Diabetes Medications and Devices

Rosny Daniel, MD (he/him)

Objectives

Recognize	Recognize the stress of chronic disease
Identify	Identify common diabetes management technology
Discuss	Discuss emergent risks and side effects of diabetes medications

Medication adherence

- When is the last time you had to take medications?
- Was it long term or short term?
- How well do you think you "complied" with the medications?
- What were factors that played into this?

Medication adherence

Primary Medication Non Adherence – defined by not renewing prescriptions on monthly basis as expected.

HTN, DM, osteoporosis, Ashtma, HLD 10-25%

Schizophrenia 41%

Medication adherence factors

Patient Factors

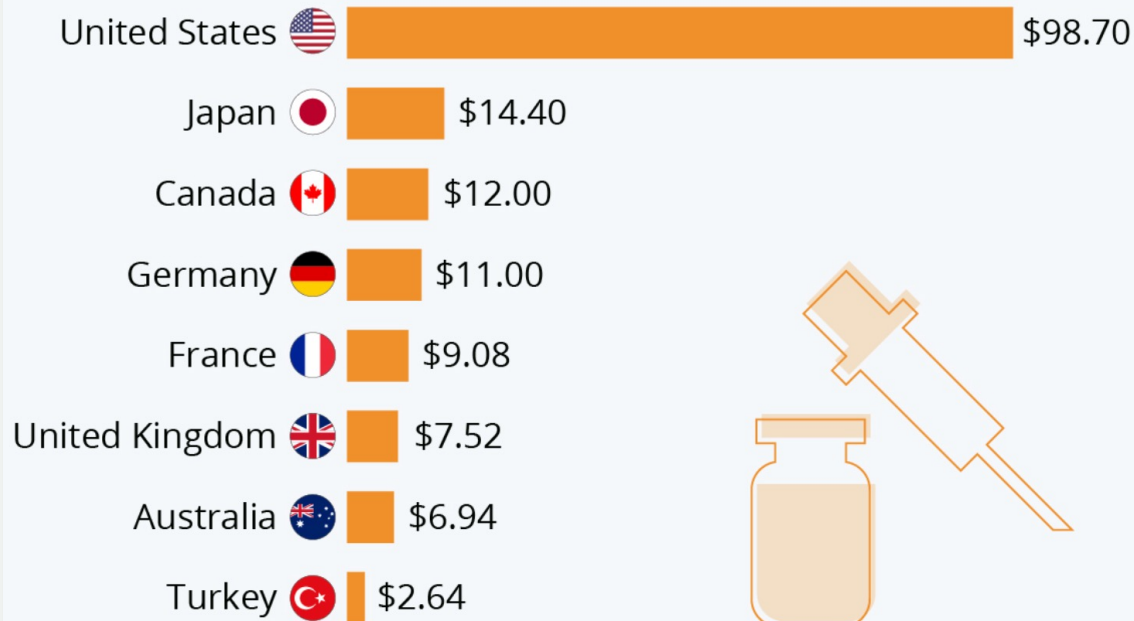Medication Factors

Physician Factors

System Based Factors

Other factors

Americans Cross Border Into Mexico To Buy Insulin At A Fraction Of U.S. Cost

For one patient, a three-month supply of insulin is $3,700 in the U.S. versus $600 in Mexico. But is it legal?

American Insulin Prices Are Off The Charts

Average price per standard unit of insulin in selected countries in 2018

Country	Price
United States 🇺🇸	$98.70
Japan 🇯🇵	$14.40
Canada 🇨🇦	$12.00
Germany 🇩🇪	$11.00
France 🇫🇷	$9.08
United Kingdom 🇬🇧	$7.52
Australia 🇦🇺	$6.94
Turkey 🇹🇷	$2.64

Source: RAND Corporation

D.j. Mattern, who has Type 1 diabetes, turned to a growing underground network of people with diabetes who share extra insulin when they have it.

Diabetes patients turn to underground insulin networks as Covid-19 exposes limits of copay caps

What can we do?

|	
Understand	Understand our patients face major challenges
Inquire	Ask what makes it difficult to access or take meds
Clarify	Ask patients about their pharmacy and ability to pay
Collaborate	Work closely with our pharmacist to figure out availability

Shame
Self doubt
Isolation
Frustration
Disbelief
Stress
Grit/resilience
Determination
Stress
Acceptance

Acceptance
Relief
Weight gain
Frustration
Stress
Patience
Self care
Understanding

