

CONSIDERATIONS FOR MANAGING DIABETES IN OLDER ADULTS

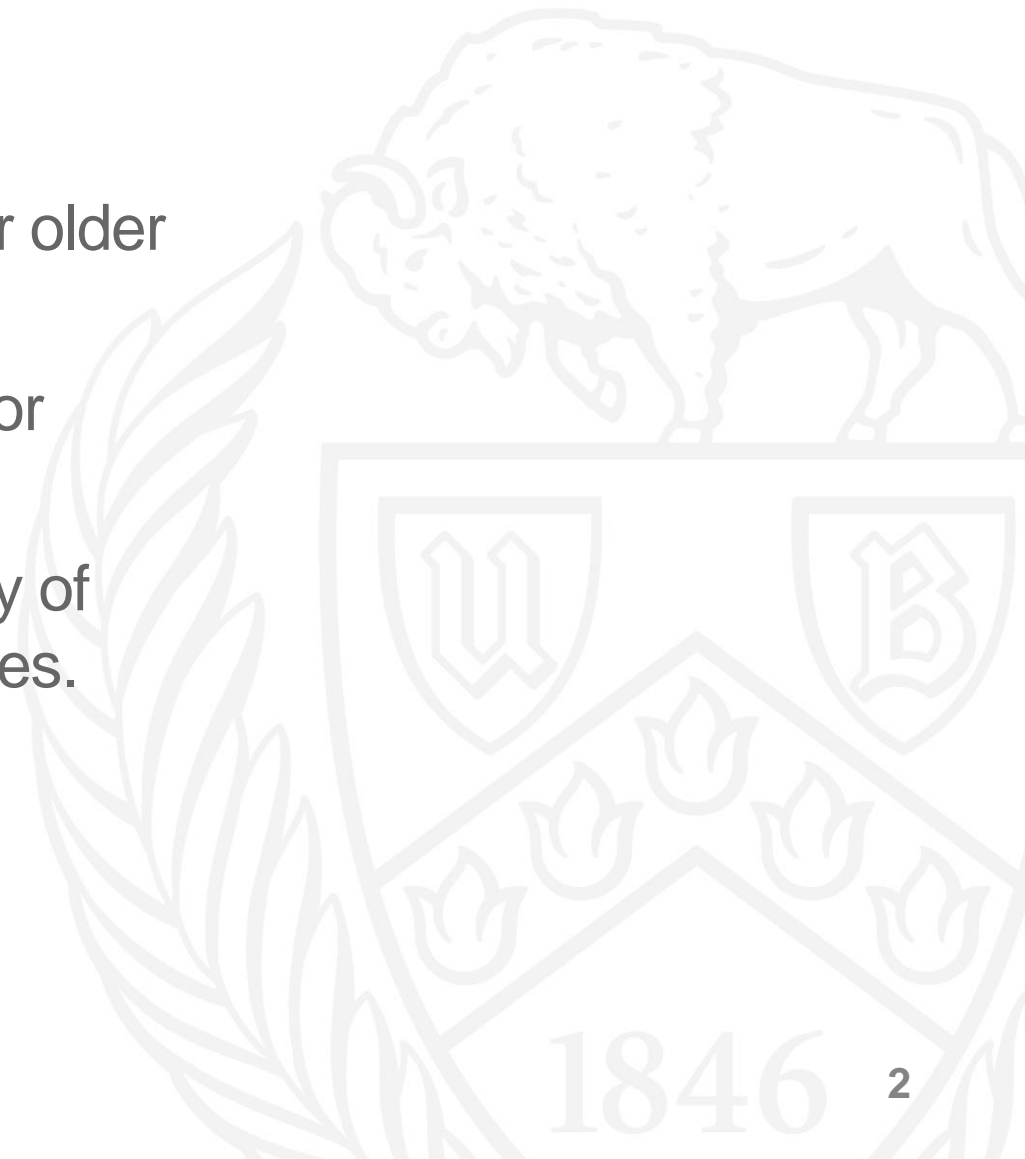
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Learning Objectives

- Discuss the management of and goal setting for older patients with diabetes.
- Explain comprehensive cardiovascular risk factor modification for older patients with diabetes.
- Describe risk factors for hypoglycemia and utility of glucagon products for older patients with diabetes.



EPIDEMIOLOGY

In older adults



Prevalence of Type 2 Diabetes (T2DM)

- ✓ 29.2%, or 15.9 million seniors (diagnosed and undiagnosed) over the age of 65, have diabetes
- ✓ About half of older adults have prediabetes
- ✓ If diagnosed before age 65:
 - ✓ Higher A1C's
 - ✓ More likely to use insulin
 - ✓ Retinopathy is more common
- ✓ If diagnosed after age 65:
 - ✓ Lower A1C
 - ✓ Less likely to use of insulin

Prevalence of Type 2 Diabetes (T2DM)

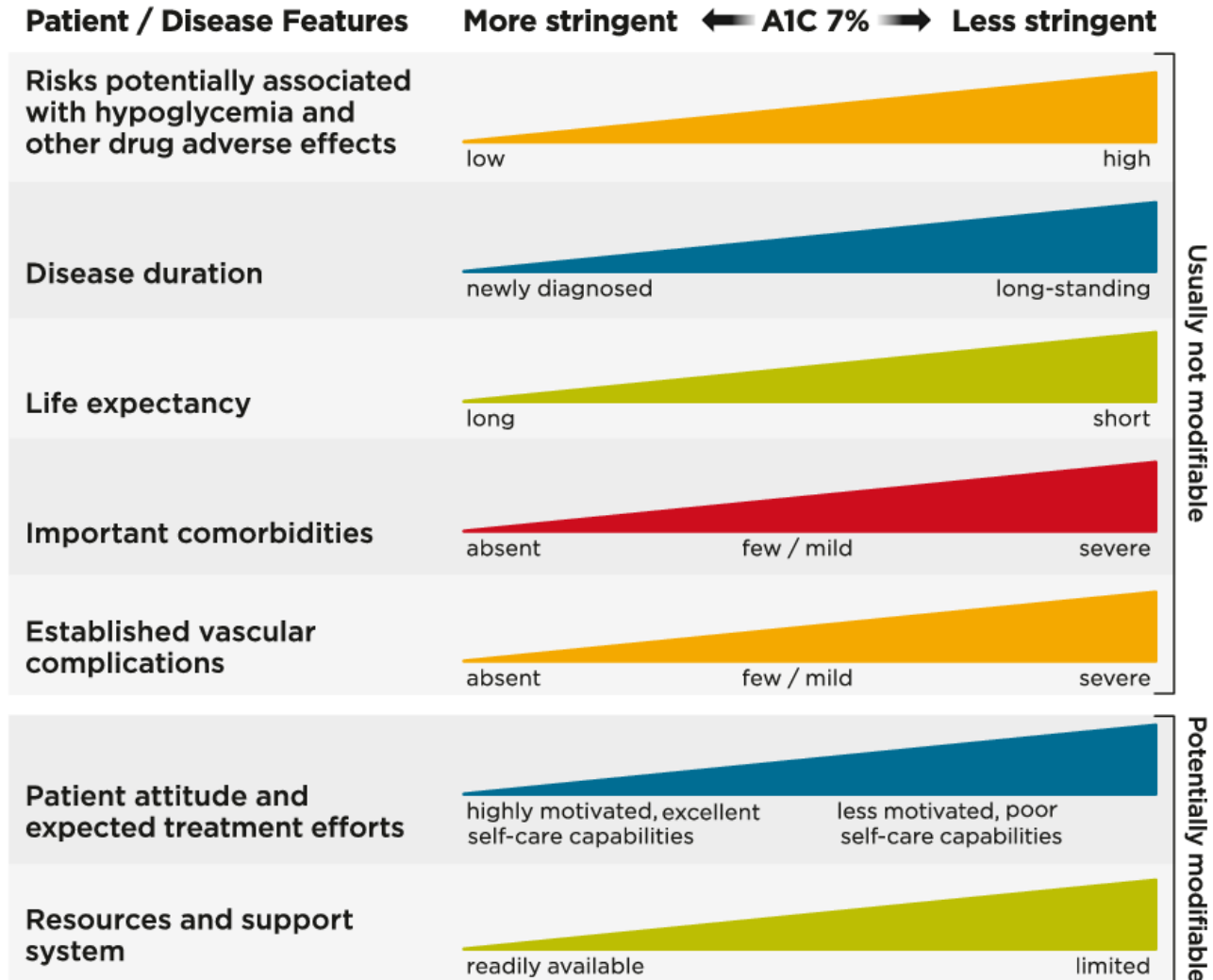
- ✓ Older adults have the highest rates of:
 - ✓ Lower-extremity amputation
 - ✓ MI
 - ✓ Visual impairment
 - ✓ ESRD
- ✓ Patients with T2DM who are ≥ 75 years old, have double the rate of ED visits for hypoglycemia.

