Understanding and Treating Diabetes in the Post-Transplant Patient

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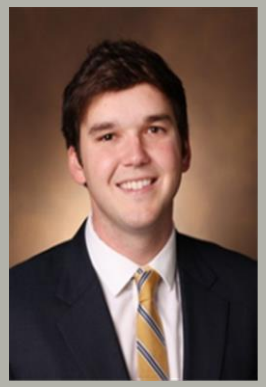
Glucose Management Service

Ann Hackett, APRN



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Disclosures

- None to disclose.

Goals of This Lecture:

- Let's learn something new!
- Get excited about treating Diabetes!

https://www.chariotlearning.com/get-excited-about-your-big-tests/

Diabetes in the Transplant Patient

- Risk Factors, Screening, Diagnosis
- Inpatient Management
- Outpatient Management

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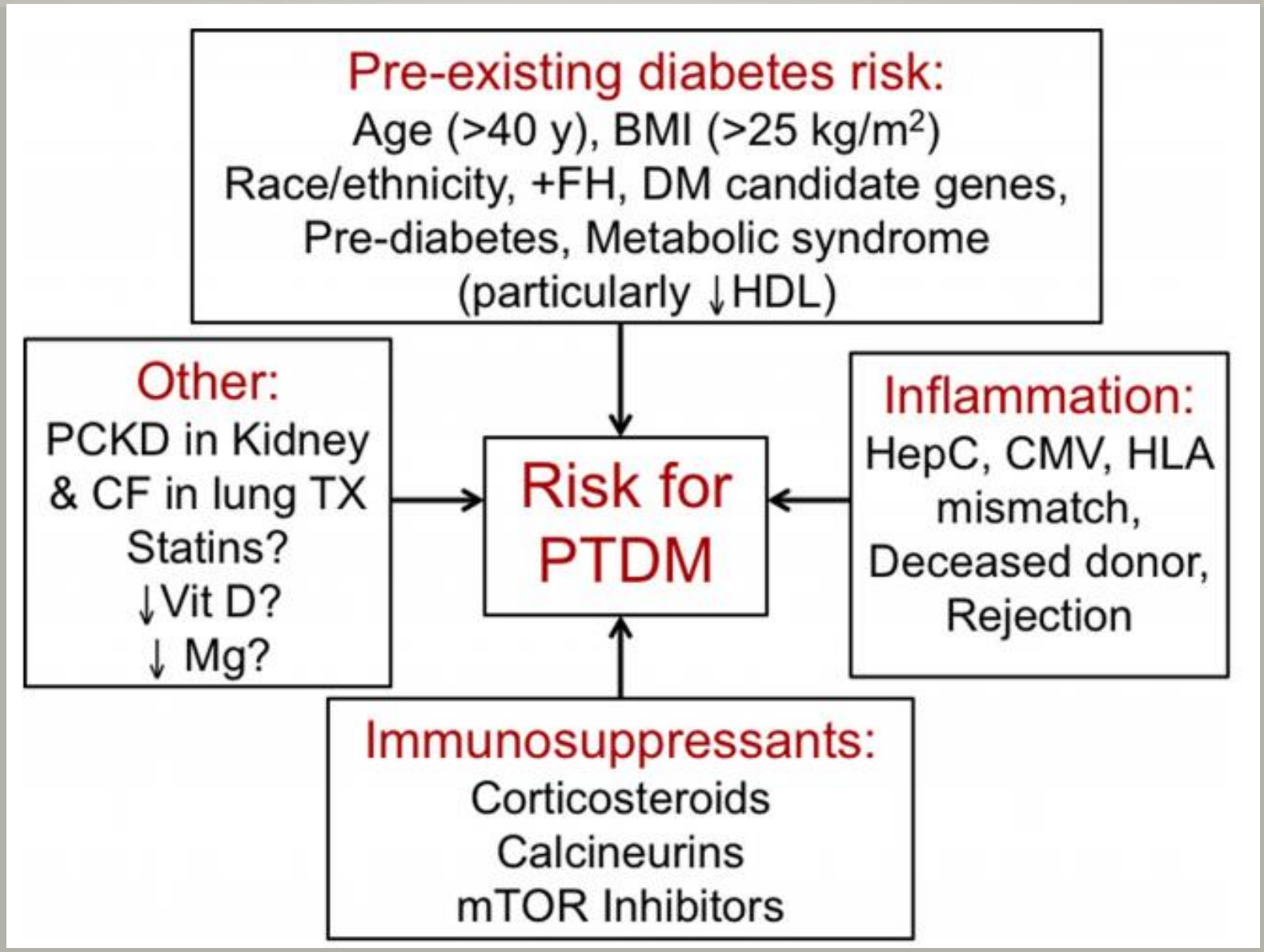
Risk Factors

- Meds: Chemotherapeutic agents, Immunosuppressants
- Nutrition: TPN, TF
- Infection
- Stress
- Age >40-45
- Obesity
- AA, Hispanic Races
- Family History
- Hepatitis C, CMV
- Polycystic Kidney Ds
- Certain Genetic Mutations

Post-transplant Diabetes Mellitus in Renal Transplant Recipients. Tobin, G et al, UpToDate, May 31, 2008.



Shivaswamy et. Al. *Endocr Rev*. 2016 Feb;37(1):37-61.

Rates of Occurrence

- Diabetes occurs post-transplant at
  - Kidney Transplant: 10-74%
  - Heart Transplant: 11-38%
  - Liver Transplant: 7-30%
  - Lung Transplant: 32%

Post-transplant Diabetes Mellitus in Renal Transplant Recipients. Tobin, G et al, UpToDate, May 31, 2008.

Screening

Outpatient Monitoring:

- Monitor blood sugar **prior** to transplant, typically fasting qam. Alert provider to BG >126 mg/dL.

- Monitor blood sugar **post** transplant with FBS weekly X4, recheck in 3 months, 6 months and annually thereafter if no abnormality presents

Inpatient Initiation of Monitoring:

- Check blood sugar ACHS and begin treatment with BG >140 mg/dL.

Diagnosis

Diagnosis	Test
Prediabetes: Impaired Fasting Glucose	Fasting plasma glucose of 100-125 mg/dL No clear A1c criteria for Prediabetes, although >5.7% has been suggested
Prediabetes: Inpaired Glucose Tolerance	75-g OGTT 2 hr plasma glucose of 140-199 mg/dL Fasting plasma glucose >/= 126 mg/dL
Diabetes	Fasting plasma glucose >/= 126 mg/dL OR random plasma glucose >/= 200 mg/dL with symptoms OR 75-g OGTT 2 hr plasma glucose >/= 200 mg/dL OR A1c >6.5%

*A diagnosis of diabetes must be confirmed on a subsequent day, by measurement of FPG, 2-h PG, or random plasma glucose (if symptoms are present).

American Diabetes Association: Executive Summary from the American Diabetes Association Standards of medical care in Diabetes 2009. *Diabetes Care.* 2009; 32 (suppl 1): S6-S12.

Post-Transplant DM Diagnosis

- October, 2013 → 2nd International Consensus Panel enacted key changes:
  - Change terminology from New Onset Diabetes After Transplant (NODAT) to Post-Transplant DM (PTDM)
  - Recommend evaluation/diagnosis outpatient, stable, and on long-term maintenance immunosuppression doses
  - HbA1c can be used to diagnose DM if elevated (>6.5%) but should not be used alone as a screen for PTDM (particularly in 1st year)
- Unclear full significance of timing of DM diagnosis (1 vs. 5 vs. 20 years post-transplant)

Types of Diabetes

- Pre-Existing Type 1 or Type 2
- Post-Transplant DM

Pre-Existing Diabetes

- Type 1:
  - Steroids increase insulin requirement and dose. Consider starting with double prandial and ss coverage if pt is well controlled at baseline.
- Type 2:
  - Cannot use all oral agents. Mostly consider SFU for postprandial hyperglycemia.
  - Usually requires insulin, at least short-term.
- Both: Insulin and/or oral agent dose will increase from ESRD to having a working kidney

Post-Transplant Diabetes Mellitus

- Insulin resistant phenotype
- Usually requires some insulin, at least short-term
- May be possible to taper to oral agents or monitor with lifestyle modifications alone
- Adjustments in regimen may be necessary at any time based on steroids and other factors

Diabetes in the Transplant Patient

- Risk Factors, Screening, Diagnosis
- Inpatient Management
- Outpatient Management

Diabetes in the Transplant Patient

- Risk Factors, Screening, Diagnosis
- Inpatient Management:
  - Goals and Factors to Consider
  - Weight-Based Dosing
  - Transitioning from Drip to SQ
  - Making Adjustments to Your Regimen
  - When to involve Endocrine
- Outpatient Management

NICE SUGAR Trial Goal BG

- Goal: BG 140-180 mg/dL
- Treatment should be started initially with insulin
- Several studies have assessed the benefit of tight control in hospitalized patients, but findings are not consistently positive.
- Tighter control (such as 80-110 mg/dL) increases risk of hypoglycemia.
- Know when to adjust your target BG or A1c.

