

A background image of pink cherry blossoms on dark, thin branches. The blossoms are in various stages of bloom, with some showing yellow centers. The background is a soft, out-of-focus light grey.

Diabetes Management and the Transplant Patient

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CDCES, BC-ADM

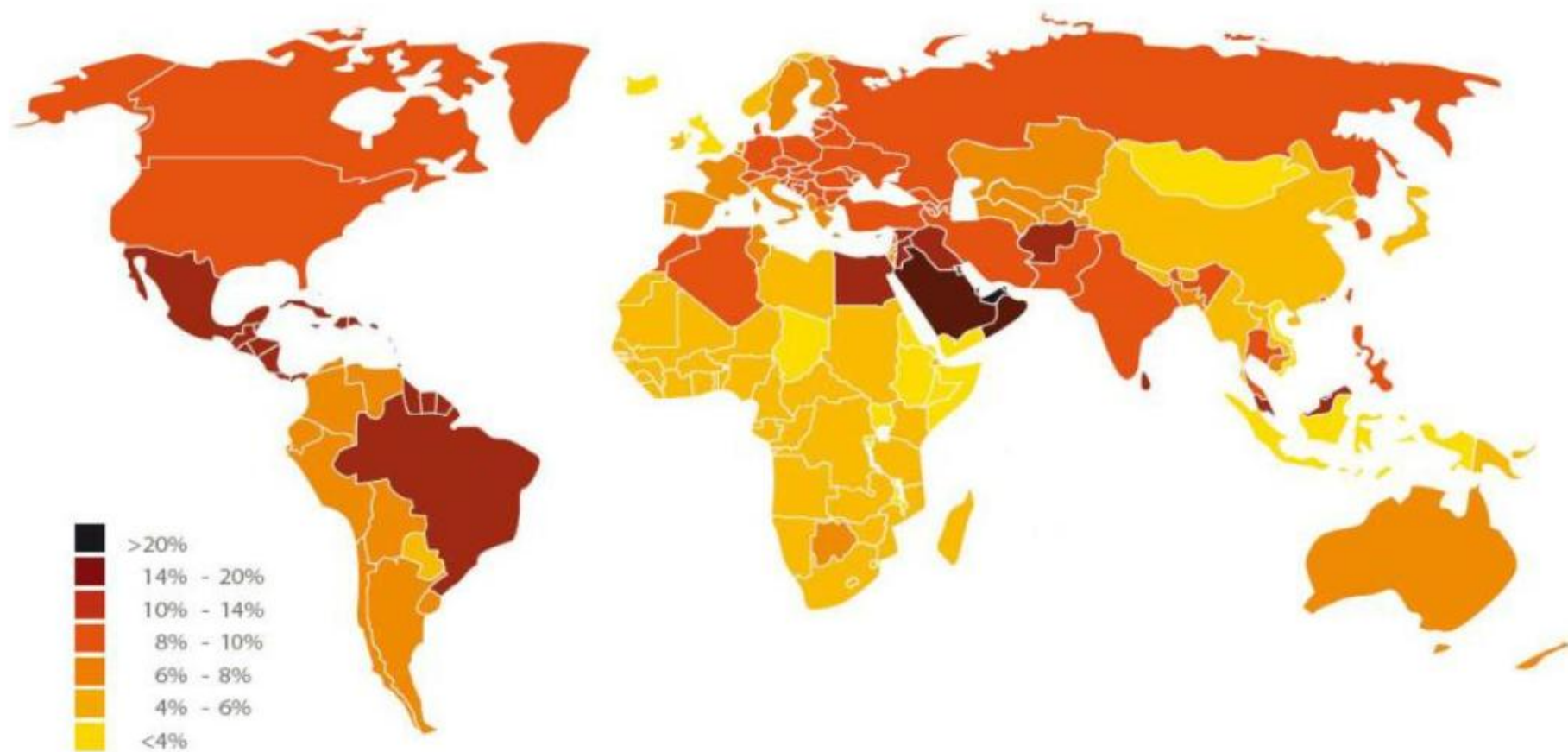
Associate in Medicine

Vanderbilt University Medical Center

Division of Endocrinology

Estimated World Prevalence of Diabetes: 2025

Prevalence estimates of diabetes, 2025



DIABETES IN THE U.S

A US REPORT CARD



DIABETES



38 million people
have diabetes



That's about **1 in every**
10 people



1 in 5 people don't
know they have it

PREDIABETES



98 million American
adults—**more than 1 in 3**
—have prediabetes



More than 8 in 10
adults with prediabetes
don't know they have it

Increasing Prevalence of Diabetes



Percent of Total Population with Diabetes (Diagnosed and Undiagnosed)



7-8%



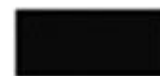
9-11%



12-14%



15-17%



18-20%

Endocrinology

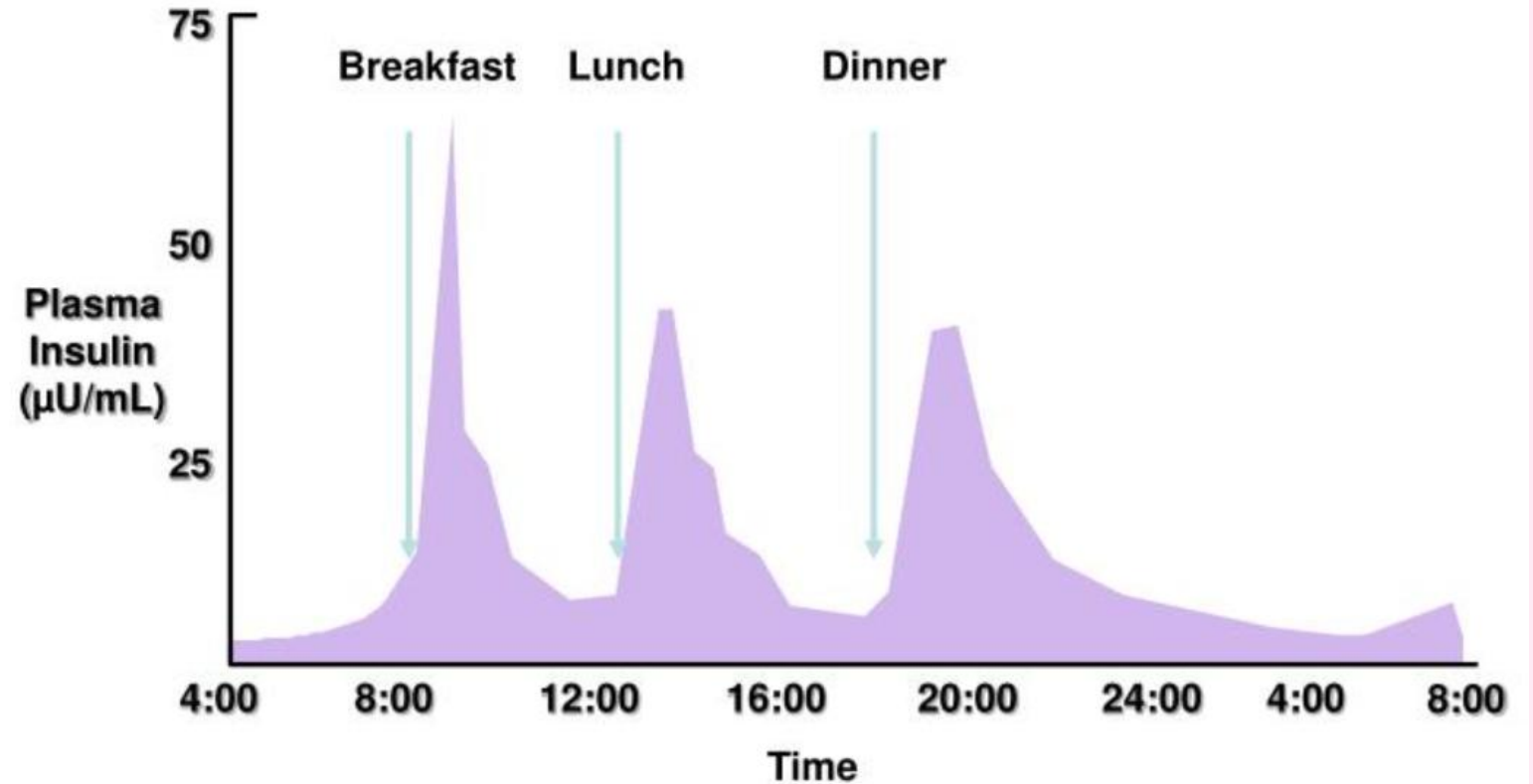
16,181 licensed Endocrinologists in the US