MANAGEMENT & GOAL SETTING

learning objective #1

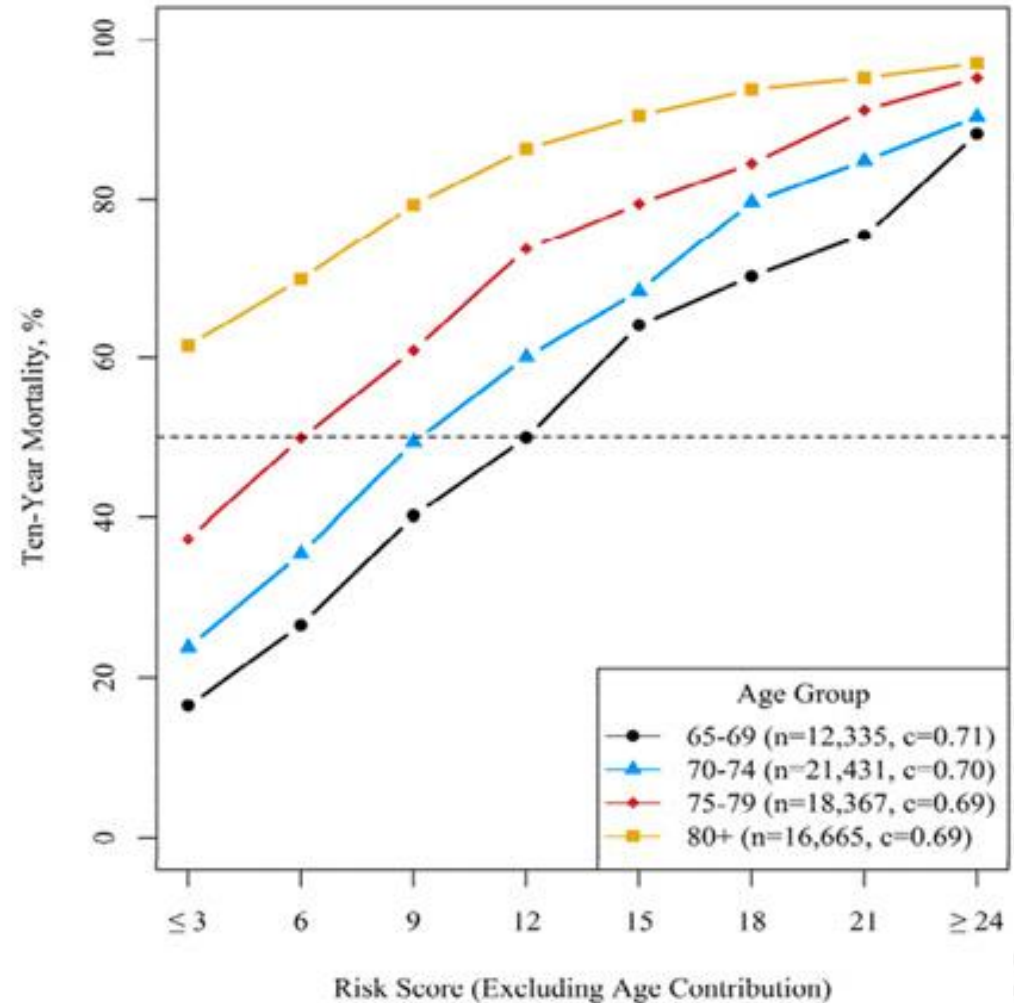
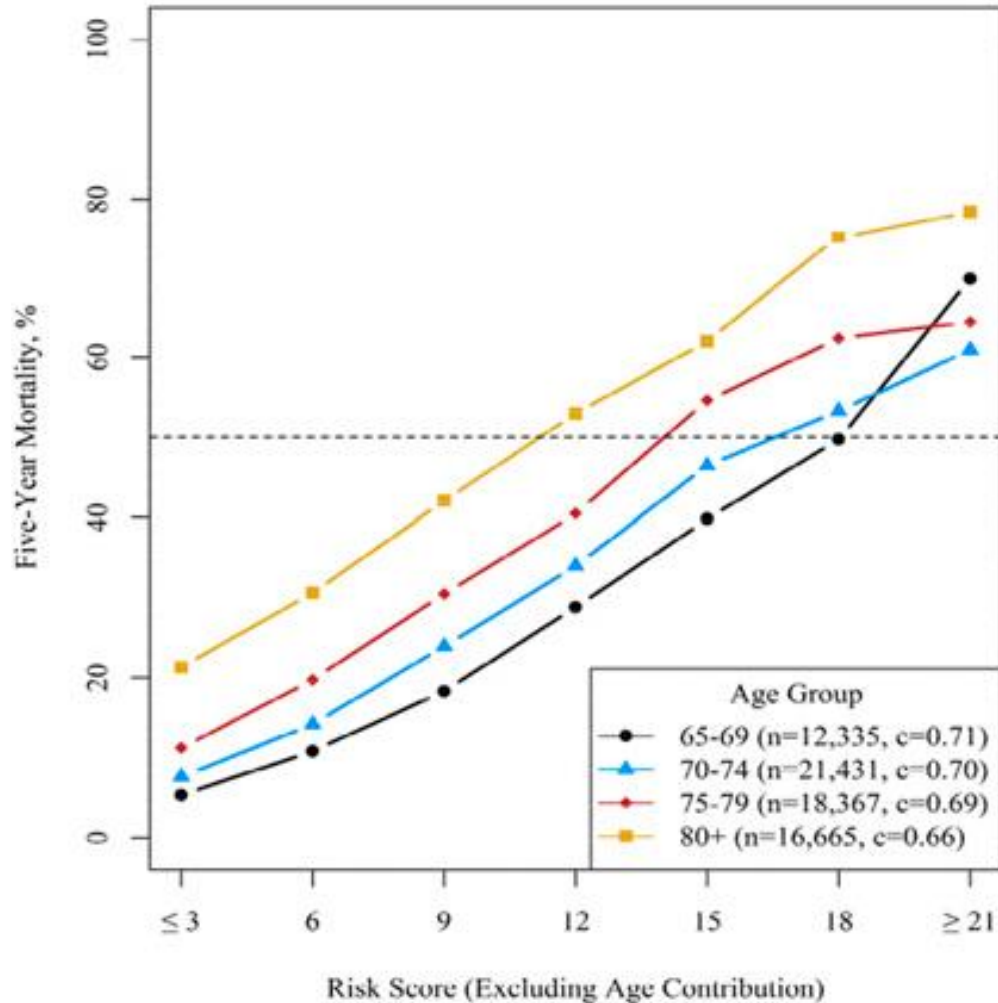