Inzucchi, S. N Engl J Med 2006;355:1903-11

Factors to Consider

- **Medications** (pressors and glucocorticoids) and severity of illness impact insulin secretion and insulin resistance.
- **Food intake** can be unpredictable
- **Tests and procedures** interrupt meals and medication dosing
- **Prior history** of DM and type if pre-existing as well as degree of prior control (A1c)
- **Nutritional status** (NPO, enteral, parenteral)

Inzucchi, S. N Engl J Med 2006;355:1903-11

PRODUCT (Chemical Name)	mg/ml	Dosage	POTENCY (When compared w/ Hydrocortisone mg to mg)	Hydrocortisone Equivalency	Route of Admin.	Type	Contains Benzyl Alcohol
Solu-Cortef® (Hydrocortisone Sodium Succinate)	50	See insert	1	50	IM or IV	Rapid Acting Short Duration	NO
Aristospan® (Triamcinolone Hexacetonide)	20	0.25-2 ml	5	100	IA & Soft Tissue	Long Acting	YES
Celestone Soluspan® (Betamethasone Sodium Phosphate & Betamethasone Acetate)	3+3	0.25-2 ml	25	150	IM, IA, IL & Soft Tissue	Both Rapid & Long Acting	NO
Kenalog®-40 (Triamcinolone Acetonide)	40	0.25-2 ml	5	200	IM, IA, IL & Soft Tissue	Long Acting	YES
Depo-Medrol®-40 (Methylprednisolone Acetate)	40	0.25-2 ml	5	200	IM, IA & Soft Tissue	Long Acting	SDV-NO MDV-YES
Depo-Medrol®-80 (Methylprednisolone Acetate)	80	0.25-2 ml	5	400	IM, IA & Soft Tissue	Long Acting	SDV-NO MDV-YES
Dexamethasone Sodium Phosphate	4	See insert	25	100	IM, IV, IA, IL & Soft Tissue	Rapid Acting Short Duration	YES
Dexamethasone Sodium Phosphate PF	10	See insert	25	250	IM or IV	Rapid Acting Short Duration	NO
Solu-Medrol® (Methylprednisolone Sodium Succinate)	40	See insert	5	200	IM or IV	Rapid Acting Short Duration	NO

Steroid Potency

- Consider strength of steroid when adjusting insulin.
- All steroids are not the same!

Weight-Based Dosing

- Stop all orals and non-insulin injectables
- Calculated starting Total Daily Dose (TDD)
  - 0.2-0.3 unit/kg if ≥70 yo or GFR <60 ml/min
  - 0.4 unit/kg if BG 140-200
  - 0.5 unit/kg if BG 201-400
- Divide TDD:
  - 50% as basal
  - 50% as nutritional (equally divided)

-Inzucchi, S. N Engl J Med 2006;355:1903-11
-Lien, Lillian F., Mary E. Cox, Mark N. Feinglos, and Leonor Corsino. *Glycemic Control in the Hospitalized Patient*. New York: Springer, 2010. Print.
-Modified from J Clin Endocrinol Metab, January 2012, 97(1):16 –38

Sliding Scale

- If patient able and expected to eat: usual
- If patient not able to eat: sensitive Q6H
- If fasting and pre-meal BG persistently >140 without hypoglycemia: resistant
- **Alternatively** you may use **5% of the TDD** per 50 pts

BG (mg/dl)	Insulin-sensitive	Usual	Insulin-resistant
>141–180	2	4	6
181–220	4	6	8
221–260	6	8	10
261–300	8	10	12
301–350	10	12	14
351–400	12	14	16
>400	14	16	18

Modified from J Clin Endocrinol Metab, January 2012, 97(1):16 –38

Sliding Scale

Glucose	Insulin Dose
<70 mg/dL	Hold meal coverage
80 - 150 mg/dL	Usual dose
151 - 200 mg/dL	Add 1 unit
201 - 250 mg/dL	Add 2 units
251 - 300 mg/dL	Add 3 units
301 - 350 mg/dL	Add 4 units

Insulin Sensitivity for Sliding Scale

- DM2: Rule of “1800” for Humalog, Novolog, or Apidra pre-meals
  - 1800/total daily insulin dosage = expected BG lowering (mg/dL) of 1 unit of rapid-acting analog.
- Example:
  - Breakfast 9 u, Lunch 9 u, Supper 9 u, Bedtime 9 u Lantus = 36 units total
  - 1800÷36=50
- DM1:Rule of “1500”.

Insulin Sensitivity for Sliding Scale

- DM2: Rule of "1800" for Humalog, Novolog, or Apidra pre-meals
  - 1800/total daily insulin dosage = expected BG lowering (mg/dL) of 1 unit of rapid-acting analog.
- Example:
  - Breakfast 9 u, Lunch 9 u, Supper 9 u, Bedtime 9 u Lantus = 36 units total
  - 1800÷36=50
- DM1:Rule of "1500".

1 unit of insulin should decrease BG approximately 50 mg/dL

Example #1

- Snow White is a 40 yo F who presents following DDKT, now stable on POD 1.
- Home regimen is Linagliptin (Tradjenta) 5 mg qday, Glucotrol (Glipizide) 5 mg BID. Pt states compliance. A1c is 9.0%.
- No additional pressors, IV dextrose.
- Wt is 100 kg.
- Taking Methylprednisolone 500 mg today x1 dose with scheduled taper.

Example #1 Cont.

- Weight:100 kg x 0.5 un/kg = 50 un TDD
- Basal Dose: 25 un basal daily. Give first dose at least 2 hours prior to stopping drip.
- Bolus Dose: 8 un rapid or short acting insulin with meals (weight-based). Given high dose steroid, may consider starting at double → 16 un meal coverage.
  - May want to hold this order until pt is eating at least 50% of meal trays consistently.
- Sliding Scale: Standard dosing requirements with no complicating factors: 2 or 3 un/50>150 ACHS. May choose to double for 5/50>160 ACHS due to steroids.
- ACHS BG checks
- Diabetic Diet as tolerated.

Insulin Drip

- **IV insulin infusion** is ideal (IV insulin half-life=5-9 min.) following standard, validated protocol for at least first 24 hrs.
- **BG monitoring q1-2h** is imperative to avoiding hypoglycemia while on drip. Check more frequently with change in IV meds or nutrition.
- As status improves, **transition to subcutaneous** insulin based on most recent IV insulin infusion rate while pt is fasting. Use rates that have maintained euglycemia only.
- Be sure to **overlap IV and subcutaneous long-acting insulin** by at least 2 hrs to avoid rebound hyperglycemia after stopping insulin drip.
- Type 2 DM with <2un/h IV insulin requirement may do well on a **non-intensive subcutaneous regimen** or scheduled insulin. Can try sliding scale only at first.

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Transitioning from Drip to SQ Insulin

- Patients without a history of DM
  - If <1 unit/hour: may not require scheduled insulin
    - Treat with scheduled insulin to determine if scheduled insulin is required
- All patients with T1DM and most with T2DM
  - Require SQ long- and short-acting insulin
  - Give basal insulin 1-2 hours before discontinuation of IV insulin
- Some T2DM pts may only require mealtime + ss. Others may only require ss.

