Staying out of Death Valley….
of Complications

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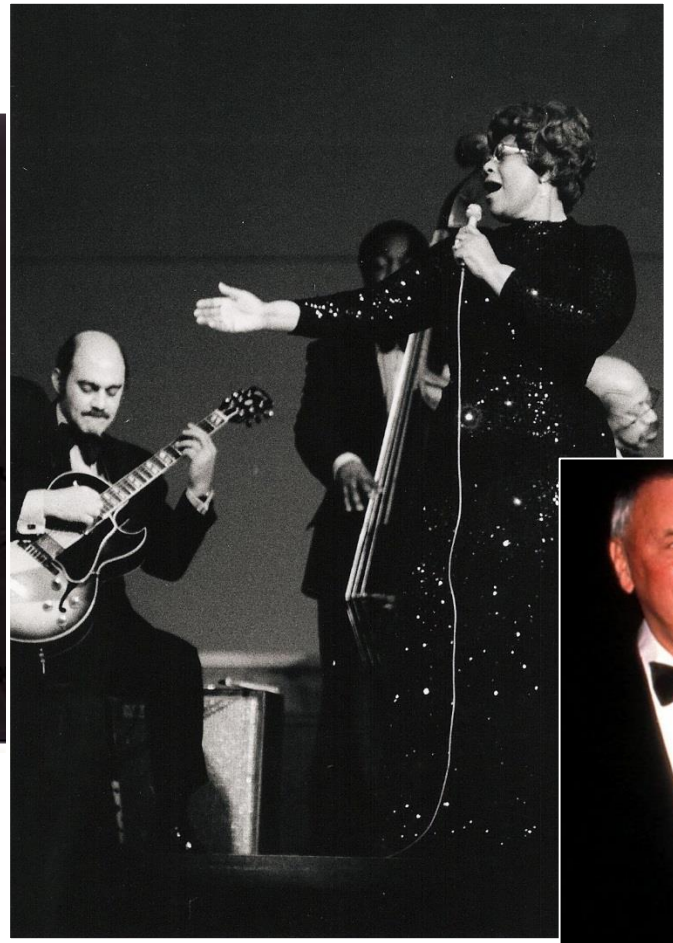
Cue: Dream a Little Dream of Me.

Ella Fitzgerald

You know Ella Fitzgerald….

1947

1968



1974

1986

Ella - 1986

- Age: 69 years old
- Emergency coronary bypass surgery after presenting with congestive heart failure
- Diagnosed with T2DM as part of pre-op
- A1C = 12.6%
- Discharged on NPH and Regular insulin, bid
  - Uptitrated to 30/20 U am and 30/20 U before dinner

Ella's Follow-up with Primary Care

- 8 wk post-discharge (2 prior follow-ups)
- A1C is down from 12.6% to 10.1%
- Glucose records, fasting and bedtime
  - Fasting: 122 – 198 mg/dL
  - Bedtime: 185*– 386 mg/dL

*If she took her insulin and didn't have a performance.

Ella's Follow-up with Primary Care

- 8 wk post-discharge (2 prior follow-ups)
- A1C is down from 12.6% to 10.1%
- Glucose records, fasting and bedtime
  - Fasting: 122 – 198 mg/dL
  - Bedtime: 185*– 386 mg/dL
- Weight: 228 lbs, height: 5'5"
- History remarkable for
  - Corrected vision
  - Neuropathy
  - Moderate CKD (eGFR = 51 mL/min/1.73 m^2)
  - Moderate microalbuminuria
  - Hypertension; treated
  - Elevated blood lipids; treated

*If she took her insulin and didn't have a performance.

- **Ella admits to erratic eating habits and occasionally missing injections due to travel, concert, and recording schedules.**
- **She asks if she can stop the injections and "just take a pill."**

- **In 1986, she had few options.**
- **In 2024, what would the best next step be?**

In 2024, what would be the most appropriate A1C target for Ella?

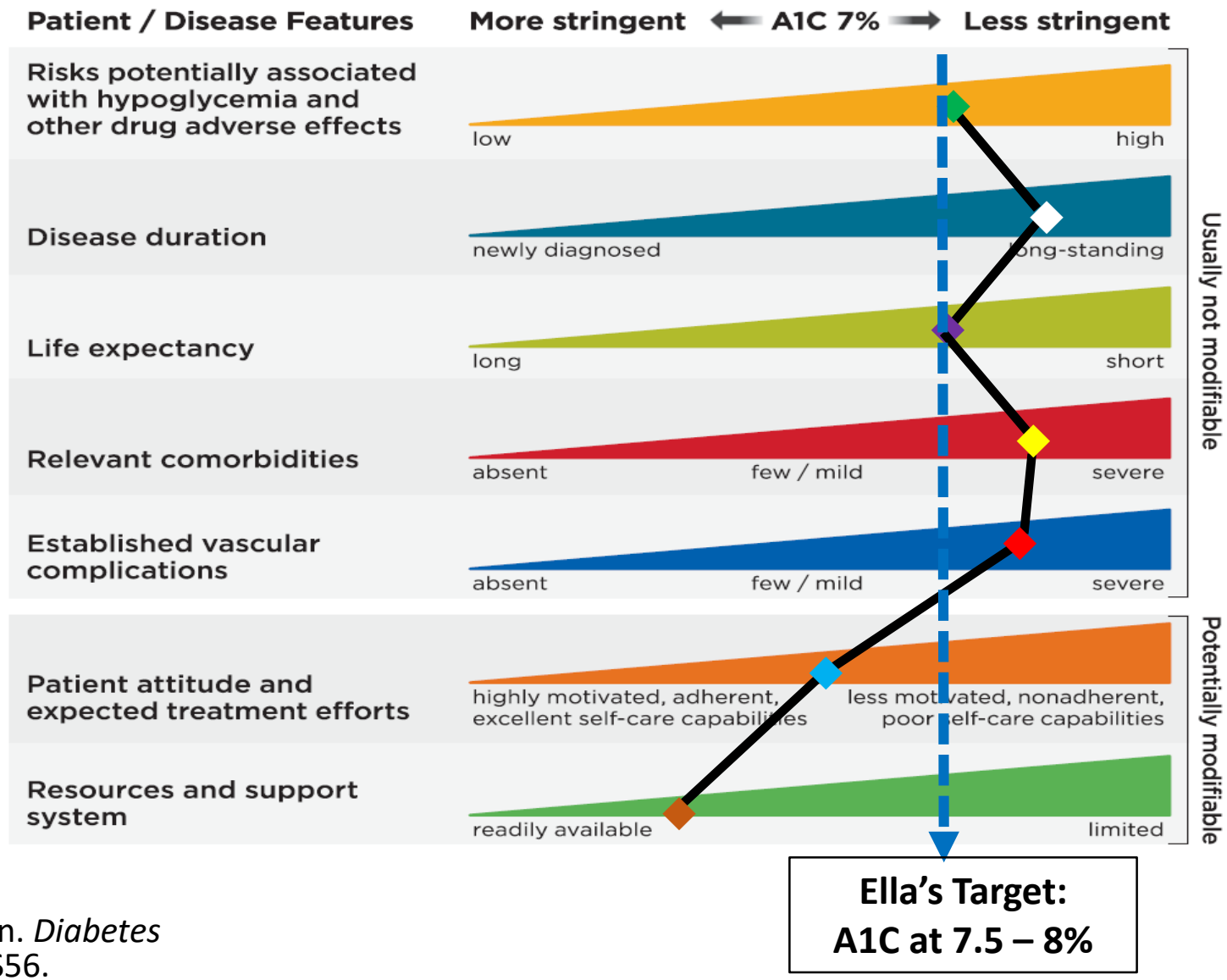
?

A. < 6.5%
B. 6.5% to 6.8%
C. 7.0% to 7.4%
D. 7.5% to 8.0%

ELLA RECAP

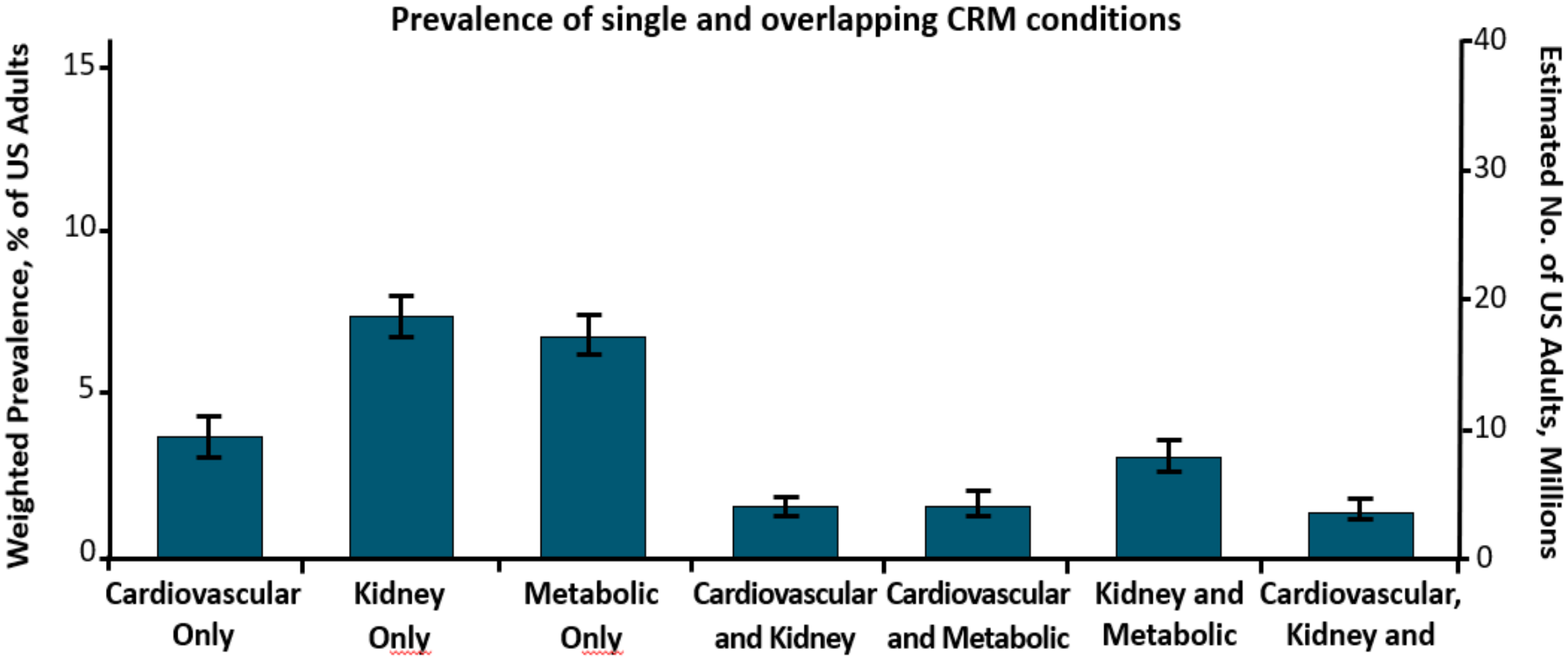
- 69 years old
- CHF
- Dyslipidemia and HTN (both treated)
- eGFR = 51 ml/min/1.73m^2; moderate microalbuminuria
- NPH and Regular insulin, bid
- Up-titrated to 30/20 U am and 30/20 U before dinner
- A1C down from 12.6% to 10.1%

Selecting Ella's Individualized A1C Target

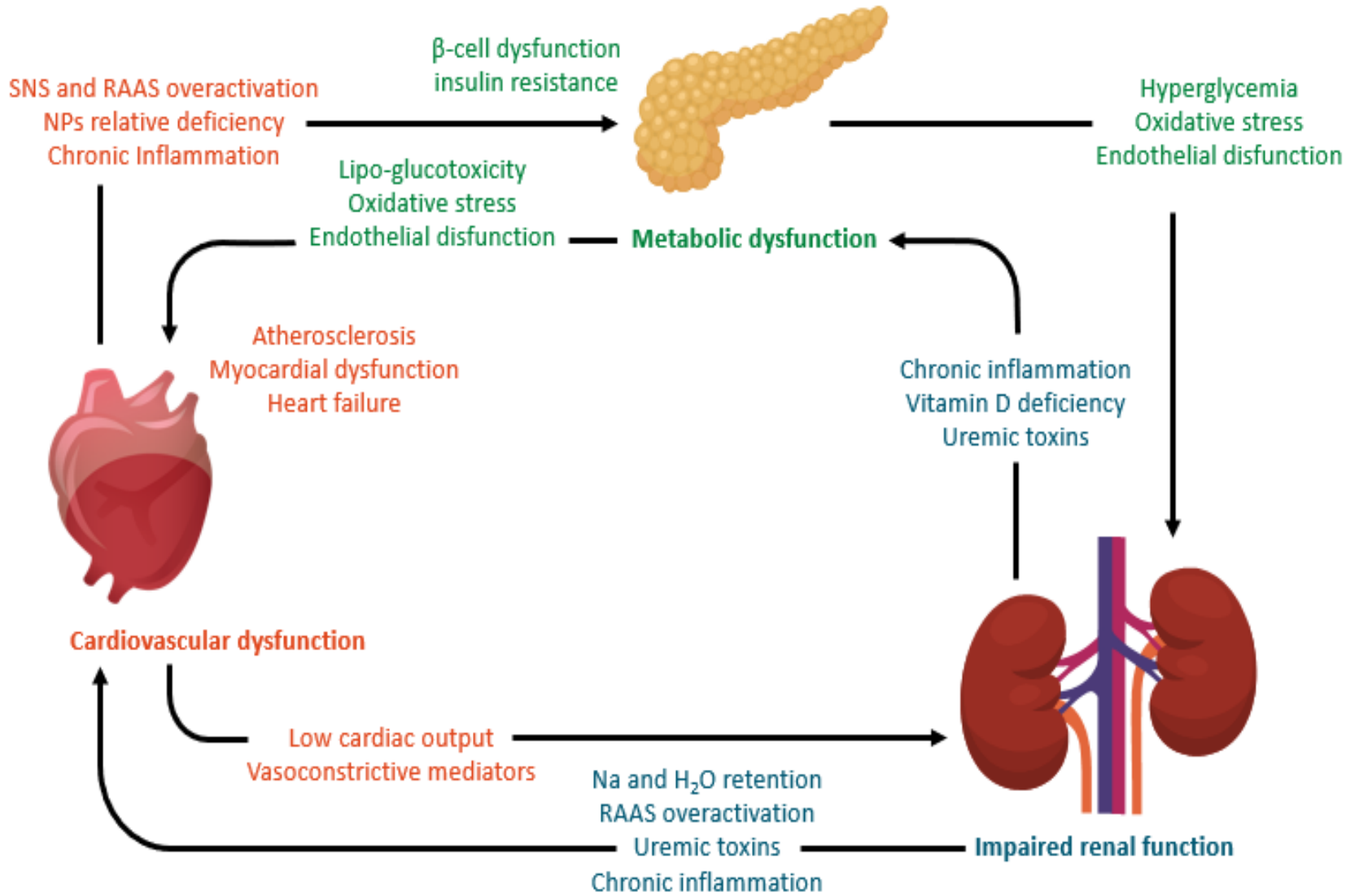


American Diabetes Association. *Diabetes Care*. 2017;40(Suppl. 1):S48–S56.