Approach to Individualization of Glycemic Targets



Glycemic Targets:
 Standards of Medical Care in
 Diabetes - 2022. Diabetes Care
 2022;45(Suppl. 1)

Life Expectancy and Risk of Mortality



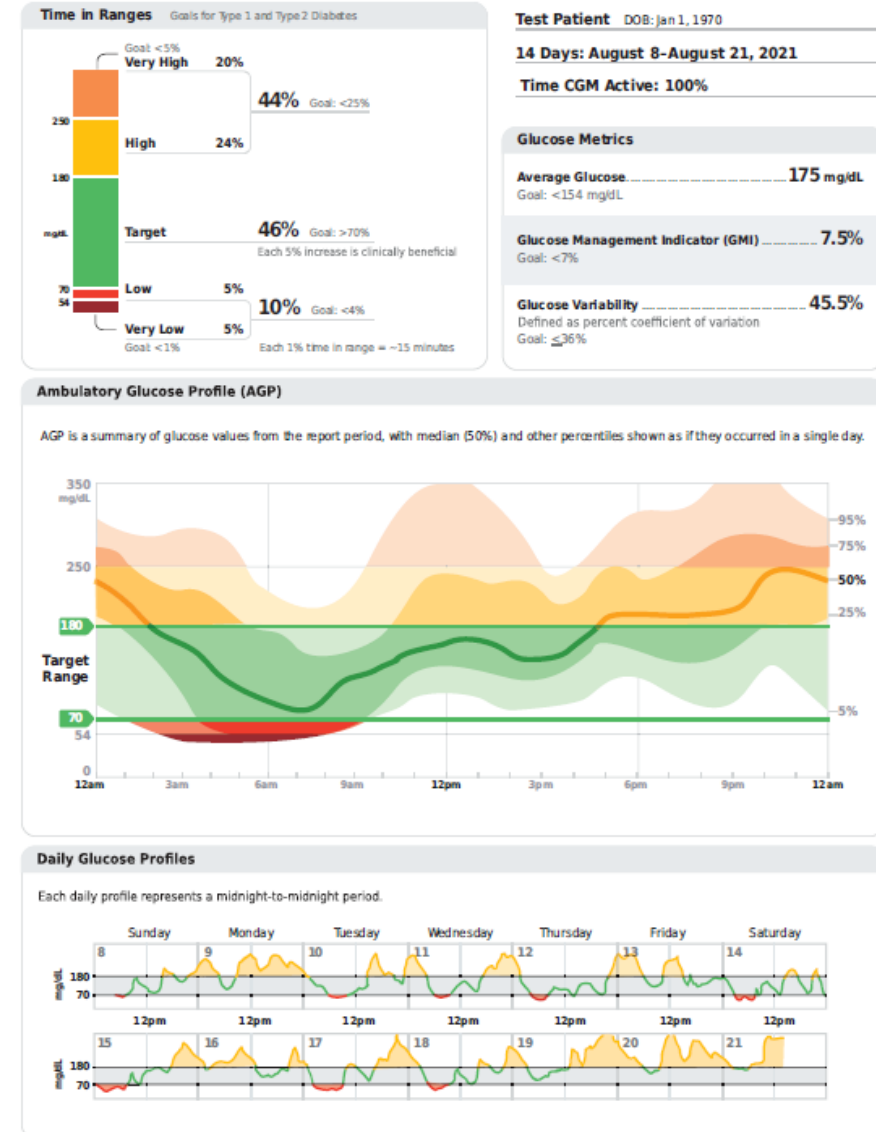
Diabetes Treatment Goals in Older Patients

Health Status	A1C Goal	Fasting Glucose	Bedtime Glucose
<i>Healthy</i> <ul style="list-style-type: none"> Few comorbidities and Intact cognitive and functional status 	< 7 – 7.5%	80 – 130 mg/dL	80 – 180 mg/dL
<i>Complex/Intermediate</i> <ul style="list-style-type: none"> Multiple comorbidities or 2+ instrumental ADL impairments or Mild/moderate cognitive impairment 	< 8.0%	90 – 150 mg/dL	100 – 180 mg/dL
<i>Very complex/Poor health</i> <ul style="list-style-type: none"> LTC or End-stage chronic disease or Moderate/severe cognitive impairment or 2+ instrumental ADL impairments 	Avoid reliance on A1C; avoid hypoglycemia	100 – 180 mg/dL	110 – 200 mg/dL

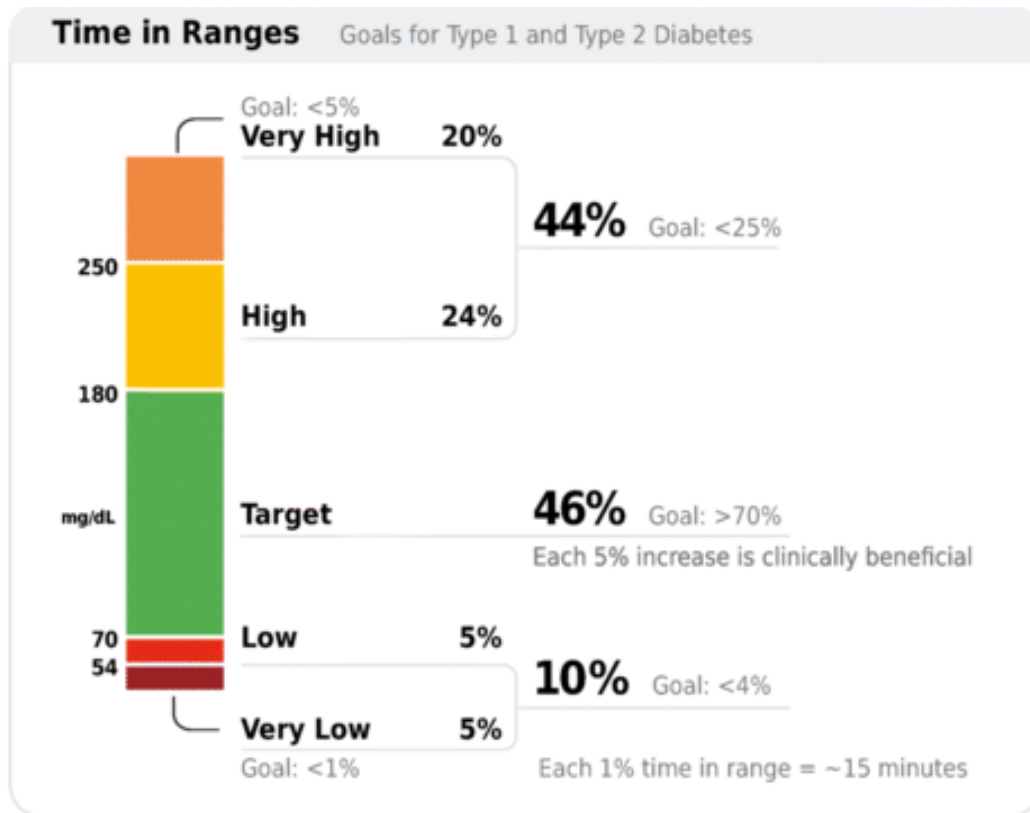
AGP Report

- ❖ Time in Range
- ❖ Ambulatory Glucose Profile (AGP)
- ❖ Daily Glucose Profiles