Vanderbilt University Medical Center: Division of Endocrinology

- 24 clinical Endocrinologists
- 24 APPs

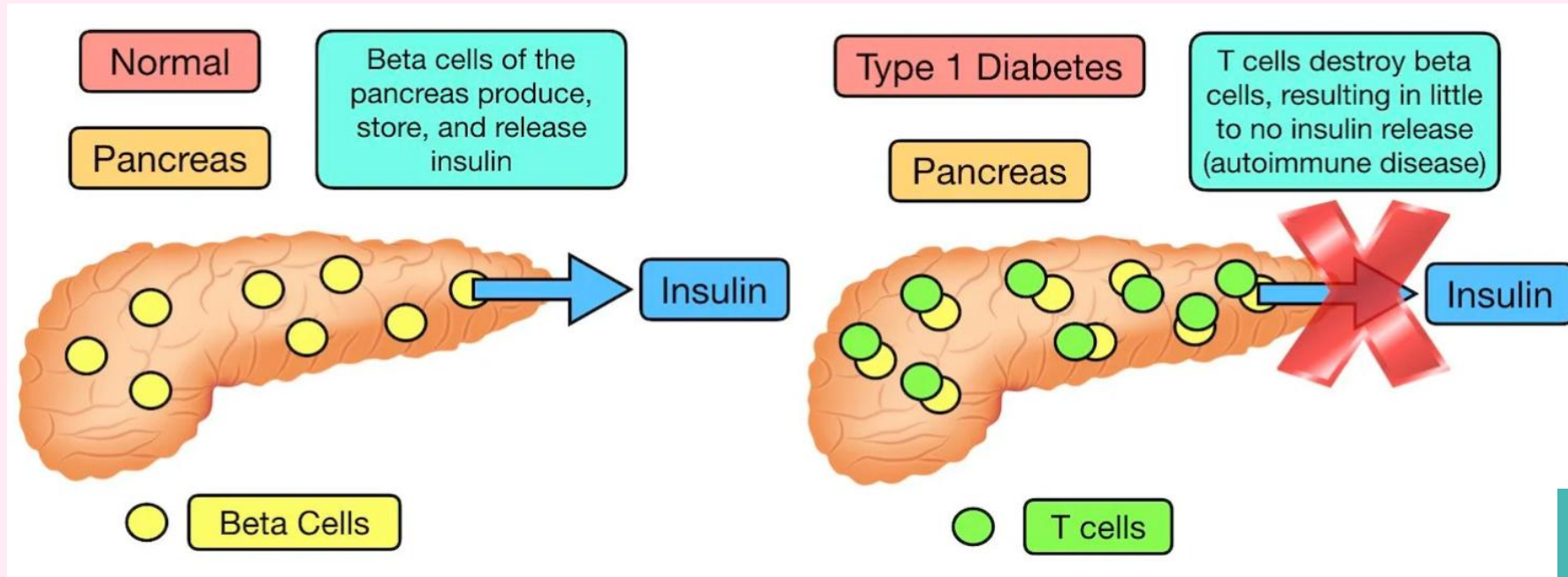
Normal Insulin Physiology

Physiologic Blood Insulin Secretion Profile



Adapted from White JR, Campbell RK, Hirsch I. Postgraduate Medicine.
June 2003;113(6):30-36.

Type 1 Diabetes



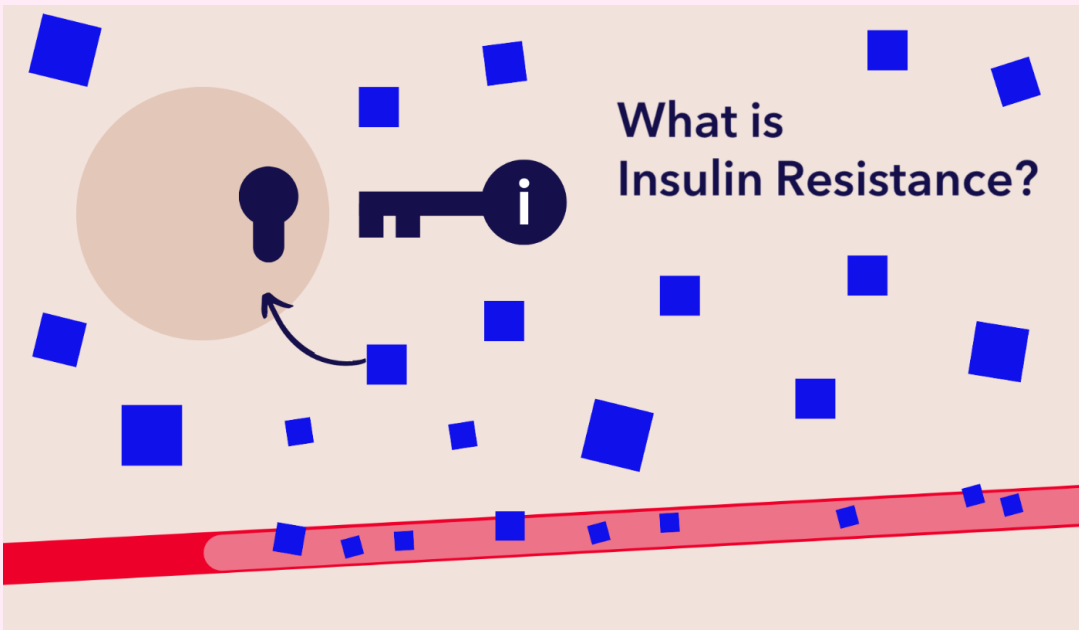
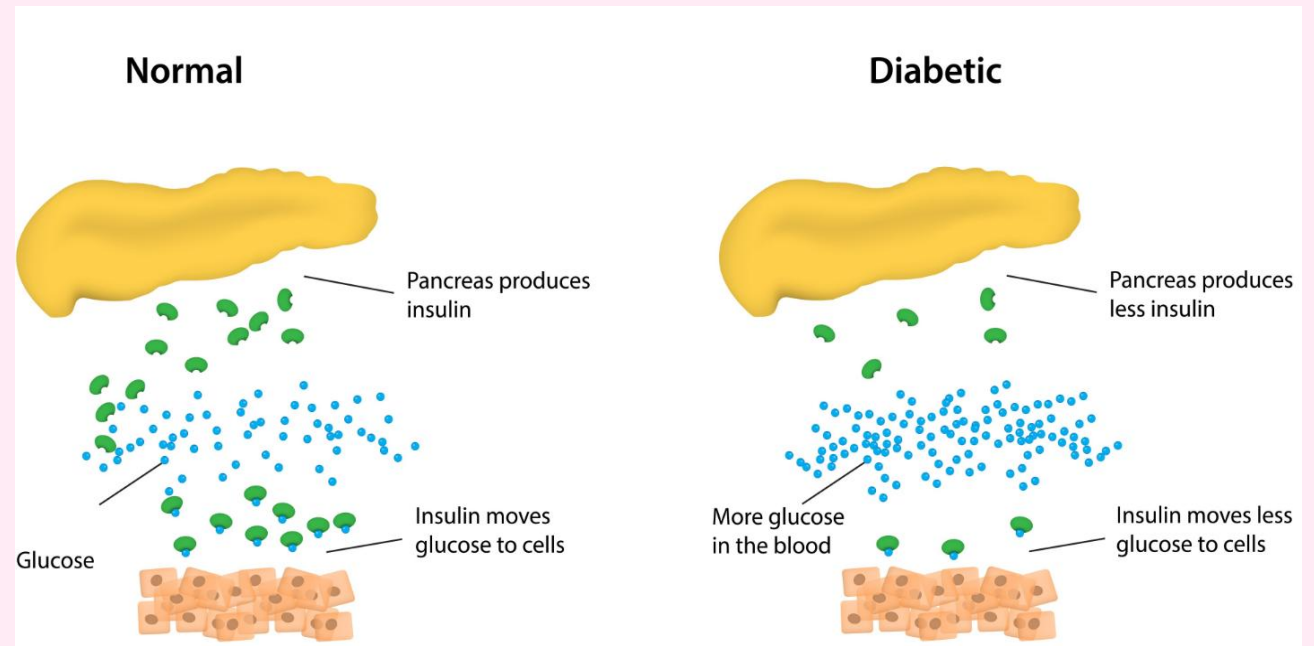
Autoimmune

Lifelong insulin treatment



Type 2 Diabetes

Insulin resistance + deficiency



Risk Factors:

- Family history
- Overweight/ Obesity
- African American, Hispanic, Asian, Native American, Pacific Islanders

