PRACTICAL APPROACHES TO USING CURRENT, NON-INSULIN PHARMACOTHERAPY FOR T2DM

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OBJECTIVES

- Describe risks and benefits of medications available for management of T2DM
- Describe how medications may positively or negatively impact glycemic control and associated morbidities
- Review considerations in prescribing individualized glucose lifestyle and pharmacologic management plans
- Appropriately integrate ADA and AACE diabetes guidelines

CASE 1: MURRAY

63 year old man with past medical history of severe HTN, ASCVD (stable since stent) and T2 diabetes (7 years).

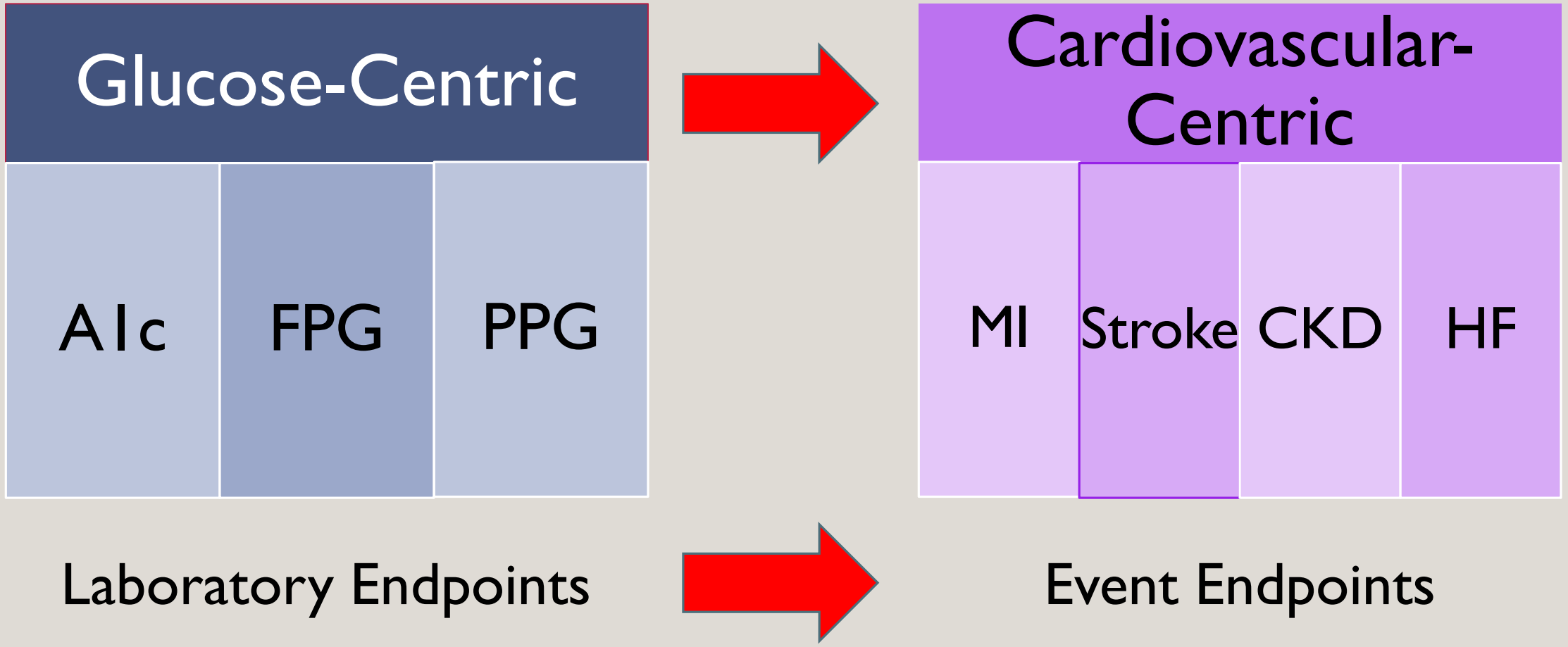
Put on metformin 5 years ago & glipizide 3 years ago no follow-up. (lower income; fears shots)

Frustrated with weight gain.

Now what?

So let's talk about T2 diabetes

PARADIGM SHIFT IN THE TREATMENT OF T2DM



While personalizing it to the patient

INDIVIDUALIZE GOALS–
THERE ARE A LOT OF *ROUND* PATIENTS SHOVED INTO *SQUARE* HOLES

- Re-evaluate often & Avoid clinical inertia
- Patient centered approach with Shared decision making
- Lower numbers may do more harm than good if higher hypoglycemia risk or excessive glycemic variability
- Ask and listen
- Barriers rather than “compliance
- Having diabetes is NOT THEIR FAULT!

POINTS TO PONDER

- Compared to persons without diabetes, persons with T2DM have:
  - 1.7 times higher risk of CV death… ***but women?***
  - 1.8 times higher risk for hospitalization for MI
  - 1.5 times higher risk for hospitalization for stroke*
  - 1.5 times higher risk of all-cause death
  - What about heart failure?*
  - Account for 60% of non-traumatic lower-limb amputations

  - Higher risk for, kidney disease, nerve damage, blindness, **NAFLD**, periodontal disease, erectile dysfunction, depression, pregnancy complications

US Centers for Disease Control and Prevention. http://www.cdc.gov/diabetes/pubs/statsreport14/national-diabetes-report-web.pdf. Accessed June 16, 2017.

BOTTOM LINE

- *Cardiologists (& nephrologists) love endocrinology*
  - ACC aligned with ADA!
  - New MACE data show positive CV impact by GLP-1 agonists, SGLT2i, and metformin
  - Focus on reducing risk of CVD and progression of DM, & CKD (DKD)

- DM leads to macrovascular disease (CVD)
- DM leads to microvascular disease (nephropathy & CKD) and retinopathy
- DM with CKD leads to greater mortality due to CVD than DM without CKD
- ***The MACE data is now driving diabetes management!***

FDA DIABETES MELLITUS GUIDANCE- 2008

Guidance for Industry

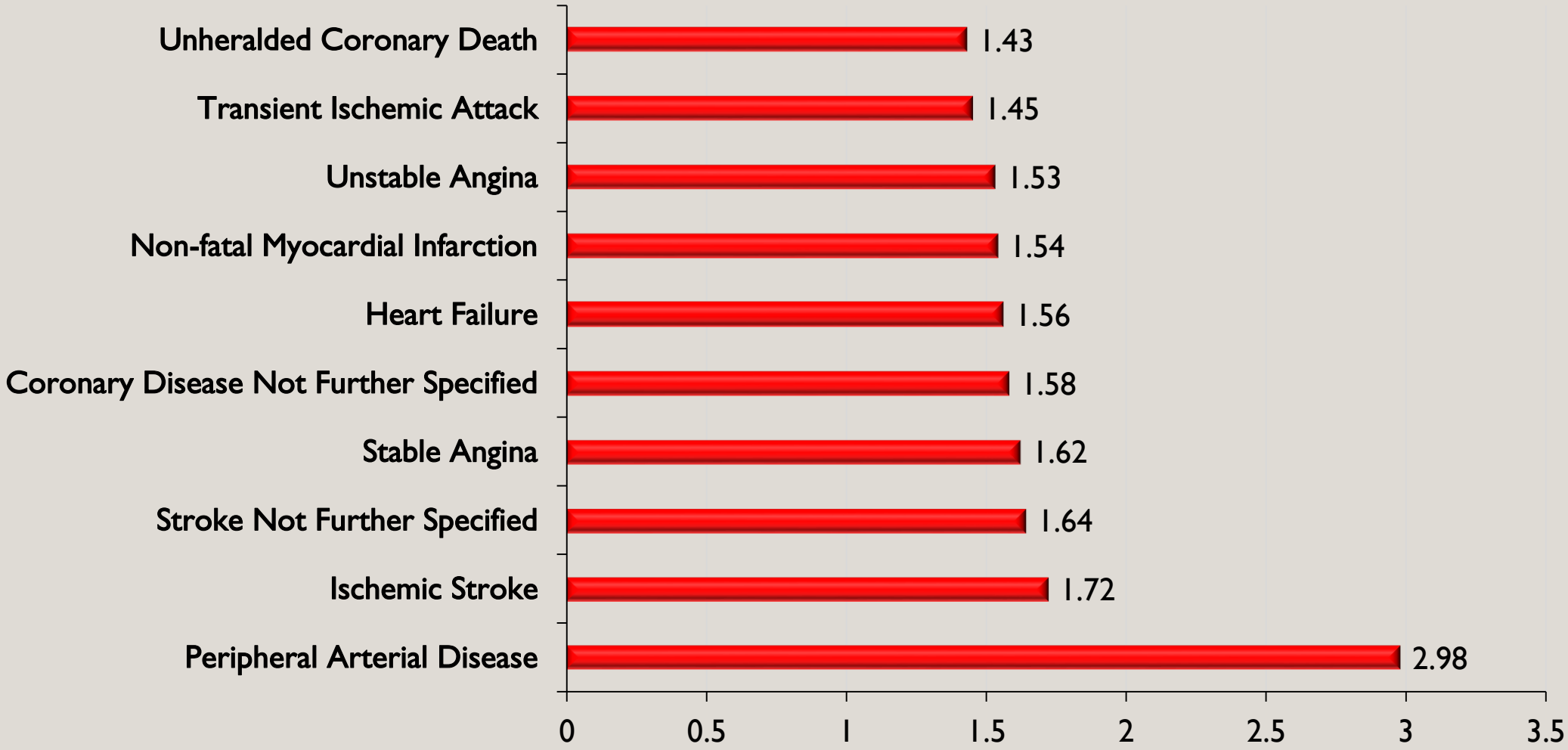
Diabetes Mellitus — Evaluating Cardiovascular Risk in New Antidiabetic Therapies to Treat Type 2 Diabetes

