Yes

ADCES Practice Paper. The Diabetes Care and Education Specialist Role in CGM. Available at: https://www.diabeteseducator.org/practice/educator-tools/diabetes-management-tools/self-monitoring-of-blood-glucose

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Poll Question 1

Which of the following drugs interact with the Libre 2?

A. Aspirin
B. Vitamin C
C. Hydroxyurea
D. Acetaminophen
E. More than 1 of the above

iCGM: The Future of Diabetes Devices

- Dexcom G6 and Libre 2 are integrated CGM (iCGM)
- Integration with digitally connected devices (eg, pumps, pens, automated insulin dosing [AID] systems)

CGM Counseling Points

- Important to check glucose when indicated
  - Symptoms do not match sensor value
  - During warm-up period
  - When making dosing decisions for select devices
- Sensors are waterproof
  - Showering, bathing, swimming OK
- Avoid with MRI, CT, diathermy
  - Exception: Eversense implantable, transmitter should be removed
- Not FDA approved
  - Pregnancy, dialysis, critically ill
  - If people choose to use, it is important they know it is off-label and discuss potential risks

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Troubleshooting Site Adhesiveness

Lag Time

- Refers to a delay in CGM sensor readings compared to finger stick blood glucose readings
  - Estimated CGM sensor reading ~5 minutes behind
- Most apparent when glucose is changing rapidly

Helping PWD Identify the Right CGM for Them

WHAT ARE CGMs?

Continuous Glucose Monitors (or CGMs) are small devices that have a tiny hair like wire that goes under the skin. Many people with diabetes refer to a CGM as a 'sensor' because it's sensing the glucose in your body. Sensors show your current sugar level and how it's changing - whether it's staying the same, going high, or going low. You can also set alarms if you want. Most CGMs come with automatic inserters that make it easy, and virtually pain-free, to put it in place on your own.

Dexcom G6 | Medtronic Guardian | Abbott Freestyle Libre | Eversense

Compare Sensors

Diabeteswise.org

Poll 2. Which of the Following is considered an iCGM?

A. Dexcom G6 Pro
B. Libre 2
C. Guardian 3
D. Eversense

Downloading CGM Data

Collaborate: How to Share Data

Data Platform	Associated Mobile Apps	Data Sources
Glooko	Glooko	Insulin pumps (Omnipod, Tandem), Dexcom, Eversense, many glucose meters, InPen
Clarity	Dexcom G6, Clarity, Dexcom Follow, Undermyfork, Sugarmate	Dexcom, InPen
LibreView	LibreLink, LibreLinkUp, Libre 2	FreeStyle Libre 14 day, Libre 2
Carelink	Guardian Connect, Carelink	Medtronic insulin pump and Medtronic CGM
Tidepool	Tidepool Mobile	Insulin pumps (Medtronic, Tandem, Omnipod), Dexcom, Guardian, many glucose meters, InPen
Eversense Data Management System	Eversense	Eversense
InPen Insights Report	InPen	InPen, Dexcom, Guardian Connect
Bigfoot Unity	Bigfoot Unity	Bigfoot Unity pen cap data, Libre 2

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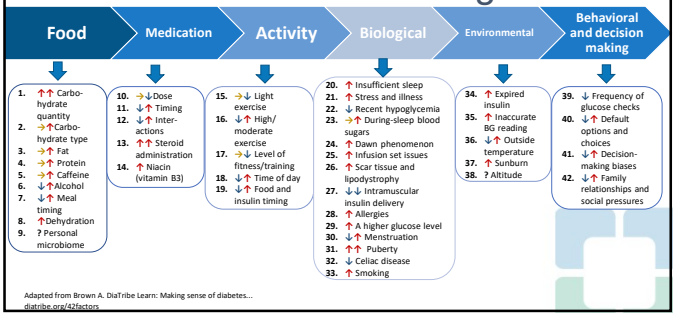
3. How does exercise affect glucose levels?