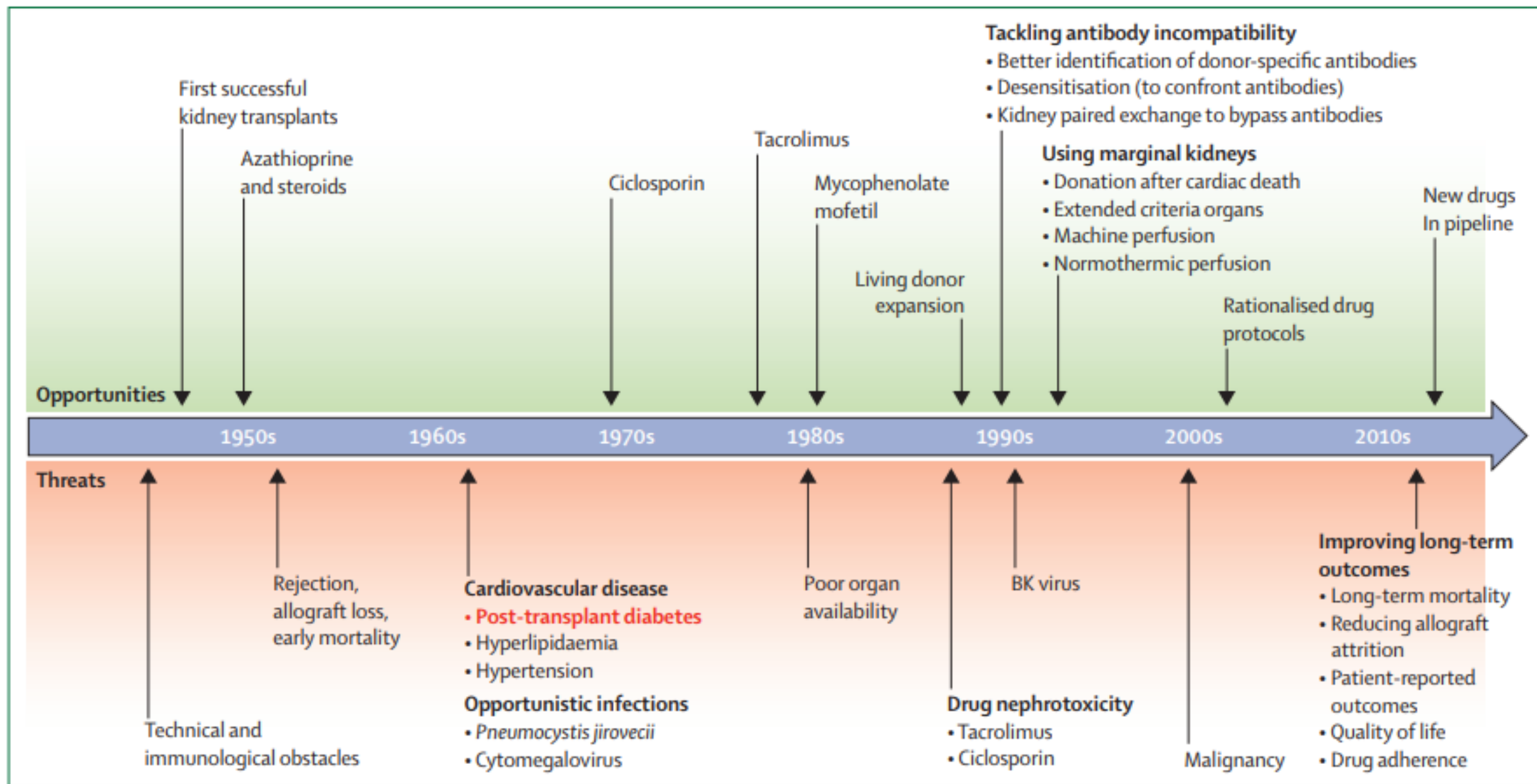


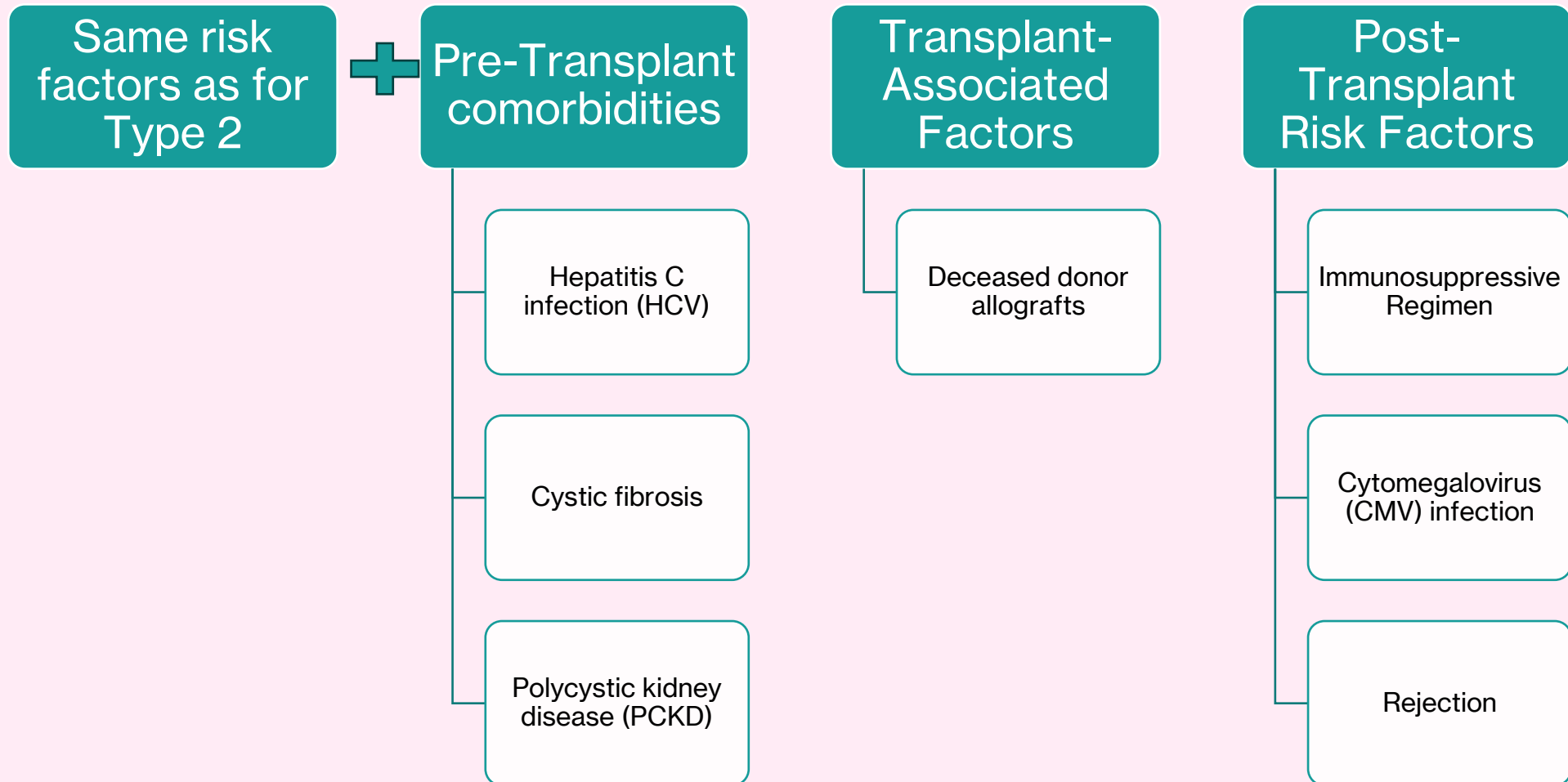
Figure 1: Timeline of kidney transplantation, threats, and opportunities that have contributed to changes in practice

The important take home message from this timeline is the need to understand the importance of post-transplant diabetes in view of competing risks and changes in clinical practice over time.

Organ	Incidence
Kidney	10-20%
Liver	30-40%
Heart	20-30%
Lung	20-40%

Incidence of PTDM

Post Transplant Diabetes Mellitus (PTDM)



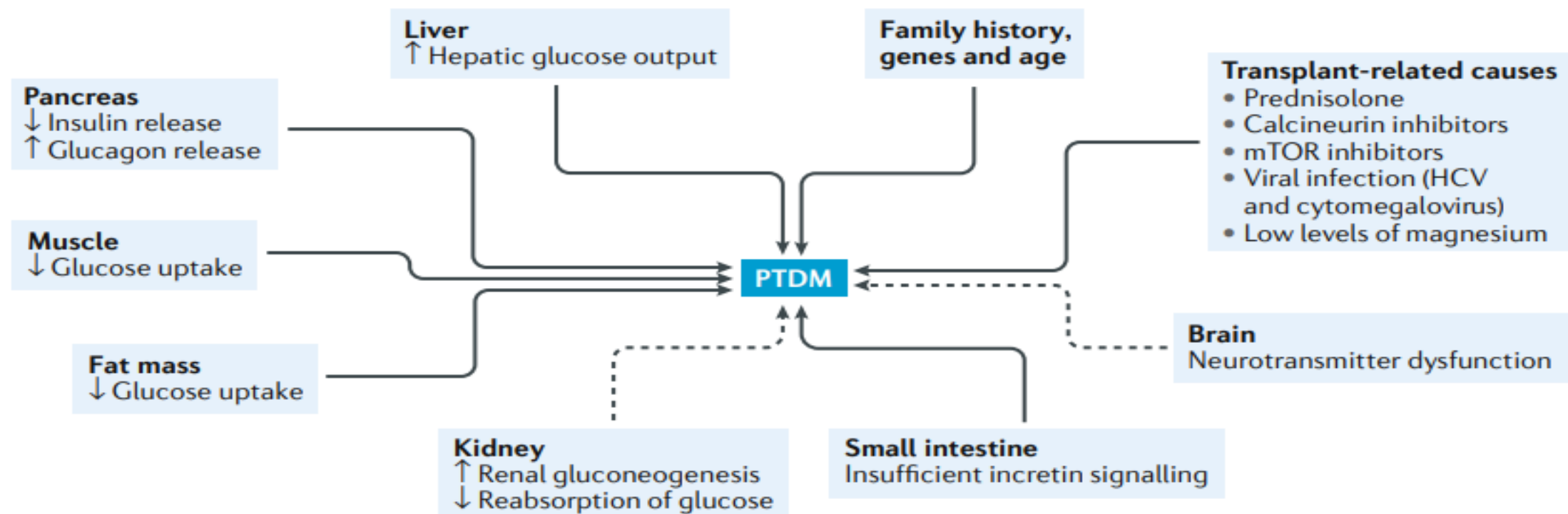


Fig. 1 | Acknowledged contributors of hyperglycaemia in PTDM. Common pathways in type 2 diabetes mellitus and post-transplant diabetes mellitus (PTDM) are impaired insulin release and impaired suppression of glucagon release. These effects are not fully compensated by glucagon-like peptide 1 (GLP1) release from the intestinal tract. Insulin-stimulated glucose uptake is reduced in muscle cells and adipocytes, and insulin-mediated suppression of hepatic glucose output is also reduced. In type 2 diabetes mellitus, it is documented that both renal gluconeogenesis and tubular reabsorption of glucose are increased, and crosstalk between insulin, the brain and systemic metabolism is also present. These mechanisms might also be operative in PTDM, but this has not yet been documented. Known contributors of hyperglycaemia in PTDM are shown with bold arrows. Broken arrows depict contributing organs in type 2 diabetes mellitus that have not yet been examined in PTDM. HCV, hepatitis C virus; mTOR, mechanistic target of rapamycin.