Provides recommendations about how to demonstrate that a new antidiabetic therapy to treat T2DM is not associated with an unacceptable increase in CV risk.

- That is, the new therapy is safe (**noninferior** to placebo)
- If so--is does it demonstrate CV benefits? (**superiority**)

US Food and Drug Administration. http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm071627.pdf. Accessed May 10, 2017.

INITIAL PRESENTATION OF CVD IN T2DM



Shah AD, et al. *Lancet Diabetes Endocrinol*. 2015;3;105-113.

Hyperglycemia → Oxidative stress

Inflammation → **Pro-thrombotic**

Increased release of cytokines (Il-6, 8, 17, 22, 23, TNFa, IFNy) VEGF

impaired NOS (nitric oxide) activity

Increase ROS

Advanced glycolation end-products (AGE)

increase fibrinogen

Altered platelet activity (decreased vWF)

Increased adhesion molecules

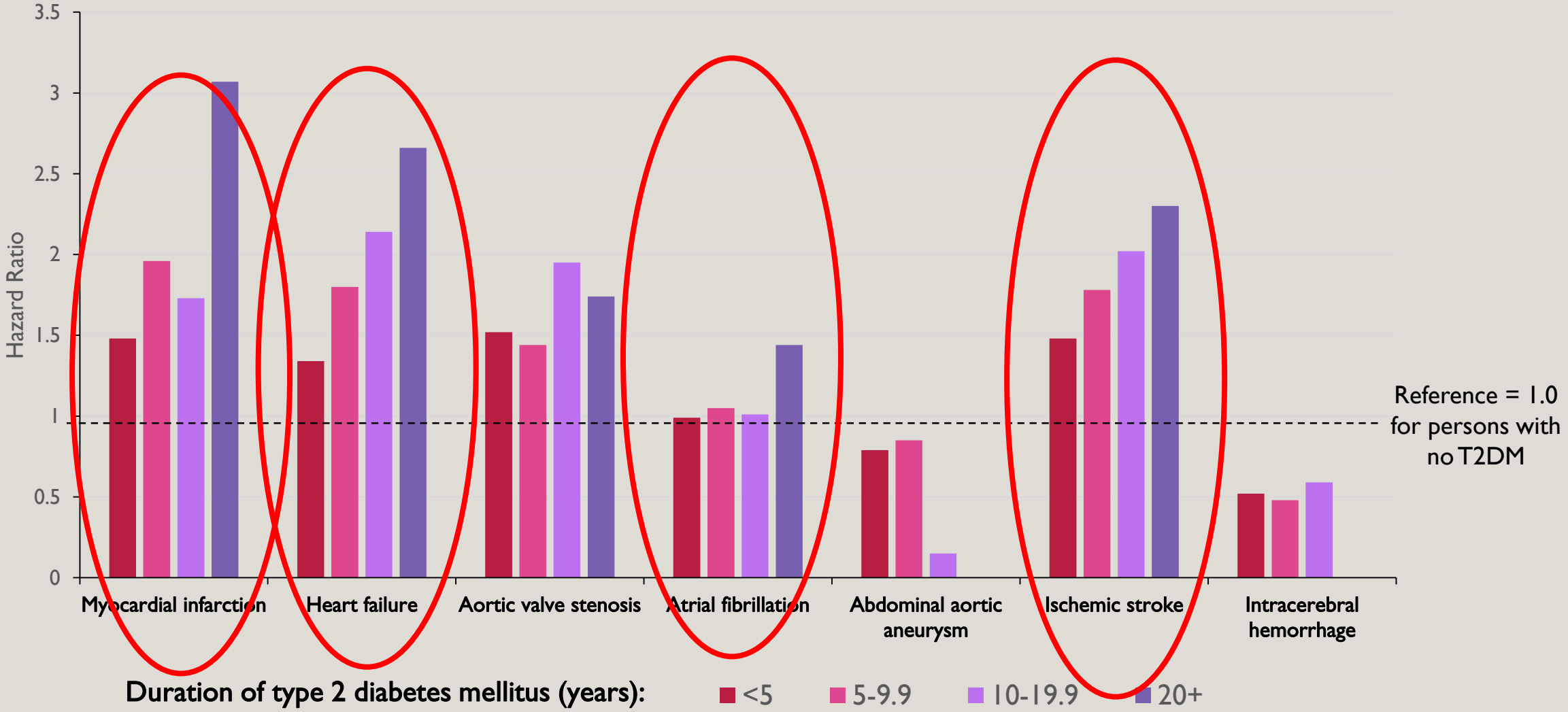
Dyslipoproteinemia

Vasoconstriction
Arterial stiffness

Clotting,
Vascular fragility
ischemia

Endothelial Dysfunction

DOES DURATION OF T2DM IMPACT CVD?



Larsson SC, et al. *Int J Cardiol*. 2018;262:66-70.

QUICK POINTS ABOUT CV SUPPORT IN T2DM

- **Lifestyle**
  - Sleep!! (sleep apnea and night shift work a BIG problem)
  - CV supporting dietary interventions (for weight loss and BG control too) *(*Safely increase
  - physical activity (cardiopulmonary impact consideration)
- **Treat underlying contributing CV risk factors (think Metabolic Syndrome)**
  - Overweight or obese (>70% of the country)—use lifestyle and anti-obesity meds
  - Dyslipidemia (*especially Triglycerides!!)*
  - Hypertension
  - Non-alcoholic fatty liver disease (NAFLD)

And consider DKD: look at UACR

- **Treat insulin resistance (IR) and hyperglycemia** – we will discuss this again
  - *Diabetes medications; ********
- **Other potential help....microbiome?**
  - *FYI: it appears that hyperglycemia causes "leaky gut" and microbiome dysbiosis*

MANAGING INSULIN RESISTANCE & HYPERGLYCEMIA

- IR and hyperglycemia are part of the Metabolic Syndrome (MetS) mosaic of systemic, messed up bio-hormonal signaling.
- The underlying result is inflammation, pro-thrombosis and endothelial dysfunction
- Must AVOID hypoglycemia!!
- Avoid weight gain! (help with weight loss?)
- **It is the glycemic swings that are believed to cause most of the endothelial micro & macrovascular damage.**

MORE ON MURRAY

BACKGROUND

- **Hx:** HTN, CAD (stent at 56), T2DM, HLD (high TGs), CKD 3 (GFR 38), albuminuria, OA, sleep apnea, NAFLD. *No heart failure*
- **FPG**: 140-160 mg/dl
- **HbA1c:** 8%
- **BMI:** 34
- **Symptoms**
  - NO CHANGE in symptoms
  - **Says he is ALWAYS hungry**

PRIOR DM TREATMENT

- **Metformin XL** 1000mg /day
- **Glipizide** 10 mg bid x 3 years

- "Reduced carb diet" was recommended
- Daily walk recommended (doing neither)

Sells insurance; sedentary d/t chronic knee pain

OKAY….

What is your immediate concern for Murray?

What to consider when prescribing:

Risk for hypoglycemia and weight gain

Will it help or hurt heart & kidneys

Cost constraints

Is he taking the medications?