Burden of chronic disease

disease

management

cognitive overload

symptoms

stress
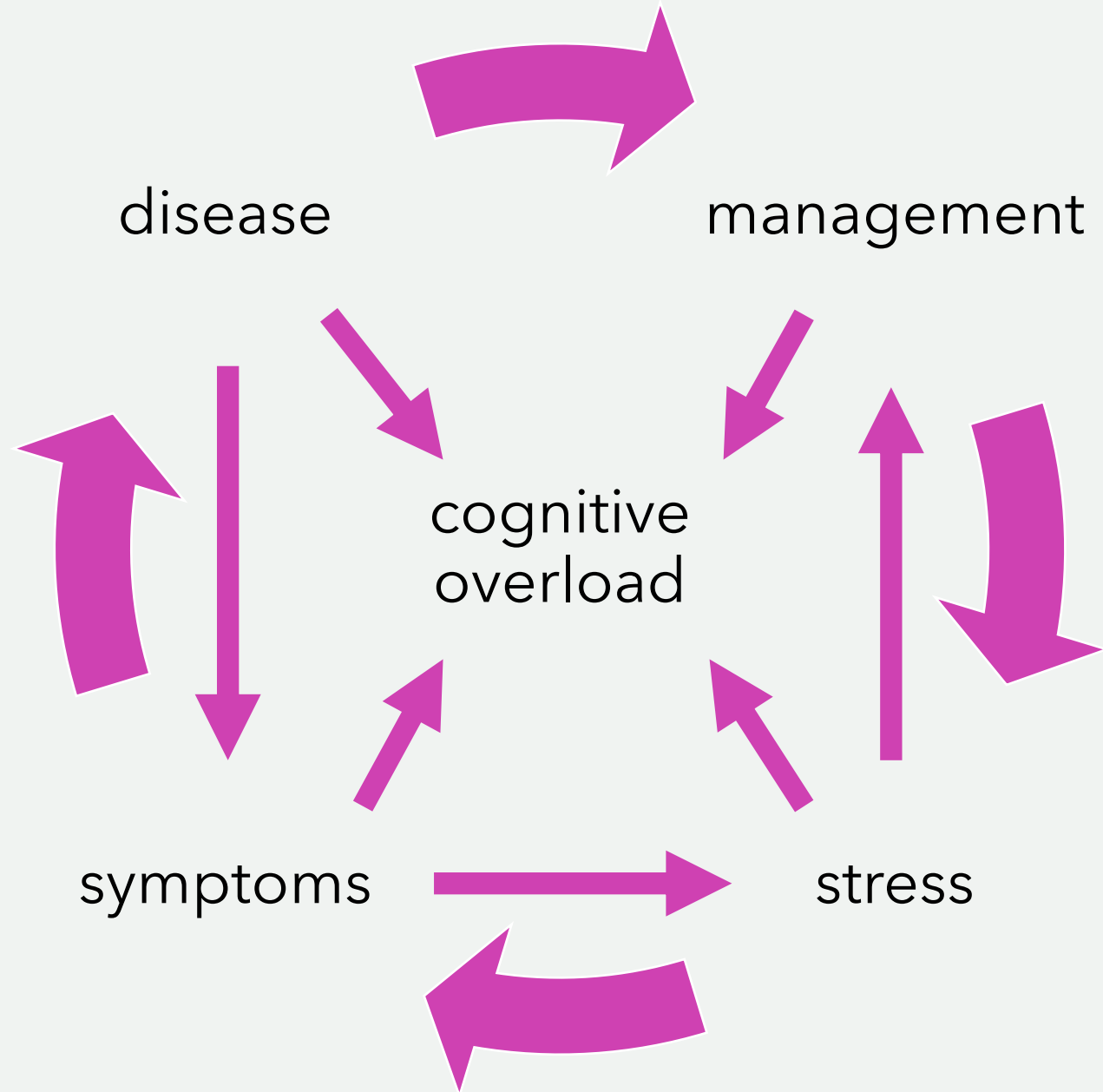
Chronic disease takeaways

- It is hard to have a (chronic) disease
- It is hard to navigate the healthcare system
- Don't judge your patients
- Think about how you can help them with navigating the system and getting medications

Evolution of diabetes technology

Insulin discovered Frederick Banting

Backpack insulin & glucagon pump

Intravenous glucose control:
Albisser et al, 1974;
Mirouze, Selam et al, 1977.
Pfeiffer et al, 1974

Understanding the Metabolic Network:
The Minimal Model of Glucose Kinetics.
Bergman & Cobelli, 1979

Subcutaneous Continuous Glucose Monitoring Minimed CGMS, 1999

The Incretin Effect:
GIP, GLP-1 and DPP-4
Nauck et al, 1986.

1920s   1960s   1970s   1980s   1990s   2000s

Ames Reflectance Meter

The Auto Syringe (Dean Kamen)

First use of s.c. insulin pump
Tamborlane et al, 1979
Pickup et al, 1978.

Quantifying Diabetes:
Glucose variability and Risk Analysis.
Kovatchev et al. 1997
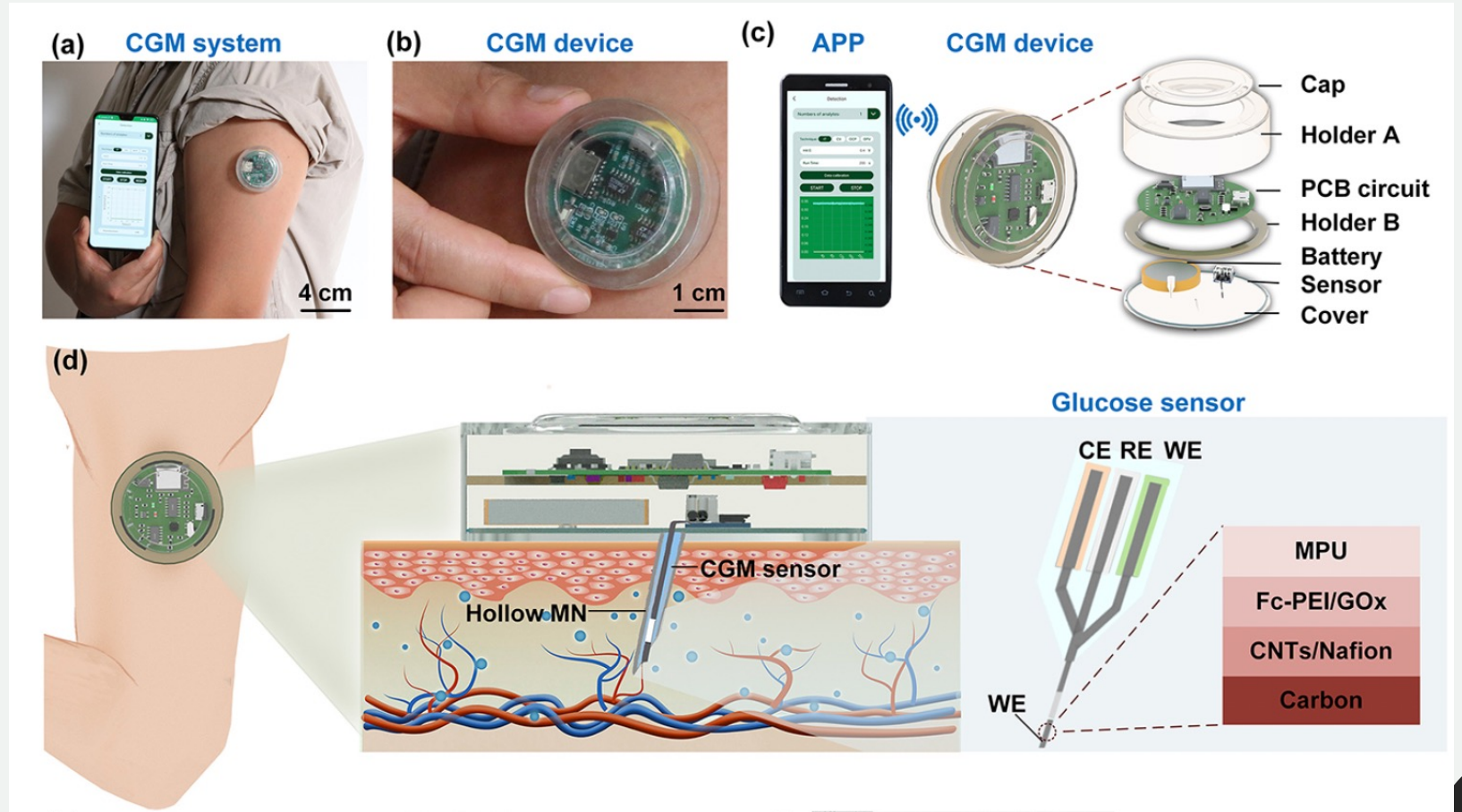
Diabetes technology in the ED