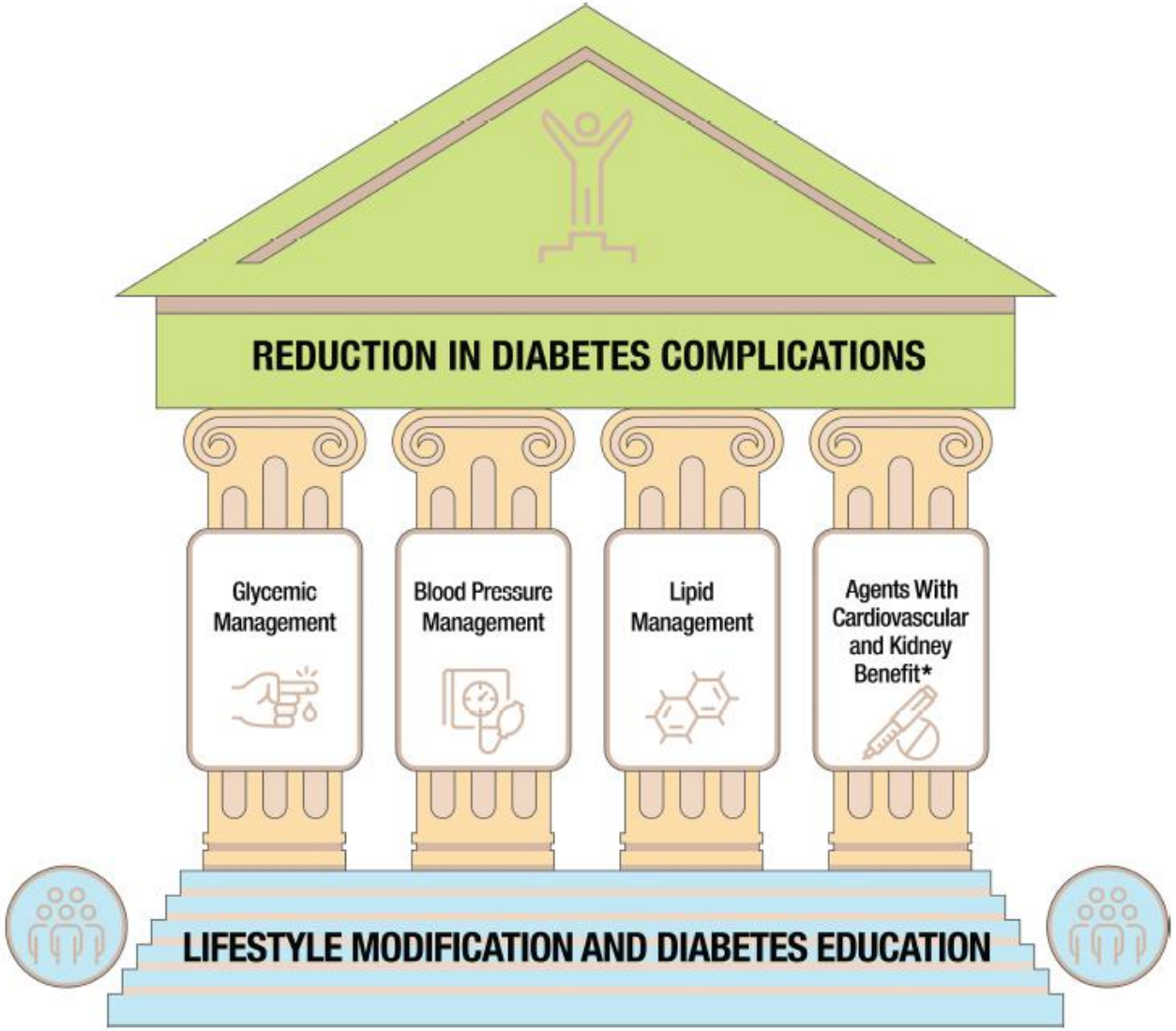
Prevalence and Overlap of Cardiac, Renal, and Metabolic Conditions in US Adults, 2015-2020



Overlapping Pathophysiology of DM, CKD, and HF

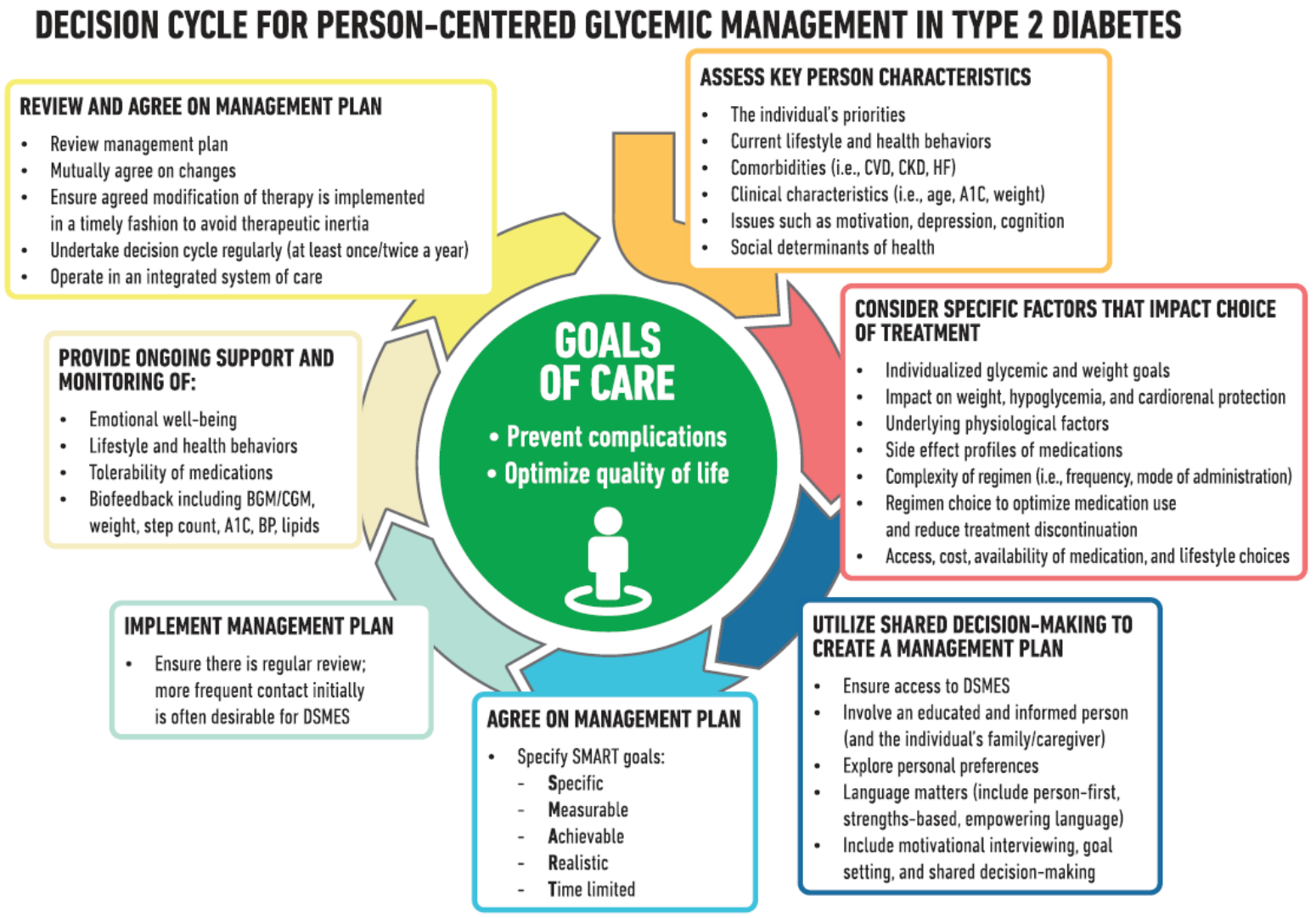


Marassi. Cardiovasc Diabetol. 2023;22:195.



Cardiovascular Disease and Risk Management:
Standards of Care in Diabetes - 2024. *Diabetes Care* 2024;47(Suppl. 1):S179-S218

COMPREHENSIVE MEDICAL EVALUATION AND ASSESSMENT OF COMORBIDITIES



Comprehensive Medical Evaluation and Assessment of Comorbidities:
Standards of Care in Diabetes - 2024. Diabetes Care 2024;47(Suppl. 1):S52-S76

COMPREHENSIVE MEDICAL EVALUATION AND ASSESSMENT OF COMORBIDITIES

Table 4.2—Assessment and treatment plan

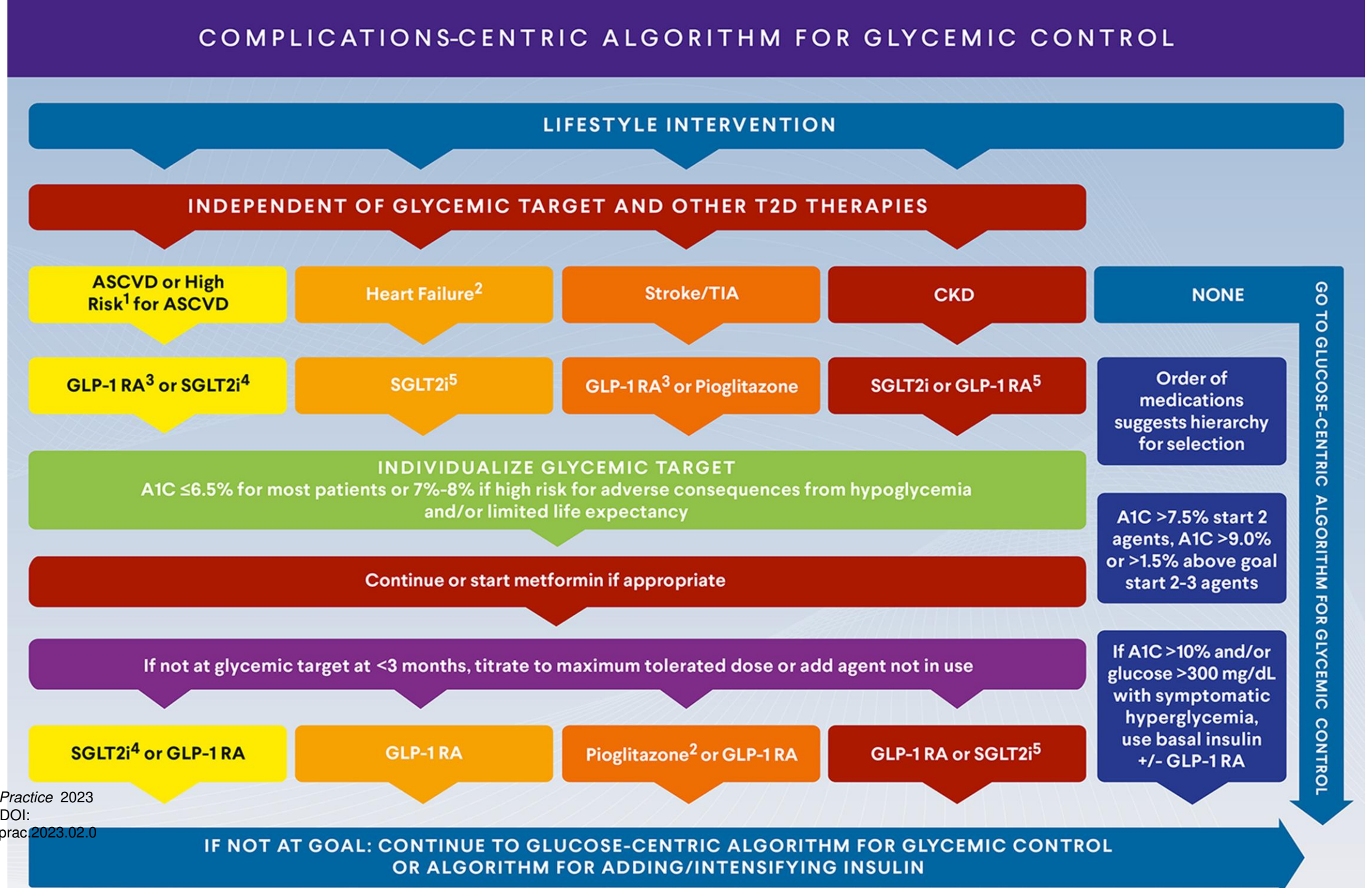
Assessing risk of diabetes complications
- ASCVD and heart failure history
- ASCVD risk factors and 10-year ASCVD risk assessment
- Staging of chronic kidney disease (see **Table 11.1**)
- Hypoglycemia risk (see Section 6, "Glycemic Goals and Hypoglycemia")
- Assessment for retinopathy
- Assessment for neuropathy
- Assessment for NAFLD/NASH

Goal setting
- Set A1C/blood glucose/time in range
- If hypertension is present, establish blood pressure goal
- Weight management and physical activity goals
- Diabetes self-management goals

Therapeutic treatment plans
- Lifestyle management
- Pharmacologic therapy: glucose lowering
- Pharmacologic therapy: cardiovascular and kidney disease risk factors
- Weight management with pharmacotherapy or metabolic surgery, as appropriate
- Use of glucose monitoring and insulin delivery devices
- Referral to diabetes education, behavioral health, and medical specialists

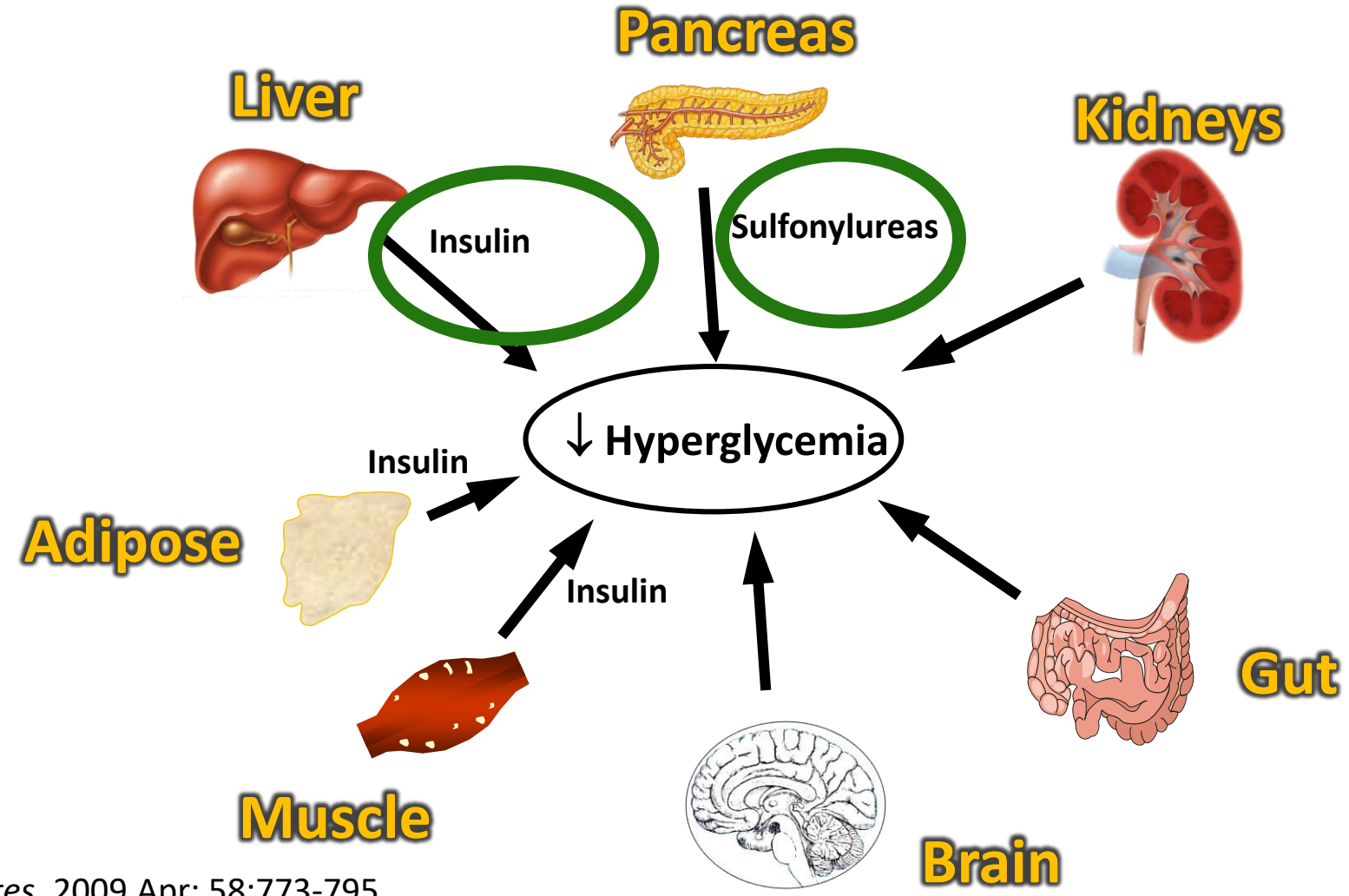
Assessment and treatment planning are essential components of initial and all follow-up visits. ASCVD, atherosclerotic cardiovascular disease; NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis.