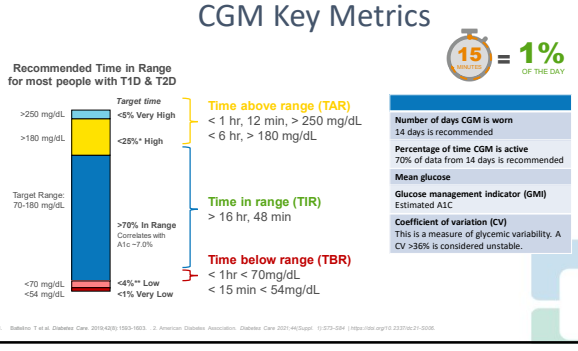
A. Increase
B. Decrease
C. No effect
D. I have no idea

At least 42 factors affect glucose!



Adapted from Brown A. DiaTribe Learn: Making sense of diabetes... diatribe.org/42factors

CGM Key Metrics



15 MINUTES = 1% OF THE DAY

Number of days CGM is worn 14 days is recommended
Percentage of time CGM is active 70% of data from 14 days is recommended
Mean glucose
Glucose management indicator (GMI) Estimated A1C
Coefficient of variation (CV) This is a measure of glycemic variability. A CV >36% is considered unstable.

1. Battelino T et al. *Diabetes Care.* 2019;42(8):1593–1603. 2. American Diabetes Association. *Diabetes Care* 2021;44(Suppl. 1):S73–S84 | https://doi.org/10.2337/dc21-S006.

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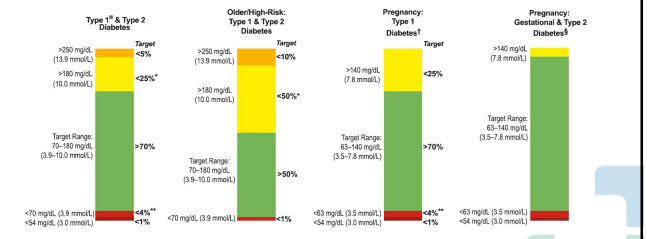
4. What is the goal time in range for most adults with type 1 or 2 diabetes?

A. ≥50%
B. ≥70%
C. ≥80%
D. ≥90%

Time in Range (TIR) Goals: International Consensus



Battelino T, et al. *Diabetes Care.* 2019;42(8):1593-1603.

Time in Range and A1C Correlation

N = 545 participants with type 1 diabetes

Measured TIR	A1C	95% CI
40%	8.4%	7.1%-9.7%
50%	7.9%	6.6%-9.2%
60%	7.4%	6.1%-8.8%
70%	7.0%	5.6%-8.3%
80%	6.5%	5.2%-7.8%

Beck RW, et al. *J Diabetes Sci Technol.* 2019;13(4):614-626.

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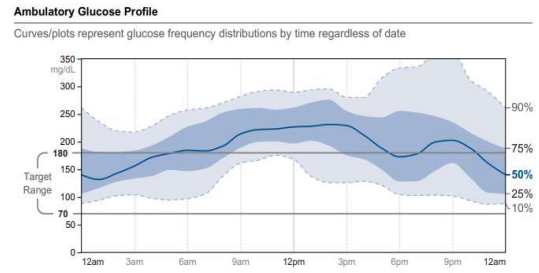
Ambulatory Glucose Profile (AGP)



Spaghetti Graph

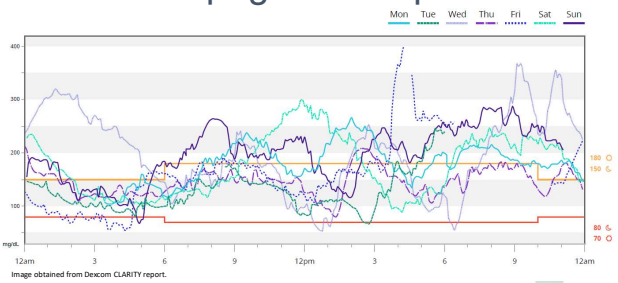


Image obtained from Dexcom CLARITY report.