48% of people with T1DM use a CGM

50% in white patients, 18% in Black patients

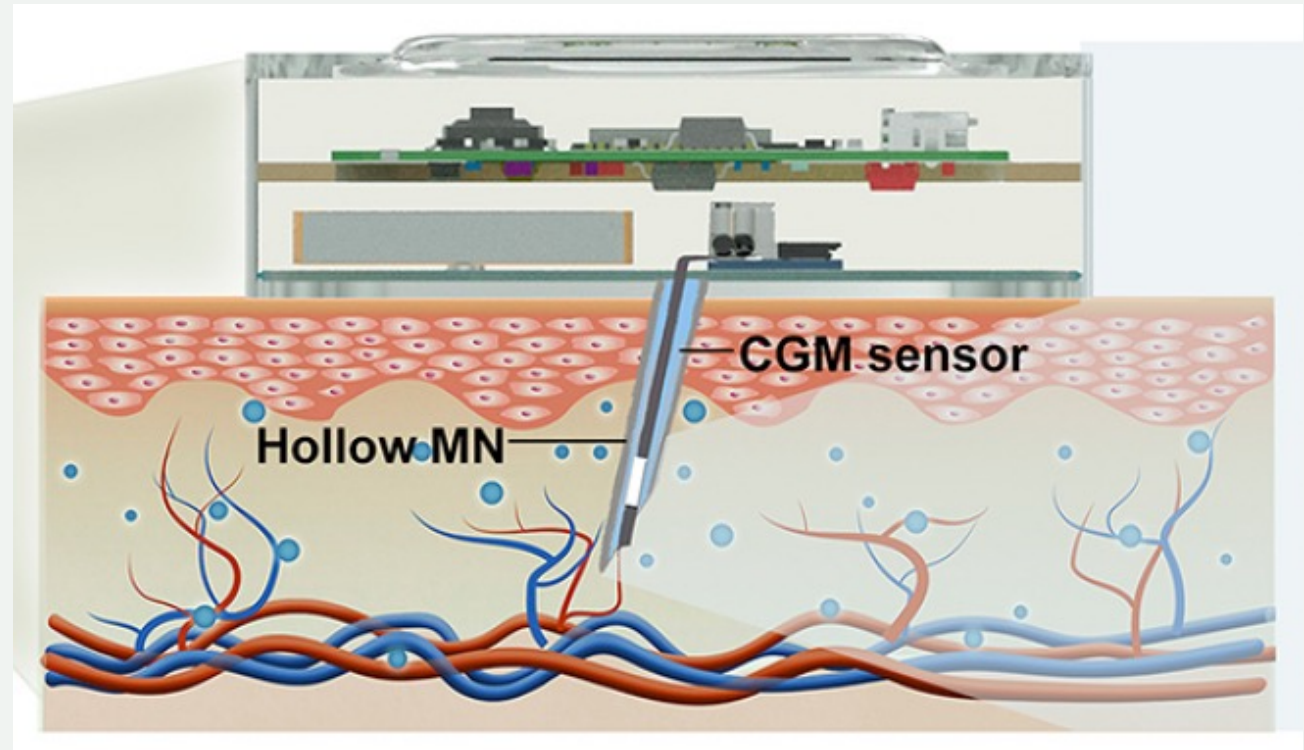57% of privately insured patients, 33% of publicly insured patients

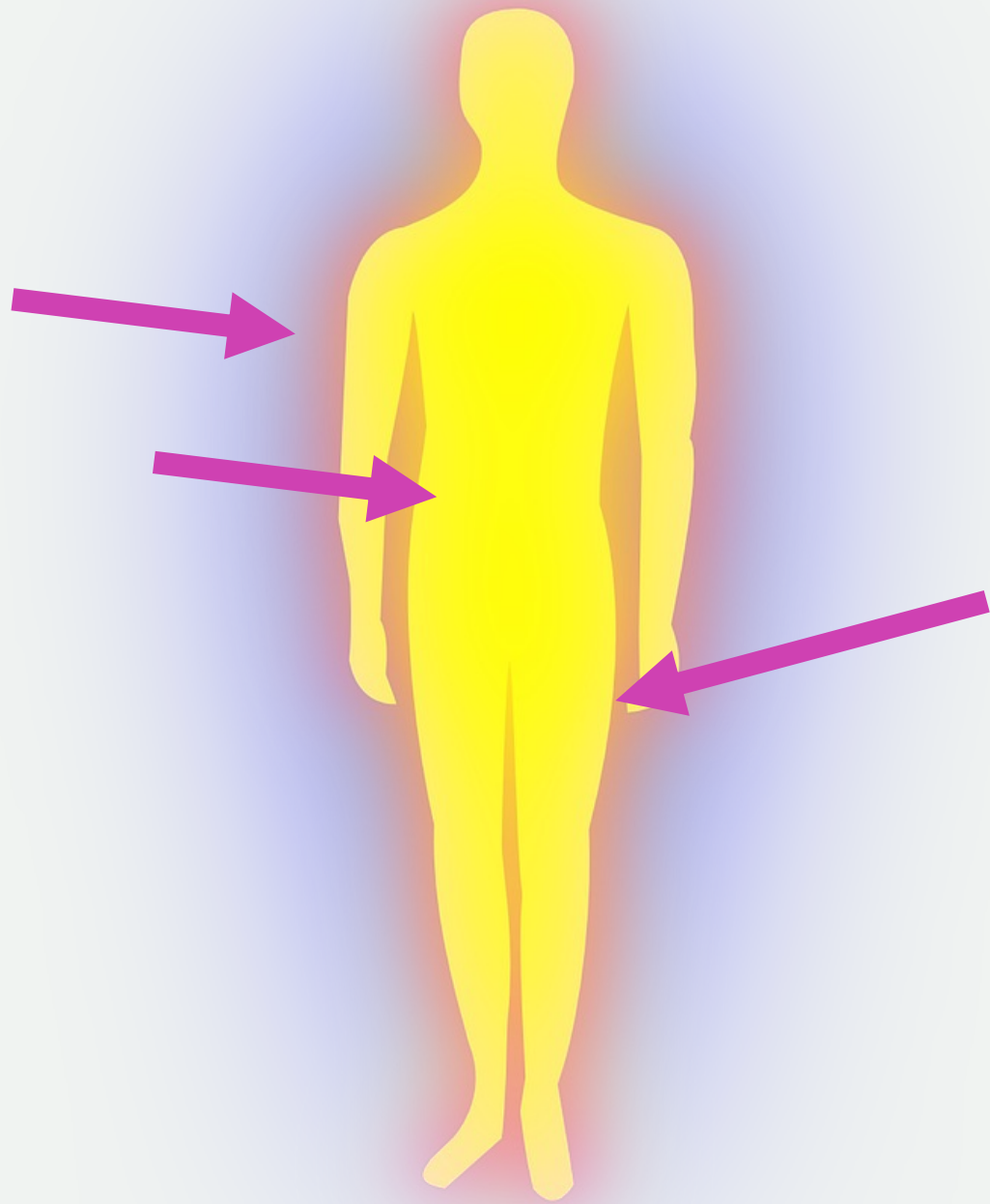30-60% of people with T1DM use an insulin pump