Comprehensive Medical Evaluation and Assessment of Comorbidities: *Standards of Care in Diabetes - 2024. Diabetes Care* 2024;47(Suppl. 1):S52-S76



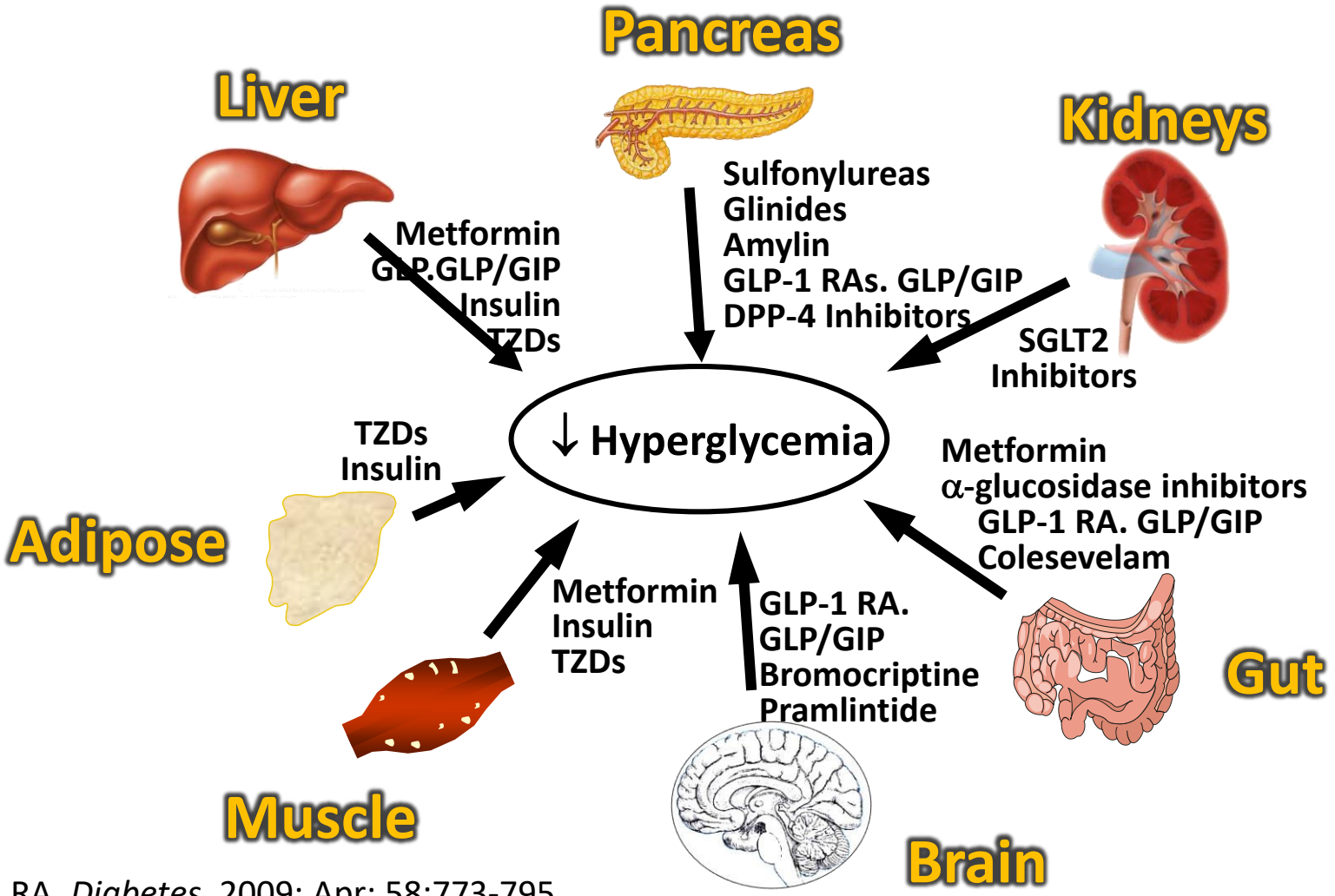
Endocrine Practice 2023
29305-340DOI:
(0.1016/j.eprac.2023.02.0
01)

1986: Available Antihyperglycemic Agents



DeFronzo RA. *Diabetes*. 2009 Apr; 58:773-795.
Holst JJ, Orskov C. *Diabetes.* 2004;53:S197-S204.
Lebovitz HE. *Diabetes Rev.* 1999;7:139-153.

2024: Available Antihyperglycemic Agents



ADA 2024. DeFronzo RA. *Diabetes*. 2009; Apr; 58:773-795.
Holst JJ, Orskov C. *Diabetes.* 2004;53:S197-S204.
Lebovitz HE. *Diabetes Rev.* 1999;7:139-153.

USE OF GLUCOSE-LOWERING MEDICATIONS IN THE MANAGEMENT OF TYPE 2 DIABETES

HEALTHY LIFESTYLE BEHAVIORS; DIABETES SELF-MANAGEMENT EDUCATION AND SUPPORT (DSMES); SOCIAL DETERMINANTS OF HEALTH (SDOH)

TO AVOID THERAPEUTIC INERTIA REASSESS AND MODIFY TREATMENT REGULARLY (3–6 MONTHS)

Goal: Cardiorenal Risk Reduction in High-Risk Individuals with Type 2 Diabetes (in addition to comprehensive CV risk management)*

+ASCVD†
Defined differently across CVOTs but all included individuals with established CVD (e.g., MI, stroke, any revascularization procedure). Variably included: conditions such as transient ischemic attack, unstable angina, amputation, symptomatic or asymptomatic coronary artery disease.

+Indicators of high risk
While definitions vary, most comprise ≥55 years of age with two or more additional risk factors (including obesity, hypertension, smoking, dyslipidemia, or albuminuria)

+ASCVD/Indicators of High Risk

GLP-1 RA# with proven CVD benefit — EITHER/OR — SGLT2i§ with proven CVD benefit

If A1C above target

- For patients on a GLP-1 RA, consider adding SGLT2i with proven CVD benefit or vice versa
- TZD^

+HF
Current or prior symptoms of HF with documented HFrEF or HFpEF

+HF
SGLT2i§ with proven HF benefit in this population

+CKD
eGFR <60 mL/min per 1.73 m² OR albuminuria (ACR ≥3.0 mg/mmol [30 mg/g]). These measurements may vary over time; thus, a repeat measure is required to document CKD.

+CKD (on maximally tolerated dose of ACEi/ARB)

PREFERABLY
SGLT2i§ with primary evidence of reducing CKD progression

Use SGLT2i in people with an eGFR ≥20 mL/min per 1.73 m²; once initiated should be continued until initiation of dialysis or transplantation

OR

GLP-1 RA with proven CVD benefit if SGLT2i not tolerated or contraindicated

If A1C above target, for patients on SGLT2i, consider incorporating a GLP-1 RA or vice versa

If additional cardiorenal risk reduction or glycemic lowering needed

Goal: Achievement and Maintenance of Glycemic and Weight Management Goals

Glycemic Management: Choose approaches that provide the efficacy to achieve goals:
Metformin OR Agent(s) including COMBINATION therapy that provide adequate EFFICACY to achieve and maintain treatment goals
Prioritize avoidance of hypoglycemia in high-risk individuals

In general, higher efficacy approaches have greater likelihood of achieving glycemic goals

Efficacy for glucose lowering

Very High:
Dulaglutide (high dose), Semaglutide, Tirzepatide
Insulin
Combination Oral, Combination Injectable (GLP-1 RA/Insulin)

High:
GLP-1 RA (not listed above), Metformin, SGLT2i, Sulfonylurea, TZD

Intermediate:
DPP-4i

Achievement and Maintenance of Weight Management Goals:

Set individualized weight management goals

- General lifestyle advice: medical nutrition therapy/eating patterns/physical activity
- Intensive evidence-based structured weight management program
- Consider medication for weight loss
- Consider metabolic surgery

When choosing glucose-lowering therapies:
Consider regimen with high-to-very-high dual glucose and weight efficacy

Efficacy for weight loss

Very High:
Semaglutide, Tirzepatide

High:
Dulaglutide, Liraglutide

Intermediate:
GLP-1 RA (not listed above), SGLT2i

Neutral:
DPP-4i, Metformin

If A1C above target

Identify barriers to goals:

- Consider DSMES referral to support self-efficacy in achievement of goals
- Consider technology (e.g., diagnostic CGM) to identify therapeutic gaps and tailor therapy
- Identify and address SDOH that impact achievement of goals

* In people with HF, CKD, established CVD, or multiple risk factors for CVD, the decision to use a GLP-1 RA or SGLT2i with proven benefit should be independent of background use of metformin; † A strong recommendation is warranted for people with CVD and a weaker recommendation for those with indicators of high CV risk. Moreover, a higher absolute risk reduction and thus lower numbers needed to treat are seen at higher levels of baseline risk and should be factored into the shared decision-making process. See text for details; ^ Low-dose TZD may be better tolerated and similarly effective; § For SGLT2i, CV/renal outcomes trials demonstrate their efficacy in reducing the risk of composite MACE, CV death, all-cause mortality, MI, HHF, and renal outcomes in individuals with T2D with established/high risk of CVD; # For GLP-1 RA, CVOTs demonstrate their efficacy in reducing composite MACE, CV death, all-cause mortality, MI, stroke, and renal endpoints in individuals with T2D with established/high risk of CVD.

Pharmacologic Approaches to Glycemic Treatment: *Standards of Care in Diabetes - 2024*. *Diabetes Care* 2024;47(Suppl. 1):S158-S178

If it were today, which of the following therapeutic regimens might you select for Ella?

ELLA RECAP

- 69 years old
- CHF
- Dyslipidemia and HTN (both treated)
- eGFR = 51 ml/min/1.73m^{2}; moderate microalbuminuria
- NPH and Regular insulin, bid, titrated to 30/20 U am and 30/20 U before dinner
- A1C down from 12.6% to 10.1%

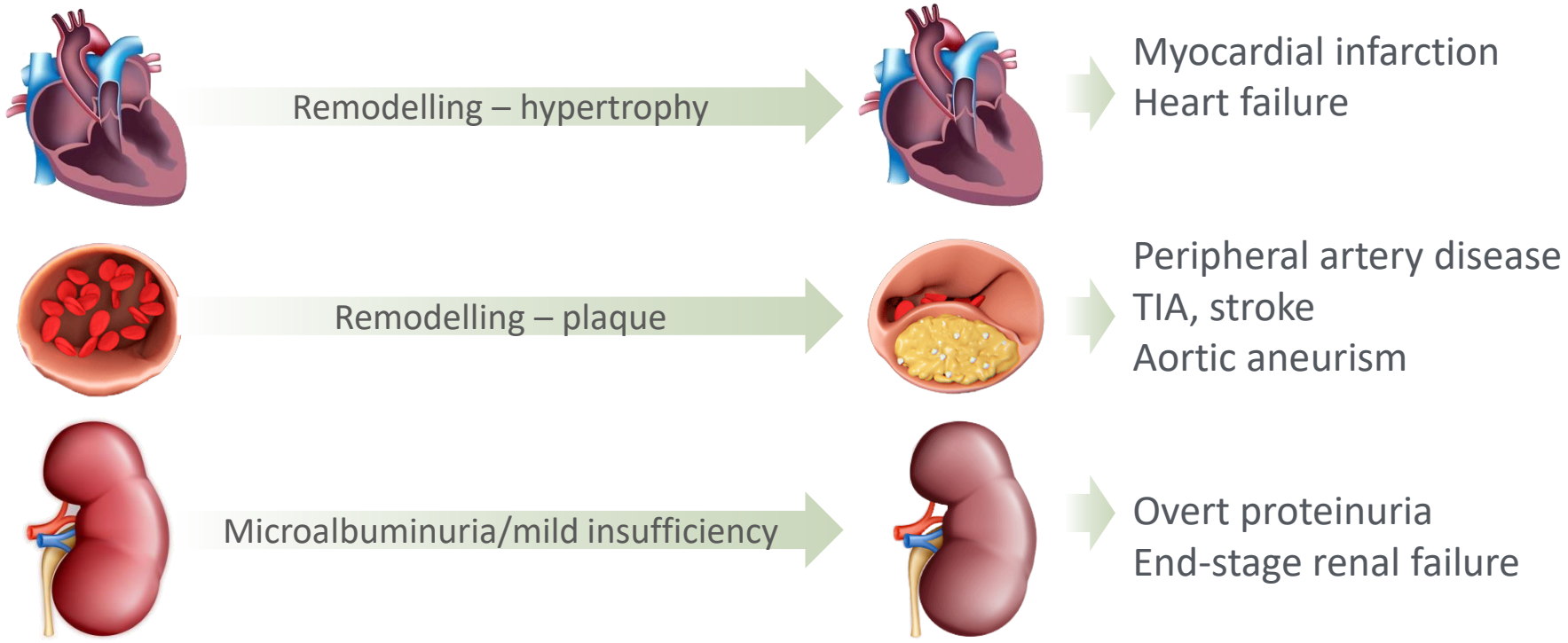
A. Maintain NPH/Reg as-is; add metformin XR 500 mg/d; titrate to maximum tolerated dose

B. Replace NPH/Reg with a pioglitazone/metformin combination pill at 15 mg/500 mg/day; titrate to maximum tolerated dose

C. Add metformin XR starting at 500 mg/d and titrate to maximum tolerated dose; Switch to basal insulin (Reduce TDD by ~ 50%) Start SGLT2

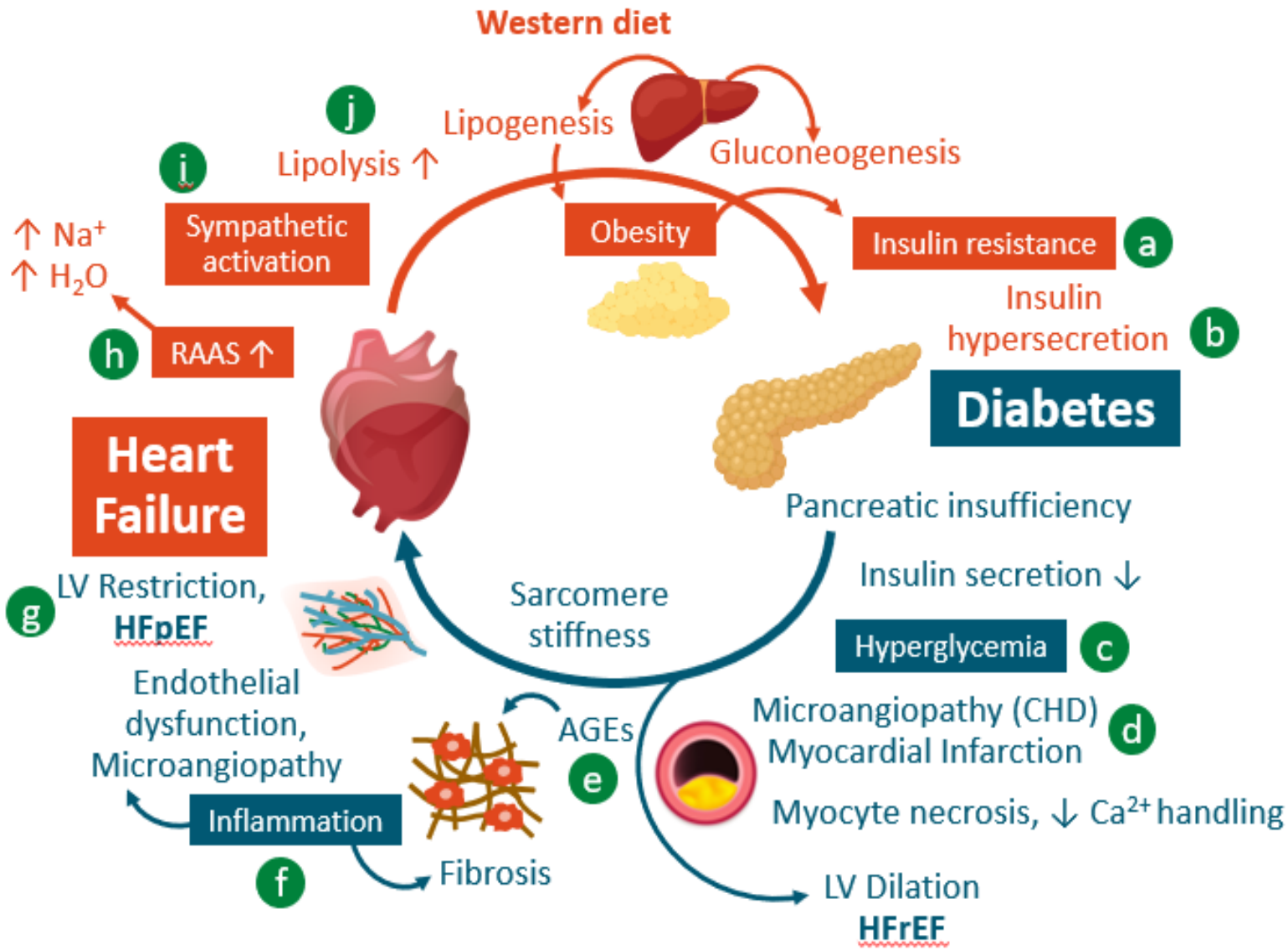
D. Add metformin XR starting at 500 mg/d and titrate to maximum tolerated dose; switch out NPH/Reg for GLP-1 RA or GLP/GIP plus basal insulin (half total dose).