Snapshot to Assess Hypoglycemia

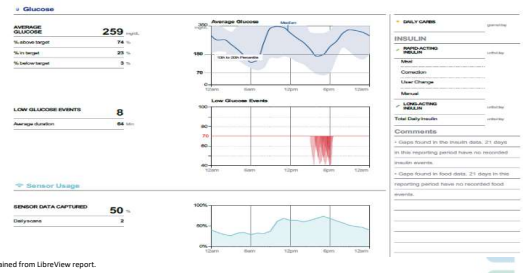


Image obtained from LibreView report.

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- Day by Day Graphs

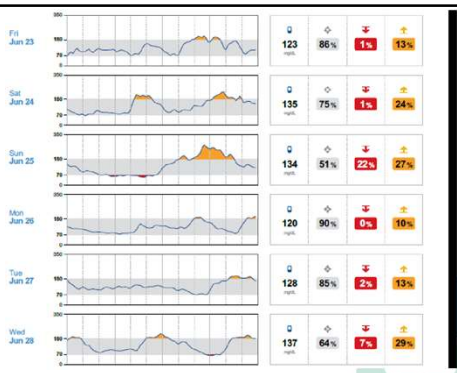


Image obtained from LibreView report.

Review of CGM - DATAA

D	Download Data	• Key metrics, AGP, day by day or spaghetti graph • Start with global overview; what AGP, key metrics mean, ask what the person learned/what is going well with self-management
A	Assess Safety	• Hypoglycemia - identify times below range, % time in hypoglycemia, # events • Interactive discussion: possible causes and solutions
T	Time in Range	• Focus on the positive - identify days or times where time in range is highest • Interactive discussion: how to replicate what is working well
A	Areas to Improve	• Hyperglycemia - Identify times above range, % time in hyperglycemia, # events • Interactive discussion: possible causes, solutions, and adjustments to self-management
A	Action Plan	• Develop collaboratively with the person with diabetes

At each step, express that this is information, not good or bad

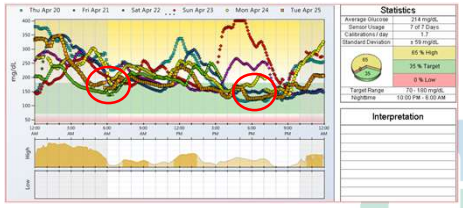
Isaacs D, Cox C, Schwab K, et al. Technology Integration: The Role of the Diabetes Care and Education Specialist in Practice. The Diabetes Educator. 2020;46(4):323-334. doi:10.1177/0145721720935123

Case Studies & 2 min Stretch

Meet Derek

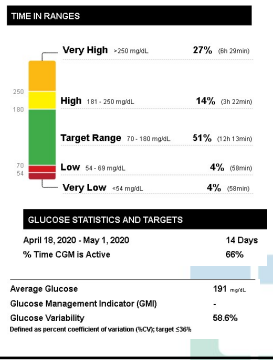
- 48-year-old man, type 2 diabetes x 10 years, maxed out on metformin, GLP-1 agonist, SGLT2 inhibitor, sulfonylurea
- A1C = 9%-9.5% for 12 months, FBG and pre-dinner BG ≈150 mg/dL
- He agreed to wear a professional CGM for 7 days

Derek was shocked by what happened between breakfast and dinner; he agreed to start insulin.



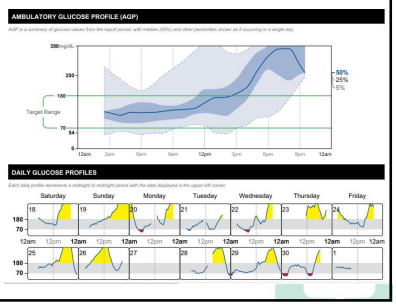
Meet Adriane

- 47 year old with T1DM
- A1C = 8.1%
- Insulin glargine 16 units BID
- Insulin aspart: 1 unit for10 grams CHO
- Correction factor: 1:25



Adriane's AGP

- What do you notice?
- Is Adriane meeting targets?
- What questions to ask?