Continuous Glucose monitors

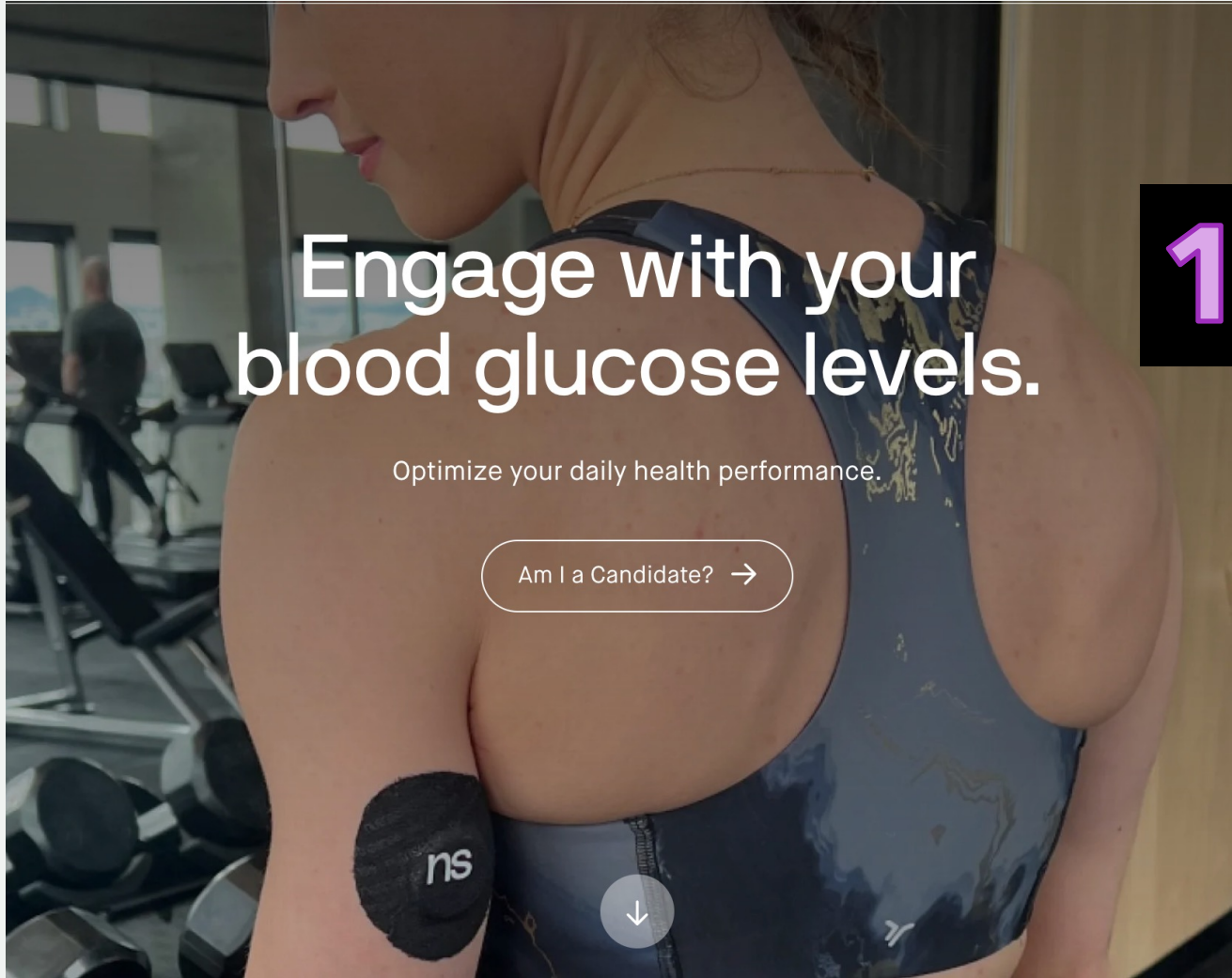# *Continuous Glucose monitors*

Eligibility?

- People who use insulin multiple times daily
- People with hypoglycemic episodes
- Elderly patients
- Patients with disabilities
- People who use a pump

Model	FreeStyle Libre Pro	FreeStyle Libre	FreeStyle Libre 2	FreeStyle Libre 3
Year of FDA Approval	2016	2017	2018	2022
MARD	12.3%	12%	9.5%	7.9%
Wear Length Time	14 days			
Warm Up Time	1 hour			
Repeated Calibrations Needed	None			
Measures Glucose	Every 15 minutes	Every 1 minute		
Wireless Data Sharing	N/A	20 people		
Alerts	N/A		Yes; when scanned	Yes
Transmitter Duration	14 days			
Interference With	Hydroxyurea	Vitamin C Aspirin		
Pump Integration	N/A			

Model	Short Term Sensor (STS)	Dexcom SEVEN PLUS	Dexcom G4	Dexcom G5	Dexcom G6	Dexcom G6 Pro	Dexcom G7
Year of FDA Approval	2006	2007	2012	2015	2019	2019	Not Approved
MARD	26%	16%	13%	9%	9%	9%	8.1% in arm 9.1% in abdomen
Wear Length Time	3 days	7days			10 days		10.5 days
Warm Up Time	2 hours						27 minutes
Repeated Calibrations Needed	Every 6 hours				No		
Measures Glucose	Every 5 minutes						
Wireless Data Sharing	N/A		5 people	10 people		N/A	10 people
Alerts	Only for hypoglycemia	Yes					
Transmitter Duration	6 months			3 months		1 month	10 days
Interference With	Aspirin Vitamin C	Acetaminophen	Acetaminophen Hydroxyurea		Hydroxyurea	Ascorbic Acid Salicylic Acid	Unknown
Pump Integration	N/A		Tandem		Tandem Omnipod 5	N/A	Unknown

Model	Dexcom Implantable Sensor	Eversense	Eversense XL	Eversense (E3)
Year of FDA Approval	Not approved by FDA	2018	Not approved by FDA	2022
MARD	16-25%	11.2%	11.6%	8.5%
Wear Length Time	3 months	90 days	180 days	180 days
Warm Up Time	N/A	24 hours		
Repeated Calibrations Needed	Every 12 hours			2 calibrations per day, for the first 21 days of wear. Then, every 24 hours.
Measures Glucose	Every 5 minutes			
Wireless Data Sharing	N/A	5 people		
Alerts	Yes			
Transmitter Duration	51-58 days	3 months	6 months	
Interference With	N/A	Tetracycline Mannitol		
Pump Integration	N/A			