Endothelial dysfunction is common to microvascular and macrovascular events



Versari et al. Diabetes Care 2009;32(suppl 2):S314-321.

Interplay Between Diabetes and Heart Failure



Braunwald. Prog Cardiovasc Dis. 2019;62:298.

If this were today, which of the following therapeutic regimens might you select?

ELLA RECAP

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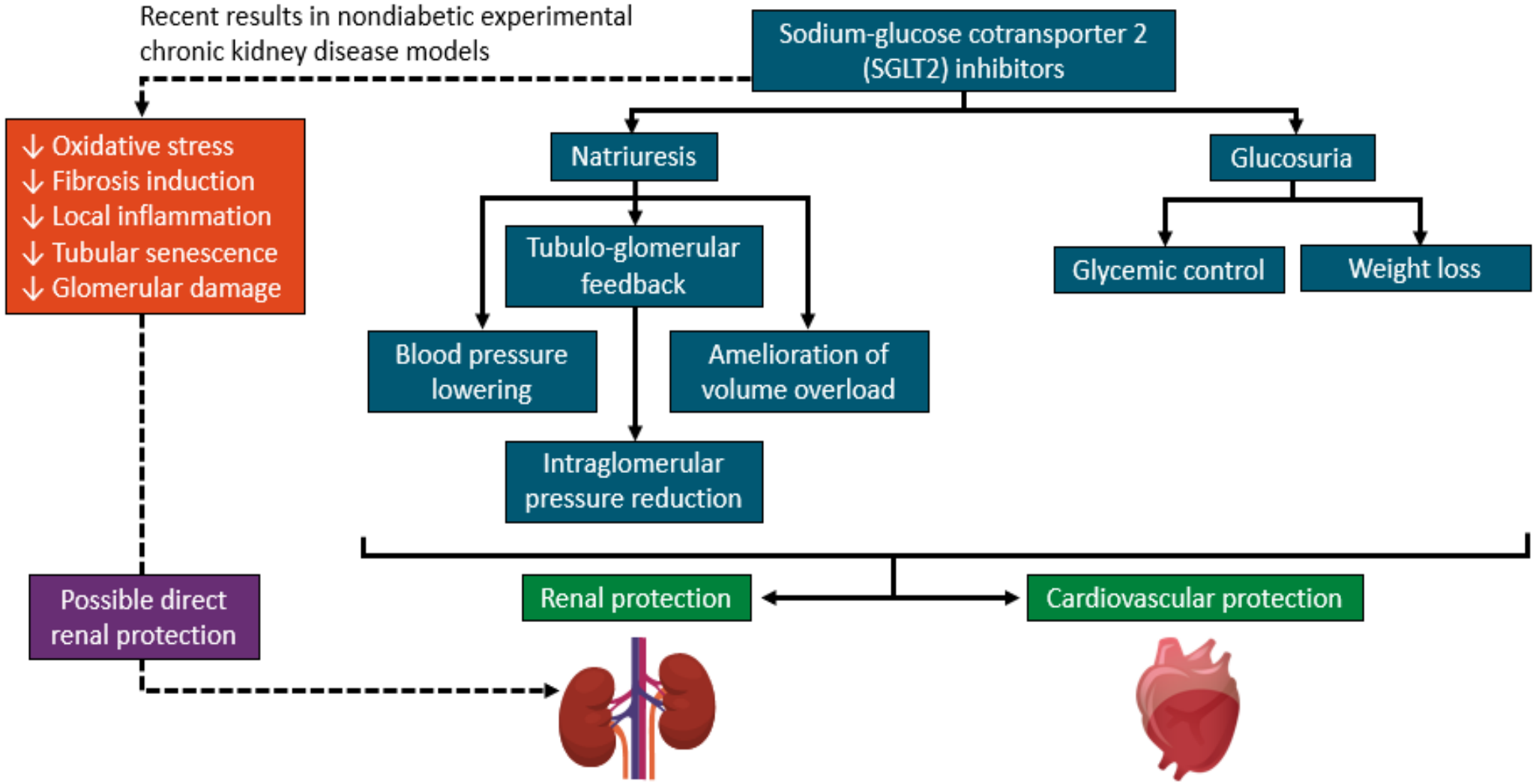
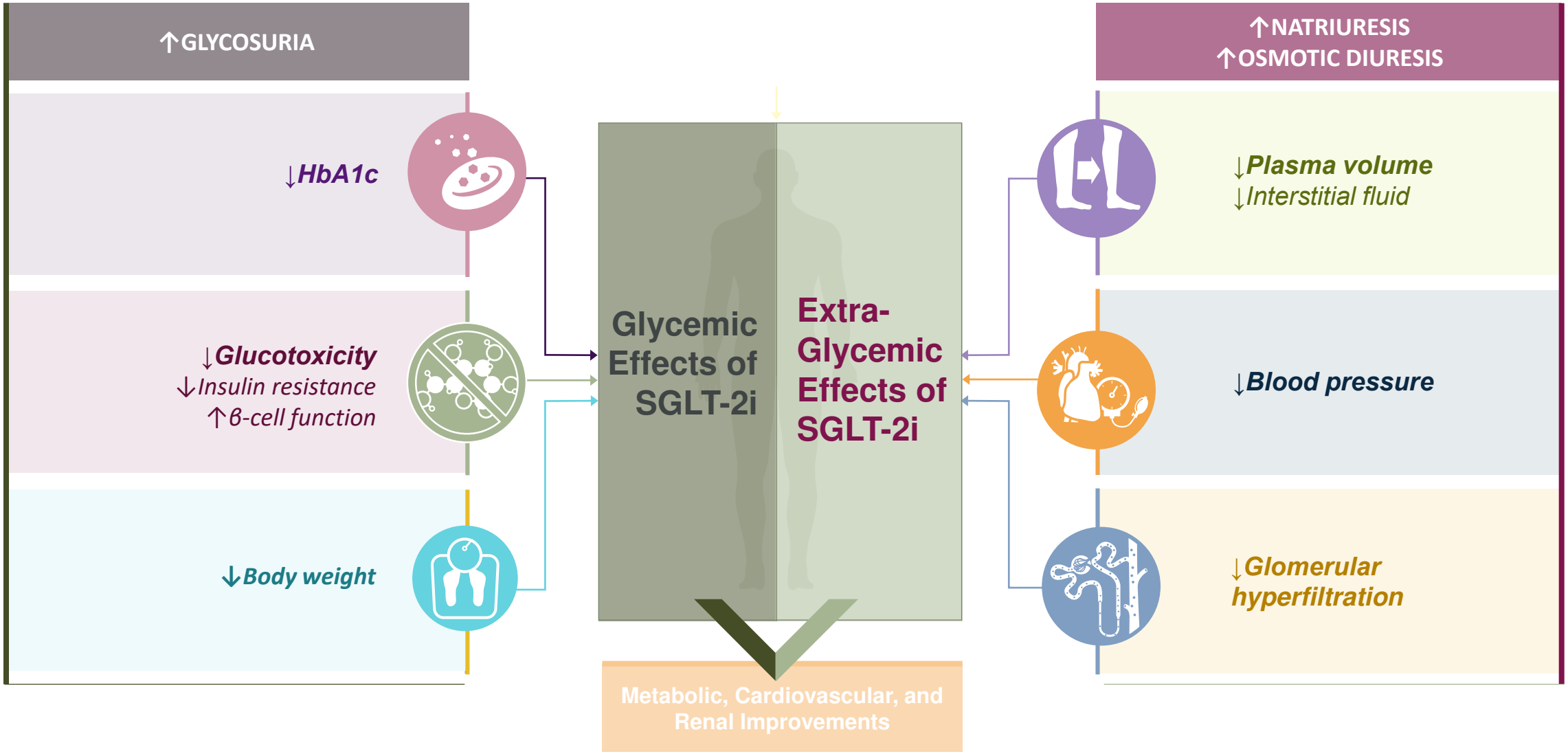
Mechanisms for Cardiorenal Protection With SGLT2i



Zelniker. J Am Coll Cardiol. 2020;75:422.

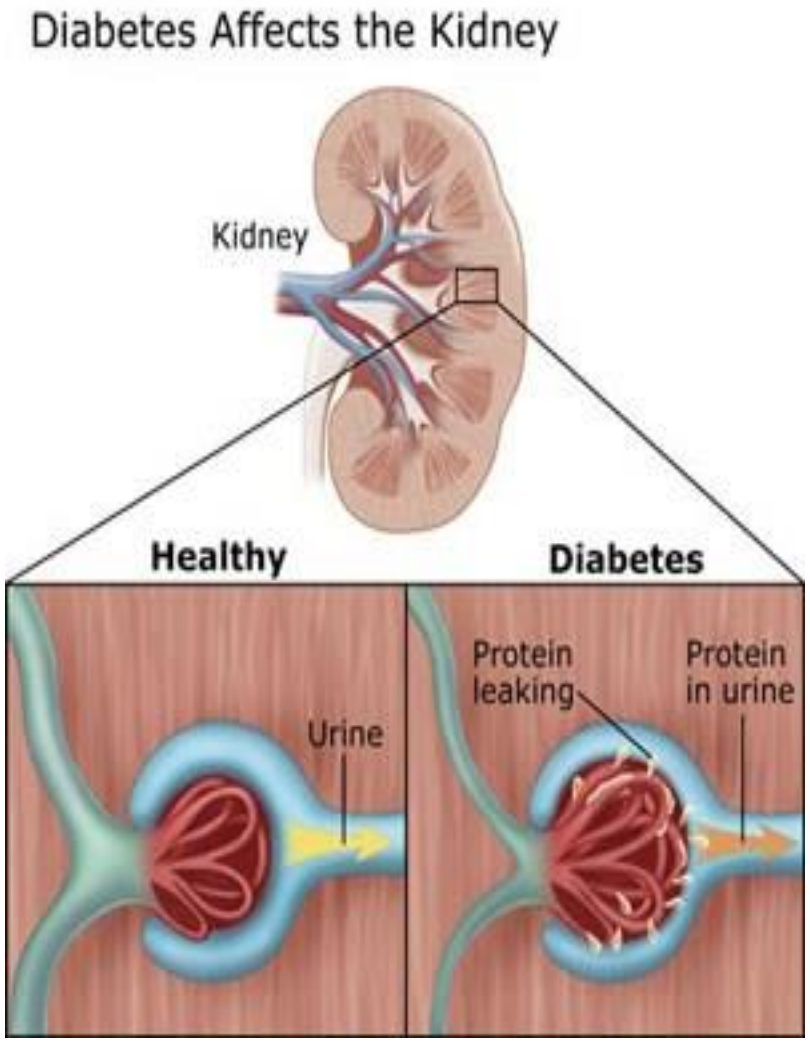
Key Physiological Effects of SGLT-2 Inhibition



HbA1C=hemoglobin A1C; SGLT-2=sodium-glucose co-transporter 2; SGLT-2i=sodium-glucose co-transporter 2 inhibitor.

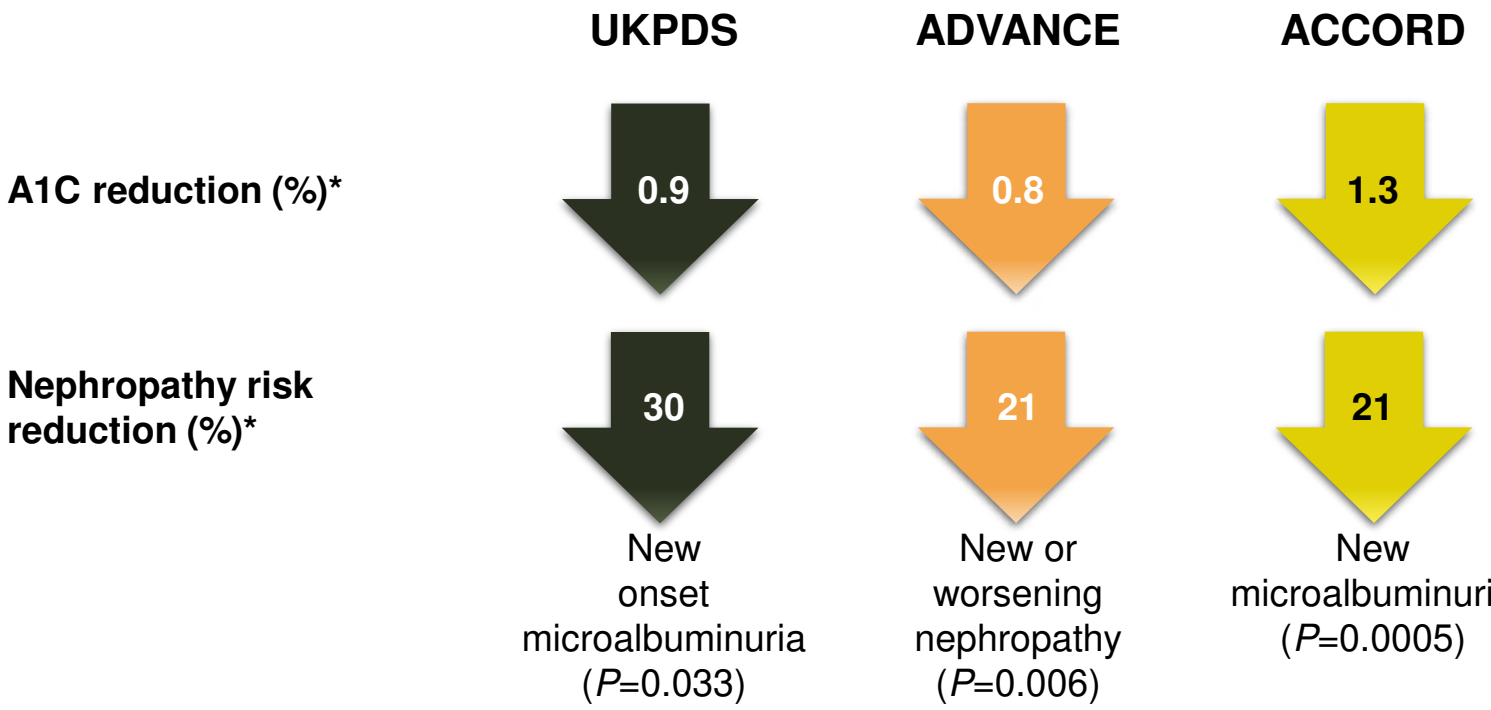
1. Heerspink HJL, et al. *Kidney Int*. 2018;94(1):26-39. 2. van Baar MJB, et al. *Diabetes Care*. 2018;41(8):1543-1556. 3. Tamargo J. *Eur Cardiol*. 2019;14(1):23-32.