Transitioning from Drip to SQ Insulin

- Extrapolate insulin requirement over preceding 6 to 8 hours to a 24-hour period
- Various approaches:
  - Surgical patients not eating:
    - 60-80% of the TDD as basal demonstrated to be safe and effective in surgical patients (Clement 2004, Schmeltz 2006)
  - Medical patients:
    - 75-80% of TDD divided between basal and bolus (Schmeltz 2006, Yeldandi 2006, Bode 2004)

Example #2:

- Sneezy Dwarf is a 50 yo M who presents following liver transplant, now POD 6.
- Euglycemia is maintained with insulin drip with rates of 2.5 un/hr on average.
- No complicating factors such as pressors or IV dextrose.
- Diet: Clear liquids. PO intake is poor.
- No current steroids.
- Wt: 100 kg

BG in mg/dL	Drip Rate in un/hr
90	1.5
110	2.5
100	2.0
140	3.0
150	3.5
120	2.5
200	5.0

Example #2 Cont:

- Take average drip rate of 2.5 un/hr and multiply by 24 hrs.
  - 2.5 x 24 = 60
- Reduce by 20%.
  - 60 x 0.8 = 50
- Use this dose to calculate TDD.
  - 50 un TDD
    - 25 un for basal coverage
    - 25 un for bolus coverage (8 un with meals)
    - Moderate insulin requirements ss: 2 or 3/50>150 ACHS

Impact of Nutrition

- No Food Intake:
  - Give continuous insulin infusion via IV (insulin drip)
  - Alternatively give basal insulin + sliding scale
  - Give basal coverage twice/day if requirements >60 un/day or pt is highly insulin sensitive.
- Continuous Enteral Feeding: Basal insulin + TF coverage + correction dose q4h or q6h.
  - *If feeding interrupted, give IV glucose to prevent hypoglycemia.*
- Total Parenteral Nutrition: Add regular insulin to IV bag and titrate dose in increments of 5-10un/liter.
- Reassess insulin requirement with any change in nutritional status.

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Confounding Variables

- Changes in caloric or carbohydrate intake
- Change in clinical status or medications (corticosteroids, vasopressors)
- Make adjustments based on daily BG patterns
- Poor coordination of BG testing and administration of insulin with meals
- Errors during patient transfer
- Renal or liver insufficiency

Adjusting Goal Targets

- Consider elevating goal target in the following situations:
  - Elderly >60 yo
  - ESRD, liver disease, partial or total pancreatectomy
  - CAD, CVA
  - Reduced hypoglycemic awareness
  - Recurrent hypoglycemia
- Watch for IV fluids with Dextrose, vasopressors, edema, snacking which can falsely increase your daily dosing.
- Be more aggressive with insulin dosing when pt has elevated TDD or BMI >35 kg/m2.

When to Involve Endocrine

- U500 insulin or High Dose Requirements
- Low Dose Requirements
- Erratic Inpatient or Outpatient Control
- Insulin Pump
- Anytime!

Watch Out!

- Common Med Errors with Insulin:
  - Insulin to Carb mismatch: Providing meal or TF insulin without meal/TF
  - Holding SS or Long-acting insulin for NPO
  - Using meal coverage when pt isn't eating to bring down a high BG
  - "Pt refused" when it seems like too much or too little.
  - Poor communication between teams and nurses
  - Overtreating Hypoglycemia. Remember Rule of 15.

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Diabetes in the Transplant Patient

- Risk Factors, Screening, Diagnosis
- Inpatient Management
- Outpatient Management:
  - Assessment
  - Lifestyle Modification
  - Oral Agents
  - Non-Insulin SQ Agents
  - Insulin
  - Hypoglycemia

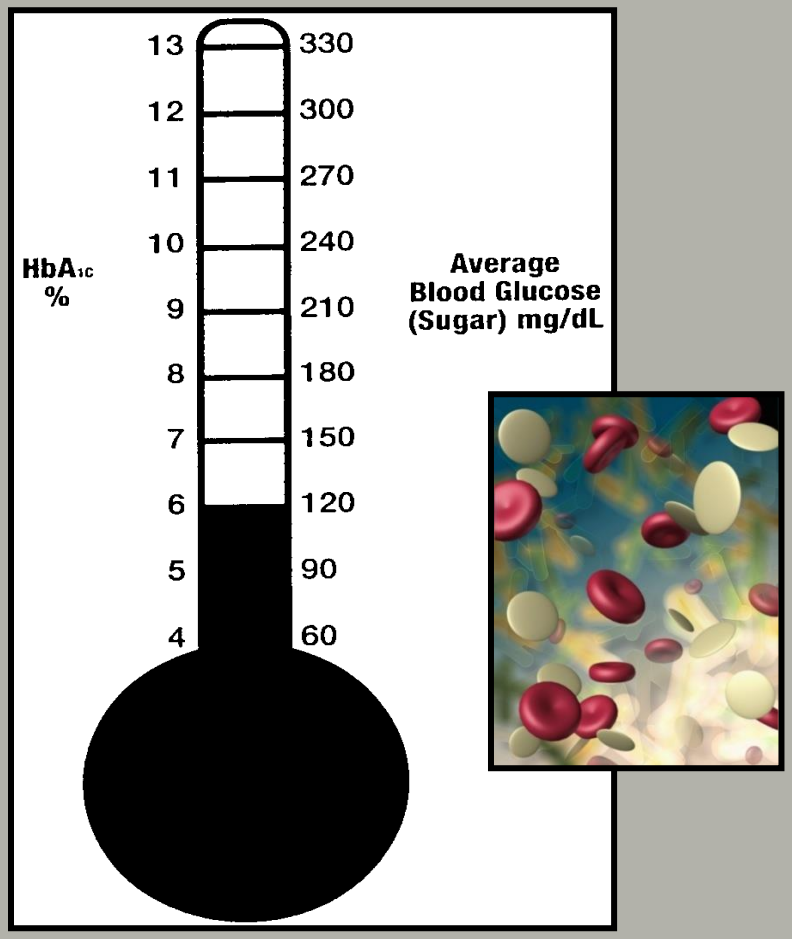
ADA Goals of Care

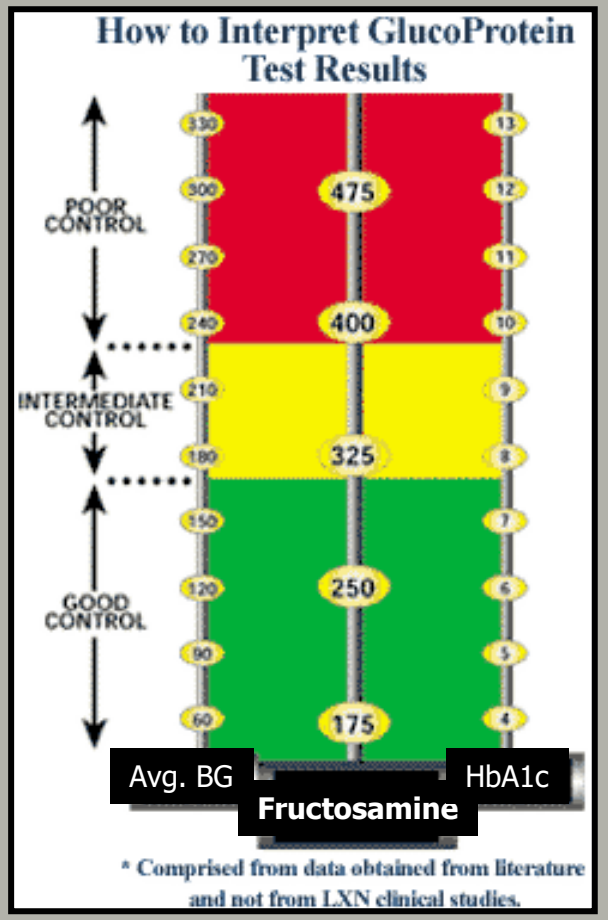
	Normal	Goal
HbA1c	4-6%	<7% *
Pre-prandial Blood Sugar	70-100 mg/dl	90-130 mg/dl (70-120)
Post-prandial Blood sugar	<140 mg/dl	<180 mg/dl (<160)

ADA Recommendation: Check A1c at least 2 x/yr if in target and stable; q 3 months if therapy has changed or not meeting goals. *Diabetes Care* 29:S4-S42, 2006