Sensor Applicator   Sensor Pack   Sensor (assembled)   Reader

Continuous Sensor – Dexcom

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Flash Sensor – FreeStyle Libre
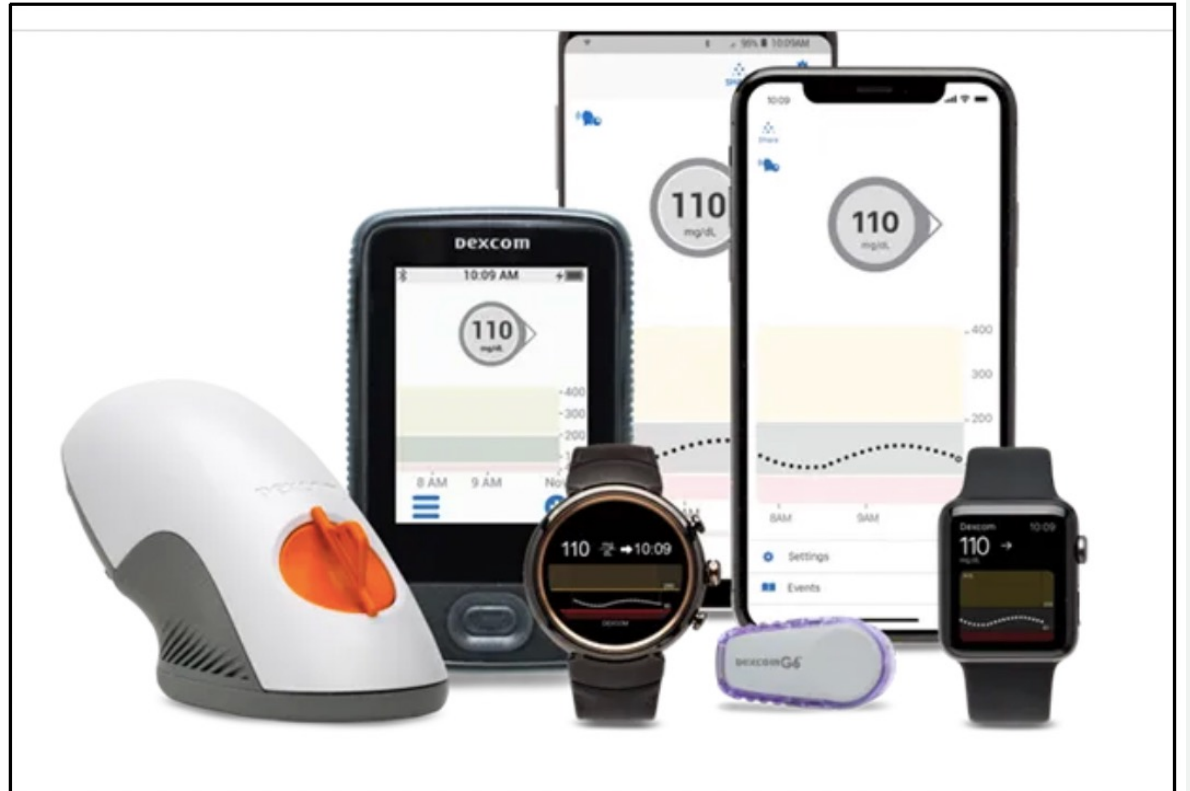
CGM Considerations