Here's another reality check

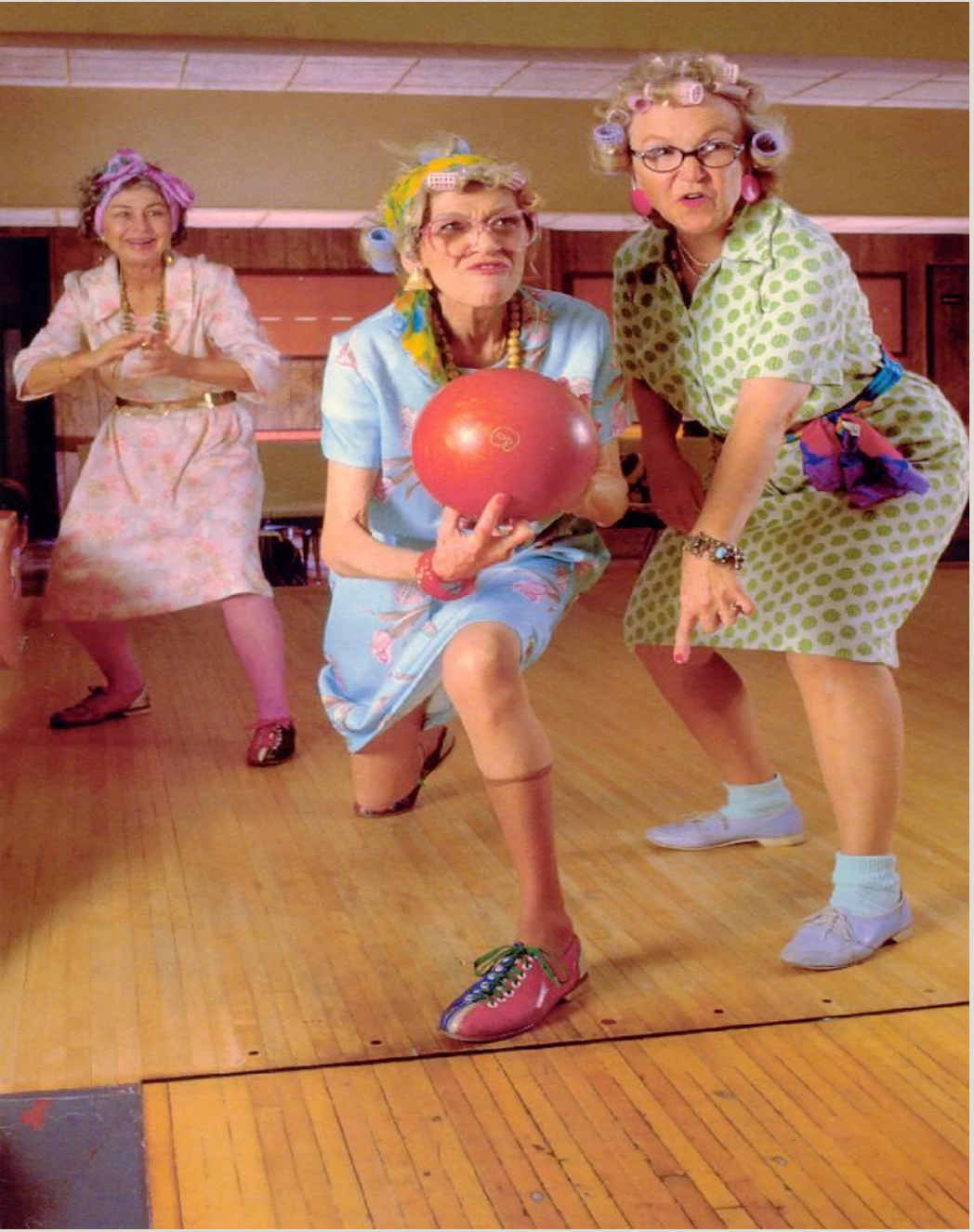
Good glycemic control does not

reduce macrovascular morbidities

But can help microvascular health

Duration "impacts" impact

American Diabetes Association Standards of Medical Care in Diabetes Glycemic targets. Diabetes Care 2023; 40 (Suppl. 1): S48-S56



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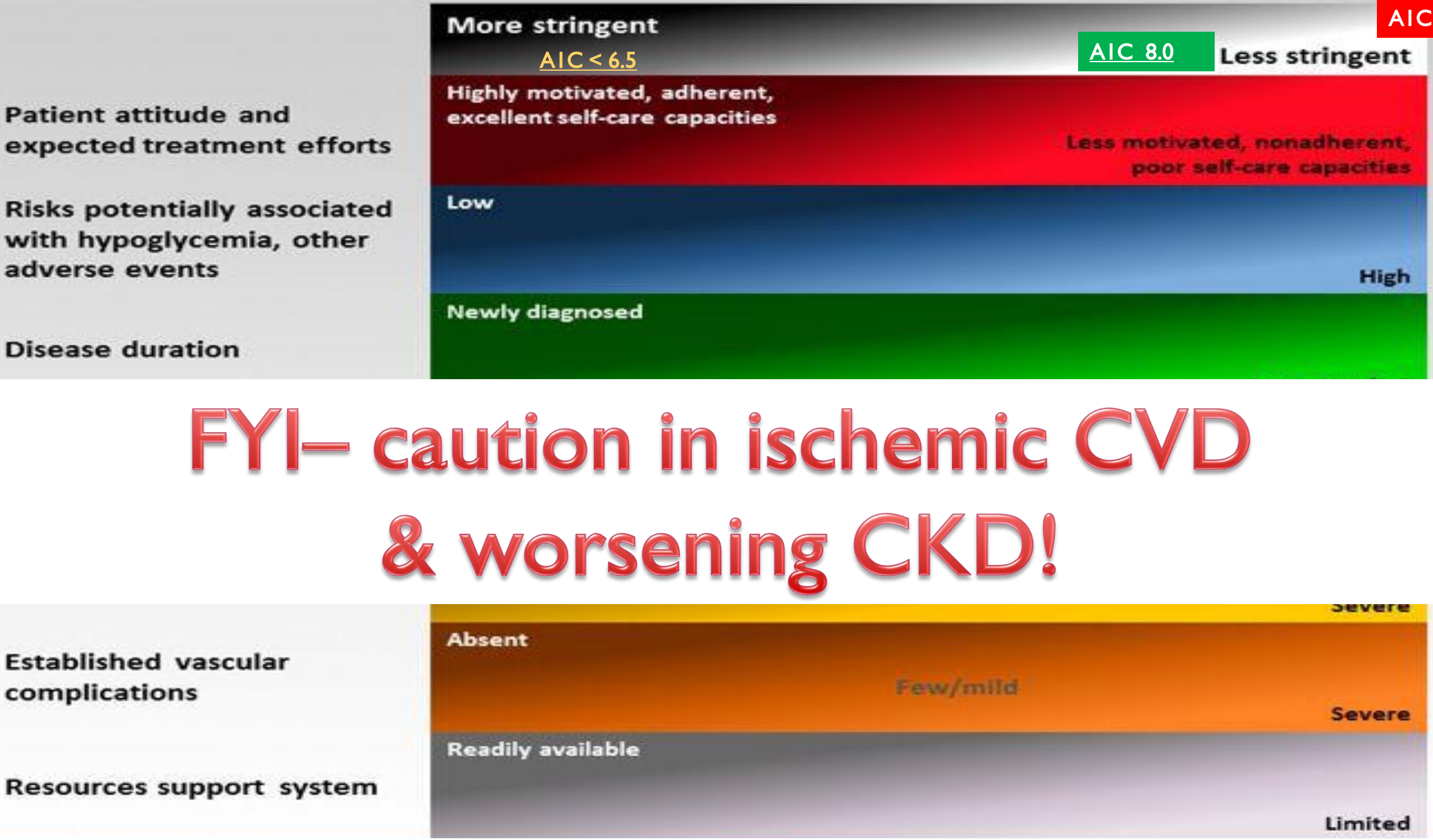
So what A1C level should we *aim* at for Murray?