Dolly

- 56-year-old female
- Type 2 DM x 15 years
- HTN, HLD
- Diabetic nephropathy -> ESRD on HD x 3 years
- DDKT- received Methylprednisolone 500mg in OR
- Steroid taper:
 - POD 1: Methylpred 250mg
 - POD 2: Methylpred 125mg
 - POD 3: Prednisone 20mg daily



Johnny

- 65-year-old male
- Type 2 DM
- NICM, HErEF (on home Milrinone), HTN, CAD, CKD III, OSA, MDD, GERD, Iron Deficiency Anemia, Glaucoma, Prostate Cancer (now in remission)
- OHT
- Steroid Course
 - Methylprednisolone 125mg q8hours x 2 doses
 - Methylpred 100mg x 1
 - Methylpred 80mg x 1
 - Methylpred 60mg x 1
 - Methylpred 40mg x 4
 - Prednisone 30mg daily until biopsy



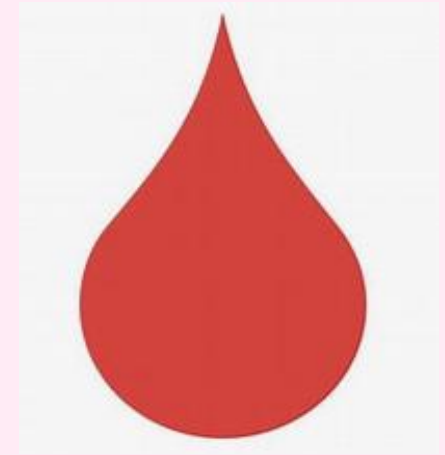
Insulin drip for the first 5 days after transplant

Pre-Transplant



Diagnosing PTDM

- Day 0-45: do not diagnose PTDM
- Day 46-365:
 - Oral Glucose Tolerance Test (OGTT)
 - Fasting glucose 126mg/dl or > **and/or**
 - 2-hour plasma glucose 200mg/dl or >
 - Fasting glucose 126mg/dl or >
 - Random glucose 200 or > WITH SYMPTOMS
 - Hemoglobin A1C 6.5% or > (may underestimate PTDM if used <1 year post-transplant)
- Greater than 1-year post-transplant
 - OGTT
 - Hemoglobin A1C
 - Fasting glucose/ Random glucose



What Alters A1C

Hematologic conditions

- Anemia
- Accelerated erythrocyte turnover
- Thalassemia
- Sickle cell disease
- Reticulocytosis
- Hemolysis

Physiologic States

- Aging
- Pregnancy

Drugs/Medications

- Alcohol
- Opioids
- Vitamin C
- Vitamin E
- Aspirin
- Erythropoietin
- Dapsone
- Ribavirin

Disease States

- HIV infection
- Uremia
- Hyperbilirubinemia
- Dyslipidemia
- Cirrhosis
- Hypothyroidism

Medical Therapies

- Blood transfusion
- Hemodialysis

Miscellaneous

- Glycation rate
- Protein turnover
- Race and ethnicity*
- Laboratory assay
- Glycemic Variability
- Smoking
- Mechanical heart valves
- Exogenous testosterone?

Fructosamine

- Glycated albumin; reflects average glucose levels over the preceding 2-3 weeks
- $A1C = 0.017 \times \text{fructosamine} + 1.61$

Table 1.

Correlations Between Estimated Average Glucose, A1c, and Fructosamine^{1,9,4}

Glucose (mg/dl)	A1c (%)	A1c (mmol/mol)	Fructosamine (μmol)
97	5	31	131
126	6	42	203
154	7	53	273
183	8	64	345
212	9	75	417
240	10	86	487
269	11	97	559
298	12	108	631

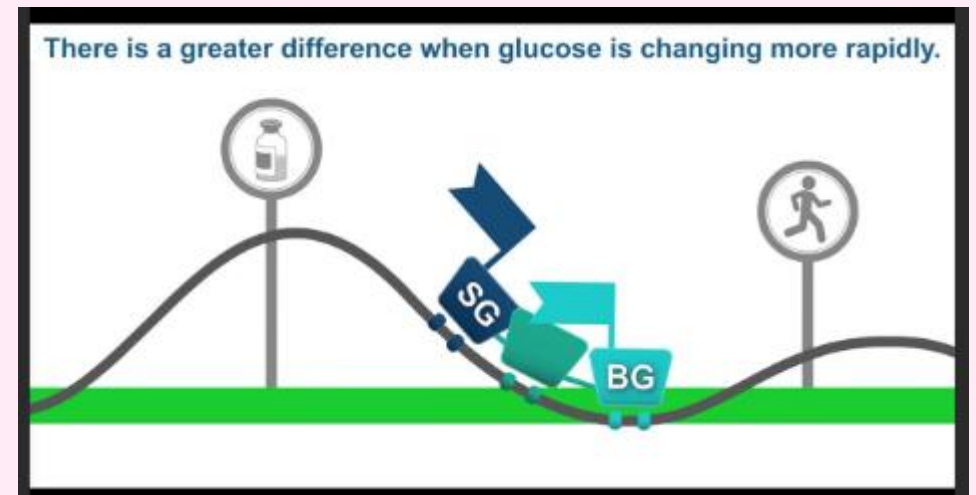
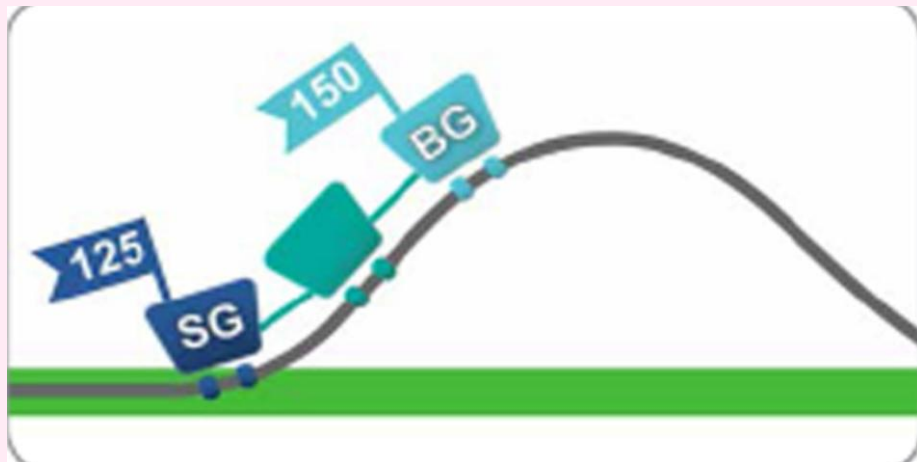
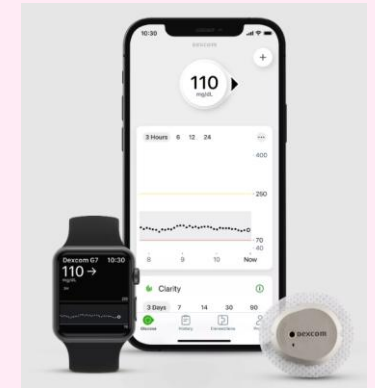
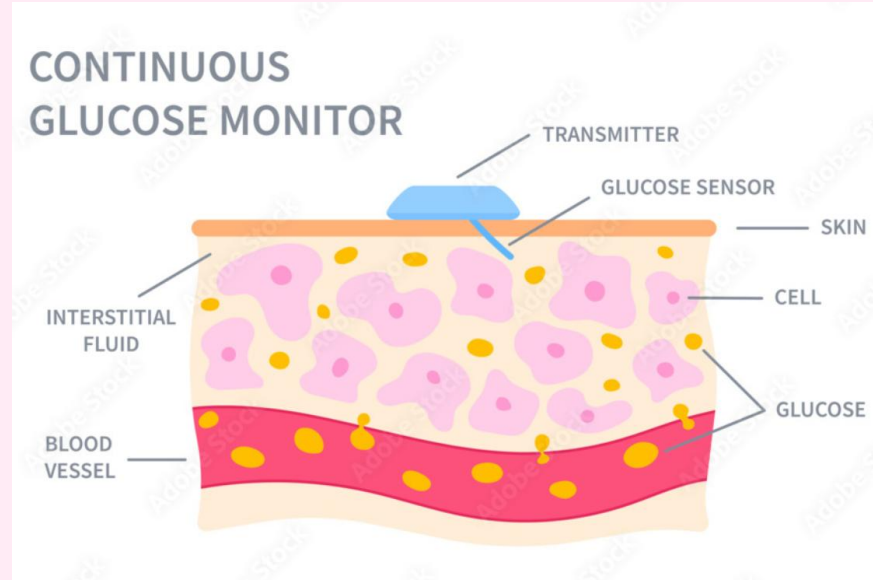
A1c hemoglobin A1c

Table 7.2—Some of the more common interfering substances and/or conditions that affect blood glucose meters (for inpatient and outpatient use)