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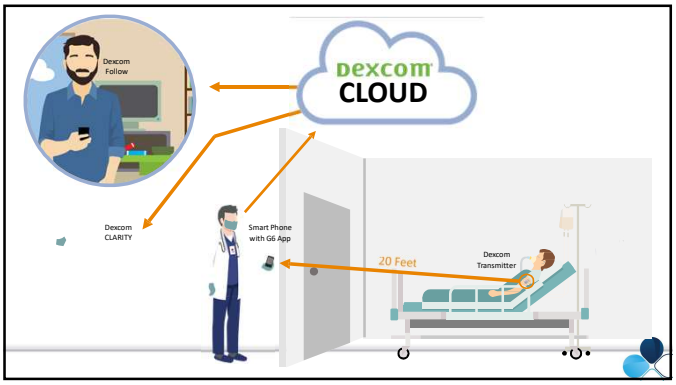
CGM in the Hospital

- Dexcom G6 and Freestyle Libre available for inpatient remote monitoring
  - FDA has temporarily approved due to the public health crisis of COVID-19 and the need to preserve PPE and reduce hospital staff exposure to coronavirus
- March 1, 2022
  - FDA grants breakthrough device designation for Dexcom hospital CGM system
  - Designed to expedite the development and regulatory review

https://www.dexcom.com/news/dexcom-cgm-hospital-covid19
https://abbott.mediaroom.com/2020-04-08-Abbotts-FreeStyle-R-Libre-14-Day-System-Now-Available-in-U-S-for-Hospitalized-Patients-with-Diabetes-During-COVID-19-Pandemic



CGM Resources

Diabetes Advanced Network Access (DANAtech)	danatech.org
Association of Diabetes Care and Education Specialists (ADCES) glucose monitoring resources	diabeteseducator.org/practice/educator-tools/diabetes-management-tools/self-monitoring-of-blood-glucose
diaTribe	diatribe.org
Senseonics Eversense	eversensediabetes.com
Medtronic Guardian Connect	hcp.medtronic-diabetes.com.au/guardian-connect
Dexcom G6	dexcom.com/g6-cgm-system
Abbott FreeStyle Libre	freestylelibre.us

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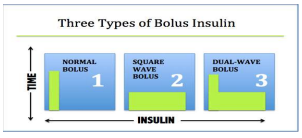
Insulin Pumps

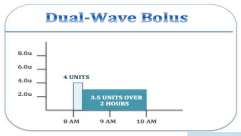
Common Insulin Pump Features

- Bolus calculator
- Temporary basal or temporary target
- Insulin-on-board/active insulin feature
- Multiple basal patterns
- Small dose increments
- Integration with CGM
- Designed to work with U100 insulin
- Most have a 4-5 year warranty/contract

Extended Boluses

- Great for high-fat foods or people with gastroparesis





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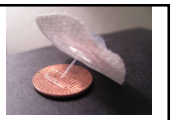
Temp Basals

- Temporarily increase or decrease basal settings
- A great option for high stress, sick days, steroid bursts, exercise
- Start the temp basal 1-2 hours prior to exercise or activity requiring the change
- Depending on pump report view, you may not see the temp basals
- Hybrid-closed loop
  - Temp target option (Medtronic), 150mg/dL
  - Exercise mode (Tandem), 140-160mg/dL
  - Hypo-protect (Omnipod 5), 150mg/dL

Safety Features

- Alarms for occlusion or low insulin reservoir
- Active insulin to prevent stacking
- Keypad lock
- Waterproof or watertight
- Communication with CGM for auto-suspend and auto adjustment of basal
- Reminders to bolus, change infusion set, etc

Infusion Sets



- Infusion sets are usually Teflon
  - Available in different sizes (ex. 9mm vs 6mm)
  - Silhouette (angled) may be better for kids/thinner/very active people
  - Steel infusion sets a good option for people with frequent site occlusions
- Insert at least 1 inch from CGM site
  - Auto-injectors vs. manually injecting
- Site selection/rotation
- Longer tubing options
  - Good if connected on leg, arm or wearing pump further from site
- Caution with kids/babies/pets-pouches available to hide pump
- When changing out infusion set, check glucose or CGM 1-2 hours after
  - Don't change right before bed

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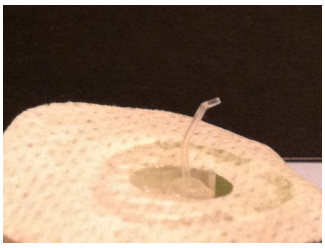
What Happens with a Bent Cannula?