Diabetes Care 29:S4-S42, 2006

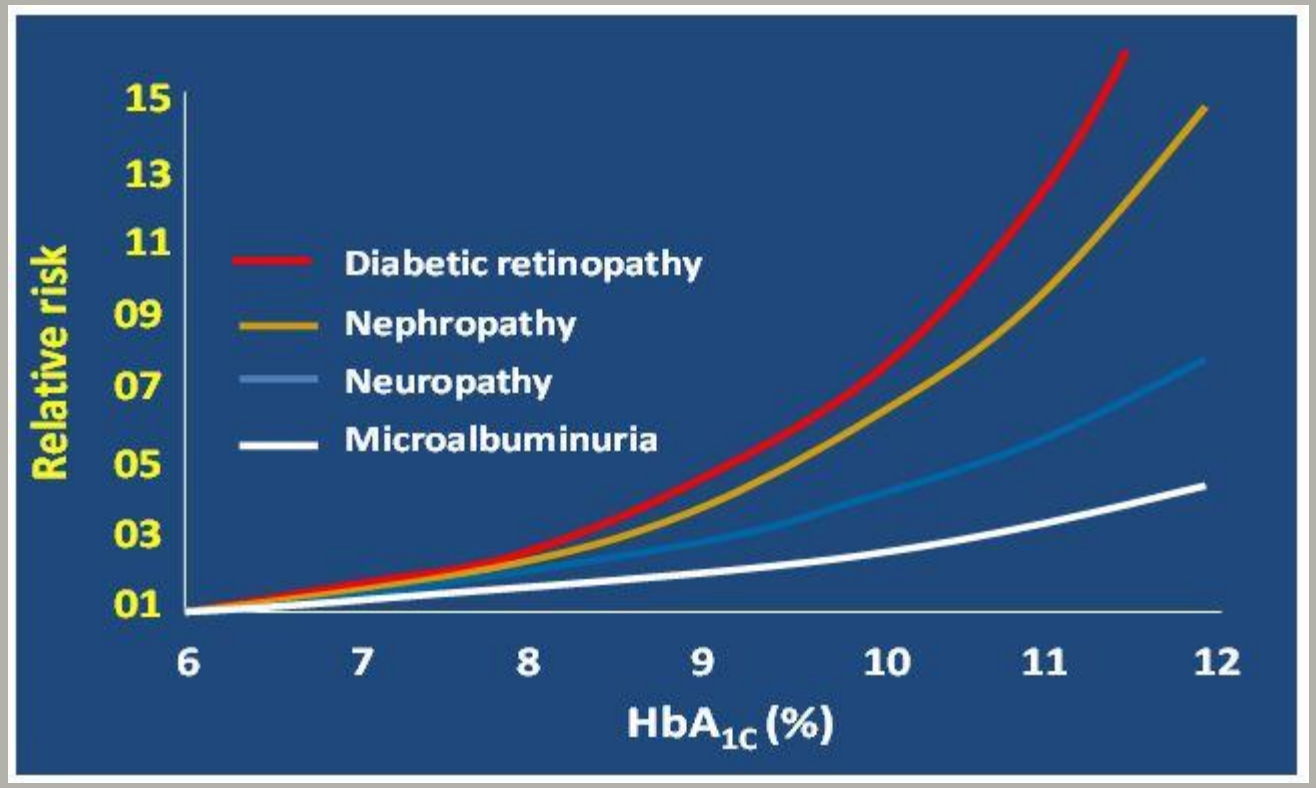
Assessment of Glycemic Control





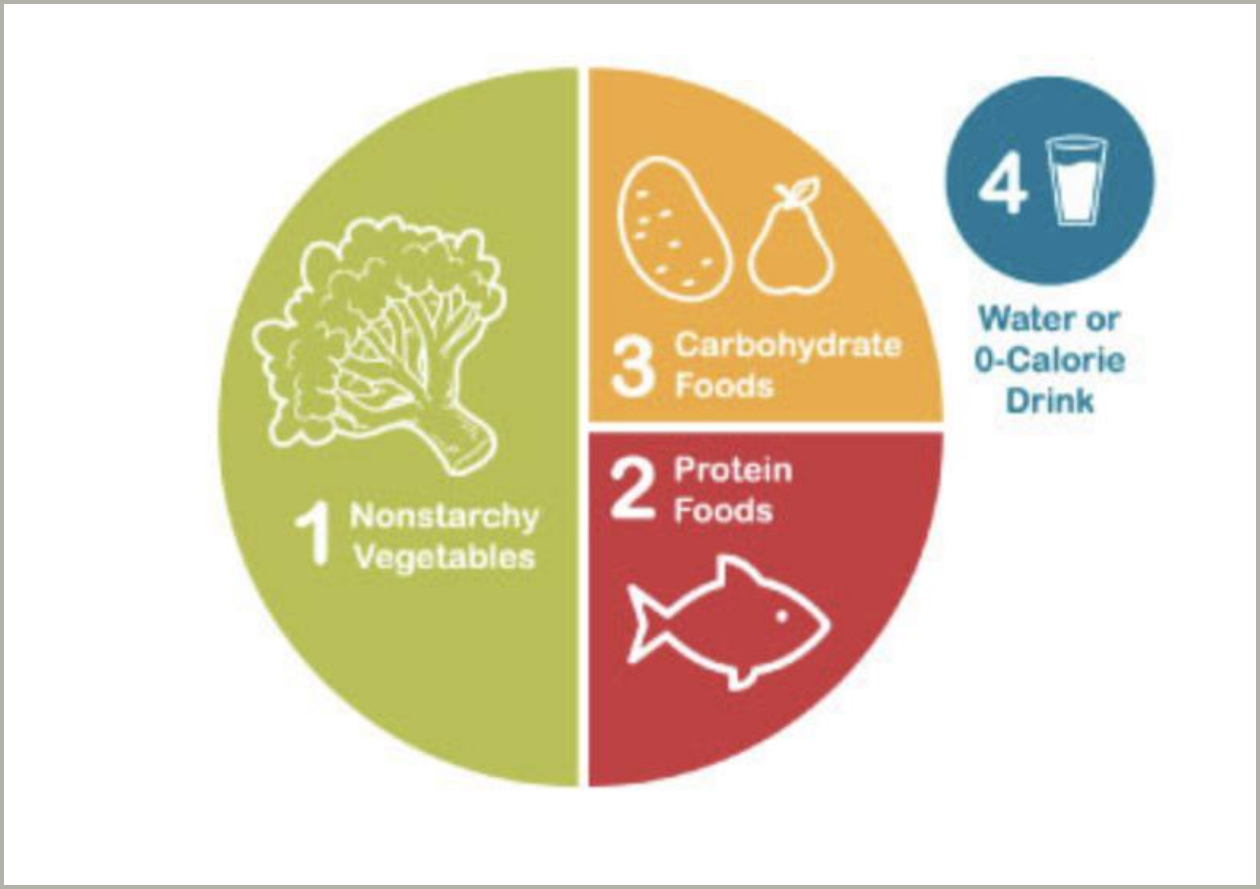
https://myendoconsult.com/learn/fructosamine-to-a1c-conversion-calculator/

A1c and Risk of Complications



The relative risk is exponential!

Diet: The Plate Method



American Diabetes Association: https://diabetes.org/healthy-living/recipes-nutrition/eating-well

Examples!

Avocado Toast with Turkey Bacon and Tomato
Avocado toast is a quick and easy breakfast that includes whole grains and healthy fats. Add a slice of turkey bacon and some sliced tomato for some more protein and veggies. For a more filling breakfast, add a ½ cup of nonfat Greek yogurt and a handful of fresh blueberries (or other seasonal fruit)

Lean protein: turkey bacon, Greek yogurt
Nonstarchy vegetables: Tomato, avocado
Carbohydrate foods: whole-wheat bread, blueberries

Apple Pie Yogurt Parfait
Enjoy the flavors of the all-American dessert, apple pie, in a healthy, balanced breakfast parfait. These are great for making ahead—just store the granola separately and add just before eating so it stays crunchy.

Lean Protein: Greek Yogurt
Carbohydrate foods: granola, apple

This perfect weeknight meal features **Lemon Chicken with Rosemary and Garlic**. Fill half your plate with a double serving of **Collard Greens with Yellow Squash** and complete your plate with half of a roasted sweet potato topped with a little bit of butter.

Lean Protein: Chicken
Nonstarchy Vegetables: Collards, yellow squash
Carbohydrate foods: sweet potato

We gave classic meatloaf a healthy makeover with this **Southwest-Style Turkey Meatloaf**. Pair with simple **Mashed Red Potatoes** and a **Green Salad with Orange, Avocado, and Onion**.

Lean Protein: ground turkey
Nonstarchy Vegetables: salad greens, onion
Carbohydrate foods: potatoes; oranges

This meal is perfect for lunch or dinner and works great for meal prepping. **Easy Beef Chili** is paired with a sweet and savory **Kale Apple Slaw**. Top the chili with a dollop of Greek yogurt and **Almost Smooth Salsa**.

Lean Protein: lean ground beef, beans
Nonstarchy Vegetables: kale; tomatoes, onion; salsa
Carbohydrate foods: apple; beans; yogurt

Here is a light, vegetarian meal, perfect for dinner or lunch. Veggie-packed **Slow-Cooker Ratatouille** gets a protein boost by adding white beans. Complete the plate with a simple **Side Greek Salad with Red Wine Vinaigrette**.