AGP Report: Continuous Glucose Monitoring



Time in Range



Test Patient DOB: Jan 1, 1970

14 Days: August 8-August 21, 2021

Time CGM Active: 100%

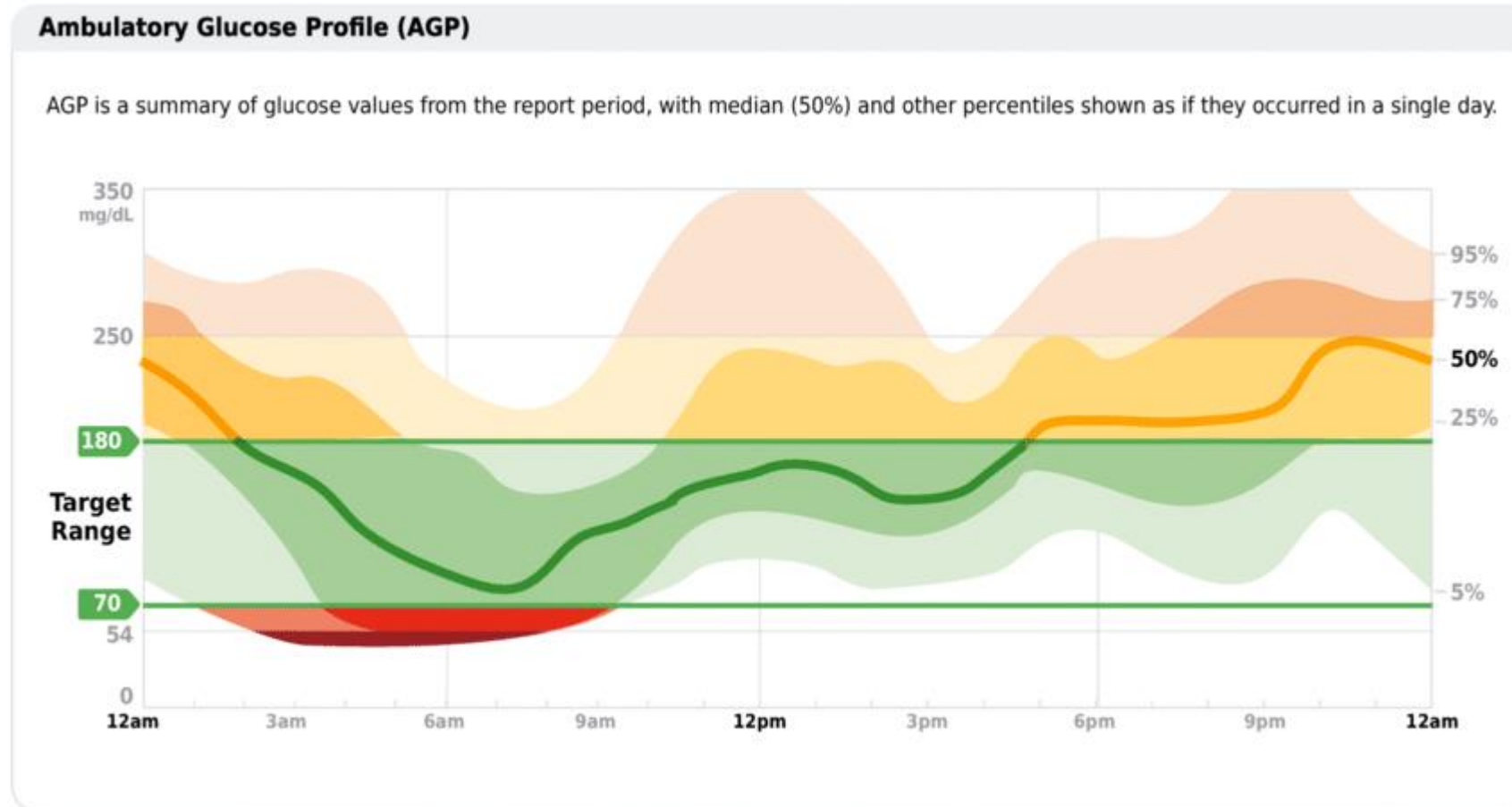
Glucose Metrics

Average Glucose **175 mg/dL**
Goal: <154 mg/dL

Glucose Management Indicator (GMI) **7.5%**
Goal: <7%

Glucose Variability **45.5%**
Defined as percent coefficient of variation
Goal: ≤36%

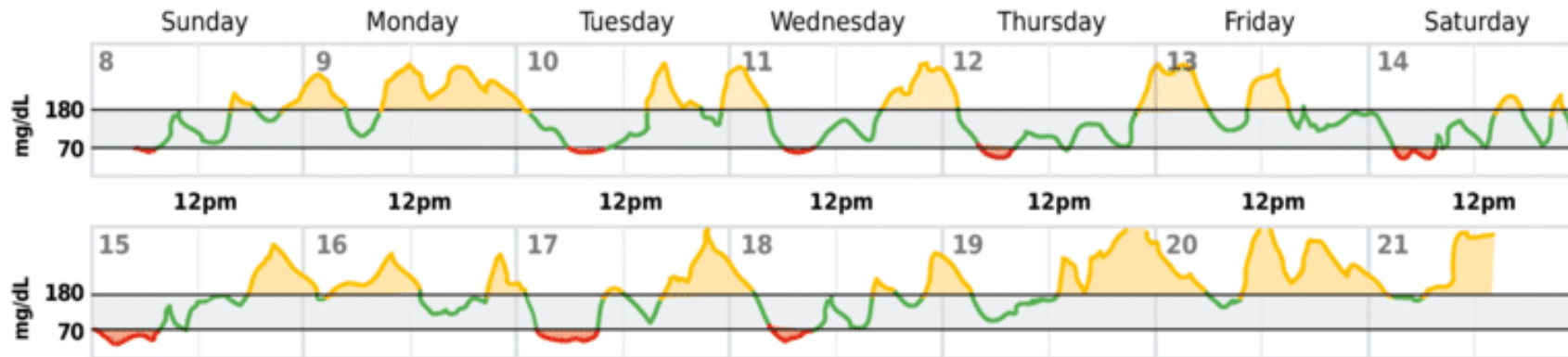
Ambulatory Glucose Profile



Daily Glucose Profile

Daily Glucose Profiles

Each daily profile represents a midnight-to-midnight period.