Diagnosing diabetes

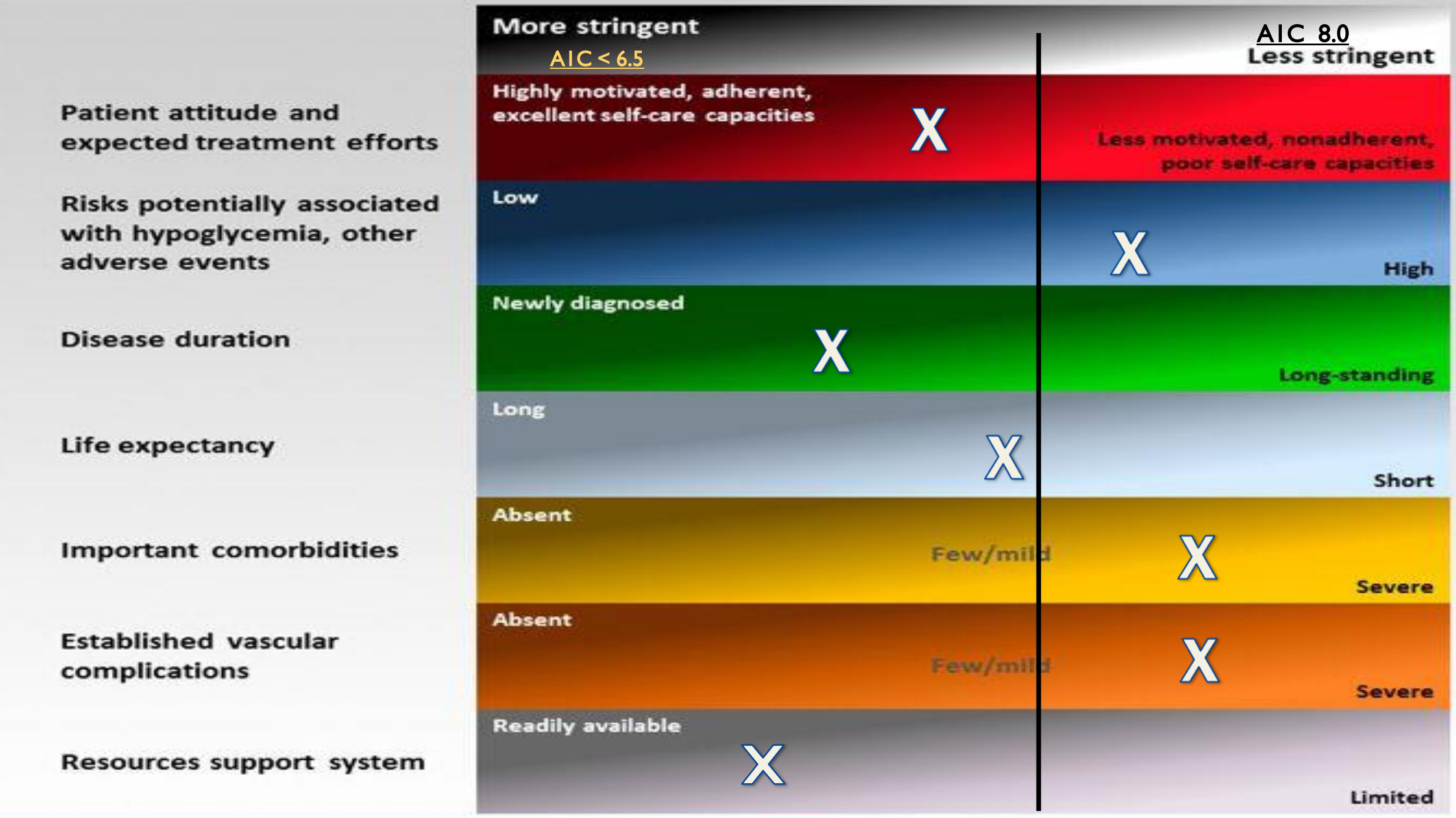
	Normal	Pre Diabetes	Diabetes
Fasting	< 100	100-125	126+
Postprandial	<140	140-199	200+
HbA1c	<5.7	5.7-6.4	6.5+

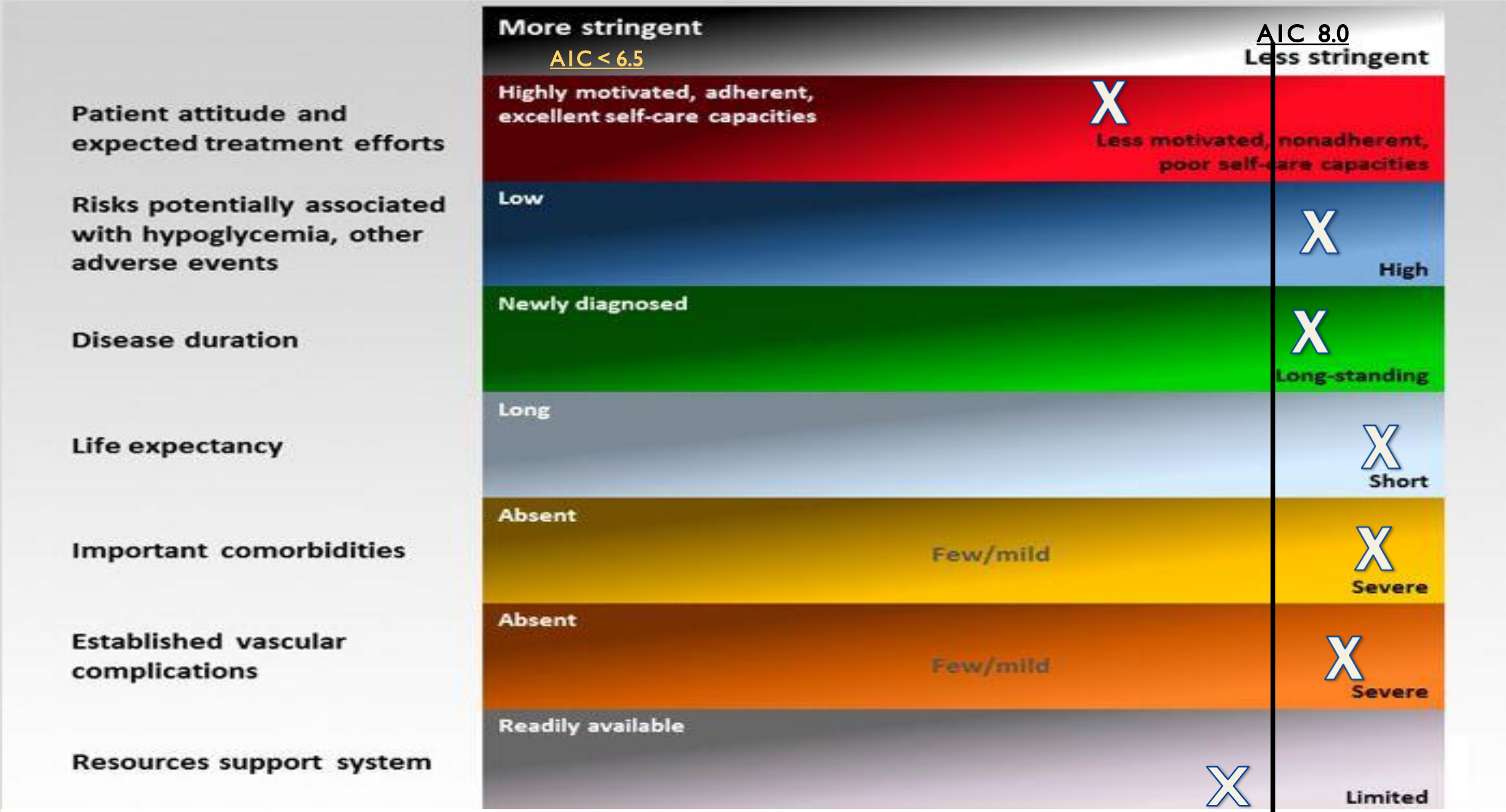
ElSayed, N. A., Aleppo, G., Aroda, V. R., Bannuru, R. R., Brown, F. M., Bruemmer, D., ... & Gabbay, R. A. (2023). 2. Classification and Diagnosis of Diabetes: Standards of Care in Diabetes—2023. *Diabetes Care*, *46*(Supplement_1), S19-S40

AIC 9%



FYI– caution in ischemic CVD & worsening CKD!





REMEMBER THE TREATMENT PRIORITIES FOR DIABETES CARE?