A. Hyperglycemia
B. Hypoglycemia
C. No effect

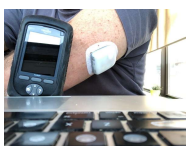
Filling the Pump

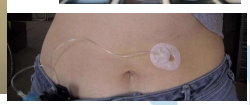
- Only fill with how much insulin you expect to use in 3 days + ~30 units
- Pumps hold 200-300 units
- Caution with air bubbles
- Fill cannula amount
  - Steel needle (0 units)
  - 6mm cannula (0.3 units)
  - 9mm cannula (0.5 units)
- If cannula overfilled, can lead to lows
- If cannula under-filled or air bubbles, can lead to highs

https://princessofpavement.com/2011/11/10/like-a-pin-cushion/

Where to Wear?

- Infusion set can go any place where insulin can be injected
- Pump can be worn on belt, in pocket or in a pouch





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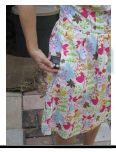
Where to Wear?







Hybrid-Close Loop (HCL)

- Automates insulin delivery based on CGM readings
- All systems auto-adjust basal rates
- Some systems give auto-corrections
- All systems require the user to bolus for carbohydrates
- Requires user to use CGM and maximize time spent in HCL to get most benefits
- Current systems: Medtronic 670G/770G, Tandem Control IQ
- Up-coming: Medtronic 780G, Omnipod 5, Beta bionics ilet

Ideal Pump Candidates

- Motivated
- Checking BG 4+ times/day or wearing CGM
- A1C <10%
- Carbohydrate counting or good with estimates
- Ability to learn pump programming
- Willing to follow up regularly with health care team
- Can afford the pump/supplies
- Following hyperglycemia treatment instructions

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Insulin Pump Options

OmnipodDash
(Insulet)

t:slim X2 with G6 CGM
(Tandem/Dexcom)
Basal IQ
Control IQ

670G & 770G with
Guardian 3 (Medtronic)

Cleveland Clinic

"Smart" Insulin Pumps

Omnipod DASH
(Insulet)

Omnipod 5
(Insulet/Dexcom)

T:slim X2 with G6 CGM
(Tandem/Dexcom)
Basal IQ
Control IQ

770G with Guardian 3
(Medtronic)

Omnipod DASH

- No tubing
- Pod (pump) includes infusion set
- All programming done via PDM
  - Locked Android smartphone
  - Bluetooth connection
- Rechargeable battery
- Food database
- Holds 200 units
- 0.05 unit basal increment
- Automatic cannula insertion and priming
- Dash blue tooth connected with contour meter

https://www.omnipod.com/what-is-omnipod

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Omnipod 5

- HCL system
- Glucose targets from 110-150mg/dL adjustable by time or d
- Adaptive basal rates
- HypoProtect for times to reduce risk of lows
  - Reduce insulin to target of BG 150
- SmartBolus calculator informed by Dexcom G6 CGM value and trend
- Control system from a compatible personal smartphone
- Adjustable settings: carb ratio, sensitivity, active insulin time, recommended bolus dose
- Plans to integrate with Libre 2 in the future

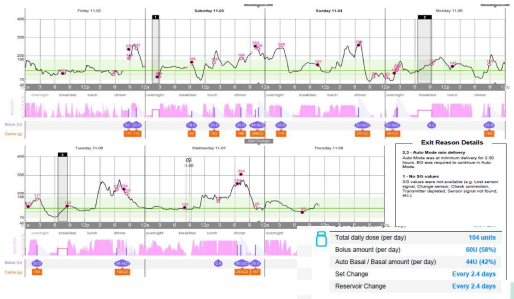
Device Comparison — Panther Program (bdcpantherdiabetes.org)