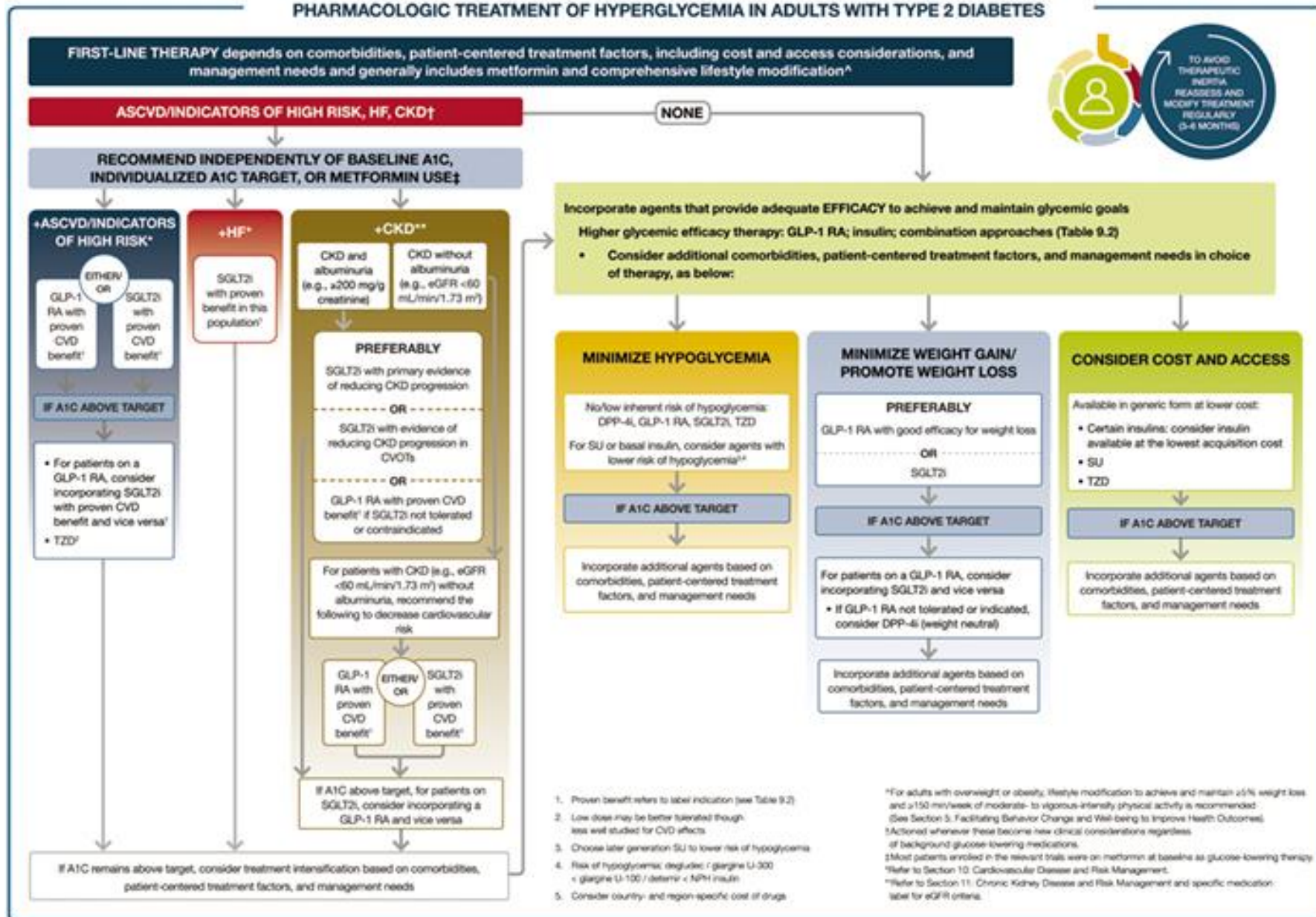
Lifestyle Management

- **Optimal nutrition and protein intake is recommended**
 - Frailty and sarcopenia risk can ↑
- **Regular exercise**
 - Aerobic activity
 - Weight-bearing exercise and/or resistance training
- **Those with T2DM who are overweight/obese and can safely exercise**
 - Intense lifestyle intervention with modest weight loss goals of 5-7%

Pharmacologic Therapy

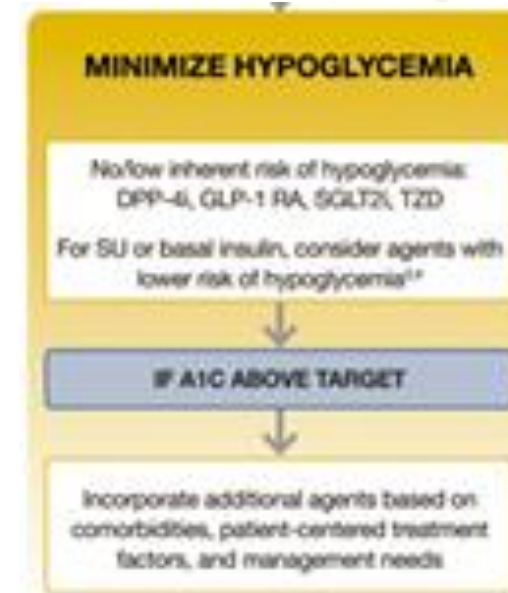
GUIDING PRINCIPLES

1. Choose medications with low risk of *hypoglycemia*.
2. De-intensify/simplify complex regimens to reduce the risk of *hypoglycemia*.
3. Consider cost and insurance coverage to avoid nonadherence.



Minimize Hypoglycemia

- Medication classes with **no/low risk of hypoglycemia**:
 - DPP-4i
 - GLP-1 RA
 - Metformin
 - SGLT2i
 - TZD
- Medication classes with **moderate risk of hypoglycemia**:
 - Secretagogues
 - Basal insulin



Dipeptidyl peptidase-4 inhibitors (DPP-4i)

- Low risk of hypoglycemia 👍
- Few side effects 👍
- Costly \$\$\$ 👎
- No CV risk reduction 👎
- Efficacy: *Intermediate*
 - A1C lowering ~0.75% 👎

Medication Options:

- Alogliptin (Nesina)
- Linagliptin (Tradjenta®)
- Saxagliptin (Onglyza®)
- Sitagliptin (Januvia®)

Glucagon-like peptide-1 receptor agonist (GLP-1 RA)

- Low risk of hypoglycemia 🍀
- ASCVD benefit 🍀
- Slows CKD progression 🍀
- Weight loss 🍀
- Costly \$\$\$ 🚫
- Significant GI side effects 🚫
- Injectable 🚫
- Efficacy: *High*
 - A1C lowering ~1-2% 🍀

Medication Options:

- Dulaglutide (Trulicity®)*^
- Exenatide ER (Bydureon®)
- Liraglutide (Victoza®)*^
- Lixisenatide (Adlyxin®)
- Semaglutide SQ (Ozempic®)*^
- Semaglutide PO (Rybelsus®)

*with proven ASCVD benefit

^with proven CKD benefit

Glucose-dependent insulinotropic polypeptide (GIP)/ Glucagon-like peptide-1 receptor agonist (GLP-1 RA)