Lean Protein: beans
Nonstarchy Vegetables: lettuce, tomato, onion; eggplant, cabbage, bell pepper
Carbohydrate foods: beans

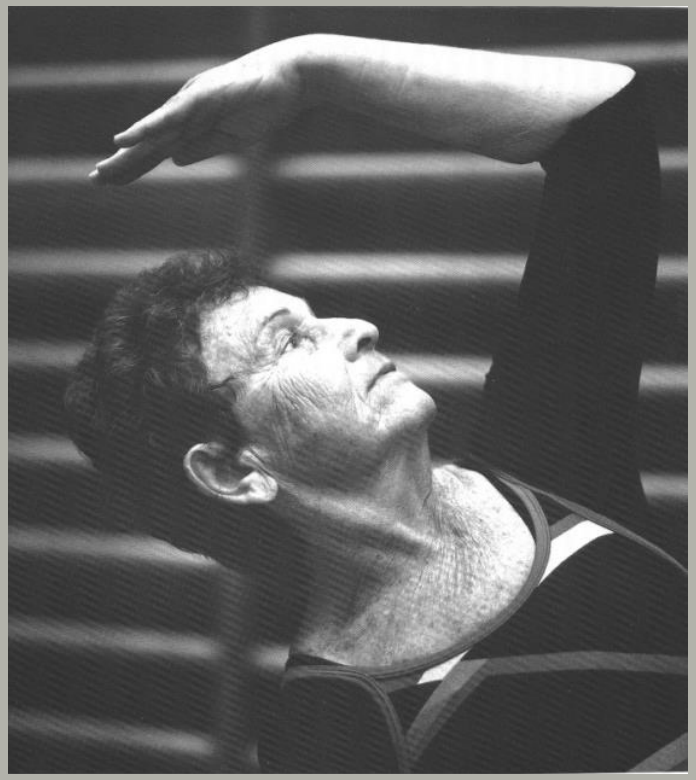
American Diabetes Association: https://diabetes.org/healthy-living/recipes-nutrition/eating-well

Resources

- App and Websites
  - My Fitness Pal
  - Calorie King (Also available in a book)
  - Live Strong
  - Spark People (Look for Meal Plan, Grocery List)

Physical Activity

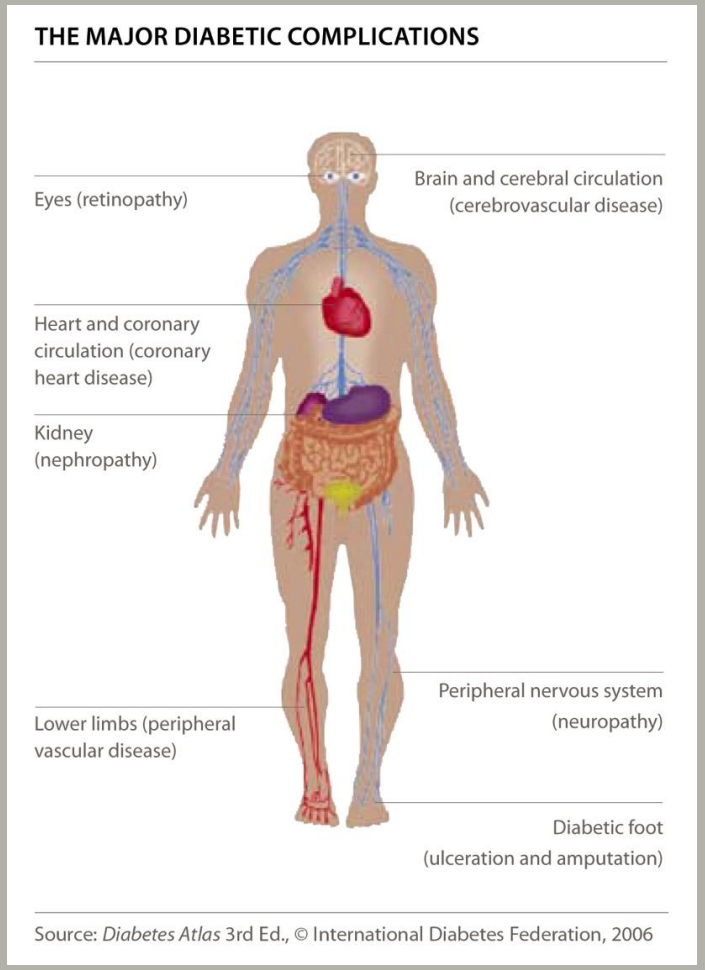
- Set small, reasonable goals: **Something is better than nothing!**
- Aim for **30 minutes** of moderate-to-vigorous intensity aerobic exercise **at least 5 days a week** or a total of **150 minutes per week**.



"What We Recommend." American Diabetes Association, 19 May 2015. Web. 15 Aug. 2016.

Chronic Effects of Diabetes

- Macrovascular
- Microvascular
- Consider short-term risks in the post-op setting



Oral Diabetes Meds

Drug Class	Action	Names
Insulin Secretagogues	Increase Glucose Secretion	**Sulfonylureas:** Glipizide, Glyburide, Glimepiride (Amaryl®) **Meglitinides:** Nateglinide (Starlix®) Repaglinide (Prandin®)
Biguanides	Increase insulin sensitivity, decrease hepatic glucose output	Metformin (Glucophage®)
Alphaglucosidase Inhibitors (AGI's)	Inhibit absorption of glucose from the gut	Acarbose (Precose®) Miglitol (Glyset®)
Thiazoladindiones (TZD's)	Increase insulin sensitivity	Rosiglitazone (Actos®) Pioglitazone (Avandia®)
DPP-4 Inhibitors	Increase insulin secretion, decrease glucagon secretion	Sitagliptin (Januvia®) Saxagliptin (Onglyza®)
SGLT2 Inhibitors *NEW CLASS!*	Increase glucose reabsorption in kidney	Canagliflozin (Invokana®) Dapagliflozin (Farxiga®) Empagliflozin (Jardiance®)
Bile Acid Resins	Cholesterol-lowering med that also reduces BG by binding bile acids in the digestive tract	Colesevelam (Welchol®)

Non-Insulin Injectables

Drug Class	Action	Names
GLP-1 Receptor Agonists	stimulate insulin production while suppressing the liver's glucose output, slows gastric emptying	· Albiglutide (Tanzeum) weekly · Dulaglutide (Trulicity) daily · Exenatide (Byetta) twice daily · Exenatide Extended Release (Bydureon) weekly · Liraglutide (Victoza) daily
Amylin Analogue	slows food from moving too quickly through the stomach and helps keep after-meal glucose levels from going too high, also reduces glucose production from liver.	Pramlintide (Symlin)

Table 1. Hypoglycemic Agents for Treating Type 2 Diabetes Mellitus

Medication	*Average A1C reduction*	*Potential adverse effects*	*Precautions/contraindications*
Alpha-glucosidase inhibitors Acarbose (Precose) Miglitol (Glyset)	0.5% to 0.8%	Flatulence, diarrhea, abdominal bloating	Avoid when creatinine clearance < 25 mL per minute per 1.73 m^2 (0.42 mL per second per m^2) Most effective when given with a starchy, high-fiber diet Reverse hypoglycemia with glucose, not sucrose
Biguanides Metformin	1.0% to 1.3%	Nausea, diarrhea, abdominal bloating Extended-release preparations have fewer gastrointestinal adverse effects	Estimated GFR 30 to 44 mL per minute per 1.73 m^2: review use of metformin Estimated GFR < 30 mL per minute per 1.73 m^2: discontinue use Discontinue during acute illness or procedure that could predispose patient to lactic acidosis
Dipeptidyl-peptidase-4 inhibitors Alogliptin (Nesina)* Linagliptin (Tradjenta)* Saxagliptin (Onglyza)* Sitagliptin (Januvia)*	0.5% to 0.9%	Headache, pancreatitis (rare)	Linagliptin does not require dosage adjustment in renal insufficiency Saxagliptin dosage adjustment required when administered with concomitant CYP3A4 inhibitors