Medtronic 770G

- 770G with SmartGuard™ Auto Mode
  - Adjusts basal insulin every 5 min based on CGM readings to target glucose of 120 mg/dL
  - Bluetooth connectivity
  - 780G software upgrade when approved
- Suspend before/on low options (in manual mode)
- Temp target of 150 available
- 300 unit reservoir
- Connected Accu-check Guide meter and Guardian 3 CGM
- Mobile app for data sharing/viewing
- 300-unit reservoir
- 0.025 unit basal increment

https://www.medtronic.com/us-en/healthcare-professionals/products/diabetes/insulin-pump-systems.html

Medtronic 770G Example



Tandem t:slim X2

- Touch screen
- Rechargeable
- 300-unit reservoir
  0.001 unit basal increment
  Integrated Dexcom G6 CGM
  Software updates available
- 2 algorithms:
  - Basal IQ – basal adjusts and suspends for lows
  - Control IQ – basal adjusts for lows and highs; automatic hourly correction boluses for highs

Tandem T:Slim X2 with Basal IQ

- Touch screen
- Lithium rechargeable battery
- 300-unit reservoir
- Indicated ages ≥ 6 years
- 0.001 unit basal increment
- Integration with Dexcom G6
- Basal IQ- suspends basal if CGM predicted to decrease to < 80 mg/dl within 30 minutes

BASAL IQ Example

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Tandem T:Slim X2 with Control-IQ

- Advanced hybrid-closed loop system
- Algorithm adjusts insulin delivery from programed "manual" settings
- Automatic correction doses
  - Up to 1 every hour
  - Calculated at 60% of programmed correction factor (target of 110)
- User must still bolus for carbs (and additional correction doses)
- FDA approved 6+ years
- Basal-IQ users who update to Control-IQ cannot switch back to Basal-IQ mode

Control IQ Targets

	Control-IQ	Sleep Activity	Exercise Activity
Delivers — Delivers an automatic correction bolus if sensor glucose is predicted to be above ___ mg/dL	180	---	180
Increases — Increases basal insulin delivery if sensor glucose is predicted to be above ___ mg/dL	160	120	160
Maintains — Maintains active Personal Profile settings when sensor glucose is between ___ - ___ mg/dL	112.5 - 160	112.5 - 120	140 - 160
Decreases — Decreases basal insulin delivery if sensor glucose is predicted to be below ___ mg/dL	112.5	112.5	140
Stops — Stops basal insulin delivery if sensor glucose is predicted to be below ___ mg/dL	70	70	80

Coming Soon: Dose off Phone app

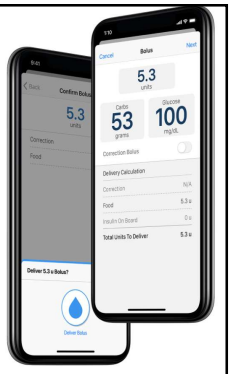
Give yourself the freedom to more easily manage your diabetes with the t:slim X2 insulin pump and t:connect mobile app

With this much-anticipated feature, expected summer 2022,* you'll have the freedom to bolus without having to touch your t:slim X2 insulin pump. That increased flexibility decreases how often you need to interact with your pump. Read our press release announcing FDA clearance to learn more. We'll let you know as soon as it becomes available.

Enjoy the Freedom to See Clearly
Conveniently view your pump data, including basal and bolus events, pump and sensor status, insulin on board, carbs, and settings on your compatible smartphone.

Enjoy the Freedom to be Discreet
Serving as a secondary display for your t:slim X2 insulin pump, the t:connect mobile app allows you to view alerts from your pump as push notifications.†

See Smartphone Compatibility



Future Pumps

Beta Bionics iLet

Medtronic 780G

Tidepool Loop

Medtronic 780G

- Basal rate automation
- Automatic correction boluses
- Adjustable target to 100mg/dL
- Increased time in closed loop
- Bluetooth connectivity, remote software upgrades
- Mobile app for secondary data display and wireless data uploads
- CE-marked in Europe
- >80% time in range goal
- Guardian Sensor 4 non-adjunctive (no calibrations)
- Future:
  - Synergy sensor: disposable, 50% smaller