- Improving glycemic control
- Preventing Beta Cell failure
- Cardiometabolic health *(macrovascular)*
  - Weight (adiposity) reduction
  - Reducing NAFLD
  - Lipid & BP stabilization
  - Monitor for PAD
  - Monitor for hypothyroidism & other CMD risk
- Screening for & treatment of the "opathies" *(microvascular)*
  - Retinopathy
  - Nephropathy
  - Neuropathy (peripheral & autonomic)

Real focus on lifestyle: dietary, activity, behaviors

ADA guidelines for lipid management

Guidelines for lipid lowering in patients with DM

Patient Characteristics	LDL target
Diabetes	Less than 70 mg/dl or no greater than 55mg/dl based on CV risk
Age 40-75 with DM and 1 or more atherosclerotic RF	Reduce LDL by 50% from baseline and target less than 70 mg/dl
Addition of ezetimibe of PCSK9 inhibitor in addition to statis	LDL remains >70 mg/dl on max tolerated statin

STATIN CONCERNS IN DIABETES?

- Statins have been associated with a modest increase in risk in some people developing diabetes
- But it is believed that primary prevention of ASCVD and of ASCVD mortality
- outweigh the risks so not ADA does NOT recommend stopping the statin

WHAT ARE THE GOALS FOR BP IN T2DM?

- < 130/80 is the overall all goal suggested by the AACE guidelines 2023
- <120/70 in the presence of DKD or moderate to severe ASCVD
- Higher BP goals in the presence of autonomic neuropathy, acute coronary syndrome, or frailty
- Drugs of choice ACE or ARB; CCB, thiazide
- Dual therapy to start if BP >150./100

Weight management will be discussed in last session

SUMMARY OF TREATMENT GOALS IN TYPE 2 DM
BEYOND GLUCOSE CONTROL

Blood Glucose
A1c < 7.0%

+

Blood Pressure
<140/90 mmHg*

Blood Lipids
TG <150 mg/dL
HDL-cholesterol ≥40 mg/dL (men)
HDL-cholesterol ≥50 (women)

Body Weight
Body mass index <25 kg/m^{2**}

Cardiovascular Risk Reduction

*In individuals with diabetes and hypertension at higher cardiovascular risk (existing atherosclerotic cardiovascular disease or 10-year ASCVD risk ≥15%), a blood pressure goal of <130/80 mmHg may be appropriate, if it can be safely attained.
**<23 kg/m^2 in Asian Americans

American Diabetes Association. *Diabetes Care*. 2018;41(suppl 1):S1-S159.
American Diabetes Association. *Diabetes Care*. 2022;45(suppl 1):S1-S264.

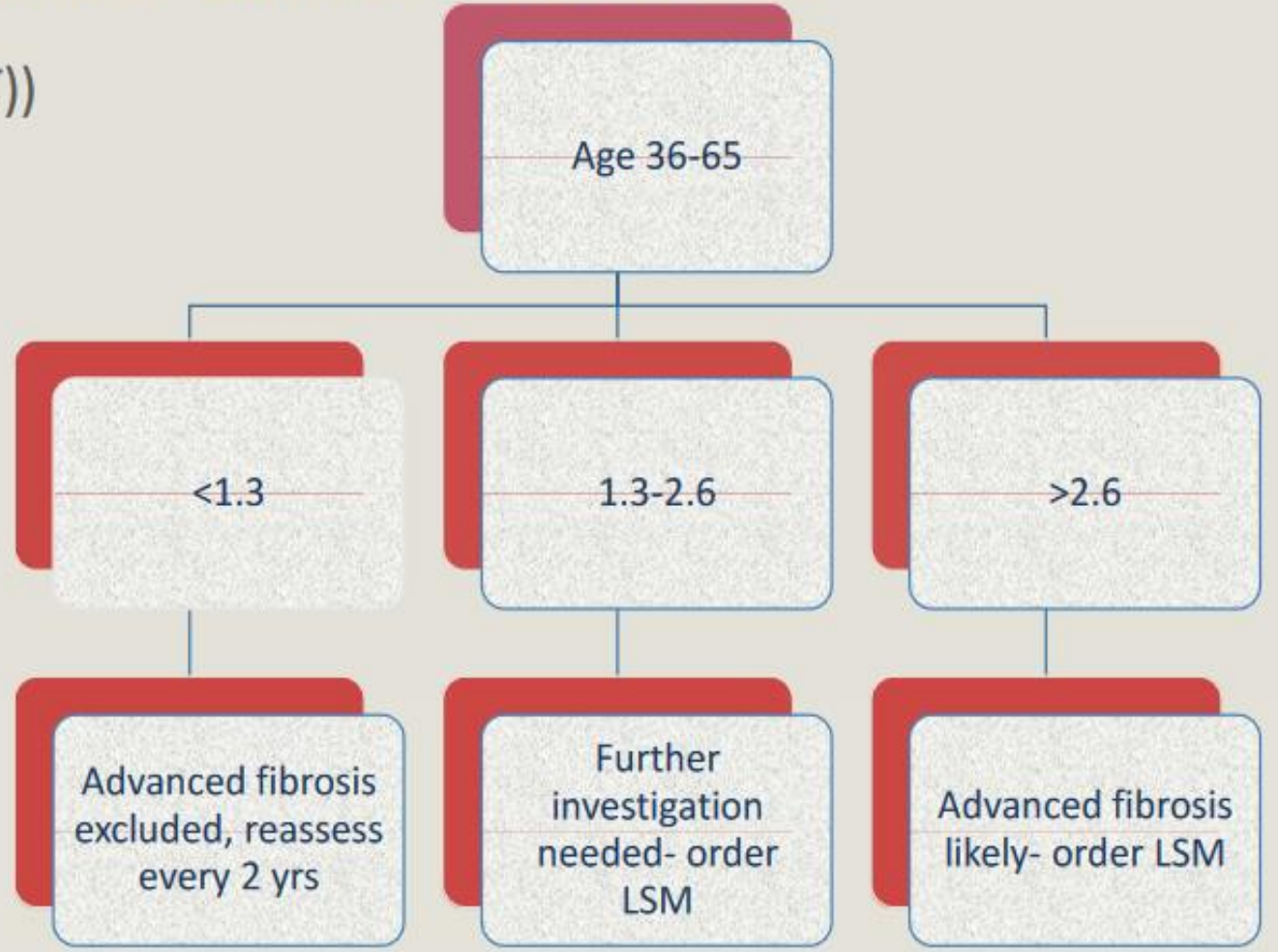
EVALUATE FOR NAFLD IN PATIENT WITH T2DM

- Diabetes major risk factor NAFLD with prevalence estimated at >70%
- NASH- >5% steatosis with inflammation hepatocyte injury with or without fibrosis and 50% prevalence in T2DM with NAFLD
- NASH #1 leading cause of hepatocellular carcinoma

Fibrosis-4 (FIB-4) Index for Liver Fibrosis

FIB-4 Score = (Age* x AST) / (Platelets x √(ALT))

- AGE (Validated for ages 36-65)
- Aspartate aminotransferase (AST)
- Alanine aminotransferase (ALT)
- Platelet Count



https://www.mdcalc.com/calc/2200/fibrosis-4-fib-4-index-liver-fibrosis

WHAT TO DO ABOUT YOUR PATIENTS WITH NAFLD

- If < 8.0 kPa or Low risk, repeat every 2 years
- Emphasize weight loss (5-10%), exercise, Mediterranean diet
  - or diet with reduced fat, starches, and added sugar
- Obesity pharmacotherapy or bariatric surgery
- Consider pioglitazone, SGLT2i, GLP1RA ,and combination GIP/GLP-1RA
- • If >8kPa- refer to Gastroenterologist or Hepatologist

So what labs or physical assessments would you do and which T2DM medications changes are best for Murray at this time?

REMEMBER THE MEDICATIONS FOR DIABETES

Biguanides
*metformin

Sulfonylureas
*glipizide
*glyburide
*glimepiride

Thiazolidinediones (TZDs)
*pioglitazone (Actos)
rosiglitazone (Avandia)

GLP-1 agonists
semaglutide (Rybelsus)

DPP-4 Inhibitors
sitagliptin (Januvia)
saxagliptin (Onglyza)
linagliptin (Tradjenta)
alogliptin (Nesina)

SGLT 2 Inhibitors
dapagliflozin (Farxiga)
canagliflozin (Invokana)
empagliflozin (Jardiance)
ertugliflozin (Steglatro)
Bexagliflozin (Brenzavvy)

And injectable incretins!!