Am Fam Physician. 2015;92(1):27-34

Glucagon-like peptide-1 receptor agonists Albiglutide (Tanzeum)* Dulaglutide (Trulicity)* Exenatide (Byetta, Bydureon)* Liraglutide (Victoza)*	0.8% to 2.0%	Nausea, vomiting, sense of fullness Weight loss of 1 to 4 kg (2.2 to 8.8 lb) is likely Pancreatitis (rare)	Exenatide is not recommended if creatinine clearance < 30 mL per minute per 1.73 m^2 (0.50 mL per second per m^2) Boxed warning for personal or family history of medullary thyroid carcinoma; patients with multiple endocrine neoplasia type 2
Meglitinides Nateglinide (Starlix)* Repaglinide (Prandin)	0.5% to 1.0%	Hypoglycemia	Metabolized primarily by the liver (CYP3A4 and CYP2C9)
Sodium-glucose cotransporter 2 inhibitors Canagliflozin (Invokana)* Dapagliflozin (Farxiga)* Empagliflozin (Jardiance)*	0.5% to 0.9%	Increased urinary tract and genital infections, increased low-density lipoprotein cholesterol level Weight loss of 0.7 to 3.5 kg (1.5 to 7.7 lb) is typical	Dosage adjustment required in renal insufficiency
Sulfonylureas Glimepiride (Amaryl) Glipizide (Glucotrol) Glyburide	0.4% to 1.2%	Hypoglycemia, weight gain	Dosage adjustment required in renal insufficiency Administer with meals
Thiazolidinediones Pioglitazone (Actos) Rosiglitazone (Avandia)	0.5% to 1.4%	Weight gain, edema	Contraindicated in patients with New York Heart Association class III or IV congestive heart failure Decrease concomitant insulin dose at initiation

Considerations for Transplant Pts

Table 4. Non-Insulin Diabetes Treatments: Potential Considerations for Use in the Solid Organ Transplant Patient

Agent	Safety or Efficacy Studies in Transplant Patients	Potential Considerations in Organ Transplant Patient
Metformin	Effective in stable KTX patients but contraindicated for many other TX groups, including during acute hospitalizations (177, 214)	Should not be used during acute hospitalization, with ↓ GFR, ↑ LFTs, CHF, or active, significant infection; and should be held for planned iv contrast procedure
Sulfonylureas	Efficacy is not well documented in transplant patients. Did not alter cyclosporine pharmacokinetics in a small study of KTX recipients with PTDM (215–218)	Increased risk of more frequent and more prolonged hypoglycemia with ↓ GFR
Repaglinide	Effective and safe with no interaction with CNIs in a small study of KTX recipients with PTDM (180)	Less risk of hypoglycemia with ↓ GFR than sulfonylureas
Thiazolidinediones (eg, pioglitazone)	Effective and safe in small studies of KTX recipients (177, 180, 183, 219, 220)	Known risk for weight gain, edema, heart failure, and reduced bone mass; contraindicated with known elevated liver function tests with the exception for known fatty liver disease including after liver transplant; contraindicated with known heart failure; unknown impact on risk for heart failure risk after transplant

Shivaswamy et. Al. *Endocr Rev*. 2016 Feb;37(1):37-61.

More Considerations

Table 4. Non-Insulin Diabetes Treatments: Potential Considerations for Use in the Solid Organ Transplant Patient

Agent	Safety or Efficacy Studies in Transplant Patients	Potential Considerations in Organ Transplant Patient
α-Glucosidase inhibitors	No studies of safety or efficacy to date in organ transplant populations	Avoid with ↓ GFR; unlikely to be an effective single agent
GLP-1 agonists (exenatide, liraglutide, lixisenatide)	Liraglutide did not affect tacrolimus concentration in a very small study of KTX recipients (185)	Decreases bowel motility, which may impact absorption of immune suppression agents and has not yet been studied; should not use if GFR < 40 mL/min
DPP-4 inhibitors (sitagliptin, vildagliptin, saxagliptin, linagliptin, allogliptin)	Retrospective and small random controlled trials of KTX recipients show safety of several DPP-4 inhibitors (8, 181–184)	Reduce dose of all but linagliptin with ↓ GFR
SGLT-2 inhibitors (dapagliflozin, canagliflozin, empagliflozin)	Known to increase risk of genitourinary infections in those with previous history, which is a concern in immunocompromised transplant patients, known to cause volume dehydration and hypotension, which may also be a concern in these patients as well as recent reports of diabetic ketoacidosis raise concerns of safety for most transplant populations (186, 187)	Avoid until safety studies are performed

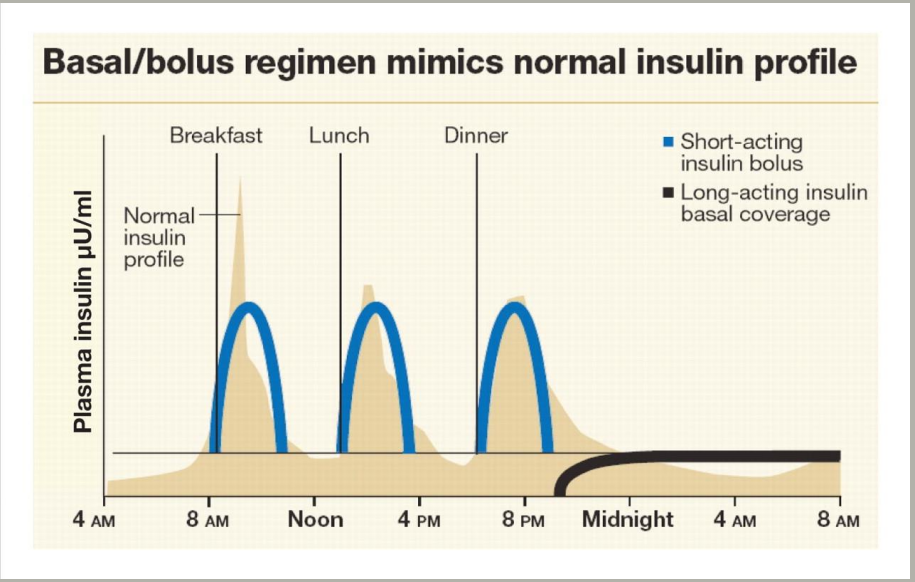
Shivaswamy et. Al. *Endocr Rev*. 2016 Feb;37(1):37-61.

Insulin

- Maintenance Insulin (Basal) – NPH, Levemir, Lantus, Toujeo, Tresiba, Basaglar
  - 50% of daily needs
  - Suppresses glucose production while fasting
- Prandial and SS Coverage (Bolus)
  - Limits hyperglycemia after meals
  - Immediate risk and sharp peak at 1-2 hrs
  - 10-20% of total daily insulin requirement at each meal

Normal Endogenous Insulin Secretion

- Guidelines just a starting point.
- When correction is required before most meals, ↑ basal
- When BG remains consistently elevated at one time point, ↑ preceding bolus
- Fasting BG also a good measure of basal insulin dose but be wary of the bedtime snack!



Modified from J Clin Endocrinol Metab, January 2012, 97(1):16 –38, Volume 29, Number 1, 2011 • Clinical Diabetes

Insulin Duration of Action: Rapid-Acting

Type of Insulin (Trade Names)	Supplier	Appearance	Begins Working	Peak Activity	All gone
RAPID ACTING					
Afrezza (Regular insulin)	MannKind	Inhaled	12 minutes	30–45 minutes	2 hours
Lyumjev® (insulin lispro)	Eli Lilly	Clear	15–17 minutes	57 minutes	4.6-7.3 hours
Fiasp® (insulin aspart)	Novo Nordisk	Clear	16–20 minutes	90–120 minutes	5–6 hours
NovoLog® / NovoRapid® (insulin aspart)	Novo Nordisk	Clear	15–20 minutes	60–180 minutes	3–5 hours
Apidra® (insulin glulisine)	Sanofi	Clear	15–20 minutes	60–120 minutes	4–5 hours
Humalog® (insulin lispro)	Eli Lilly	Clear	20–45 minutes	60–120 minutes	4–5 hours
Admelog® (insulin lispro)	Sanofi	Clear	20–45 minutes	45–150 minutes	3.5–4.75 hours

https://childrenwithdiabetes.com/cwd-news/insulin-options-in-the-us-as-of-january-2022/

Insulin Duration of Action: Long-Acting

Type of Insulin (Trade Names)	Supplier	Appearance	Begins Working	Peak Activity	All gone
LONG ACTING					
LANTUS® (insulin glargine U-100)	Sanofi	Clear	4–6 hours	No pronounced peak	Up to 24 hours (depends on injected dose)
Toujeo® (insulin glargine U-300)	Sanofi	Clear	4–6 hours	No pronounced peak	Up to 24 hours (depends on injected dose)
Basaglar® (insulin glargine U-100)	Eli Lilly	Clear	4–6 hours	No pronounced peak	Up to 24 hours (depends on injected dose)
SEMGLEE™ (insulin glargine U100)	Viatris	Clear	4–6 hours	No pronounced peak	Up to 24 hours (depends on injected dose)
Levemir® (insulin detemir)	Novo Nordisk	Clear	1–2 hours	2 - 12 hours (mild, varies by dose)	Up to 24 hours (depends on injected dose)
Tresiba (insulin degludec U-100 or U-200)	Novo Nordisk	Clear	1–2 hours	About 12 hours	42+ hours