CGMs can be inaccurate

Skin irritation is common

Beware of meds/conditions that interfere with readings

CGM Considerations

Look for a CGM if a patient is hypoglycemic

Let the patient leave the CGM on

Some are not compatible with MRI

Check to see if your hospital allows you to document CGM readings

Consult endocrine if you are concerned

cannula

tubing

controller

reservoir

omnipod

EXTER BG
103 mg/dL

10/23/15
9:34 AM

103 mg/dL
Sent

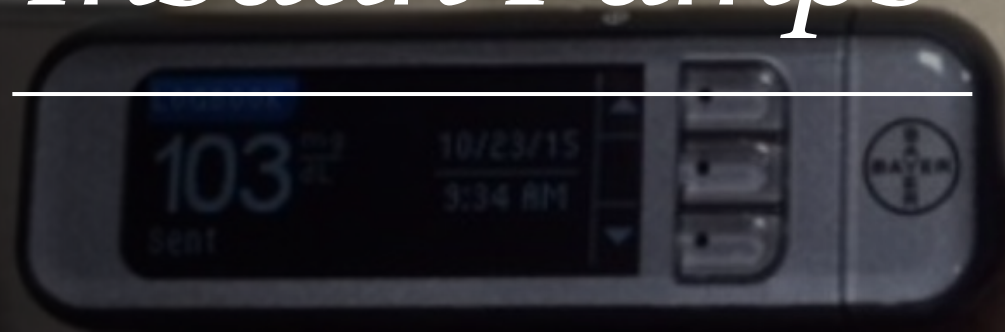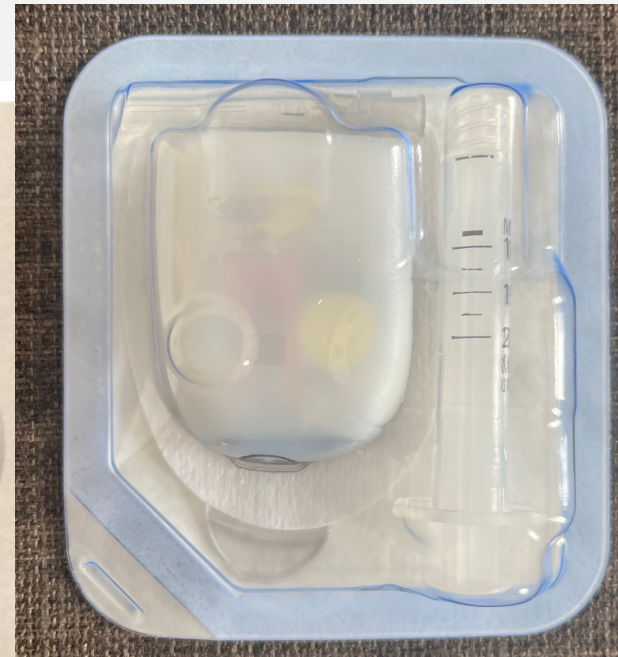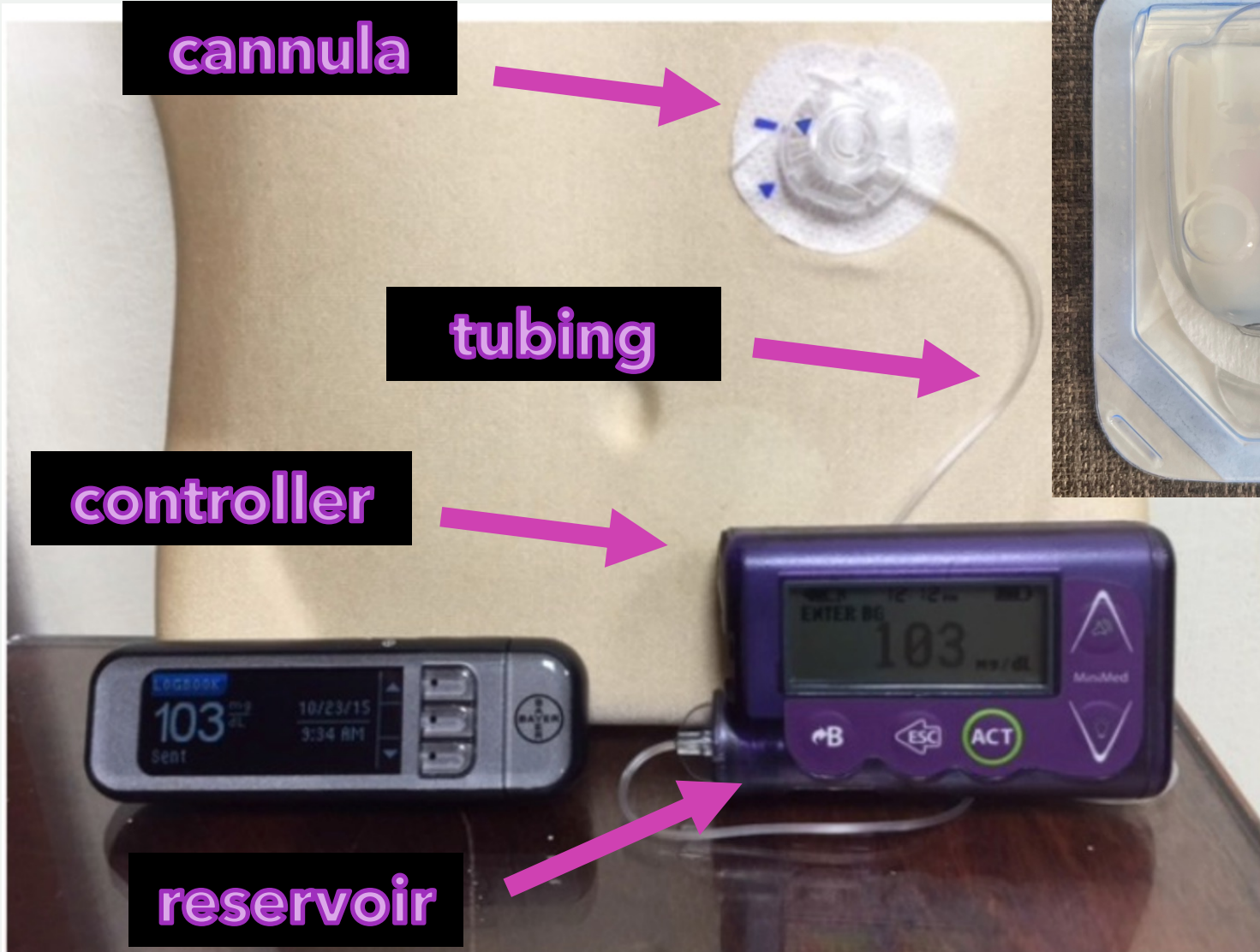| Model	Medtronic 670G/ 770G	Medtronic 780G	Tandem t:slim X2 Basal-IQ	Tandem t:slim X2 Control-IQ	Omnipod 5
FDA Approval	2017/2020	Not yet approved	2018	2020	2022
CGM Used	Guardian 3	Guardian 3 or 4	G6		
Auto-Mode	After 48 hours		Immediately		
Basal adjusted	Every 2-6 days		Based on previous basal program		With each pad change
Target Range (mg/dL)	120	100, 110 or 120	N/A	112.5-160	110, 120, 130, 140, or 150
Correction Target (mg/dL)	Fixed at 150	Fixed at 120	N/A	Fixed at 110	Flexible
Modified Parameters	ICR DIA	ICR DIA	ICR ISF Basal Rate		ICR ISF DIA
Fixed Parameters	Basal Rate ICF	Basal Rate ICF	DIA is 5 Hours	DIA is 5 Hours Correction Target	Basal rate
Exercise Mode (mg/dL)	Temporary Target (150)	Exercise Mode (150)	N/A	Exercise Mode (140-160)	Activity Mode (150)
Sleep mode (mg/dL)	N/A	N/A	N/A	Sleep Mode (112.5-120)	N/A
Additional Features (mg/dL)	Recommended Bolus	Auto-Bolus	N/A	Extended Bolus Insulin Delivery	N/A
Upload program	CareLink		t: Connect		Glooko

Insulin Carb Ratio (ICR), Duration Insulin Action (DIA), Insulin Sensitivity Factor (ISF)

Table 1. Pharmacokinetic Profiles of Insulin Therapies

Insulin type	Onset	Peak	Duration
Long-acting			
Detemir (Levemir)	3 to 4 hours	6 to 8 hours	6 to 23 hours
Glargine (Lantus)	90 minutes	None	24 hours
Intermediate-acting			
NPH (Humulin N)	1 to 2 hours	4 to 10 hours	14 or more hours
Short-acting			
Aspart (Novolog)	15 minutes	1 to 3 hours	3 to 5 hours
Glulisine (Apidra)	15 to 30 minutes	30 to 60 minutes	4 hours
Lispro (Humalog)	15 minutes	30 to 90 minutes	3 to 5 hours
Regular	30 to 60 minutes	2 to 4 hours	5 to 8 hours
Mixed*			
NPH/lispro or aspart	15 to 30 minutes	Dual	14 to 24 hours
NPH/regular	30 to 60 minutes	Dual	14 to 24 hours

*—NPH/regular: Humulin 70/30, Novolin 70/30, Humulin 50/50; NPH/lispro or aspart: Humalog 75/25, Novolog 70/30, Humalog 50/50.

Adapted with permission from Endotext.org. Insulin pharmacology, types of regimens and adjustments. http://www.endotext.org/diabetes/diabetes17/diabetesframe17.htm. Accessed December 6, 2010.

Initiating and Managing pumps

- Education before starting on a pump
- Data shared with endocrinologist
- Program created with basal insulin expectation
- Insulin/carb ratio determined
- Patients learn how to use the pump over time
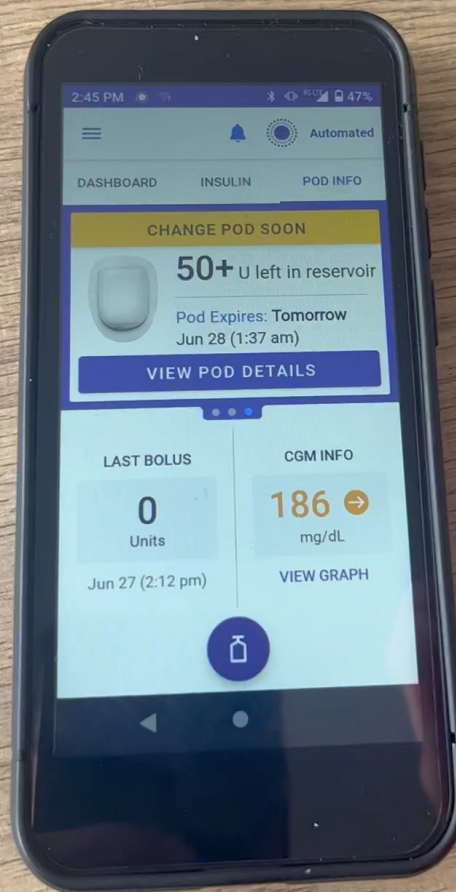
Pump Safety