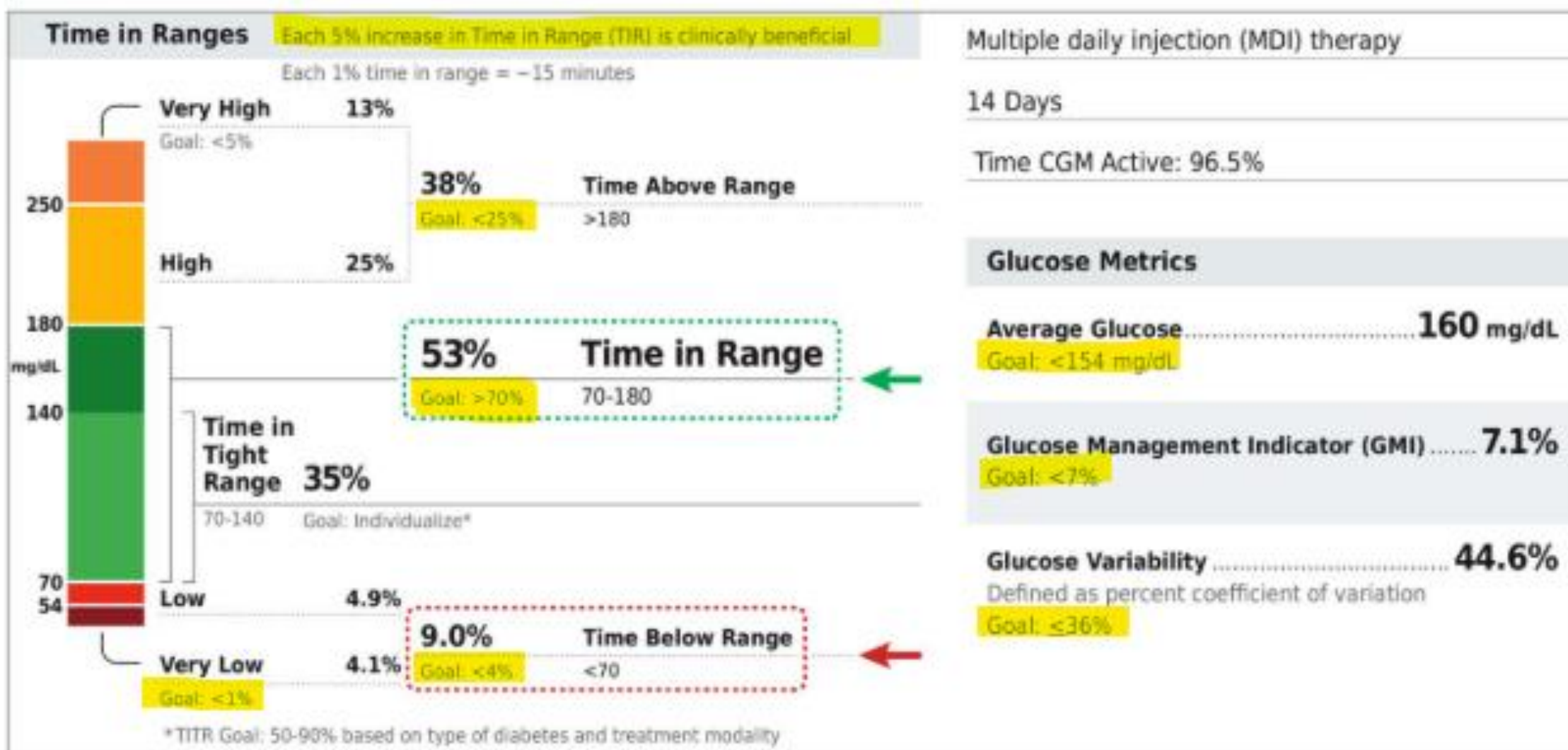
Substance or condition	Potential effects on glucose readings measured by BGMs*
Maltose†	Falsely higher blood glucose readings
Galactose	Falsely higher blood glucose readings
Xylose	Falsely higher blood glucose readings
<i>N</i> -Acetylcysteine	Falsely higher or lower blood glucose readings (depending on BGM design)
Acetaminophen	Falsely higher or lower blood glucose readings (depending on BGM design)
Dopamine	Falsely higher or lower blood glucose readings (depending on BGM design)
Pralidoxime (2-PAM)	Falsely higher or lower blood glucose readings (depending on BGM design)
Hydroxyurea	Falsely higher or lower blood glucose readings (depending on BGM design)
Vitamin C	Falsely higher or lower blood glucose readings (depending on BGM design)
Hematocrit (high)	Falsely lower blood glucose readings
Hematocrit (low)	Falsely higher blood glucose readings

*These are potential effects. There are blood glucose monitors (BGMs) that behave differently than listed in this table. Refer to product labeling for product-specific information.
 †Unmodified glucose dehydrogenase pyrroloquinoline quinone (GDH/PQQ) enzyme method only. Modern BGM designs do not incorporate unmodified GDH-PQQ enzyme.

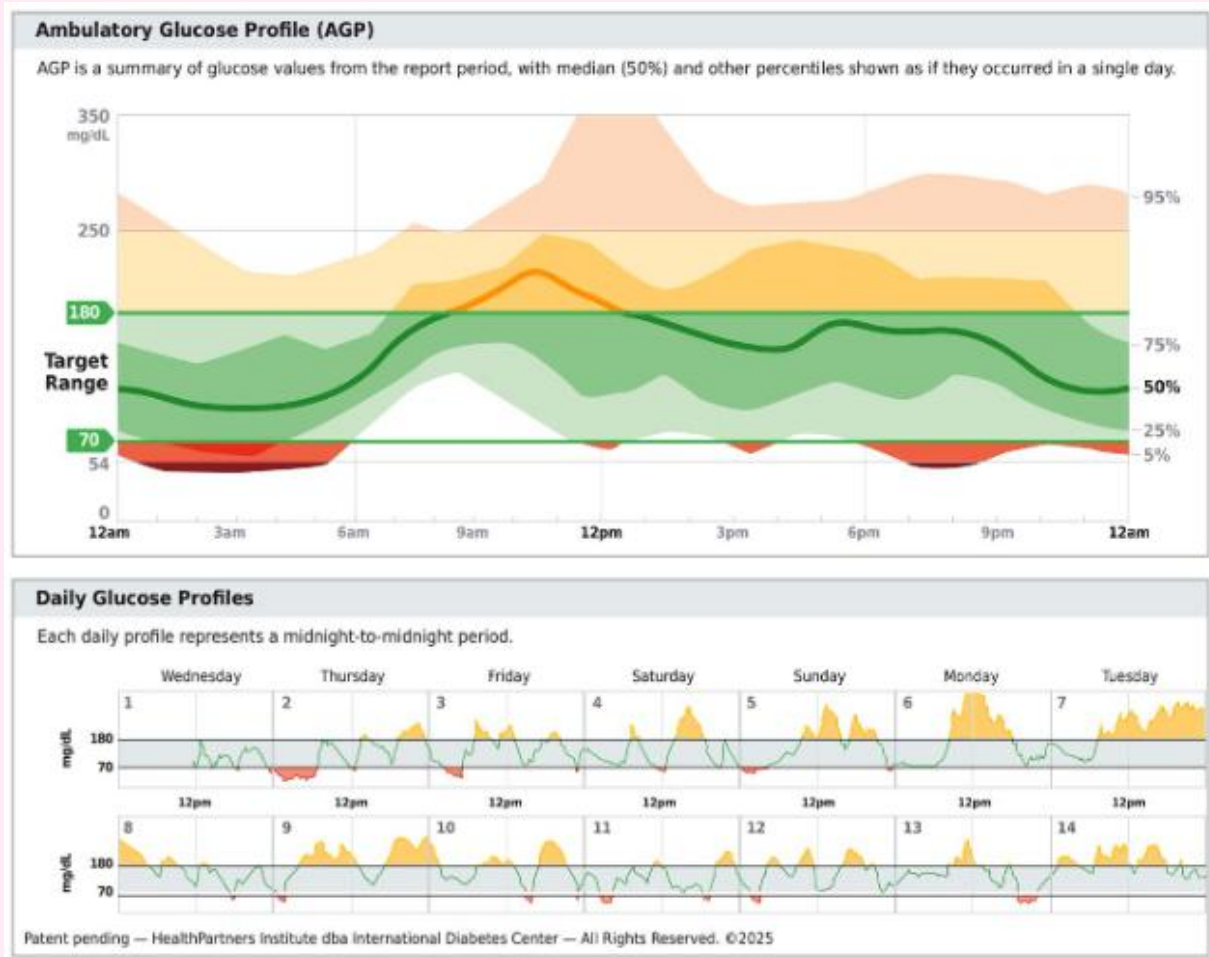
Continuous Glucose Monitors (CGMs)



CGM Data



CGM Data



1. Address hypoglycemia

2. Address hyperglycemia



More affordable CGM at half
the cost of other CGMs[†]

Present this copay card
to save money on your
FreeStyle Libre CGM
systems prescription
each month.[†]

Get a more affordable price
right at the register^{†1}

Copay savings for all eligible users,
including non-insulin and GLP-1

BIN: 610020 | GROUP: 99992546
STATIC ID: ERXCONSUMERWEBLIBRE



Present this **COPAY CARD**
to your pharmacist each time
you fill your prescription.



Copay savings for commercially insured or uninsured patients.

FOR PATIENTS: Present this FreeStyle Libre CGM systems copay card to your pharmacist.

FOR HCPs: Print and give this copay card to your patients to present at the pharmacy.