Diabetic Nephropathy



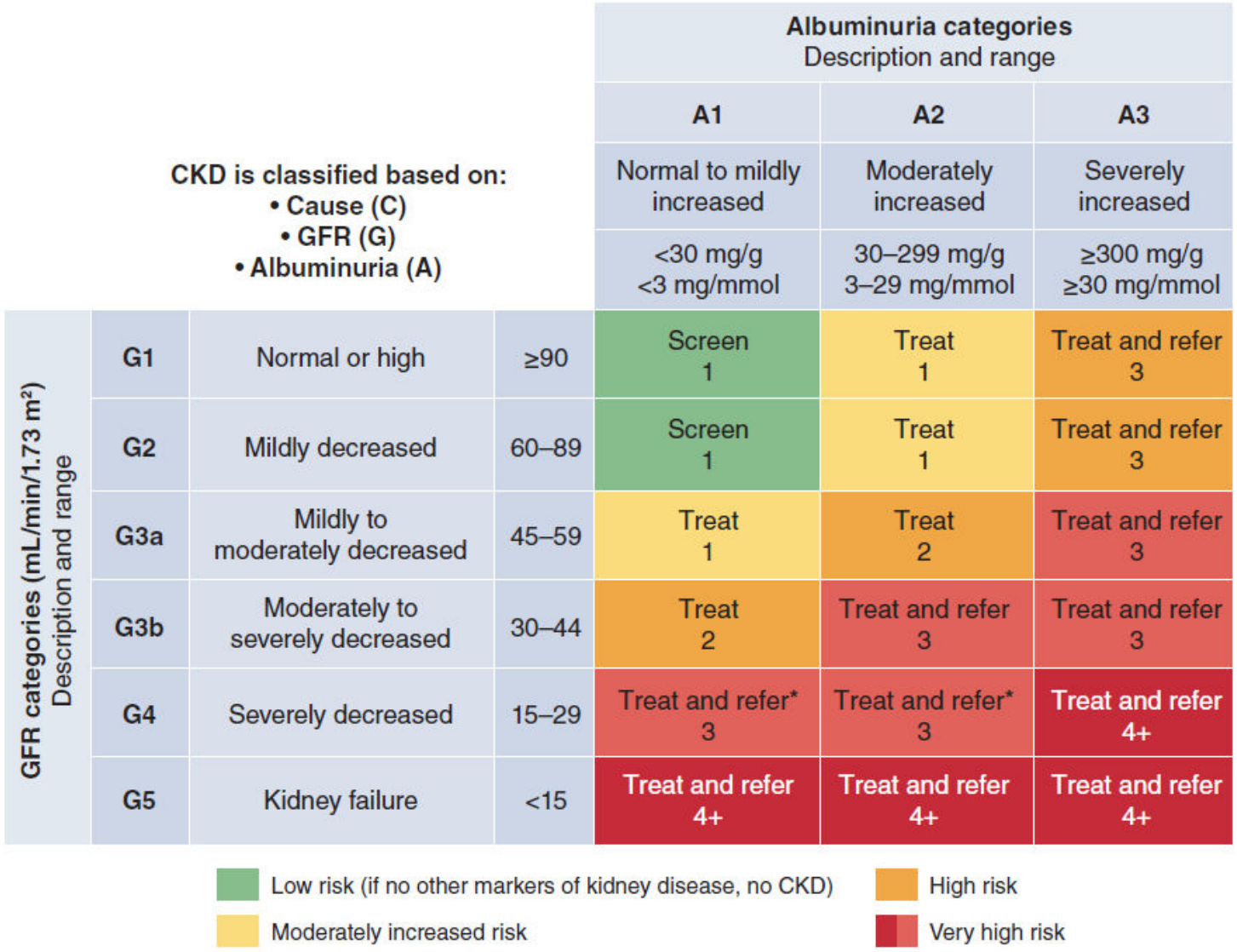
- (UACR) Microalbumin or random Albumin to Creatinine Ratio.
  - URINE test done once yearly
- Creatinine/ eGFR –blood work) yearly
- UACR- if > 30, retest;
- if persistently 30-299; recommended treatment with ACEI/"pril" or ARB/ "sartan"
  - Watch for dry cough, w ACEI
  - BP goal < 130/80

Reducing A1C Reduces Nephropathy Risk in Type 2 Diabetes



*Intensive vs standard glucose control.

UK Prospective Diabetes Study (UKPDS) Group. *Lancet*. 1998;352:837-853. ADVANCE Collaborative Group. *N Engl J Med*. 2008;358:2560-2572. Ismail-Beigi F, et al. *Lancet*. 2010;376:419-430.

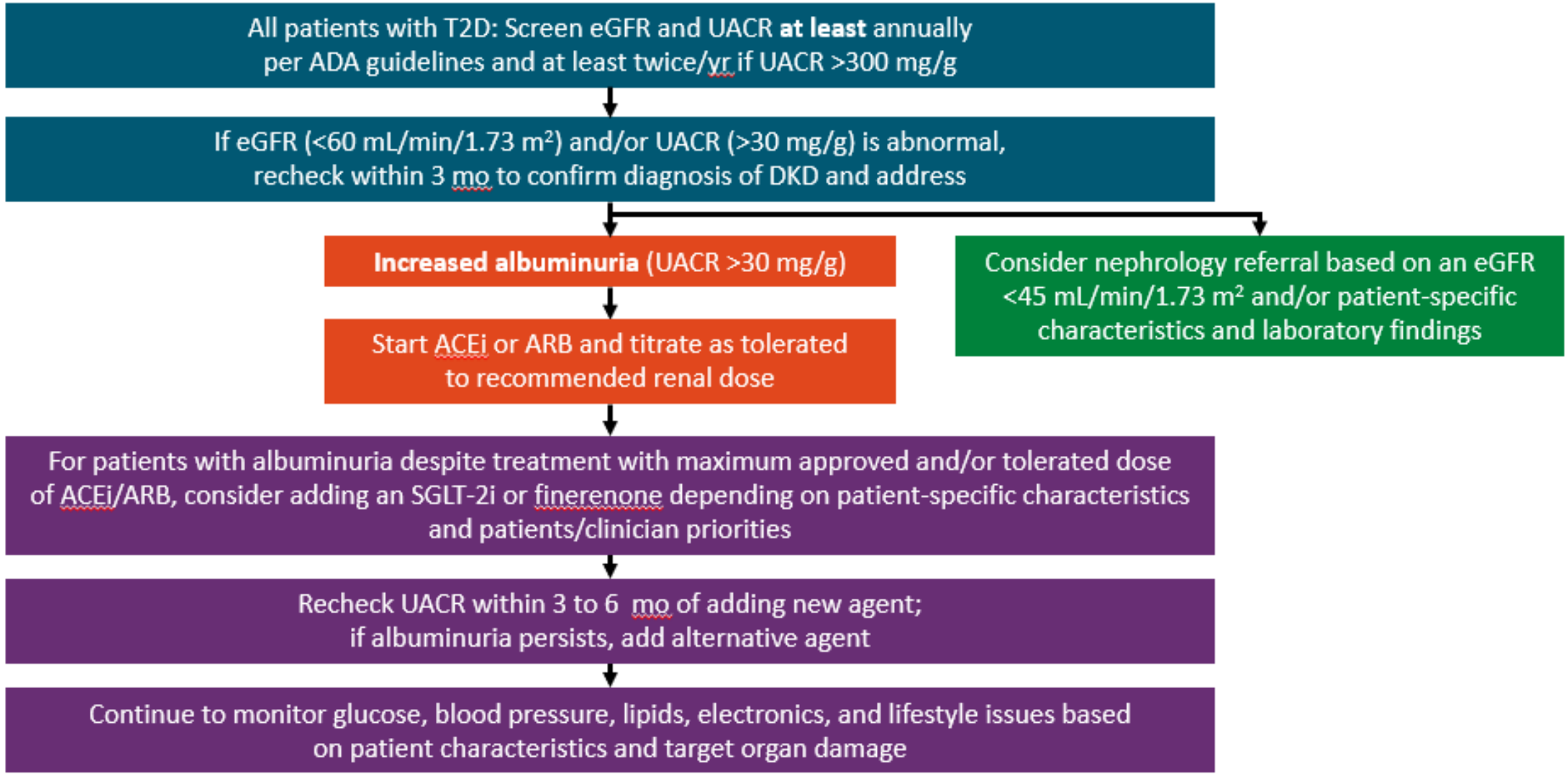


CKD is classified based on: • Cause (C) • GFR (G) • Albuminuria (A)				Albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–299 mg/g 3–29 mg/mmol	≥300 mg/g ≥30 mg/mmol
GFR categories (mL/min/1.73 m²) Description and range	G1	Normal or high	≥90	Screen 1	Treat 1	Treat and refer 3
	G2	Mildly decreased	60–89	Screen 1	Treat 1	Treat and refer 3
	G3a	Mildly to moderately decreased	45–59	Treat 1	Treat 2	Treat and refer 3
	G3b	Moderately to severely decreased	30–44	Treat 2	Treat and refer 3	Treat and refer 3
	G4	Severely decreased	15–29	Treat and refer* 3	Treat and refer* 3	Treat and refer 4+
	G5	Kidney failure	<15	Treat and refer 4+	Treat and refer 4+	Treat and refer 4+

Figure 11.1—Risk of chronic kidney disease (CKD) progression, frequency of visits, and referral to nephrology according to glomerular filtration rate (GFR) and albuminuria.

Chronic Kidney Disease and Risk management:
Standards of Care in Diabetes - 2024. Diabetes Care 2024;47(Suppl. 1):S219-230

Proposed Algorithm

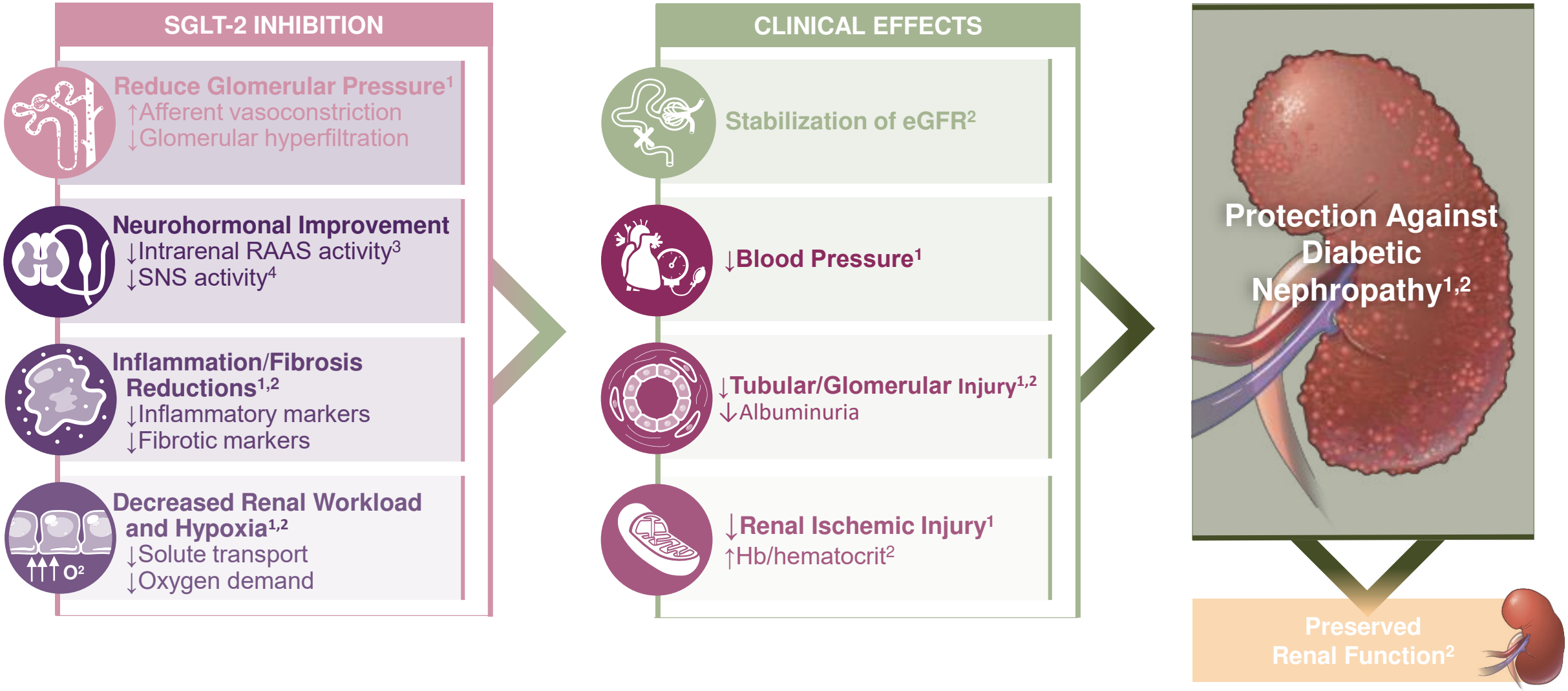


Shubrook. Postgrad Med. 2022;134:376.

Finerenone (Krendia)

- Mineracordicoid. Non-steroidal MR antagonist.
- Indication: Finerenone is indicated to reduce the risk of sustained eGFR decline, end state kidney disease, cardiovascular death, non-fatal myocardial infarction, and hospitalization for heart failure in pts with CKD and T2D
- MOA:
  - Selectively blocks MR and blocks MR overactivation in the heart and kidneys.
  - Mediated-sodium reabsorption.
- Adverse Reactions:
  - Hyperkalemia 14%v6.9%, hypotension 4.6% v 3.9% and hyponatremia 1.3% v 0.7%
  - Concomitant use with strong CYP3A4 inhibitor is contraindicated

Potential Effects of SGLT-2 Inhibition to Improve Renal Outcomes



eGFR=estimated glomerular filtration rate; Hb=hemoglobin; RAAS=renin angiotensin aldosterone system; SNS=sympathetic nervous system.

1. Heerspink HJL, et al. *Kidney Int*. 2018;94(1):26-39. 2. Tamargo J. *Eur Cardiol*. 2019;14(1):23-32. 3. Shin SJ, et al. *PLoS One*. 2016;11:e0165703. 4. Sano M. *J Cardiol*. 2018;71(5):471-476.

Other Options for Ella?

- Finerenone
- Basal insulin plus bolus
- Weekly GLP1-RA or GLP/GIP
- Fixed Ratio Basal/GLP
  - iGlar/Lixi (Soliqua)
  - iDeg/Lira (Xultophy)
- Obesity meds/Diabetes meds with weight benefits
- Cognitive screening
- Complications screening
  - Possible Anti-VEGF retinal treatment

Thinking about the multiple co-morbidities, which of the following therapeutic regimens might you select for Ella?

ELLA RECAP

- 69 years old
- CHF
- Dyslipidemia and HTN (both treated)
- eGFR = 58 ml/min/1.73m^{2,}; moderate microalbuminuria
- Glargine 50u at hs
- Empagliflozin 25mg
- Metformin XR 1500mg
- A1C down from 12.6% to 9.2%
- Weight down to 219 lbs (9lbs)