- Activity/Exercise feature
- Maximum basal rate
- Shut off feature
- Short acting insulin only
- Hypoglycemia alerts from phone/controller

Pump Considerations

- In hypoglycemia, remove the pump
- In hyperglycemia consider that the reservoir is empty, kinked or disconnected tube, kinked cannula
- Patients have a high risk of DKA after pump is removed
- If admitting, consult endocrinology
- Not all pumps are compatible with MRI

Diabetes tech Summary

- CGM and pumps are more commonplace
- Ask patients about their technology, they likely have a lot of knowledge
- Leave CGMs in place
- Remove pumps in hypoglycemia
- Patients are at high risk of DKA when pumps are removed
- Consult endocrinology with questions

Diabetes Med Case 1

A healthy 36 y/o man presents with nausea, abdominal cramping and vomiting. He has no fevers, urinary symptoms, history of abdominal surgeries. His vitals are normal and his exam is unremarkable. He recently reached out to PlushCare and was started on semaglutide for weight loss. It turns out that he accidentally took about 5x the dose.

GLP 1 Receptor Agonists

GLP1 Receptor Agonists

- Once weekly shots or daily pill

- Increase insulin, decrease glucagon, delay gastric emptying

- Potentially increase satiety, reducing weight and calorie intake

- "quieting of food noise"

- Possible CV and renal protection

- Main side effects: **nausea, vomiting, diarrhea, abdominal pain**
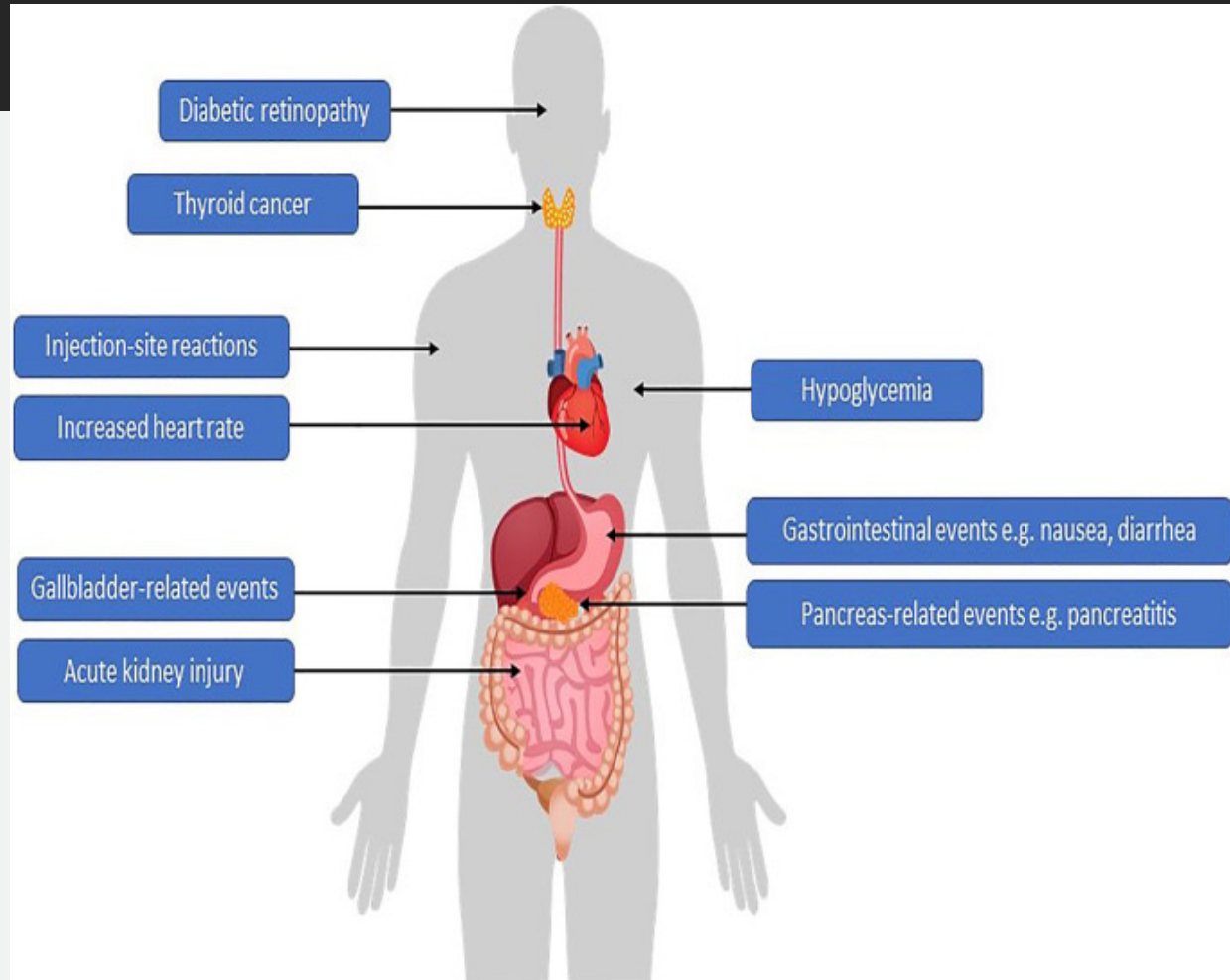
GLP1 Receptor Agonist Adverse Event Treatment

- Most effects go away over time

- Supportive care

- Monitor for hypoglycemia – maximum effect likely 6-24 hours after injection

Case outcome

Toxicology/Poison Control consulted. Patient was treated with Zofran, Compazine and 3 Liters of fluid. Abdominal pain, nausea and vomiting persisted so they were given droperidol 2.5 mg and stayed in the observation unit overnight with good outcome. Patient never had hypoglycemia.

Diabetes Med Case 2

A 63 year old transwoman with type 2 diabetes presents with chest pain. They recently had a long flight and they have pleuritic chest pain. On exam their HR is 104, BP is normal. EKG neg acute. Trop is 0.07. You want to order a CT pulmonary angiogram but see they are on metformin and your departmental policy states "patients must hold metformin for 24 hours after contrast".

Metformin Can Be Safely Used in Patients Exposed to Contrast Media: A Systematic Review and Meta-Analysis

[Hua Qiao](#), [a] [Yimin Li](#), [b,*] [Bao Xu](#), [c] [Zhiping Lu](#), [d] [Jing Zhang](#), [c] [Danxin Meng](#), [d] [Shenghu He](#), [c] and [Jin Huang](#) [d]

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Conclusion

Metformin can be safely used in patients with moderate renal impairment (eGFR $\geq$ 30 mL/min/1.73 m^2) during CM exposure.