FOR PHARMACISTS: Important—DO NOT combine with other prescription sensor fill transactions.
For insured patients, submit the SECONDARY Claim to PDMI under BIN 610020. For uninsured
patients, submit PRIMARY/Cash Claim to PDMI under BIN 610020.

A PCN code is not required to process the copay card.

For questions about the product or about using your copay card, please call 1-855-632-8658.
(Monday–Friday 8 AM–8 PM ET, excluding holidays.)

Steroids

1

Decrease insulin sensitivity

2

Increase hepatic gluconeogenesis

3

Increase appetite -> weight gain

4

Effect on glucose is dose dependent

Calcineurin Inhibitors (CNIs)

Tacrolimus
>
Cyclosporin

Increased
islet cell
apoptosis

Decreased
beta cell
mass



Mammalian Target of Rapamycin Inhibitors (mTORI)

- Sirolimus
 - Impaired insulin secretion
 - Reduction in insulin signaling

Goals



Optimize long-term outcomes



Prevent microvascular and macrovascular complications



Lessen premature mortality



Decrease risk of graft loss



Lower glucose by targeting cause of hyperglycemia



Avoid interaction with immunosuppression meds

Glucose targets



- During hospitalization: 140-180mg/dl
- At home:
 - Fasting: 80-130mg/dl
 - Post-prandial: <180mg/dl
- Continuous Glucose monitor (CGM):
 - > 70% time in range (TIR)
 - Target range is 70-180mg/dl
- Hemoglobin A1C <7%

Treatment of PTDM



Continue education



**Nutritional
counseling**



Exercise



Insulin

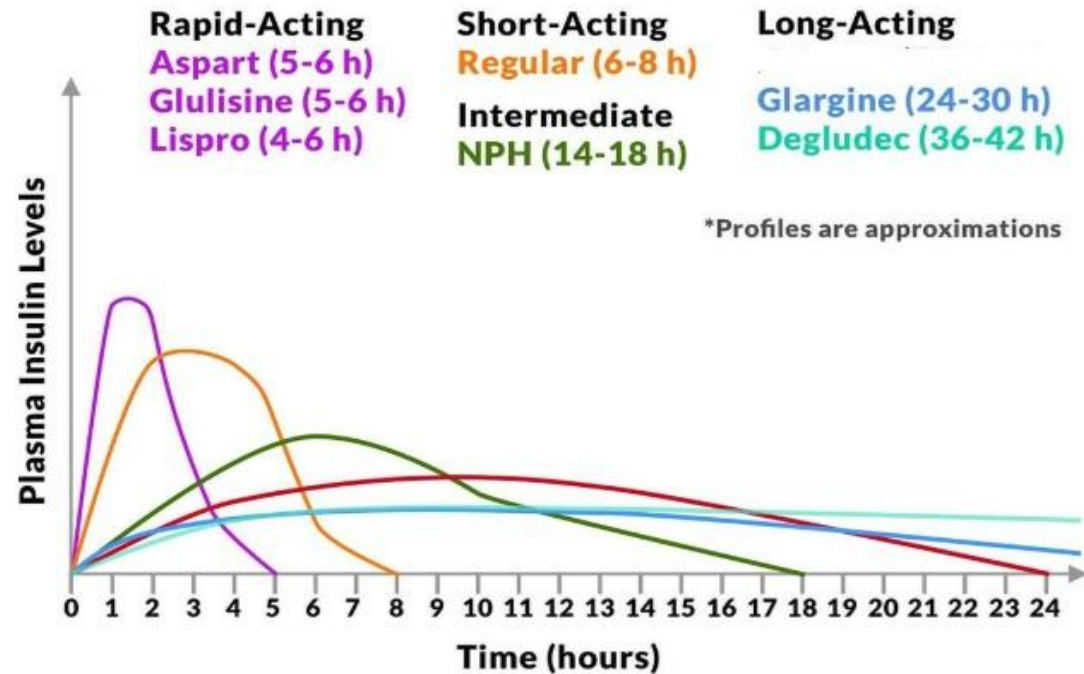


**Consider other
medications**

Doses of
immunosuppression
medications are stable

Less than 20 units of
insulin/day

Insulin Action Profiles



Adapted and referenced from: Hirsch IB. Insulin analogues. N Engl J Med. 2005 Jan 13;352(2):174-83. <https://www.ncbi.nlm.nih.gov/pubmed/15647580> and individual product labels.

Insulin	Onset	Peak	Duration
Ultra-Rapid Acting Insulin lispro (Lyumjev™) Insulin aspart (Fiasp®)	10-15 mins 10-15 mins	1-2 hrs 1-2 hrs	4-6 hrs 4-6 hrs
Rapid-Acting Insulin lispro (Admelog®, Humalog®) Insulin aspart (Novolog®) Insulin glulisine (Apidra®)	15 mins 15 mins 15 mins	1-2 hrs 1-2 hrs 1-2 hrs	4-6 hrs 4-6 hrs 4-6 hrs
Short-Acting Regular (Humulin R, Novolin R)	30 mins	3 hrs	8 hrs
Intermediate-Acting NPH (Humulin N, Novolin N)	1-2 hrs	4-8 hrs	12 hrs
Long-Acting Insulin degludec (Tresiba®) Insulin detemir (Levemir®) Insulin glargine (Basaglar®, Lantus®, Toujeo®, Semglee®)	1 hr 2 hrs 2 hrs	9 hrs 3-9 hrs --	42 hrs 20-22 hrs 24 hrs

Initiating Insulin

0.3 units/kg: BMI <18.5 or high risk for hypoglycemia

0.4 units/kg: Normal (BMI 18.5-24.9)

0.5 units/kg: Overweight (BMI 25-29.9)

0.6 units/kg: Obesity (BMI >30) or highly insulin resistant

TDD= Total Daily Dose

Initiating Insulin Part 2

Basal insulin: 50% of TDD

Bolus insulin: divide remaining 50% into 3 equal doses before meals

Correction scale:

- Low-dose: Insulin naïve, AKI, ESRD, Type 1 DM
- Moderate-dose: steroids, tube feeds, obesity, or requiring high insulin doses

Dolly- POD 1

- Methypred 250mg
- Weight: 107.4kg/ BMI 33.69
- Insulin regimen: start 0.6 units/kg TDD
 - $107.4 \times 0.6 = 64$ units
 - $64 / 2 = 32$ units
 - Glargine: 32 units qhs
 - Lispro 32/3 meals= 10 units
 - **Double prandial insulin for steroids
 - Lispro 20 units with meals
 - Correction scale 4 units:50mg/dl for BG >150mg/dl ACHS



Dolly- POD 2&3



Glucose	Lispro
B- 118	20
L- 218	28
D- 186	24
HS- 145	0

POD 2

Methylpred 125mg

No change in insulin

POD 3

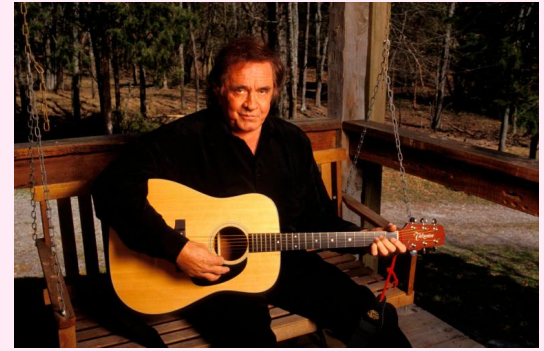
Prednisone 20mg daily

Decrease Lispro to 16 units
with meals

Decrease correction scale to 3
units:50mg/dl for BG
>150mg/dl

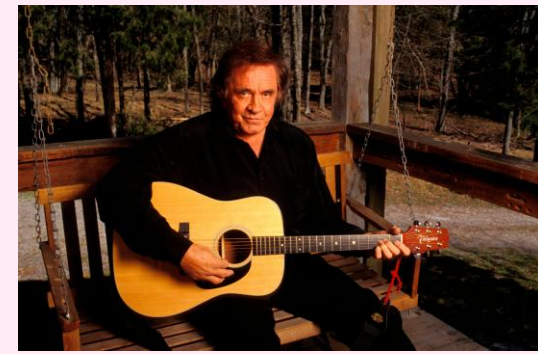
Glucose	Lispro
B- 124	20
L- 165	24
D- 82	20
HS- 110	0

Johnny



- Transitioned off insulin drip
 - **give basal insulin at least 2 hours before stopping insulin drip
- Methylpred 40mg daily
- Weight: 84.2kg
- BMI 27.81
- Start weight-based insulin dosing
 - 0.3 units/kg TDD
 - Basal: 12 units
 - Prandial: 8 units with each meal
 - Correction scale: 2 units:50mg/dl for BG >160mg/dl ACHS

Johnny



Time: ◀	10/07 0700 - 10/08 0659						10/08 0700 - 10/09 0659						▶		
	1804	2115	2118	2119	0607	0617	0735	0736	1141	1211	1212	1634		1800	2111
Glucose (mg/dl) Graphs cannot display in the current view															
▼ Glucose															
POC glucose		233				197			273			225		249	POC glucose
Blood glucose					172										Blood glucose
▼ Medication Dosing															
insulin glargine, hum.r...			12												insulin glargi...
insulin lispro SUBQ (...)	14			4				10		9	12		18		insulin lispro ...
methylprednisolone s...							40								methylpredni...