Beta Bionics iLet

- HCL system
- Holds 160 units of insulin
- Dual hormone automation with glucagon and insulin
- Programmed by entering body weight and starting CGM
  - No other insulin pump settings
- Enter in meal estimates (less, usual, more)
- Ability to use prefilled insulin cartridges

https://www.betabionics.com/

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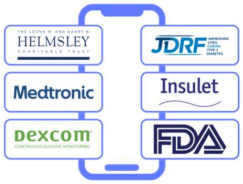
Tidepool Loop

- The Tidepool Loop app will be submitted to FDA as a controller (iAGC) that pairs with an ACE insulin pump and an iCGM using Bluetooth wireless communication.
- Goal is for the app to be FDA approved and available for download from the App Store and compatible with commercially-available, in-warranty insulin pumps and CGMs.



Automated insulin dosing | Tidepool

5. Which pump is considered a hybrid-closed loop?

A. Cequr simplicity
B. Tandem Basal IQ
C. Medtronic 770G
D. Omnipod Dash

HCL Pump Comparison

	MiniMed™ 670G / 770G	MiniMed™ 780G*	t:SLIM X2 WITH CONTROL-IQ	OMNIPOD 5*
		*AVAILABLE OUTSIDE US, NOT FDA APPROVED.		* NOT FDA APPROVED, SUBJECT TO CHANGE.
CALCULATE				
What is automation called?	Auto Mode	Auto Mode	Control-IQ	Automated Mode
Basal automation?	Automated basal insulin delivery calculated based on total daily insulin from past 2-6 days ("auto basal")	Automated basal insulin delivery calculated based on total daily insulin from past 2-6 days ("auto basal")	Automated basal insulin delivery that increases or decreases programmed basal rates	Automated basal insulin delivery calculated from total daily insulin from last pod change (~3 days) ("adaptive basal")
Bolus automation?	No (auto basal only to respond to hyperglycemia)	Auto-correction bolus if glucose > 120 mg/dL and at maximum "auto basal" delivery	Auto-correction bolus (max 1/hour) if glucose predicted to be >180 mg/dL delivers 60% of calculated dose	No (adaptive basal only to respond to hyperglycemia)
Algorithm target BG/range?	120 mg/dL	100 mg/dL OR 120 mg/dL	112.5-160 mg/dL (range)	110, 120, 130, 140, 150 mg/dl

Automated Insulin Delivery — Panther Program (bdcpantherdiabetes.org)

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Critical Thinking

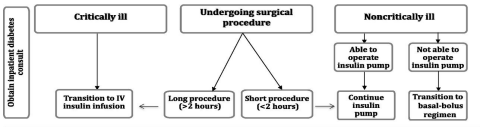
When should a provider consider discontinuing an insulin pump during hospitalization?

Technology in the Hospital

- Several inpatient studies have shown that CGM detected a greater number of hypoglycemic events than POC glucose testing
  - Overall, did not improve glucose control
- Patients who are comfortable using their diabetes devices (insulin pumps, sensor) should be given the chance to use them in an inpatient setting if they are competent to do so.
- Health care institutions must have clear policies and procedures to maximize safety and to comply with existing regulations related to self-management of medication.

Diabetes Care 2020 Jan; 43(Supplement 1): S77-S88
Umpierrez G et al. Diabetes Care 2018 Aug; 41(8): 1579-1589..

Patient With Insulin Pump Admitted to Hospital



Changes to Pump Therapy With Imaging Studies	
X-ray/CT	Pump should be covered by lead apron
MRI	Pump and metal infusion set should be removed
Ultrasound	No need to remove pump but transducer should not be pointed directly at the pump
Cardiac catheterization	Pump should be covered by lead apron
Pacemaker/automatic implantable cardioverter defibrillator (AICD)	Pump should be covered by lead apron
Colonoscopy/EGD	Pump can remain in place
Laser surgery	Pump can remain in place

Umpierrez G et al. Diabetes Care 2018 Aug; 41(8): 1579-1589.