Meglinatides
*nateglinide (Starlix)
*repaglinide (Prandin)

Alpha-glucosidase inhibitors
*acarbose (Precose)
*miglitol (Glyset)

Bile acid sequestrants
*colesevelam (Welchol)

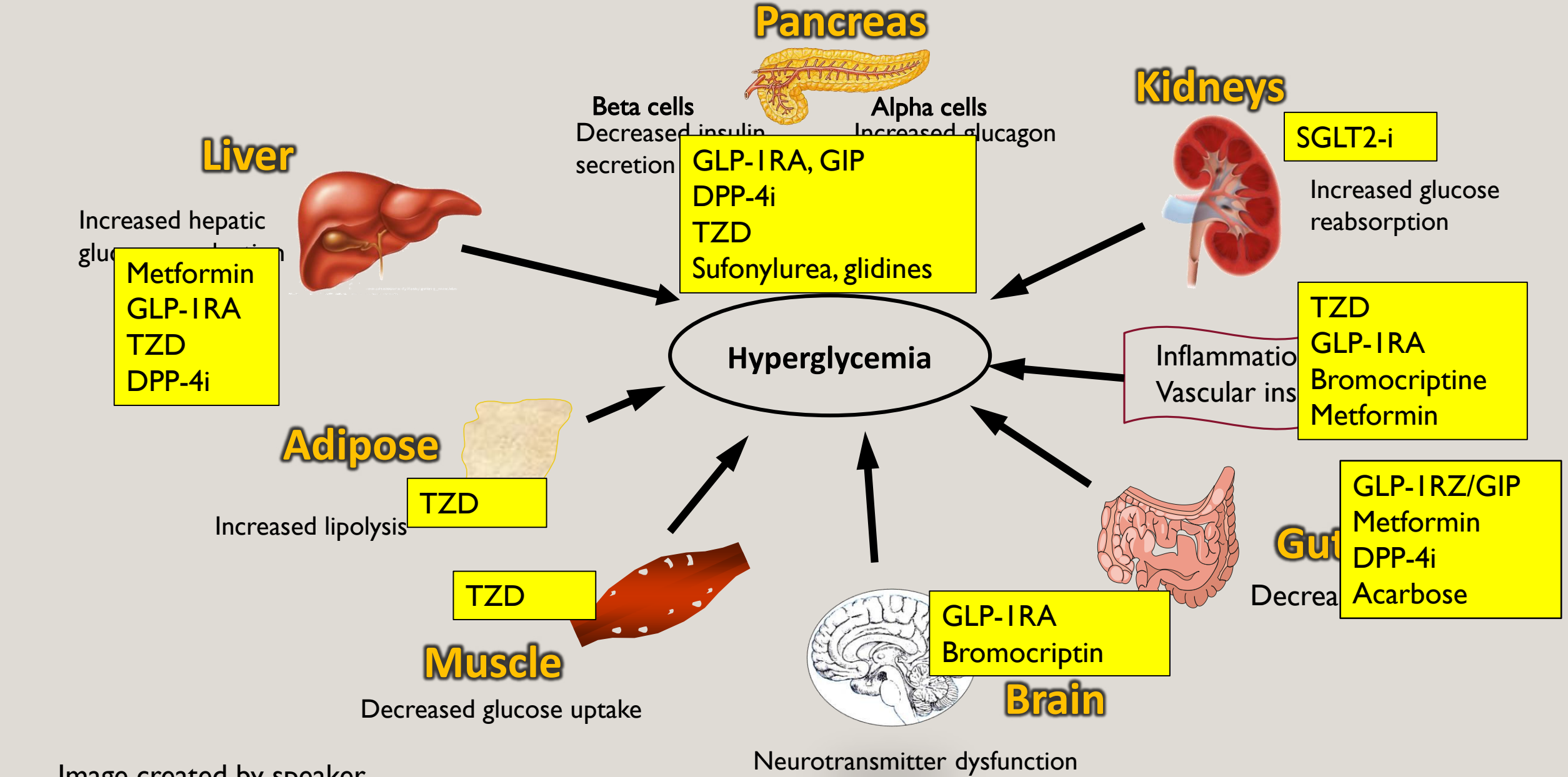
Dopamine agonist
bromocriptine (Cycloset ONLY)

* = generic available

WHEN AND HOW TO TREAT

- *When life style changes are not adequate to manage blood glucose levels, pharmacological approaches should be used*
- **Classes of Non-Insulin drugs help**
  - **Increase insulin secretion (from beta cells)**
    - **GLP-1, secretagogues, glinides**
  - **Increase glucose uptake by cells (receptor insulin sensitivity)**
    - **TZD, metformin (mild), bromocriptine (Cycloset)**
  - **Decrease glucogenolysis & glycogenesis (glucose production)**
    - **Glucagon-like peptide (GLP1 agonists), DPP4 antagonists**
  - **Decrease digestion of starch (converts to glucose)**
    - **A-glycosidase inhibitors**
  - **Decrease reuptake of glucose by kidney (pee more sugar)**
    - **Sodium glucose cotransporter-2 (SGLT-2) inhibitors SGLT2i**

PATHOGENESIS OF DIABETES & FOCUS OF DIABETES MEDS
(INFLAMMATION & INSULIN RESISTANCE)



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Metabolic Effects of Anti-DM Drugs

Don't forget these

Drug	↓Inflammation	↓Insulin resistance	↓Beta Cell demise	↓CVD risk	↓Weight / NAFLD	No Hypoglycemia risk
Metformin	✓	✓	✓	✓	✓ / ✓	✓
TZD*	✓	✓	✓	✓	X / ✓	✓
Bromocriptine	✓	✓	?	✓	✓ / ✓	✓
GLP-1	✓	✓	✓	✓	✓ / ✓	✓
SGLT2i	✓	✓	✓	✓	✓ / ✓	✓

* Thiazolidinediones (TZD), especially Pioglitazone (Actos) is weight neutral at low dose but increases weight in doses at =/> 30 mg/day.

Table created by speaker

INJECTABLE MEDICATIONS FOR DIABETES

GLP-1 agonist
liraglutide (Victoza)
dulaglutide (Trulicity)
exenatide ER (Bydureon, Bcise)
exenatide (Byetta)
Semaglutide (Ozempic)

GLP-1/GIP agonist
tirzapetide (Mounjaro)

Basal Insulin
insulin glargine u100*
(Lantus, Basaglar)
insulin detemir u100 (Levemir)
insulin glargine u300 (Toujeo)
insulin degludec u100 or u200
(Tresiba)

Rapid Acting Insulin
insulin glulisine (Apidra)
insulin lispro u100 or u200
(Humalog)
insulin lispro-aabc u100or u200
(Lyumjev)
insulin aspart (Novolog, Fiasp)
insulin human inhaled (Afrezza)

Regular Insulin
insulin regular human u100
(Humulin R, Novolin R, Relion R)
Insulin regular human u500
(Humulin R u500)

Intermediate Insulin
Human insulin isophane, aka NPH
(Humulin N, Novolin N,Relion N)

Split mixes
Humulin 70/30 (70% NPH, 30% regular)
Novolin 70/30 (70% NPH, 30% regular)
Relion 70/30 (70% NPH, 30% regular)
Humalog 50/50 (lispro /lispro protamine)
Humalog 75/25 (75% lispro protamine, 25% lispro

Mixed injectables – GLP1 and basal insulin
insulin degludec and liraglutide (Xultophy)
insulin glargine and lixisenatide (Soliqua)

Amylin mimetic
Pramlinitide (Symlin)

*Indicates units per mL:
u100 = 100 units/mL,
u300 = 300 units/mL, etc.

METFORMIN

Would you keep Murray on Metformin?

Once initiated, metformin should be continued as long as it is tolerated and is safe.
Other agents, including insulin are added to metformin.

RECALL METFORMIN USE IN CKD

EGFR (ML/MIN/1.73 M2)	WHAT YOU SHOULD CONSIDER
≥ 60	No renal contraindication (regardless of creatinine); Monitor GFR annually
≥ 45 and ≤ 60	Continue use; monitor GFR every 3-6 months
<45 and > 30	Initiating metformin not recommended Use lower dose (50% maximum dose) Monitor GFR every 3 months
<30	Metformin contraindicated--stop

Exercise caution in patients low muscle mass or on concurrent nephrotoxic drugs (e.g. NSAIDS)

Cochrane Database Syst Rev. 2017 Feb 3;2:CD011880. doi:10.1002/14651858.CD011880.pub2

If Murray has GFR <30 and a lot of insulin resistance and he needs a sensitizer…

Consider using a TZD

Like pioglitazone (Actos)

Low dose

Unless patient has beta–cell burn out, insulin resistance will present with High C-PEPTIDE levels

GENERAL AGREEMENT THAT FOR PEOPLE WITH ASCVD AND/OR HEART FAILURE USE:

- **GLP-1RA or GLP-RA/GIP combo**
  - If ASCVD predominates
- **SGLT-2i**
  - If heart failure predominates
    - Also for kidney protection

Folks—these are the GO-TO drugs in diabetes!