- Increase Lantus to 15 units
- Increase Lispro to 12 units with meals
- Continue correction scale 3 units: 50mg/dl for BG >150mg/dl
- Diabetes education- including insulin teaching

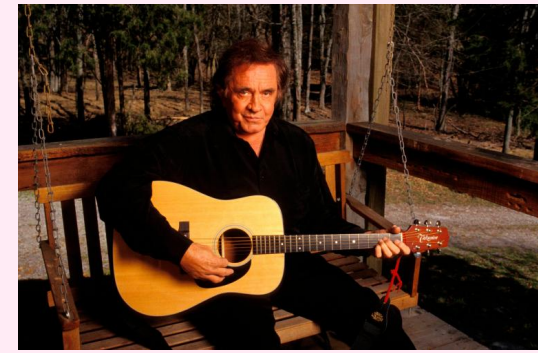
Johnny



Time: ◀	10/08 0700 - 10/09 0659				10/09 0700 - 10/10 0659									▶
	2220	2221	0607	0611	0841	1015	1136	1156	1636	1820	2121	2232	2257	0506
Glucose (mg/dl)	Graphs cannot display in the current view													
▼ Glucose														
POC glucose				192			139		190		195			POC glucose
Blood glucose			173										122	Blood glucose
▼ Medication Dosing														
insulin glargine,hum.r...	15												16	insulin glargi...
insulin lispro SUBQ (...)		6			21			18		21		3		insulin lispro ...
PredniSONE ORAL (...)						30		10						PredniSONE...

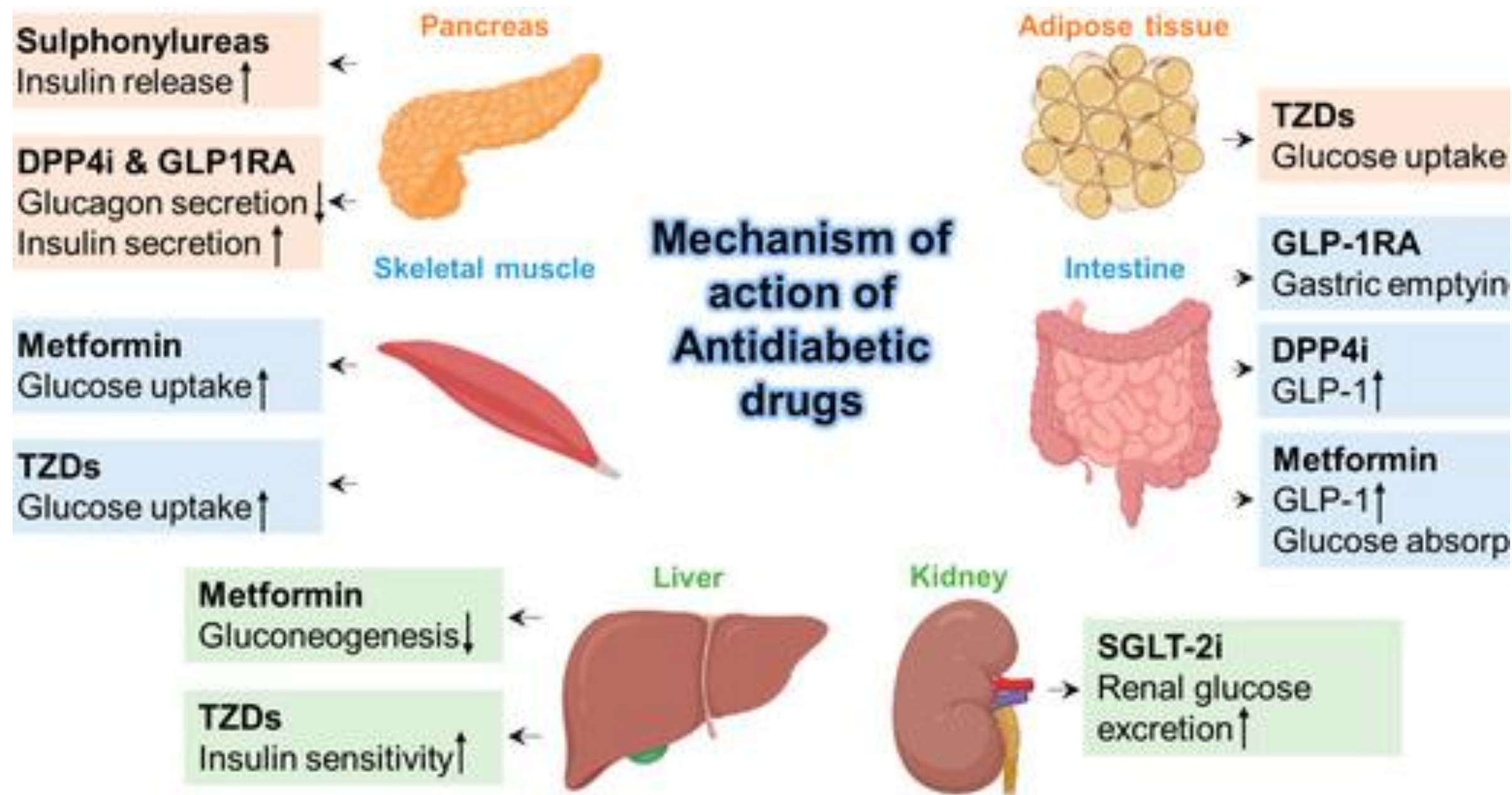
- Prednisone 40mg daily
- Increase Lantus to 16 units
- Increase Lispro to 18 units with meals
- Continue correction scale 3 units: 50mg/dl for BG >150mg/dl
- Diabetes education- including insulin teaching

Johnny



10/09 0700 - 10/10 0659												10/10 0700 - 10/11 0659		
Time: ◀	0841	1015	1136	1156	1636	1820	2121	2232	2257	0506	0620	0834	1025	1120 ▶
Glucose (mg/dl) Graphs cannot display in the current view														
▼ Glucose														
POC glucose			139		190		195				134		284	POC glucose
Blood glucose										122				Blood glucose
▼ Medication Dosing														
insulin glargine, hum.r...									16					insulin glargi...
insulin lispro SUBQ (...)	21			18		21		3				18		insulin lispro ...
PredniSONE ORAL (...)		30		10									40	PredniSONE...

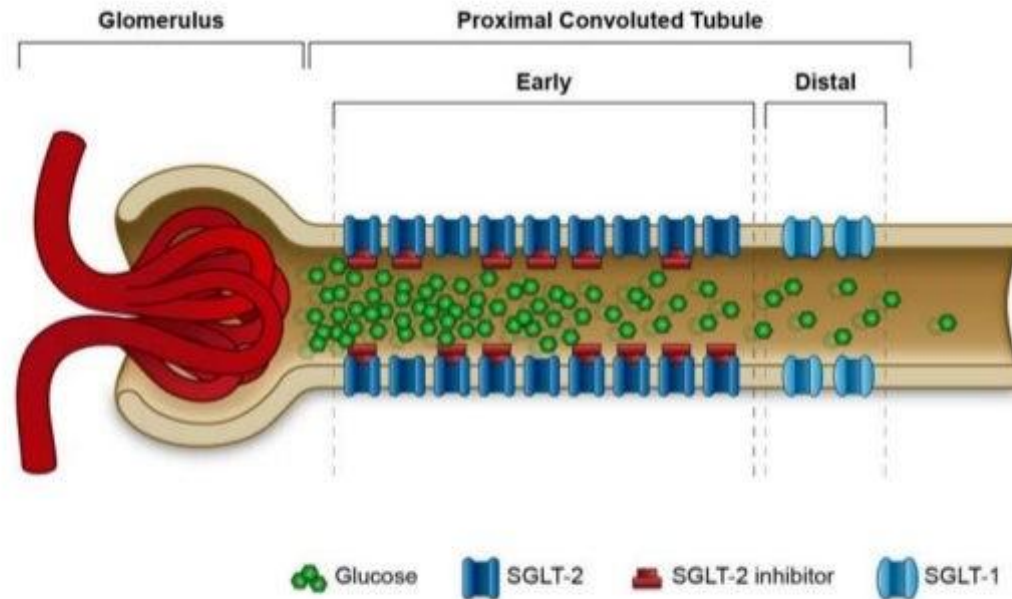
- Continue Lantus 16 units
- Increase Lispro to 24 units with meals
- Increase correction scale to 5 units: 50mg/dl for BG >150mg/dl



Sodium Glucose Transport 2 Inhibitors (SGLT2)

Mechanism of Action

Increase the removal of glucose via SGLT2 inhibitors



Kanai Y, et al. *J Clin Invest.* 1994;93:397-404^[18]; You G, et al. *J Biol Chem.* 1995;270:29365-29371^[19]; Rothenberg PL, et al. EASD 2010:Abstract 876.^[20]

Glucagon-Like Peptide

- **Tablet:** Ozempic
- **Daily:** Victoza
- **Weekly:**
 - Ozempic
 - Trulicity
 - Mounjaro (+ GIP)