Diabetes Med Case 3

60 year old woman with history of DM1 presents after 2 days of feeling unwell with some nausea and vomiting. ROS reveals dysuria. She recently started a new medication she cannot recall. Exam notable for dehydration. Vitals notable for low grade temp and tachycardia.

Labs show: pH 7.23, Anion gap 18 (nl <12), Serum Glucose 174

Euglycemic DKA and **SGLT2 Inhibitors**

- Acidosis and Ketosis with glucose <250
- Pregnancy, stimulant use, infection, fasting, chronic liver disease, glycogen storage disease
- SGLT2 inhibitors
- 0.2% in DM2 9.4% in DM1
- Usually happens within the first 2 months
- Precipitants: Infections, stimulant use, dehydration, discontinuation of insulin

Table 1. Available SGLT2 inhibitor preparations.

Medication	Dose (mg)	Frequency
Dapagliflozin	5; 10	Once daily
Dapagliflozin/ metformin	5/850; 5/1000	Twice daily, with food
Dapagliflozin/ saxagliptin	10/5	Once daily
Canagliflozin	100; 300	Once daily, before first meal of day
Canagliflozin/ metformin	50/850; 50/1000; 150/850; 150/1000	Twice daily, with food
Empagliflozin	10; 25	Once daily
Empagliflozin/ metformin	5/850; 5/1000; 12.5/850; 12.5/1000	Twice daily, with food
Empagliflozin/ linagliptin	10/5; 25/5	Once daily
Ertugliflozin	5; 15	Once daily
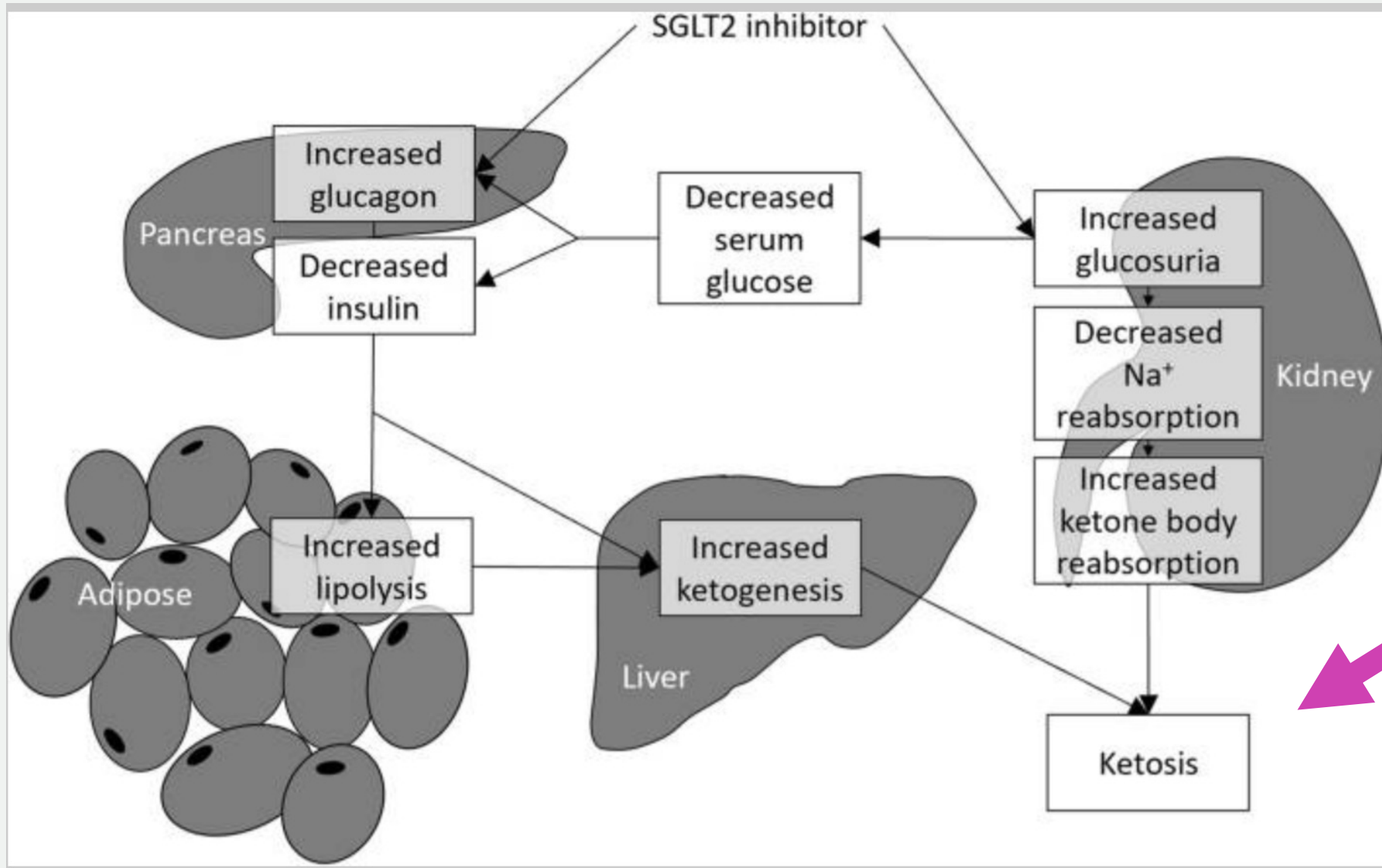
Case resolution

- Patient treated with IV fluids with dextrose, insulin drip, UTI treated. She improved and was discharged home 2 days later.

- Treat these patients as you would DKA, consult endocrinology.

The SQuID protocol (subcutaneous insulin in diabetic ketoacidosis): Impacts on ED operational metrics

Richard T. Griffey MD, MPH ✉, Ryan M. Schneider MSN, ACNP-BC, CPPS, Margo Girardi MD, Julianne Yeary Pharm D, BCCCP, Craig McCammon Pharm D, BCCCP ... See all authors ⌄

DISCUSSION

In this study, we found that a SQ fast-acting insulin protocol is an excellent option for MTM-severity DKA patients in the ED, reducing EDLOS and holding the potential for reductions in ICU admissions for MTM DKA. We observed excellent performance on our metric for fidelity to the protocol and had equivalent safety compared to a traditional insulin infusion pathway. Our project was met with a high degree of enthusiasm by ED providers and by the inpatient teams, leading to a forthcoming expansion of the SQuID protocol to a general medical floor and liberalization of criteria to include more complex patients. We anticipate this will result in a greater impact on reducing ICU admissions for DKA. This study adds to literature demonstrating efficacy of SQ insulin for this purpose and suggests that this might be a useful strategy for patient throughput in facilities where lack of ICU or intermediate care bed availability result in patient delays and prolonged EDLOS.

Diabetes medication takeaways

GLP1 agonists are popular, watch for n/v

Metformin is safe to continue using in patients getting contrast studies with GFR >30

SGLT2 inhibitors (flozins) predispose people to euglycemic DKA

Consider subcutaneous insulin treatment of DKA

Thank you