- Low risk of hypoglycemia 👍
- ASCVD benefit ??
- Slows CKD progression ??
- Weight loss 👍
- Costly \$\$\$ 🙄
- Significant GI side effects 🙄
- Injectable 🙄
- Efficacy: *High*
 - A1C lowering ~2-2.4% 👍

Medication Option:

- Tirzepatide (Mounjaro®)

Biguanide

- Low risk of hypoglycemia 👍
- Weight loss 👍
- Cheap 👍
- Significant GI side effects 👎
- Efficacy: *High*
 - A1C lowering ~1-2% 👍

- Medication Option:
- Metformin IR (Glucophage®)
- Metformin ER (Glucophage®)
- Metformin ER MOD (Glumetza®) 👎
- Metformin ER OSM (Fortamet) 👎

Sodium-glucose cotransporter-2 inhibitor (SGLT2i)

- Low risk of hypoglycemia 👍
- ASCVD benefit 👍
- HF benefit 👍
- Slows CKD progression 👍
- Weight loss 👍
- Costly \$\$\$ 🙅
- Numerous side effects 🙅
- Efficacy: *Intermediate*
 - A1C lowering ~1-1.5% 👍

Medication Options:

- Canagliflozin (Invokana®)*+^
- Dapagliflozin (Farxiga®)+^
- Empagliflozin (Jardiance®)*+^
- Ertugliflozin (Steglatro®)+

*with proven ASCVD benefit

^with proven CKD benefit

+with proven HF benefit

Thiazolidinediones (TZD)

- Low risk of hypoglycemia 👍
- Cheap 👍
- No ASCVD, HF or CKD benefits 🚫
- Weight gain 👍🚫
- Cautionary use in HF, osteoporosis, falls/fractures, and macular edema 🚫
- Efficacy: *High*
 - A1C lowering ~1-2% 👍

Medication Options:

- ~~Rosiglitazone (Avandia)~~
- Pioglitazone (Actos®)

Insulin Secretagogues

- High risk of hypoglycemia 🚫
- Cheap 👍
- No ASCVD, HF or CKD benefits 🚫
- Weight gain 👍🚫
- Efficacy: *High*
 - A1C lowering ~1-2% 👍

Medication Options:

Sulfonylureas

- Glyburide (Glynase®)
- Glipizide (Glucotrol®)
- Glimepiride (Amaryl®)

Meglitinides

- Nateglinide (Starlix)
- Repaglinide (Prandin)

Basal Insulin

- Risk of hypoglycemia 🚫
- Costly \$\$\$ 🚫
- No ASCVD, HF or CKD benefits 🚫
- Weight gain 👍🚫
- Requires good visual & motor skills and cognitive ability 🚫
- Efficacy: *High*
 - A1C lowering unlimited 👍

Medication Options:

Long-acting insulin analogues

- Insulin glargine (Lantus®, Toujeo®, Basaglar®)
- Insulin glargine-yfgn (Semglee®)
- Insulin detemir (Levemir®)
- Insulin degludec (Tresiba®)

Intermediate-acting human insulin

- NPH (Novolin-N® and Humulin-N®)

CARDIOVASCULAR RISK FACTOR MODIFICATION

learning objective #2



Cardiovascular Treatment Goals in Older Patients

Health Status	Blood pressure	Lipids
<i>Healthy</i> <ul style="list-style-type: none"> • Few comorbidities and • Intact cognitive and functional status 	< 140/90 mmHg	Statin unless CI or not tolerated
<i>Complex/Intermediate</i> <ul style="list-style-type: none"> • Multiple (≥ 3) comorbidities or • 2+ ADL impairments or • Mild/moderate cognitive impairment 	< 140/90 mmHg	Statin unless CI or not tolerated
<i>Very complex/Poor health</i> <ul style="list-style-type: none"> • LTC or • End-stage chronic disease or • Moderate/severe cognitive impairment or • 2+ ADL impairments 	< 150/90 mmHg	Consider likelihood of benefit with statin

Hypertension Management in Older Patients

- Relax BP goals
- Encourage home BP monitoring
- Rely on:
 - Thiazides
 - ACEIs
 - ARBs
 - CCBs
- Confirm adherence before increasing doses or adding therapy

Hypertension Management in Older Patients

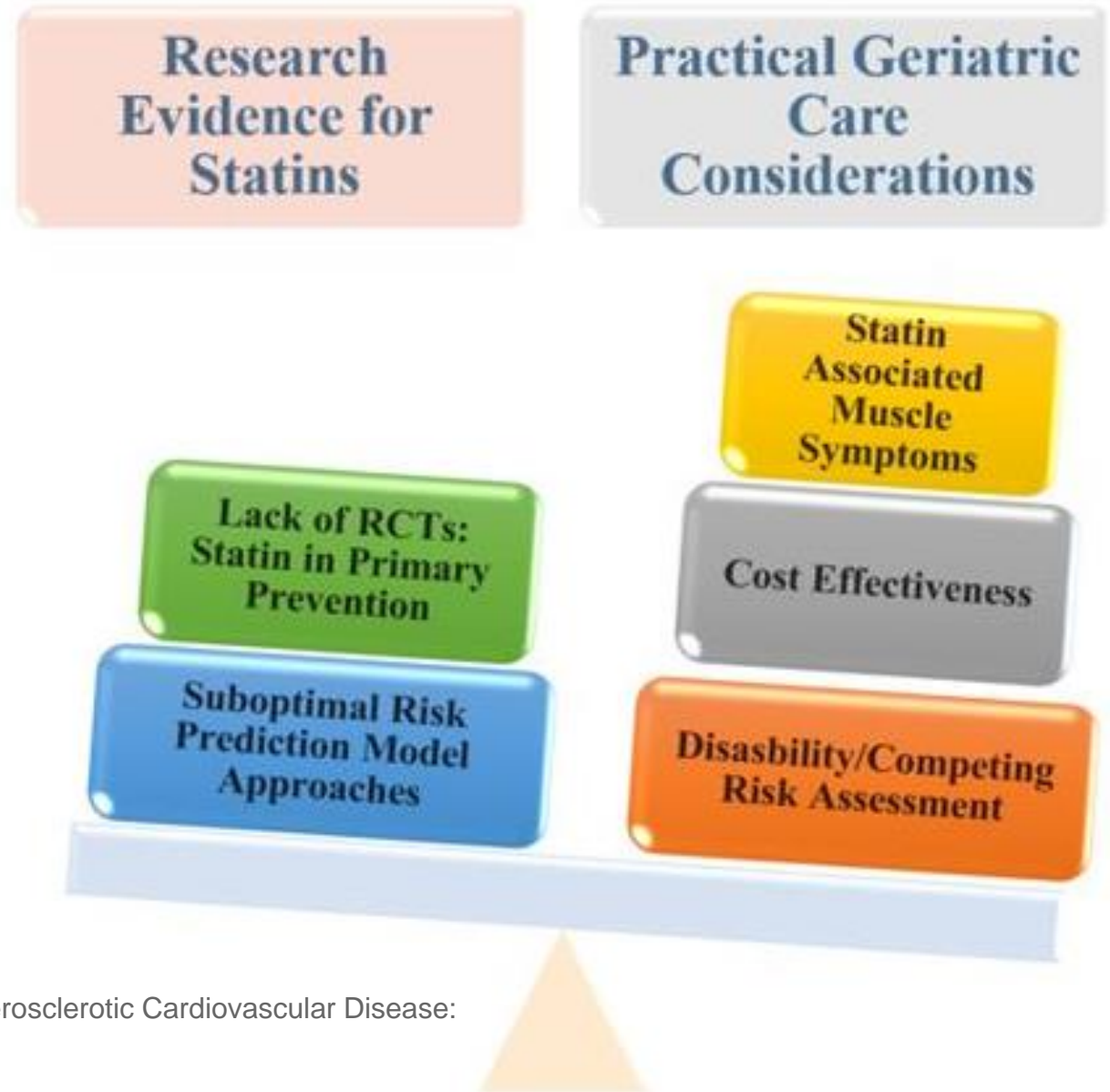
- Closely monitor sodium, potassium and renal function
- Ask about side effects
- Avoid NSAIDs
- Stay hydrated
- At least one medication should be taken at bedtime, remaining can be give QAM