GLUCAGON-LIKE PEPTIDE RECEPTOR AGONIST (GLP-1RA)

- **Mechanism:** Delayed gastric emptying, improved glucose-dependent insulin secretion, gut- brain axis effects on weight, decreased glucagon response
- **Contraindications**: Personal or family hx of medullary thyroid CA or
- **Serious Adverse reactions**: Pancreatitis (rare)
- **Common Side effects**: Nausea/GI upset/dyspepsia, Constipation/diarrhea, **Monitoring**: Renal function at initiation and consider if severe GI sx, A1c q3-6 months, watch for signs/symptoms of pancreatitis, retinal exams (retinopathy)
- DON'T COMBINE WITH DPP-41 or other GLP-1s
- TITRATE SLOWLY

Tips for using

Available GLP-1RAs

Agent	Frequency	Starting & titration	Therapeutic dose	Renal Adjustments
exenatide	Twice daily (within 60 min before 2 meals ≥6 hrs apart)	5 mcg ≥ 1 month	5 mcg or 10 mcg	Caution with CrCl 30-50 mL/min. Do not use if CrCl <30
exenatide ER	Once weekly	2 mg	2 mg	Not recommended CrCl <45
dulaglutide	Once weekly	0.75 mg, increase every 4 weeks	0.75 mcg, 1.5 mg, 3 mg or 4.5 mg	Caution in impairment
liraglutide	Once daily	0.6 mg, increase by 0.6 mg each week	1.2 mg or 1.8 mg	Caution in impairment
lixisenatide	Once daily	10 mcg once daily for 14 days then increase to 20 mcg daily	20 mcg	GFR<15 not recommended, caution in impairment
semaglutide	Once weekly	0.25 mg for 4 weeks, 0.5 mg at least 4 weeks	0.5 mg or 1 mg	None
tirzapetide GLP-1/GIP	Once weekly	2.5 mg once weekly 4 weeks, then increase 2.5 mg/week increments every 4 weeks	5-15 mg	None

Semaglutide PO (Daily 3 mg PO /Day x30 days Then increase to 7 mg/d 3-7 mg None

GLP-1RAS: CV OUTCOME TRIALS

Medication	CVOT	Use/ Prevention	CV Safety vs Placebo	MACE*	HF Benefit	Renal Benefit
Dulaglutide	REWIND	1° & 2°	✓	✓	✓	✓
Exenatide once-weekly	EXSCEL	1° & 2°	✓		✓	
Liraglutide	LEADER	1° & 2°	✓	✓	✓	✓
Lixisenatide	ELIXA	2°	✓		✓	
Semaglutide	SUSTAIN 6 (SC)	1° & 2°	✓	✓	✓	✓
	PIONEER 6 (PO)	1° & 2°	✓			

*CV reduction vs placebo for composite of CV death, nonfatal MI, nonfatal stroke

Sodium-glucose cotransporter-2 (SGLT2) inhibitors

Available agents: canagliflozin (Invokana), dapagliflozin (Farxiga), empagliflozin (Jardiance), ertugliflozin (Steglatro), Bexagliflozin (Brenzavvy)

Dosing: Taken once daily before first meal of the day.

Mechanism: Impair re-uptake of glucose in renal tubules

Common side effects: increased urinary frequency, some UTI or mycotic infections, dizziness or lowered BP

Cautions: increased risk of bone fractures (canagliflozin and dapagliflozin), electrolyte imbalances, acute renal injury, ketoacidosis (can be normoglycemic), necrotizing fasciitis of the perineum (aka Forurnier gangrene), increased risk of amputation

Monitoring A1c, renal function (before initiating, 3 months, then annually or as clinically indicated or q3 months if GFR <60), volume status (BP)

Tips on using

SGLT2-I Dosing

Agent	No renal impairment	Mild	Moderate/Severe	ESRD or dialysis
bexagliflozin	20 mg once daily	No adjustment GFR >30	Not recommended if GFR <30	Contraindicated
canagliflozin	Start 100 mg May increase to 300 mg	GFR 30-60: Max 100 mg	GFR<30 – with albuminuria may continue 100 mg	Contraindicated
dapagliflozin (also labeled for CKD, HF)	Start 5 mg May increase to 10 mg Can start at 10 if CKD or HF	GFR 25-<45: not recommended for DM but no dose adjustment for HF, CKD	May continue if already on for HF, CKD	Contraindicated
empagliflozin (also labeled for HF)	Start 10 mg May increase to 25 mg	No adjustment GFR >30;	GFR <30 not recommended but HF benefits at 10 mg until <20	Contraindicated
ertugliflozin	Start 5 mg May increase to 15 mg	GFR >45 no adjustment	Stop if GFR persists <45	Contraindicated

Remember to hydrate!

A REMINDER ABOUT BONE CONCERNS

- Diabetes increases fracture risk
- SGLTs and TZDs may further increase risk – weigh risk/benefit
- Get DXAs when indicated

A word about other DM meds..

DPP4-antagonists

Mechanism: Impairs breakdown of GLP-1, which slows gastric emptying, reduces inappropriate glucagon secretion, stimulates insulin secretion response – incretin

Cautions: Use with caution if history of pancreatitis; Increased risk of hospitalization for heart failure with saxagliptin, alogliptin

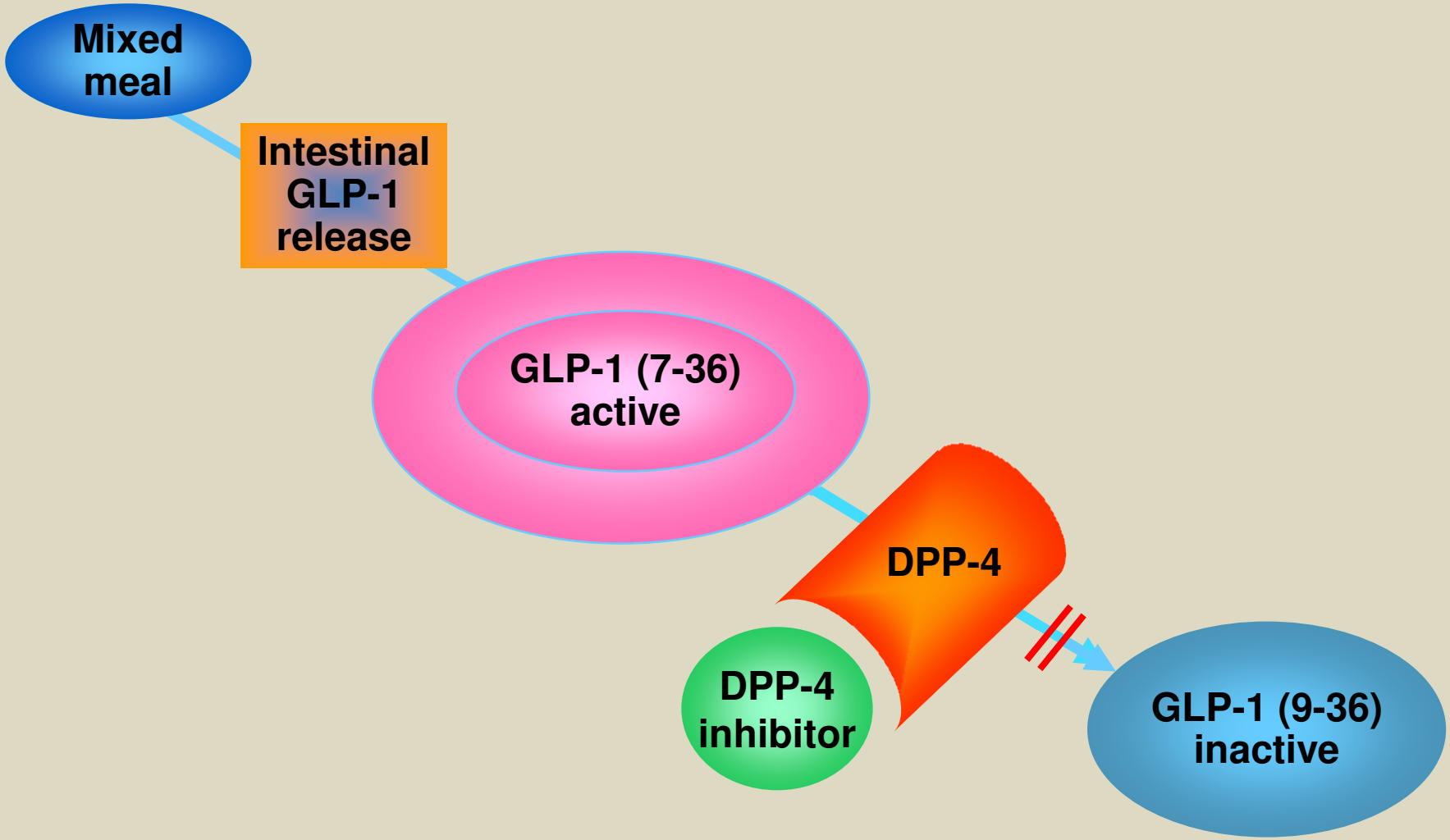
Adverse reactions: Joint pain, pancreatitis