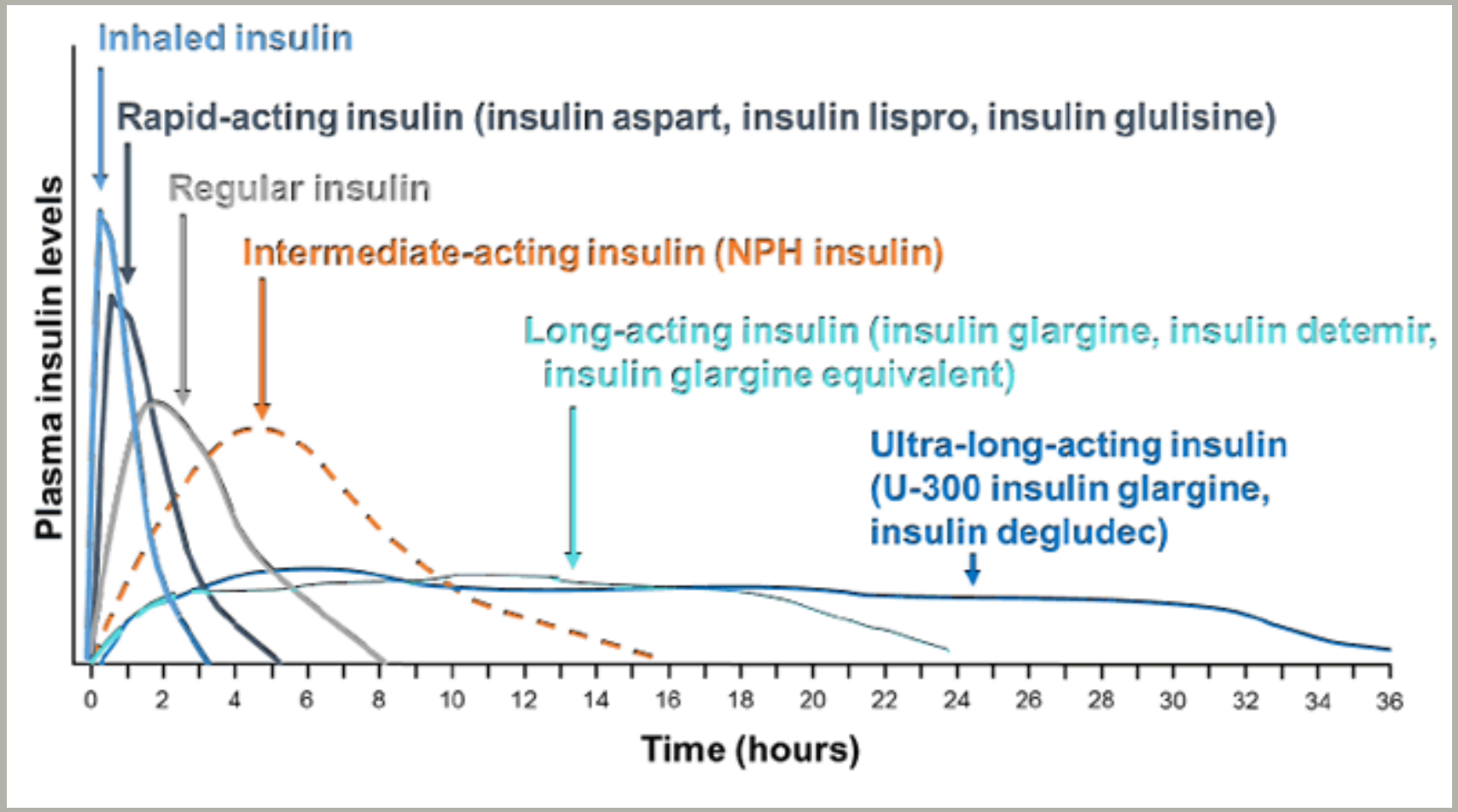
https://childrenwithdiabetes.com/cwd-news/insulin-options-in-the-us-as-of-january-2022/

Short-Acting, Intermediate, and Mixed Insulin Options

Type of Insulin (Trade Names)	Supplier	Appearance	Begins Working	Peak Activity	All gone
SHORT ACTING					
Regular (Humulin, Actrapid, Velosulin®)	Eli Lilly and Novo Nordisk	Clear	30 minutes	2–4 hours	5–8 hours
INTERMEDIATE ACTING					
NPH (Insulatard®)	Eli Lilly and Novo Nordisk	Cloudy	2–4 hours	6–8 hours	12–15 hours
Human Regular U-500	Eli Lilly	Clear	30 minutes	5–6 hours	18–20 hours
PRE-MIXED (ACTION VARIES)					
NPH/Regular 70/30 or 50/50 are common mixes	Eli Lilly and Novo Nordisk	Cloudy	30 minutes	Varies	18–24 hours
NPL/Humalog 75/25 and 50/50	Eli Lilly	Cloudy	10–15 minutes	Varies	12–15 hours
NovoLog Mix 70/30	Novo Nordisk	Cloudy	10–15 minutes	Varies	10–12 hours

https://childrenwithdiabetes.com/cwd-news/insulin-options-in-the-us-as-of-january-2022/

Insulin Duration Of Action



Practical Insulin. 4th ed. Alexandria, VA: American Diabetes Association; 2015:1-68.
https://www.powerpak.com/course/print/113133

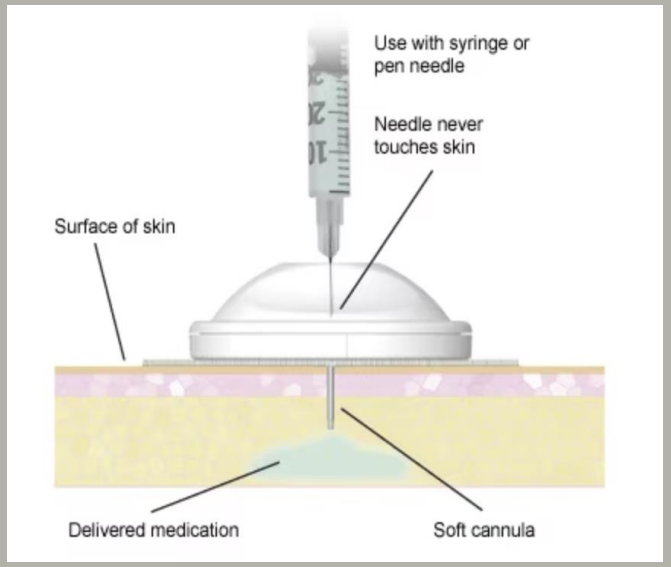
Inhaled Insulin

- Inhaled insulin begins working within 12 to 15 minutes, peaks by 30 minutes, and is out of your system in 180 minutes.
- Types: Technosphere insulin-inhalation system (Afrezza® Human Insulin)
  - Rapid acting human insulin
  - Take prior to your meals
  - Each puff is approximately 4 un, 8 un, or 12 un. Depending on dose prescribed.
  - Similar dosing, although slightly more effective than SQ insulin.

Afrezza.com

Afraid of Needles?

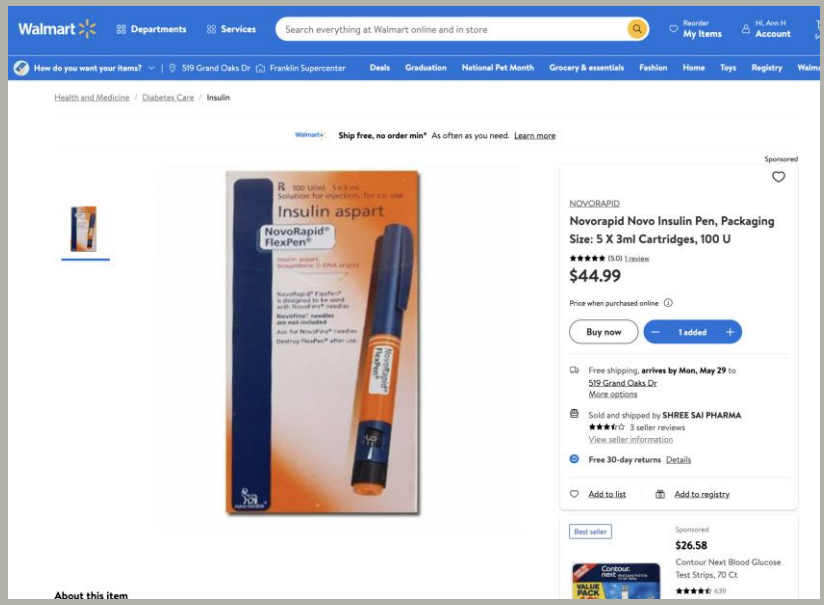
- I-Port: reduces pain and anxiety with injections by using the same site every day, instead of multiple areas
- Uses a Built-in Inserter device, which leaves a flexible cannula under the skin
- Change site every 3 days
- Used with both pens and syringes (must be 5 mm and greater)



https://www.medtronic.com/ca-en/diabetes/home/products/accessories/iport-advance.html

Affordability

- Wal-Mart's Brand: Reli-On – NPH, Regular, or 70/30 insulins $25 per vial. No Rx needed.
- As of July, 2021: Analog: Wal-Mart analog insulin vials ($72.88) and FlexPen® ($85.88). Reli-On Novolog. Also available at Sam's.