A. Maintain NPH/Reg as-is; add metformin XR 500 mg/d; titrate to maximum tolerated dose

B. Replace NPH/Reg with a pioglitazone/metformin combination pill at 15 mg/500 mg/day; titrate to maximum tolerated dose

C. Add metformin XR starting at 500 mg/d and titrate to maximum tolerated dose; Start SGLT2

D. Add a GLP-1 RA or GLP/GIP, continue to decrease basal insulin when glucose ~ 100mg.

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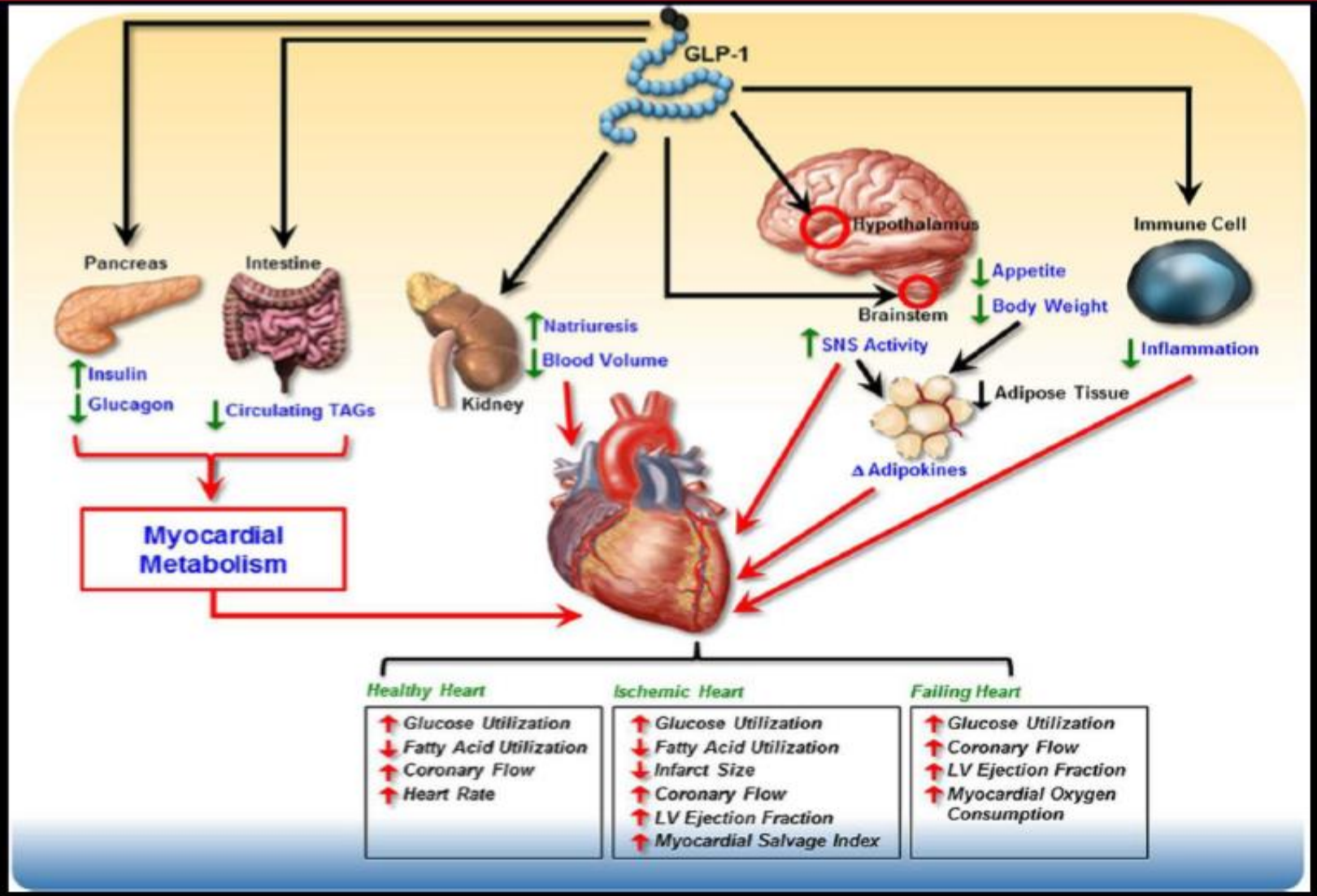
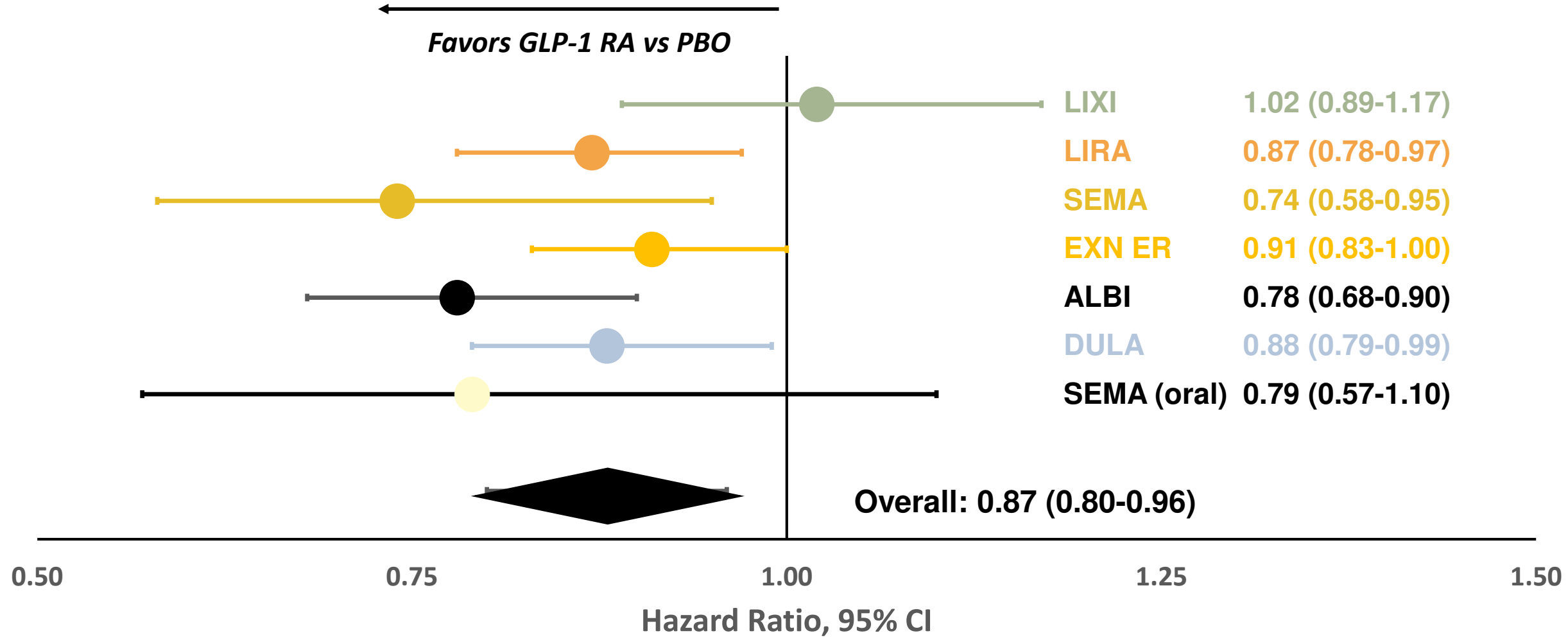
Mechanisms for CV Benefit with GLP-1



Ussher JR, Drucker DJ. *Circ Res* 2014;114:1788–803.

GLP-1 RA CVOTs: MACE[a] Outcomes[1]



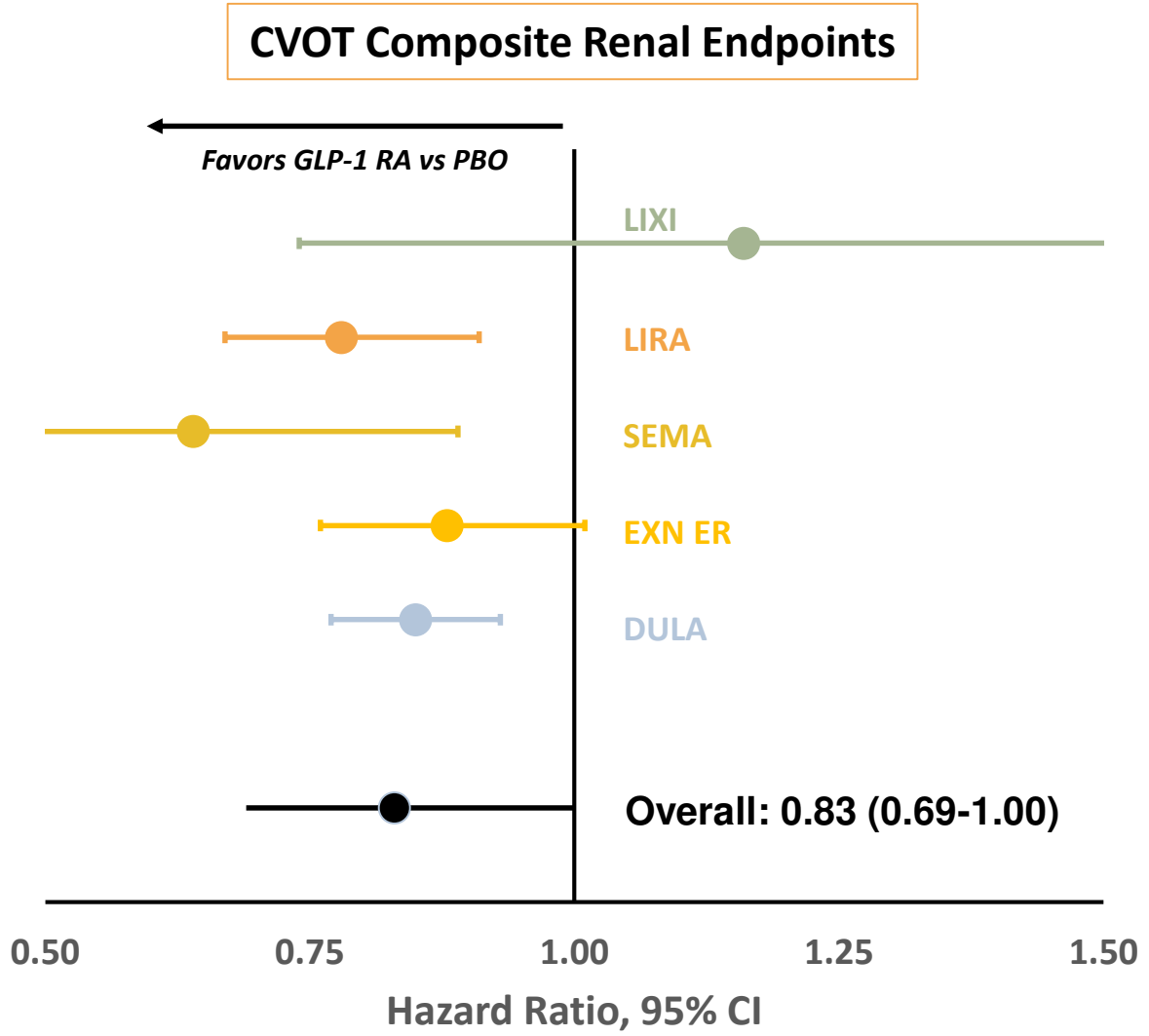
[a] CV death, nonfatal myocardial infarction, and nonfatal stroke in all 7 trials, plus hospitalization for unstable angina in ELIXA.[2-8]

1. Giugliano D, et al. *Diabetes Obes Metab*. 2019;21:2576-2580; 2. Pfeffer MA, et al. *N Engl J Med*. 2015;373:2247-2257; 3. Marso SP, et al. *N Engl J Med*. 2016;375:311-322; 4. Marso SP, et al. *N Engl J Med*. 2016;375:1834-1844; 5. Holman RR, et al. *N Engl J Med*. 2017;377:1228-1239; 6. Hernandez AF, et al. *Lancet*. 2018;392:1519-1529; 7. Gerstein HC, et al. *Lancet*. 2019;394:121-130; 8. Husain M, et al. *N Engl J Med*. 2019;381:841-851.

Heart Failure and Renal Function Effects in GLP-1 RA CVOTs

- HF
  - Meta-analysis demonstrated a 9% reduction in the risk of hospitalization for HF for GLP-1 RAs as a class
  - No significant effects on HF were identified in individual trials

- Renal effects
  - Meta-analysis demonstrated a 17% reduction in composite kidney outcomes for GLP-1 RAs as a class
  - Renal benefit driven by reduction in macroalbuminuria (HR, 0.76 [0.68-0.86])



Giugliano D, et al. *Diabetes Obes Metab*. 2019;21:2576-2580.

Ella, Age 72

- In the clinic with Ray Jr.
- A1C = 7.4; FPG = 150–180 mg/dL; weight loss (9 lbs since last visit)
- eGFR has declined to 51 ml/min/1.73m^2
- Admits to missing basal insulin injections 1–2 times/wk; unsure when she last forgot
- Poor appetite
- Discussion with Ella and Ray regarding daily medications
  - Ella says she does ok with oral medications as long as she remembers to put everything in her 7-day pill box, but admits to forgetting her insulin shots. She remembers the weekly injection because Ray is there on the weekends to remind her.
  - Ray Jr. states that she is getting more forgetful generally
  - After reassessing cognition, you recommend a neurology referral

ELLA RECAP

- 72 years old
- CHF
- Dyslipidemia and HTN (both treated)
- eGFR = 58 ml/min/1.73m^2; moderate microalbuminuria
- Met XR, Insulin, SGLT2, GLP1
- A1C up from 7.3% to 7.4%

Cordell CB, et al. *Alzheimers Dement.* 2013;9:141-150

Ella: Epilogue

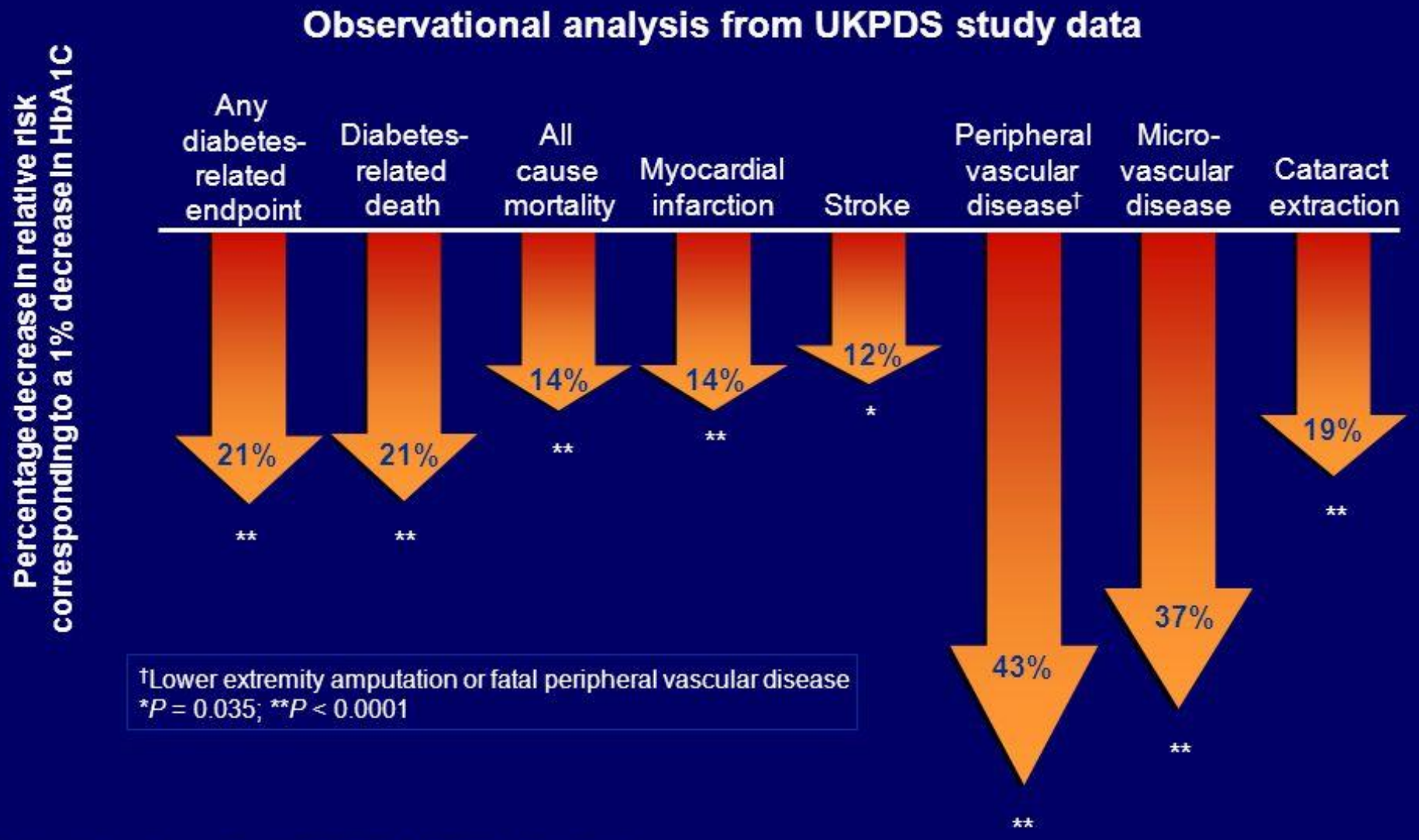
- **1993:** She was blind and underwent 2 separate, below-knee amputations
- **1996**: She decided to stay at home with her son Ray and 12-year-old granddaughter, Alice. She said “I just want to smell the air, listen to the birds, and hear Alice laugh”
- **June 15, 1996**: she died in her home at age 79. On her last day of life, she said “I am ready to go now.”

This was the end of an era; the world lost the “Queen of Vocal Jazz and Swing.” *Might she have fared better with current treatment options provided earlier in the course of her disease?* The answer is very likely *yes.*

Are Complications Inevitable? NO!