Hypertension Management in Older Patients

- Avoid *Potentially Harmful Drugs in the Elderly* (Beers List)
 - Alpha-blockers → orthostatic hypotension
 - Amiloride & triamterene [when CrCl <30 mL/min] → renal impairment
 - Clonidine
 - Guanfacine
 - Methyldopa
 - Reserpine >0.1mg/d
 - Nifedipine, short-acting → hypotension, MI
- Orthostatic hypotension
- Bradycardia
- CNS adverse effects

Lipid Management in Older Patients

Barriers of statin use in older adults



Lipid Management in Older Patients

PROSPER

- Pravastatin
- Ages 70 – 82 y
- No baseline ASCVD

- ✓ ↓ LDL 34%
- ✓ ↓ MI & CV death
- ✓ ∅ stroke reduction

Ridker et al.

- JUPITER & HOPE-3
- Rosuvastatin
- No baseline ASCVD

- ✓ ↓ composite outcome by 26%

Orkaby et al.

- All statins
- US veterans (mean age 81 y)
- No baseline ASCVD

- ✓ ↓ all-cause & CV death

Zhou et al.

- ASPREE
- Age > 70 y
- No baseline ASCVD

- ✓ ∅ disability-free survival, death, or dementia
- ✓ ↓ physical disability

1. Shepherd, et al. *Lancet*. 2002;360(9346):1623-1630

2. Ridker, et al. *Circulation*. 2017;135(20):1979-1981

3. Orkaby AR, et al. *JAMA*. 2020;324(1):68-78

4. Zhou, et al. *J Am Coll Cardiol* 2020;76:17-27

Use of statins in Older Patients

- Diabetes risk →
 - Statin use is associated with diabetes risk, however...
 - Odds ratio is 1.09
 - So, after 4 years, in 255 patients, 1 case of a new diabetes diagnosis, but 5.4 vascular events would be avoided.
- Cognitive function →
 - No differences seen between statin and placebo

Aspirin use in older patients

- USPSTF recommends
 - aged 40 to 59 who are at a higher risk for cardiovascular disease (CVD) without a history of CVD should consider using aspirin.
 - Therefore, do not use aspirin for primary prevention in patients ≥ 60 years old.
- ADA recommends
 - Generally, not recommended in age >70 for primary prevention
 - ASPREE (aspirin vs placebo)
 - CV: 10.7 vs 11.3 (HR 0.95 [95% CI 0.83–1.08])
 - Major hemorrhage: 8.6 vs 6.2 (HR 1.38 [95% CI 1.18–1.62]; $P < 0.001$)
 - Patients with documented ASCVD, use of aspirin for secondary prevention has far greater benefit than risk.

1. JAMA. 2022;327(16):1577-1584. doi:10.1001/jama.2022.4983

2. Diabetes Care December 2021, Vol.45, S144-S174. doi:https://doi.org/10.2337/dc22-S010

3. McNeil JJ, et al. Effect of Aspirin on All-Cause Mortality in the Healthy Elderly. N Engl J Med. 2018;379(16):1519-1528.