Common side effects: GI upset

Monitoring: A1c q3-6 months; renal and liver function prior to initiation and as clinically indicated; signs and symptoms of HF and pancreatitis

Tips for use

Inhibition of DPP-4 Increases Endogenous GLP-1



Adapted from Rothenberg P, et al. *Diabetes*. 2000;49(suppl 1):A39.

DPP4i Dosing

Available agents: Sitagliptin (Januvia), saxagliptin (Onglyza), linagliptin (Tradjenta), alogliptin (Nesina)

Dosing:

Agent	GFR ≥60	Renal impairment	
sitagliptin	100 mg	50 mg if GFR 30 to <45	25 mg if GFR <30
saxaglipitin	2.5mg or 5 mg (effect and tolerance)	2.5 mg recommended with GFR ≤45 mL/min	
linagliptin	5 mg	No renal adjustment	
alogliptin	25 mg	12.5 mg with CrCl 30-60 mL/min	6.25 mg with CrCl <30 mL/min

MORE POINTS ABOUT DPP4-INHIBITORS

- **Oral agents—well tolerated**
- *Works well in early T2DM and elderly*
- **Weight neutral**
- Expensive
- **Class Concerns:**
  - Rhinitis,
  - Chronic inflammatory skin issues (class IV allergies)
  - Pancreatitis?
  - Arthralgias
  - Others

What if Murrary was uninsured
and could not afford these cool newer diabetes drugs?

Can you still use a secretagogue?

Are they CV safe?

YES---THESE DRUGS WORK & ARE CHEAPER BUT ARE MORE RISKY

- Secretagogues— *release insulin*
  - **Sulfonylureas**
    - Glyburide (Glynase), **glipizide (Glucotrol), glimeperide (Amaryl)***
    - *Basal and prandial support*
  - **Metiglinide analogues** *(fast release)*
    - **Repaglinide (Prandin)***, nateglinide (Starlix)
    - Prandial support

SULFONYLUREAS—WHAT YOU SHOULD KNOW

- Vary in metabolism & elimination
- **Careful use in CKD & ischemic heart disease!!**
- ***Hypoglycemia risk!!***
  - ***Must feed!*** **Affects prandial and basal sugar**
  - Weight gain
- **Avoid glyburide in ischemic heart & CKD and elderly**
- Decrease glimeperide to 1 mg in CKD 3a-5 **(but better in CAD)**
- **Less renal dose adjusting with glipizide**

Sulfonylureas increase risk of all mortality by 26% & CV mortality by 46% per the CREST study

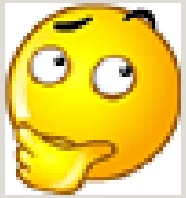
clinicalendocrinologynews.com 10(11) 2015

Can you still use them safely?

Cut dose in half (or stop) if starting GLP-1RA, SGLT2i, or insulin with it

A LITTLE SAFER SECRETAGOGUES?

- **Meglitinides** (pancreas *pops*)
  - Repaglinide (Prandin)*, nateglinide (Starlix)
  - Prandial support
  - Hypoglycemia risk if dose too high and not eat
  - ***Take with meals (or just biggest meal of day)***
  - ***R*apaglinide (Prandin) best in CKD (can use if GFR <30)!!!!**
    - Doses 0.5, 1, 2, 4 mg –generics are CHEAP
- Can you use them in DKD??
- Tips for use



Okay…how do you help the following patients?

KATHY

52 y/o with 10 year hx of T2DM (never controlled)

- **LABS**: *A1C 8.2, GFR 49, mild nephropathy,* (UACR 43) slightly elevated LFTs, TGs 500, HDL 36, TSH 5.8, normal CBC
- **TODAY**: BG in clinic was…242 mid morning (3 hrs PP). Had eaten Egg McMuffin-no fries. Reports that she took her meds.
- *Has lost some weight on Liraglutide*
- **HX**: Obesity (BMI 35), HTN, hypertriglyceridemia, hypothyroidism, depression, fibromyalgia, knee OA, PVD with edema, hx of gestational DM
- **RX**: Metformin 2000 mg/d; liraglutide 1.8 mg; ARB, HCTZ, PPI, citilapram, NSAIDs, synthroid

Is she in reasonable glycemic control?

What likely interferes with her BG control?

WHICH OF THE FOLLOWING CHANGES WOULD/ COULD YOU MAKE?

- Reduce metformin to 1000 mg/day
- Stop liraglutide
- Increase liraglutide dose
- Change to semaglitide (weekly SC or daily PO) or other GLP-1ra
- Start SGLT2-I
- Start low dose pioglitizone
- Start basal insulin

ANNA

54 y/o black, Hispanic woman seen for DM follow-up. Feels "sugars are bad" – goes "low" when she doesn't eat, gaining weight, so inconsistent with meds.

BACKGROUND

- **Hx** of MI at 48, T2DM diagnosed then
- Married; she is a school bus driver
- **BMI 31**
- **Diagnosed with**
  - **Diabetes (Hb A1C: 9.2; FBG ~200 mg/dl)**
  - **CAD with cardiomyopathy (EF 34)**
  - Hypertension (170/90)
  - Elevated triglycerides (393)
  - Depression/anxiety
  - Surgical menopause at 41
  - **GFR 46**

TREATMENT

- **Metformin** 500mg X2 daily (worried about a higher dose d/t GI issues)
- Changed to **Glimepiride** 8mg + **Metformin 1000g**
  - **Cost had been a concern**
- Atorvastatin
- Lisinopril, hydralazine, Lasix, metoprolol
- Paroxetine

WHAT CHANGES WOULD YOU MAKE FOR ANNA?

CONSIDER SHE IS A SCHOOL BUS DRIVER

- Would you add another medication?
  - If so….WHAT preferred drug would you add and why?
- Would take her off glimeperide?
- Would you stop, decrease or increase metformin?
- What about insulin?

Great pt for CGM

ANITA

- 83 y/o woman still self employed (antique dealer), lives alone with her dog.
- T2DM x 3 years controlled by diet
  - **A1C was 6.7**
  - Now **A1C has climbed to 7.5.**
  - *FBS 128-149, post prandial sugars 198-230*

HX: HLD, HTN, *Ischemic CAD*, *CKD (GFR 30),* nephropathy, spinal stenosis/pain, GERD, asthma, Hashimoto's hypothyroidism, psoriasis

Social: Vision issues (MD), Mentally SHARP, walks with cane for mild balance issues

Rx: statin, metoprolol, ASA, gabapentin, PPI, inhalers, levothyroxine, vitamins,

On NOTHNG for DM

WHAT WOULD YOU DO FOR HER DIABETES

- GLP-1RA
- SGLT2i
- Metformin
- TZD
- DPP4i
- Glinides
- Acarbose
- Nothing
- Something else

Here's the rest of the story

Let's see what you can do with these next "mystery cases"

Hint: cancer, pre-gestation, etc

ADA POINTERS ON T2DM RX

- Intensification of T2DM treatment not meeting treatment goals should not be delayed!!
- Reevaluated medication Rx at regular intervals (every 3–6 months) and adjust as needed
- If new patient with T2DM and an A1C > 1.5% over target—start 2 anti-hyperglycemic drugs!

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ADDED RESOURCES

- American Association of Clinical Endocrinologists
  - https://pro.aace.com/
- American Diabetes Association Standards of Care
  - https://professional.diabetes.org/content-page/practice-guidelines-resources

Is your brain fried?

Okay, lets stop for a while