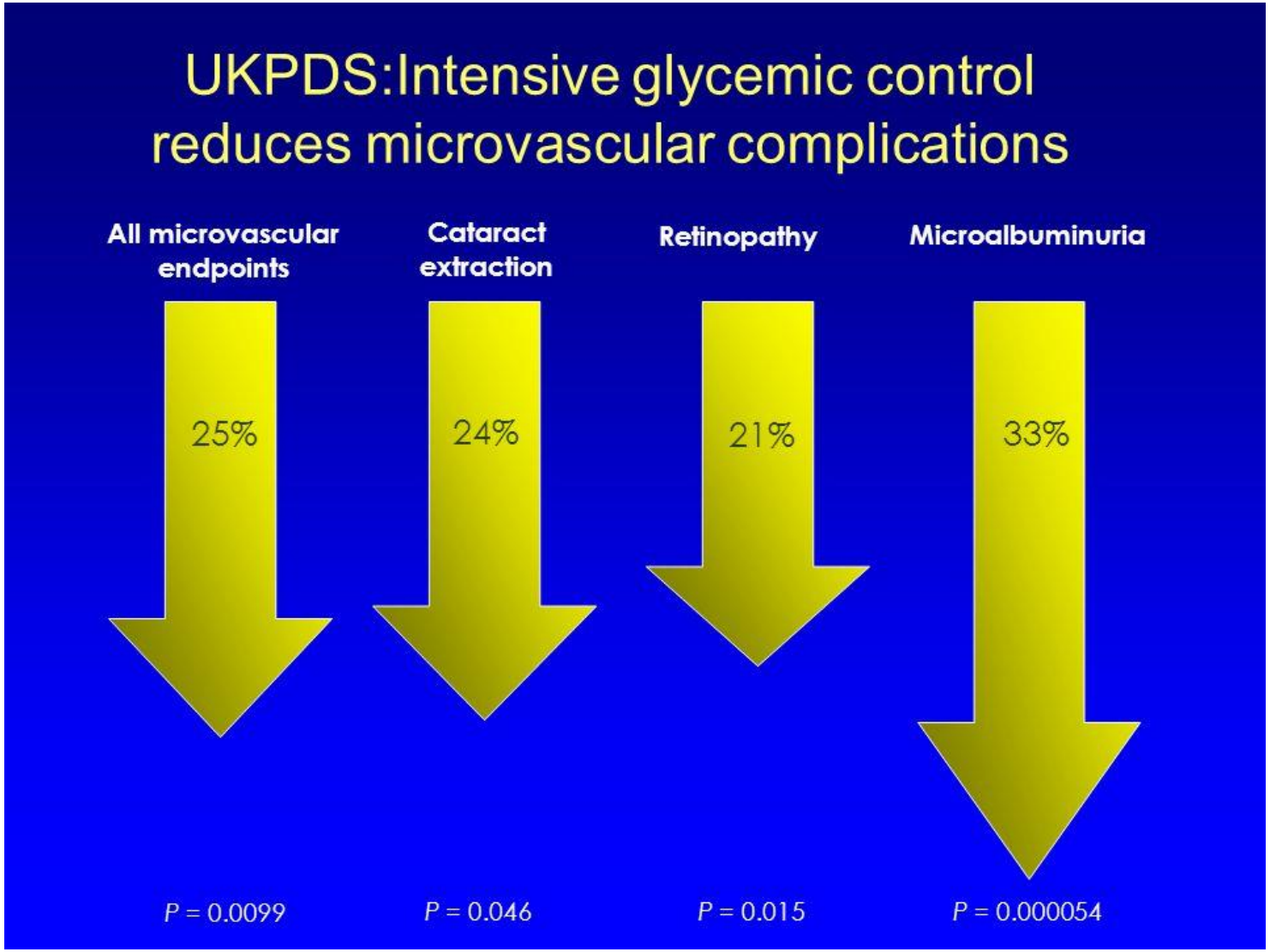
- Major studies (DCCT and UKPDS) show improved glucose control (A1c 7% or below) reduces risk of complications in micro and macro vessel.
- Studies show that newest classes of the diabetes medications reduce cardiovascular (heart) and kidney complications

UKPDS: decreased risk of diabetes-related complications associated with a 1% decrease in A1C

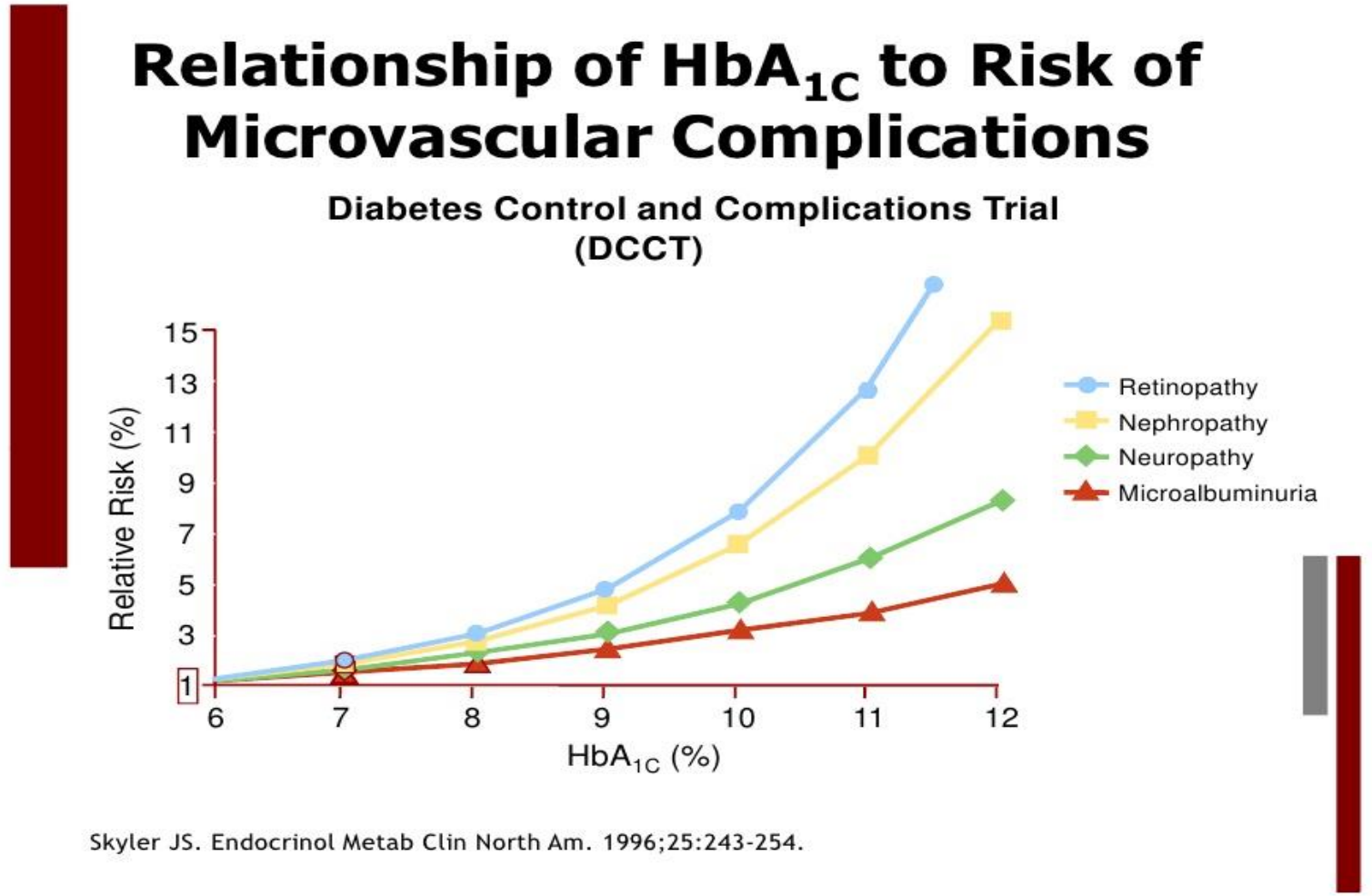


Adapted from Stratton IM, *et al.* UKPDS 35. *BMJ* 2000; 321:405–412.

UKPDS: Intensive blood sugar control decreases eye and kidney complications.

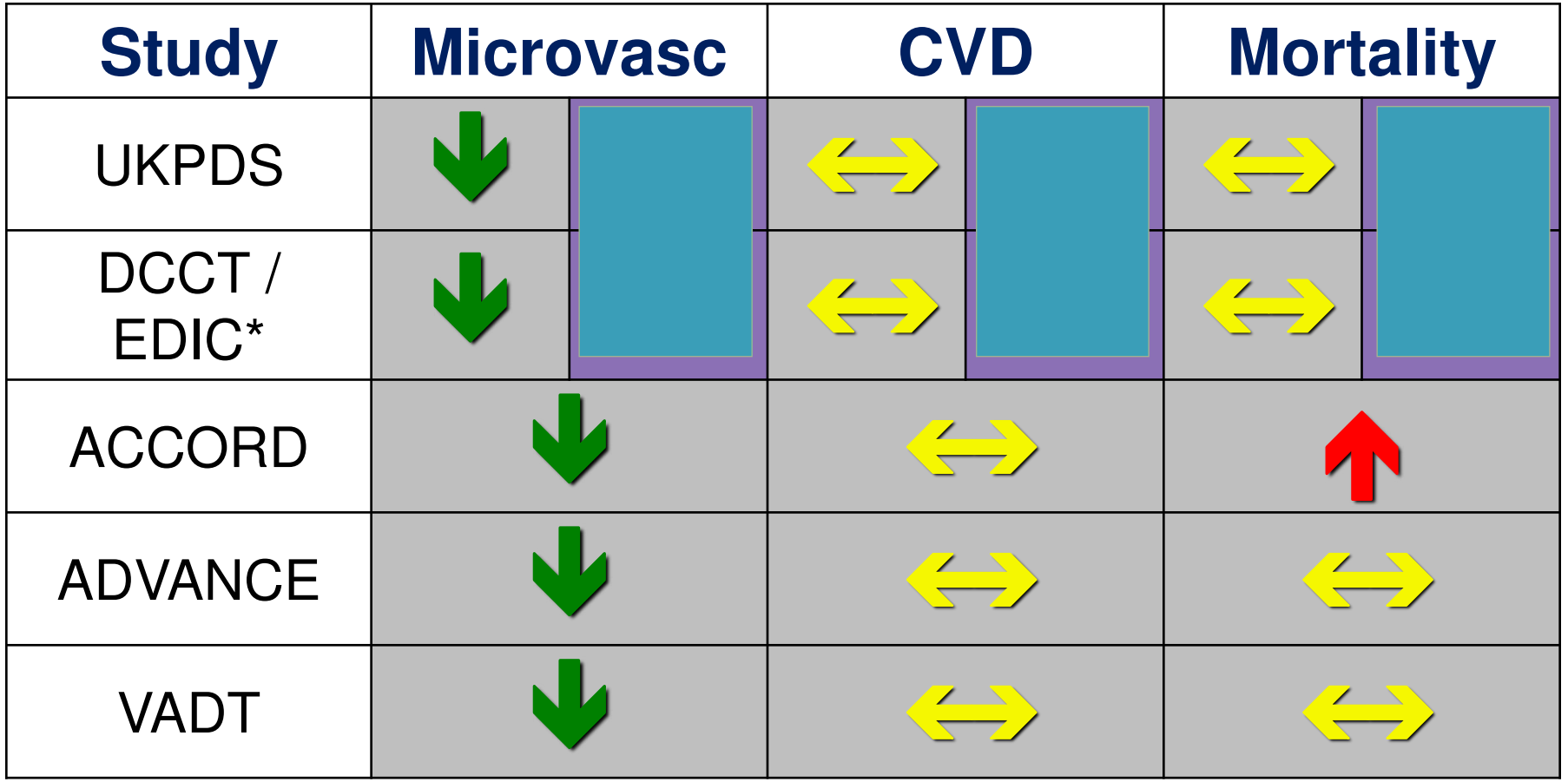


DCCT trial and relationship of small vessel disease (Eyes & Kidneys) to A1C



Skyler JS. Endocrinol Metab Clin North Am. 1996;25:243-254.

Impact of Intensive Therapy for Diabetes: Summary of Major Clinical Trials



UK Prospective Diabetes Study (UKPDS) Group. *Lancet* 1998;352:854.
Holman RR et al. *N Engl J Med*. 2008;359:1577. DCCT Research Group. N Engl J Med 1993;329;977.
Nathan DM et al. *N Engl J Med*. 2005;353:2643. Gerstein HC et al. *N Engl J Med.* 2008;358:2545.
Patel A et al. N Engl J Med 2008;358:2560. Duckworth W et al. N Engl J Med 2009;360:129. (erratum: Moritz T. *N Engl J Med* 2009;361:1024)

Initial Trial

Long Term Follow-up

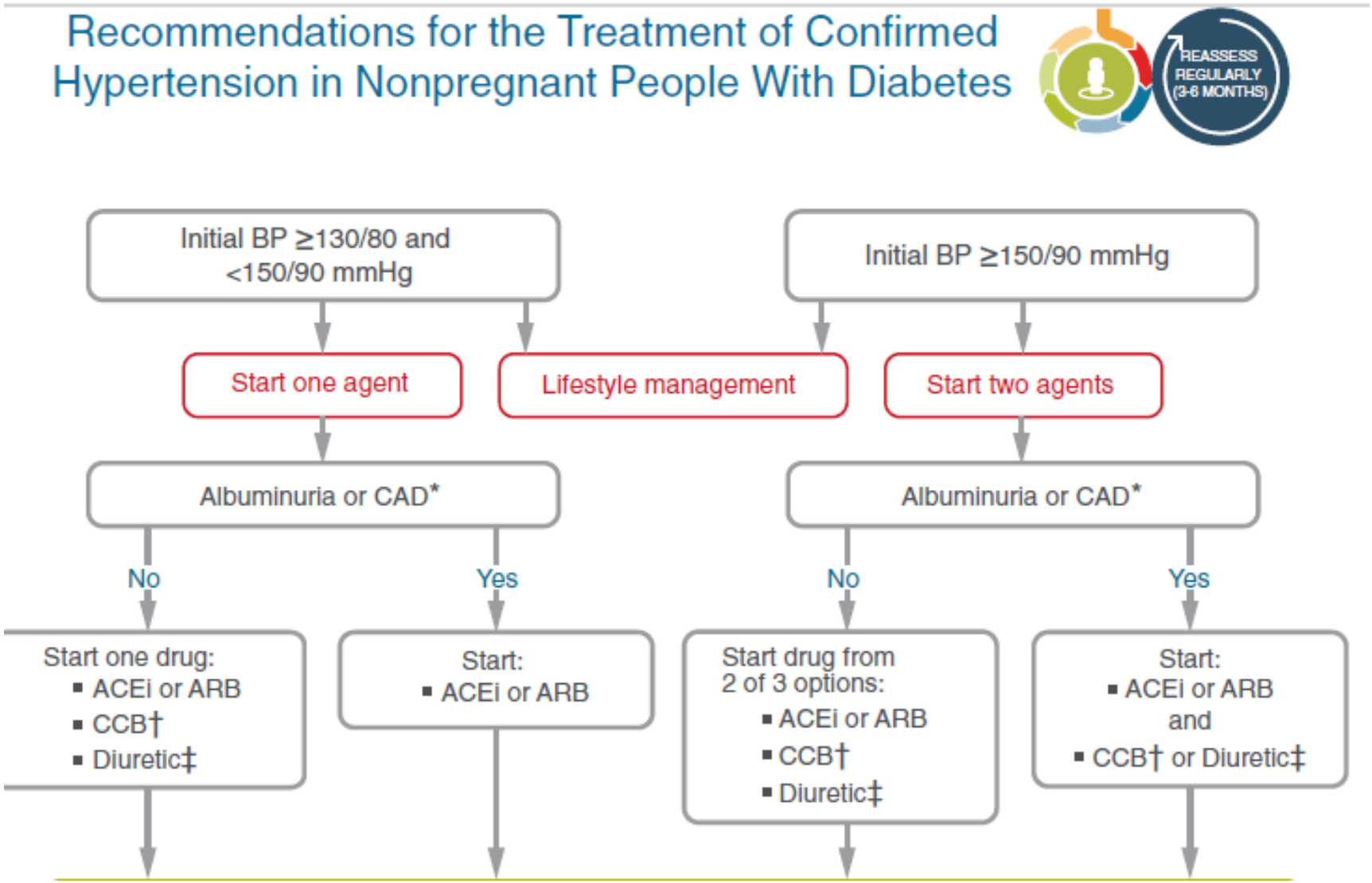
* in T1DM

Hypertension

- Hypertension affects approximately 70% of diabetic patients with a steep graded association between blood pressure and adverse cardiovascular outcomes
- Numerous classes of antihypertensive medications reduce both macrovascular and microvascular disease complications, blood pressure management is of principal importance in this high-risk population.
- Blood pressure goal of <130/80 mm Hg.