HYPOGLYCEMIA AND GLUCAGON

learning objective #3

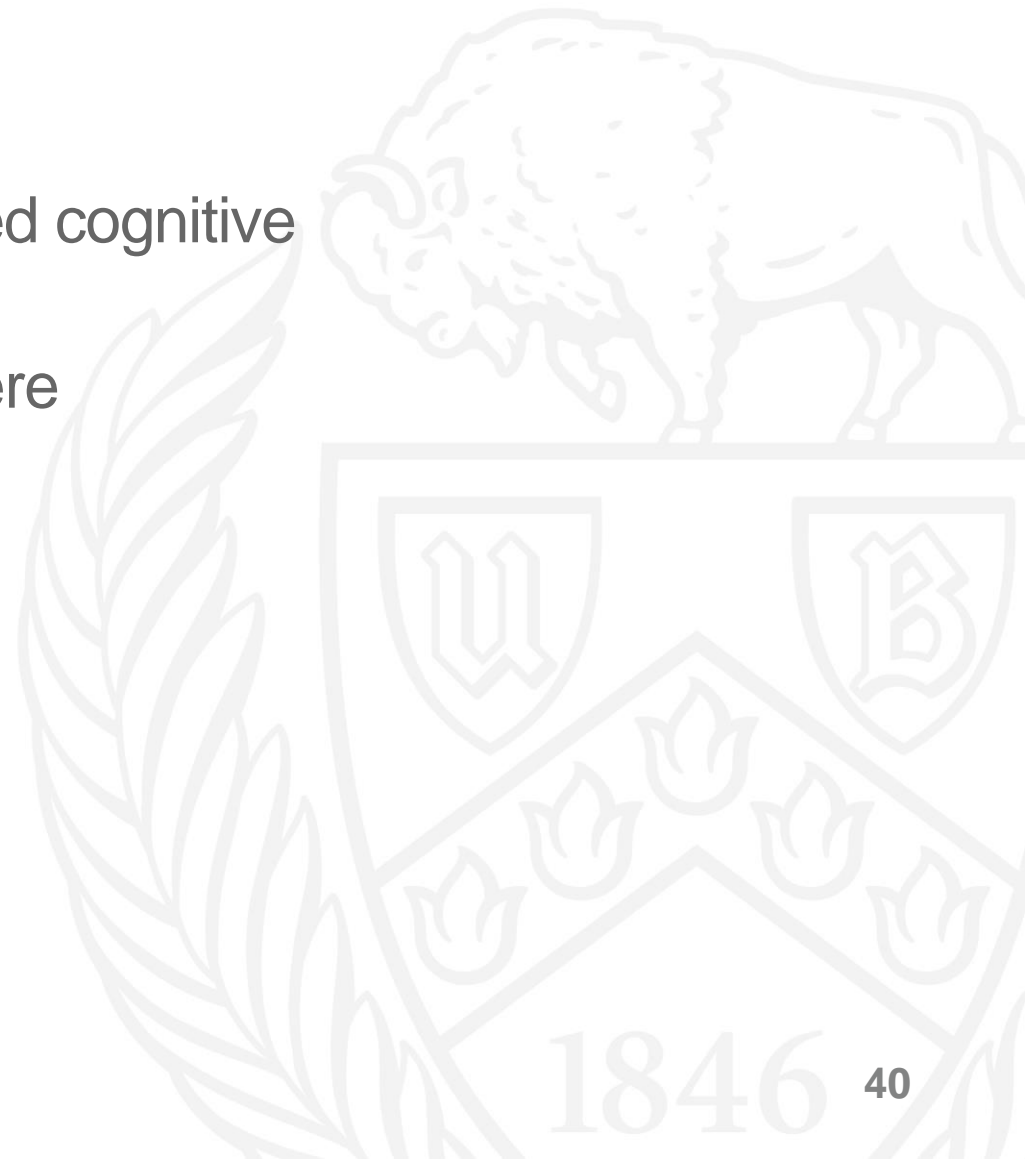


Assessing HYPOglycemic risk

- Age > 80 years
- T1DM of > 20 yr duration
- Insulin treatment
- Use of insulin secretagogues
- h/o severe hypoglycemia
- Hypoglycemic unawareness
- Reduced renal function
- Hepatic insufficiency
- Alcohol use
- Poor nutritional status
- Unpredictable food intake
- Polypharmacy
- Frailty/poor visual-motor skills
- Cognitive dysfunction or dementia
- Depression

HYPoglycemia

- Severe hypoglycemia is associated with reduced cognitive function...
- Patients with cognitive function have more severe hypoglycemia...



HYPoglycemia Classification

Table 6.4—Classification of hypoglycemia

	Glycemic criteria/description
Level 1	Glucose <70 mg/dL (3.9 mmol/L) and \geq 54 mg/dL (3.0 mmol/L)
Level 2	Glucose <54 mg/dL (3.0 mmol/L)
Level 3	A severe event characterized by altered mental and/or physical status requiring assistance for treatment of hypoglycemia

Reprinted from Agiostratidou et al. (72).

HYPOglycemia: Clinical Manifestations

Level 1 (< 70 mg/dL & \geq 54 mg/dL)

Symptoms

- Nervousness
- Anxiety
- Palpitations
- Hunger
- Tremors
- Nausea
- Angina
- Irritability
- Numbness/
tingling

Signs

- Pallor
- Diaphoresis
- Tachycardia

Level 2 (< 54 mg/dL)

Symptoms

- Sudden fatigue
- Weakness
- Feeling of coldness
- Transient hemiplegia
- Dizziness
- Headache
- Impaired mentation

Signs

- Confusion
- Amnesia
- Drowsiness
- Belligerence
- Irrationality
- Aphasia
- Seizures
- Coma
- Death

Other medication considerations

- Beta-blockers
- SSRIs
- ACE Inhibitors
- Quinolones
- Tramadol
- Quinine

1. Diabetes Care 2022;45(Suppl. 1):S46–S59
2. Ben Salem C, et al. Drug-induced hypoglycaemia: an update. *Drug Saf.* Jan 1 2011;34(1):21-45
3. Fournier J-P, et al. *JAMA internal medicine.* 2015;175(2):186-193.



HYPOglycemia Treatment



Rule of 15

Confirm
BG with
fingerstick

Consume
15g CHO

Wait
15min,
then re-
check BG

Follow up
with
substantial
snack



3–4 glucose tablets or liquid
Follow package directions, dose may vary slightly

Monosaccharide: Commercially available over the counter. Contains pure glucose. *Preferred treatment because of rapid absorption (ADA, 2017).



½ cup of fruit juice
1 tablespoon honey

Monosaccharide: Contains fructose rather than glucose



1 cup nonfat milk

Disaccharide: Contains lactose, rather than glucose



4–6 oz sweetened (nondiet) soda

Usually sucrose—disaccharide of glucose and fructose



4–5 hard candies

Potential choking hazard and difficult to ingest rapidly. Not preferred treatment. "Fruit snacks" may contain fiber that delays absorption.

Glucagon

Glucagon

Powder for solution for injection

- GlucoGen® HypoKit
- Glucagon Emergency Kit

Intranasal

- Baqsimi® 3mg

Solution for injections

- Gvoke® HypoPen
- Gvoke® PFS

Dasiglucagon

Auto-injector

- Zegalogue® 0.6mg/0.6mL

Prefilled Syringe

- Zegalogue® 0.6mg/0.6mL

Glucagon (GlucoGen® HypoKit)

- Store for up to 24 months (or to expiration date) at a temperature not to exceed 77°F
- Protect from light by keeping in original packaging
- **Administration:** powder that requires dilution with a syringe and needle to add diluent. Then dose is drawn up and injected as IM or SC
- Usual dose 1mg, use 0.5mg in children <25 kg (or if weight unknown and <6 years of age)



Glucagon (Baqsimi®)

- Store in its shrink-wrapped tube to protect it from moisture, avoid temps > 86°F
- 24-month shelf-life from date of manufacture
- Single, ready-to-use intranasal powder. Approved for ≥4 years of age
- **Administration:** insert the device tip into one nostril, then depress the plunger until the **green line** on the plunger is no longer visible
- Inhaling is not required
- Nasal congestion or use of decongestants does not affect absorption



Glucagon (Gvoke HypoPen®)

- Store in sealed pouch at room temperature
- Shelf-life is ≤ 24 months from date of manufacture
- **Administration:** prefilled autoinjector for SC administration (lower abdomen, outer thigh, or outer upper arm); push down for five seconds
- A window on the injector turns **red** when the dose has been fully administered
- Dispensed as 0.5mg/0.1mL or 1mg/0.2mL
- Each box contains 2 doses



Glucagon (Gvoke PFS®)

- Store in sealed pouch at room temperature
- Shelf-life is ≤ 24 months from date of manufacture
- **Administration:** traditional prefilled syringe for SC administration
- Remove the cap \rightarrow pinch the skin at the injection site \rightarrow insert the needle into the skin at a 90-degree angle \rightarrow push the plunger
- Dispensed as 0.5mg/0.1mL or 1mg/0.2mL
- Each box contains 2 doses



Dasiglucagon (Zegalogue®) Autoinjector

- Store in refrigerator
- Can store for up to 12 months at room temperature
 - Do not return to the refrigerator once it has been removed
- Keep in original packaging to protect from light
- Single-dose prefilled autoinjector SC administration
- 0.6mg dose ages ≥ 6 years old
- **Administration:** push the autoinjector on the skin until the **yellow needle guard** is fully pressed down (there may be a click) and holding for ten seconds
- Window turns **red** when dose has been delivered



Dasiglucagon (Zegalogue®) Prefilled Syringe

- Store in refrigerator
- Can store for up to 12 months at room temperature
 - Do not return to the refrigerator once it has been removed
- Keep in original packaging to protect from light
- Single-dose prefilled syringe SC administration
- 0.6mg dose ages ≥ 6 years old
- **Administration:** remove the cap \rightarrow pinch the skin \rightarrow insert at a 45° angle \rightarrow push the plunger



When to recommend glucagon...

- Patients at risk for Level 2 or 3 hypoglycemia
- All T1DM patients
- Older patients on insulin or sulfonylureas
- Older patients with cognitive impairment



QUESTIONS?

Thank you!

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20. Comprehensive Medical Evaluation and Assessment of Comorbidities: Standards of Medical Care in Diabetes—2022 *Diabetes Care* 2022;45(Suppl. 1):S46–S59 | <https://doi.org/10.2337/dc22-S004>
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