Walmart.com

News Release

Lilly Cuts Insulin Prices by 70% and Caps Patient Insulin Out-of-Pocket Costs at $35 Per Month

March 1, 2023

- Cutting the list price of its non-branded insulin, Insulin Lispro Injection 100 units/mL, to $25 a vial. Effective May 1, 2023, it will be the lowest list-priced mealtime insulin available, and less than the price of a Humalog® vial in 1999.
- Cutting the list price of Humalog® (insulin lispro injection) 100 units/mL1 , Lilly's most commonly prescribed insulin, and Humulin® (insulin human) injection 100 units/mL2 by 70%, effective in Q4 2023.
  - The list price for Humalog U-100, 10 mL vial will drop from $274.70 to $66.40.
  - The list price for Humulin U-100, 10 mL vials will drop from $148.70 to $44.61.
- Launching RezvoglarTM (insulin glargine-aglr) injection, a basal insulin that is biosimilar to, and interchangeable with, Lantus® (insulin glargine) injection, for $92 per five pack of KwikPens®, a 78% discount to Lantus, effective April 1, 2023.

https://investor.lilly.com/news-releases/news-release-details/lilly-cuts-insulin-prices-70-and-caps-patient-insulin-out-pocket

Lily Press Release

- Commercial Insurance: Effective immediately, Lilly will automatically cap out-of-pocket costs at $35 at participating retail pharmacies.[3]
- Uninsured: Use InsulinAffordability.com and immediately download the Lilly Insulin Value Program savings card to receive Lilly insulins for $35 per month.

https://investor.lilly.com/news-releases/news-release-details/lilly-cuts-insulin-prices-70-and-caps-patient-insulin-out-pocket

Insulin Costs Under Medicare

- The federal Inflation Reduction Act caps insulin costs at $35 a month for people on Part D plans.
- Beginning July 1, 2023, insulin covered under Medicare Part B including insulin delivered through a traditional pump that is covered under the durable medical equipment benefit will also be capped at $35 per month.
- As a result of the Senior Savings Pilot and subsequently the Inflation Reduction Act of 2022, Medicare Part D enrollees monthly cost sharing for insulin is capped at $35. A covered insulin product is one that is included on a Medicare Part D plan formulary.

American Diabetes Association:
https://diabetes.org/tools-support/insulin-affordability

Cost Of Diabetes Medications

- Cost Effective Insulin Regimens
  - Over-the-counter insulin
  - Glucometer, Strips
- May also consider use of SFU if appropriate.
  - Other generic, low-cost oral agents include Metformin, TZD (Actos), etc although these may not typically be correct for the post-transplant setting.

Pre-Mixed Insulins

- Protamine + Short or Rapid-Acting Insulin
  - Novolin 70/30® = 70% NPH+30% Regular
  - Humulin 70/30®, Humulin 50/50®
  - Humalog 75/25® = 75% NPL+25% Lispro
  - Novolog 70/30® = 70% NPH + 30% Aspart
- Time to Peak: 4-8 hours
- Duration: 17-25 hours
- Clinical Use: Elderly, cognitive or psych. impairment, multiple co-morbid illnesses, low cost, poor compliance
- Can access over-the-counter *without a prescription*
- Cost: $25 at Wal-Mart

Pen Delivery

- Improves Accuracy, especially with low dosing
- More Convenient
- Insulin Requires Priming and SQ Hold

Pumps

Continuous Glucose Monitoring Sensor

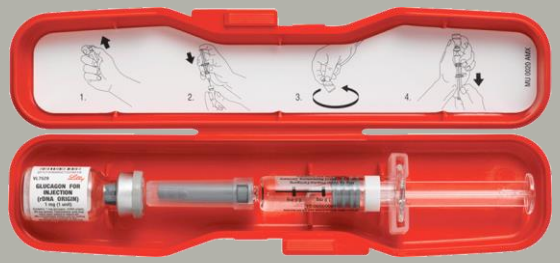
- Measures interstitial fluid
- Gives trends
- Alerts
- Poor Accuracy
- Medtronic, Dexcom

Freestyle Libre

Freestyle Libre (CGMS)

Hypoglycemia

- Below 70: **Rule of 15**
- Causes
- Severe Hypoglycemia
- Hypoglycemia Unawareness

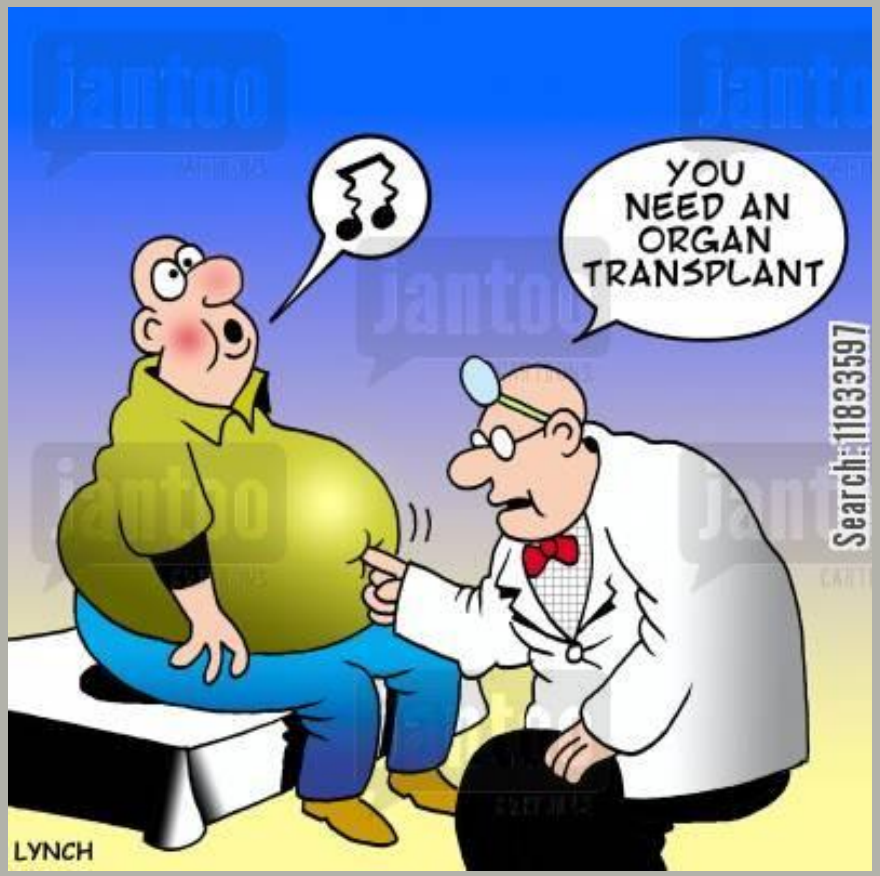


Take Home Points

- Approach med compliance, diet, and exercise in a non-judgmental way.
- Start with Weight-Based Dosing if you need a starting place.
- Educate, educate, educate!

Test/Exam	Frequency
Wgt.	Each visit
Blood Pressure	Each visit
HbA1c	Every 3 months
Dilated eye exam	Yearly if no DR
Lipid Panel	Yearly if low risk
Foot exam	Yearly if low risk
Microalbumin	Yearly

Roll With The Punches and Enjoy The Challenge of Caring For People With Diabetes!



https://www.jokejive.com/topic/kidney+transplant#&gid=1&pid=12
http://lowres.jantoo.com/health-beauty-organ_transplants-transplants-whistles-pianos-organ_transplant-11833597_low.jpg

Thank You!

Ann Hackett, APRN-BC, MSN, CDE