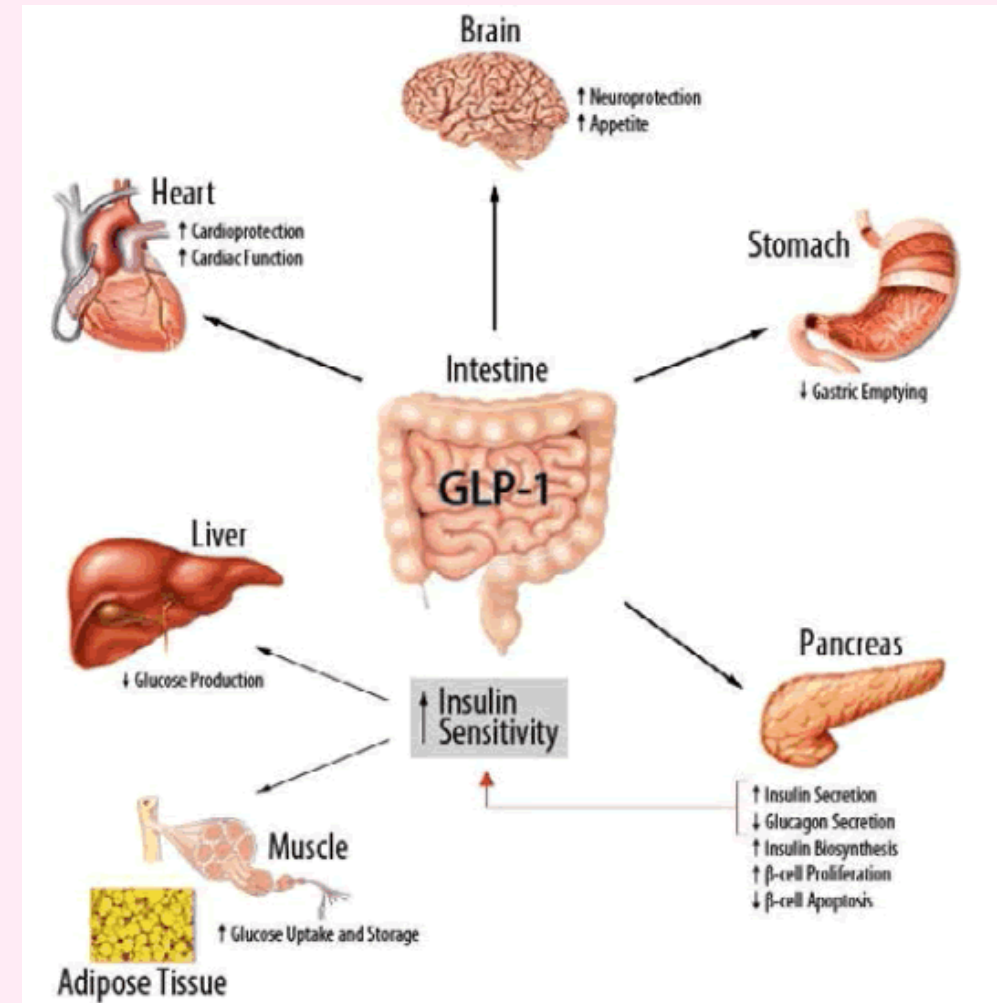


Figure 4: Biological Activities of GLP-1. The main action of GLP-1 occurs at the pancreas where GLP-1 stimulates insulin secretion and inhibits glucagon secretion in a glucose dependent manner. In addition, GLP-1 also decreases appetite, slows gastric emptying, increases β-cell proliferation, increases cardiac function as well as other physiological actions as indicated in the diagram. Redrawn from [91].

Dolly

- 8 months post-transplant
- Immunosuppression regimen stable
- Prednisone 5mg daily
- Weight up 28 pounds since transplant
- Hemoglobin A1C 7.2%
- Insulin regimen
 - Lantus 28 units qhs
 - Lispro 10 units with meals
 - Lispro correction scale 2 units:50mg/dl for BG >150mg/dl



Dolly

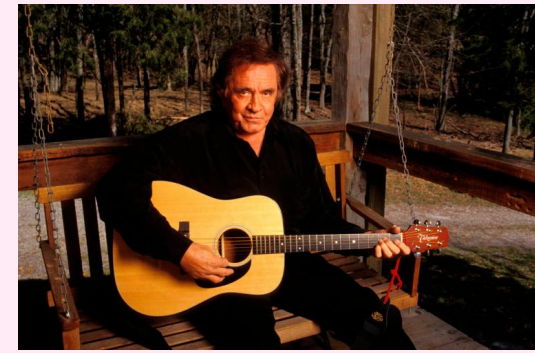
➤ Next steps

- Continue Lantus 28 units qhs
- Decrease Lispro to 8 units with meals
- Decrease Lispro correction scale to 1 unit:50mg/dl for BG >150mg/dl
- Start Mounjaro 2.5mg weekly
- Nutrition counseling
- Encourage physical activity/ exercise



Johnny

- 6 months post-transplant
- Immunosuppression regimen is stable
- Prednisone stopped
- Hemoglobin A1C 5.8%
- Fructosamine 250umol/L
- Insulin regimen:
 - Lantus 12 units qhs
 - Lispro correction scale: 1 unit:50mg/dl for BG >150mg/dl ACHS
- Adjustments?
 - Jardiance 25mg daily
 - Stop Lantus
 - Continue Lispro correction scale



Hypoglycemia



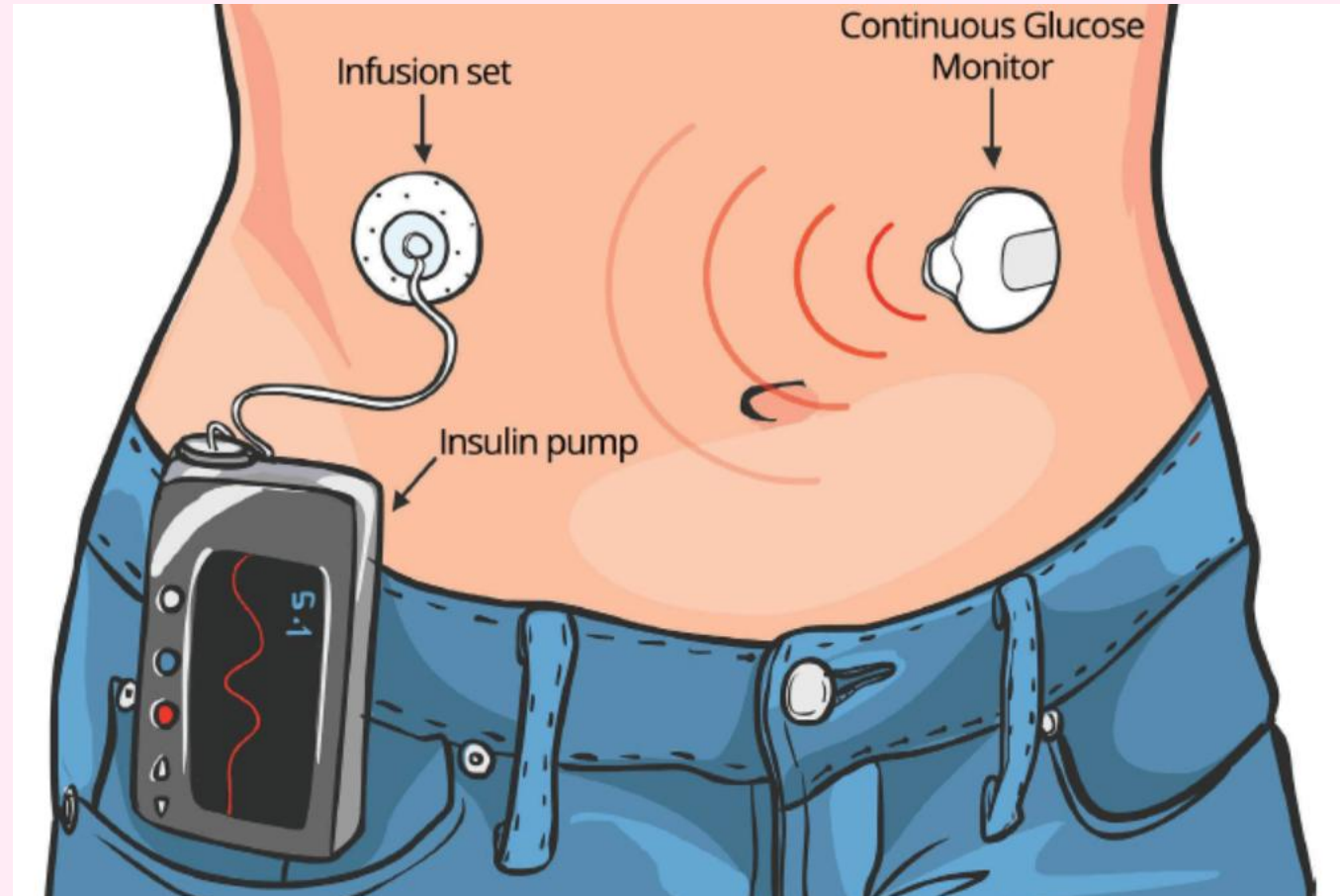
Glucose
<70mg/dl

Treatment:

- **Alert:** 15 grams of fast-acting carbohydrates
 - 4 ounces of fruit juice or REGULAR soda (NOT diet or zero)
 - 4 glucose tablets
- **Altered/ Unable to take PO**
 - Glucagon: glucagon, Gvoke, Zegalogue, Baqsimi nasal spray



Automated Insulin Pumps



Long Term Follow-Up



Monitor for
microvascular
complications

Annual eye exam
Annual foot exam
Annual microalbumin/
BMP



Cardiovascular risk
reduction

Lipids
Blood pressure

Summary

- Patients with diabetes > diabetes providers
- Treat hyperglycemia with insulin in the hospital
- When immunosuppression regimen is stable, can consider changing to oral meds/
GLP-1 to treat hyperglycemia
- Persistent PTDM should be treated as Type 2 DM, including monitoring for micro and
macrovascular complications

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