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Contraindications to Insulin Pumps in the Hospital

Impaired level of consciousness (except during short-term anesthesia)
Patient's inability to correctly demonstrate appropriate pump settings
Critical illness requiring intensive care
Psychiatric illness that interferes with a patient's ability to self-manage diabetes
Diabetic ketoacidosis and hyperosmolar hyperglycemic state
Refusal or unwillingness to participate in self-care
Lack of pump supplies
Lack of trained health care providers, diabetes educators, or diabetes specialist
Patient at risk for suicide

Umpierrez G et al. Diabetes Care 2018 Aug; 41(8): 1579-1589.

Insulin Pump Data Management Tools

System	Website	Associated Mobile Apps	Integration
Glooko	glooko.com	Glooko Omnipod Demo PodderCentral Omnipod Display Omnipod View	Insulin pumps (Omnipod, Tandem), Dexcom, Eversense, many glucose meters
Carelink	carelink.medtronic.com	MiniMed Simulator	Medtronic insulin pumps and Medtronic CGM
Tidepool	tidepool.org	Tidepool Mobile	Insulin pumps (Medtronic, Tandem, Omnipod), FreeStyle Libre, Dexcom, Guardian Connect, many glucose meters
T:Connect	tconnect.tandemdiabetes.com	T:simulator T:connect mobile	Insulin pump (Tandem), Dexcom

Connected Insulin Pens

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The Insulin Delivery Landscape

Smart Insulin Pens

Smart Insulin Pumps

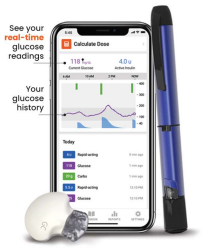
10.5% of US population with diabetes (34.2 million people)
7.2 million using insulin

Traditional Insulin Pen, Vial and Syringe

Basic Patch Pumps, Inhaled Insulin

Diabetes Care 2018 Jun; 41(6): 1299-1311

Connected Pen Options



InPen with Guardian Connect or Dexcom G6

Bigfoot Unity with Libre 2

InPen

- Delivers up to 30 units of insulin per dose
- Delivers in ½-unit increments
- Disposable needles (not included)
- 1 year life span
- Does not require charging
- Comes in blue, gray, and pink
- Integrates with Apple Health and Glooko
- Requires a prescription, uses cartridges
- Compatible with: Humalog, NovoLog, and Fiasp U100 3.0 mL prefilled cartridges
- Multiple pens can be paired to the InPen app.

https://www.companionmedical.com/InPen

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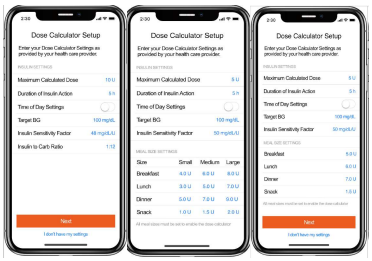
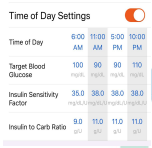
Therapy Settings





Bigfoot Unity Diabetes Management System

- Cleared by the FDA for ages over 12 years
- Smart insulin pen caps fits onto most commercially available insulin pens
- Uses glucose data from Freestyle Libre 2 CGM
- Scan the sensor with the pen cap
- Recommended dose displayed by pen cap
  - 3 options based on small, medium large or carb counts
- Will not recommend insulin within 3 hours of last dose
- Pen caps are rechargeable

In Summary

- There are several CGM, connected pen and insulin pump options, and the DCES can help PWD select the best device for their individual needs
- New era of hybrid closed loops
- No artificial pancreas yet, but we are getting closer to closing the loop
- Connected data can be used to discussion diabetes self-management with the person with diabetes and help to make meaningful changes-think DATAA

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Additional Resources

- Integrated Diabetes Services
  - https://integrateddiabetes.com/updated-insulin-pump-comparisons-and-reviews/
- ADCES Insulin pump therapy resources
  - https://www.diabeteseducator.org/practice/practice-tools/diabetes-management-tools/ipt-resources
- Diatribe.org
- Diabeteswise.org
- Danatech.org

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