ASCVD RISK REDUCTION ALGORITHM: HYPERTENSION

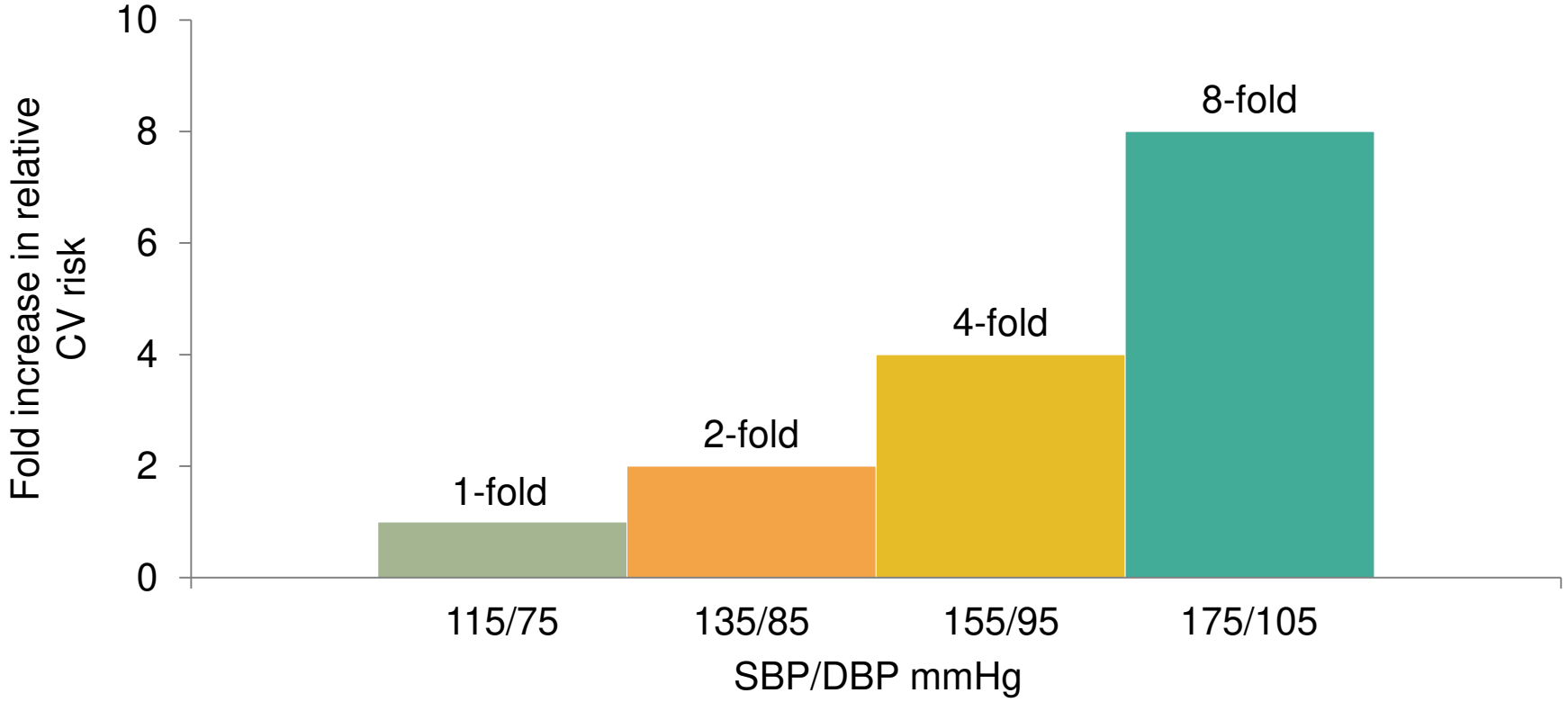
Endocrine Practe 2023
29305-340DOI:
(10.1016/j.eprac.2023.02.001)



Recommendations for the Treatment of Confirmed Hypertension in People with Diabetes (1 of 2)

Cardiovascular Disease and Risk Management:
Standards of Care in Diabetes - 2024. *Diabetes Care* 2024;47(Suppl. 1):S179-S218

Hypertension: each 20/10 mmHg BP increase doubles the risk of CV mortality



Population of 1 million adults with no previous vascular disease recorded at baseline in 61 prospective observational studies of blood pressure and mortality

Lewington et al. Lancet 2002;360:1903–13.

Blood Pressure Control Study

Blood Pressure Control Study

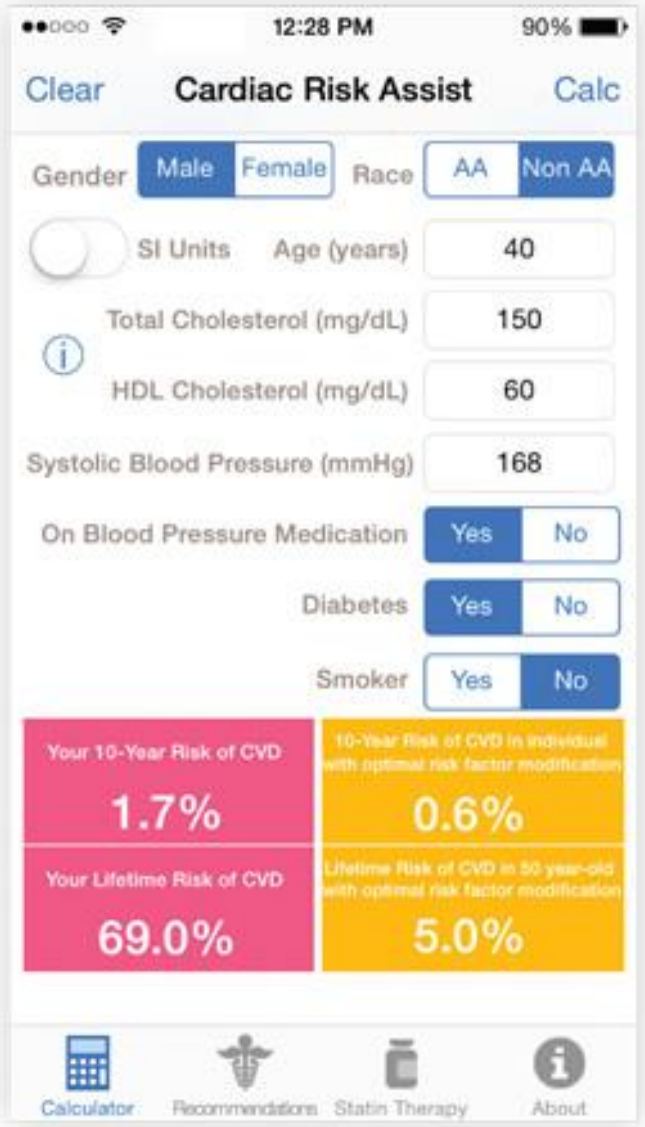
in 1148 Type 2 diabetic patients
a tight blood pressure control policy which achieved blood pressure of 144 / 82 mmHg gave reduced risk for

any diabetes-related endpoint	24%	p=0.0046
diabetes-related deaths	32%	p=0.019
stroke	44%	p=0.013
microvascular disease	37%	p=0.0092
heart failure	56%	p=0.0043
retinopathy progression	34%	p=0.0038
deterioration of vision	47%	p=0.0036

ukpds

Heart Risk: What's Your Score?

- Cardiac Risk Calculator-
  A **cardiac risk calculator** is a screening tool to assess your future risk of cardiovascular disease
- Gives you a 10 year and lifetime score of risk
- For ages 40-75
- Enter multiple risk factors
- Helps you and your provider know what treatments might be best



2013, PCE: Pooled Cohort Equations

PREVENT:
Predicting Risk of Cardiovascular EVENTs

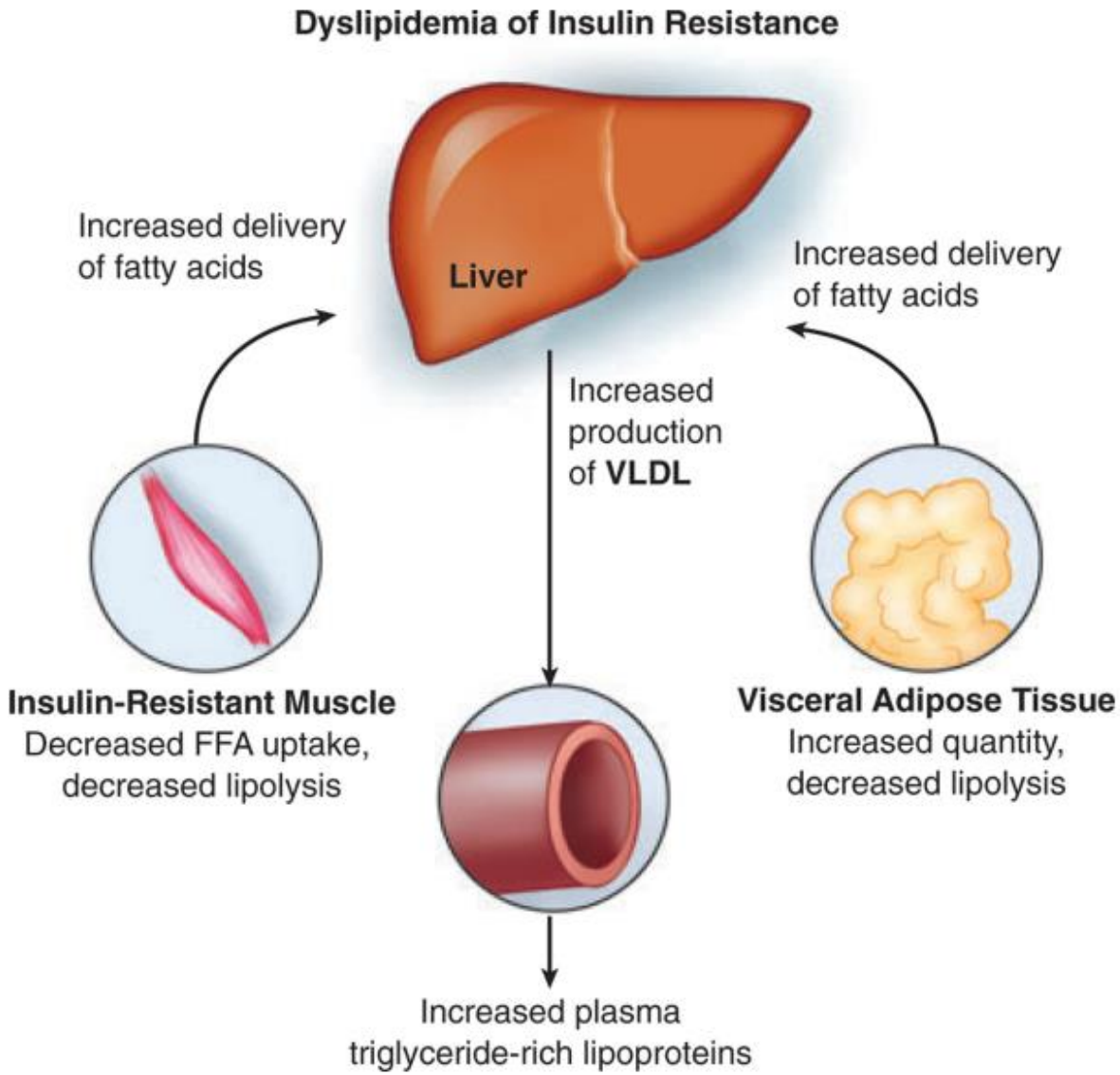
- Not formally adopted into AHA/ACC guidelines yet.
- Released in 2024, new risk calculator incorporates cardiovascular-kidney-metabolic syndrome into CVD prevention.
- May underestimate from current calculator; Statin treatment, hypertension meds
- Includes; TC, HDL, SBP, BMI, eGFR, DM, Smoking, BP and Lipid meds UACR and A1C
- Primary prevention use for pts ages 30-79
- 10-year risk for CVD is categorized as:
  - Low risk (<5%)
  - Borderline risk (5% to 7.4%)
  - Intermediate risk (7.5% to 19.9%)
  - High risk (≥20%)
- https://professional.heart.org/en/guidelines-and-statements/prevent-calculator

. 1. Khan SS, Matsushita K, Sang Y, et al. Development and Validation of the American Heart Association Predicting Risk of Cardiovascular Disease EVENTs (PREVENT™) Equations. Circulation 2023. DOI: 10.1161/CIRCULATIONAHA.123.067626(link opens in new window)(link opens in new window)(link opens in new window).
2. Khan SS, Coresh J, Pencina MJ, et al. Novel Prediction Equations for Absolute Risk Assessment of Total Cardiovascular Disease Incorporating Cardiovascular-Kidney-Metabolic Health: A Scientific Statement From the American Heart Association. Circulation 2023;148(24):1982-2004. DOI: 10.1161/CIR.0000000000001191(link opens in new window)(link opens in new window)(link opens in new window

Cerebrovascular Disease

- Diabetes increases the risk of stroke.
- For example, the risk of stroke among patients taking hypoglycemic medications was increased 3-fold among the nearly 350 000 men in the Multiple Risk Factor Intervention Trial.
- In the Baltimore-Washington Cooperative Young Stroke Study, stroke risk increased more than 10-fold in diabetic patients younger than 44 years of age, ranging as high as 23-fold in young white men.
- Diabetes also increases stroke related mortality, doubles the rate of recurrent stroke, and trebles the frequency of stroke-related dementia.

DYSLIPIDEMIA in Diabetes



ASCVD RISK REDUCTION ALGORITHM: DYSLIPIDEMIA

ASSESS LIPID PANEL (LDL-C, HDL-C, Non-HDL-C, TG, Apo B)[1]

LIFESTYLE INTERVENTION: increase ↑ dietary fiber | ↑ healthy fat | ↓ saturated fat | ↓ simple carbs | ↓ added sugars | ↑ physical activity | weight management

PREDIABETES OR T2D + RISK FACTORS: USE ASCVD 10-YEAR RISK CALCULATOR
Major ASCVD Risk Factors: Age >40 | HTN | CKD >3a | Smoking | Family History of Premature ASCVD | Low HDL-C | High Non-HDL-C

INITIATE STATIN THERAPY

		HIGH RISK <10% T2D <10 years <2 other risk factors No target organ damage	VERY HIGH RISK 10%-20% T2D >10 years Age >40 years No ASCVD No target organ damage ≥2 additional risk factors	EXTREME RISK >20% T2D & ASCVD Severe target organ damage: eGFR <45 mL/min/1.73 m^2, UACR >300, ABI <0.9, LV systolic/diastolic dysfunction
		Moderate-intensity statin	High-intensity statin	
GOAL	LDL-C (mg/dL) <100		<70	<55
	Non-HDL-C (mg/dL) <130		<100	<80
	TG (mg/dL) <150		<150	<150
	Apo B (mg/dL) <90		<80	<70

Monitor and titrate therapy every 3-6 months to achieve lipid targets according to risk[2]

Intensify statin and lifestyle & optimize glycemic control

Add ezetimibe

Consider additional therapy: bile acid sequestrant, bempedoic acid, PCSK9 inhibitor, inclisiran

HYPERTRIGLYCERIDEMIA MANAGEMENT:

TG 135-199 | **TG 200-499[3]** | **TG ≥500** | **TG >1000[4]**

Intensify Lifestyle & Achieve Glycemic Targets

If TG >135: Consider addition of icosapent ethyl to statin if DM and CVD or ≥2 risk factors

Fibrate or/and Rx Grade Omega-3

TG target achieved: Continue lifestyle therapy, maximally tolerated statin and achieve glucose targets

+Niacin[5]

[1] Baseline LDL-C >190 mg/dL, consider familial hypercholesterolemia. [2]Statin intolerance: Use alternative statin with lower incidence of myopathy (pitavastatin, extended-release fluvastatin) or decrease dose/frequency, use non-statin Rx, check for Rx interactions, consider CoQ10. [3]If TG >200 and HDL <40, add fibrate/omega-2 to achieve apo B and non-HDL goals. [4]Elevated triglycerides >500 mg/dL to >1000 mg/dL can cause acute pancreatitis. Urgent intervention with dietary management and fibrate/omega 3 therapy is needed. Suspect familial chylomicronemia syndrome or lipodystrophy, refer to lipid specialist. [5]For severe hypertriglyceridemia >1000 refractory to previous interventions, consider niacin to reduce the risk of pancreatitis. Niacin may lower TG and Lp(a) but does not reduce ASCVD and can promote hyperglycemia.

Table 10.2—High-intensity and moderate-intensity statin therapy

High-intensity statin therapy (lowers LDL cholesterol by ≥50%)	Moderate-intensity statin therapy (lowers LDL cholesterol by 30–49%)
Atorvastatin 40–80 mg	Atorvastatin 10–20 mg
Rosuvastatin 20–40 mg	Rosuvastatin 5–10 mg
	Simvastatin 20–40 mg
	Pravastatin 40–80 mg
	Lovastatin 40 mg
	Fluvastatin XL 80 mg
	Pitavastatin 1–4 mg

Once-daily dosing. XL, extended release.

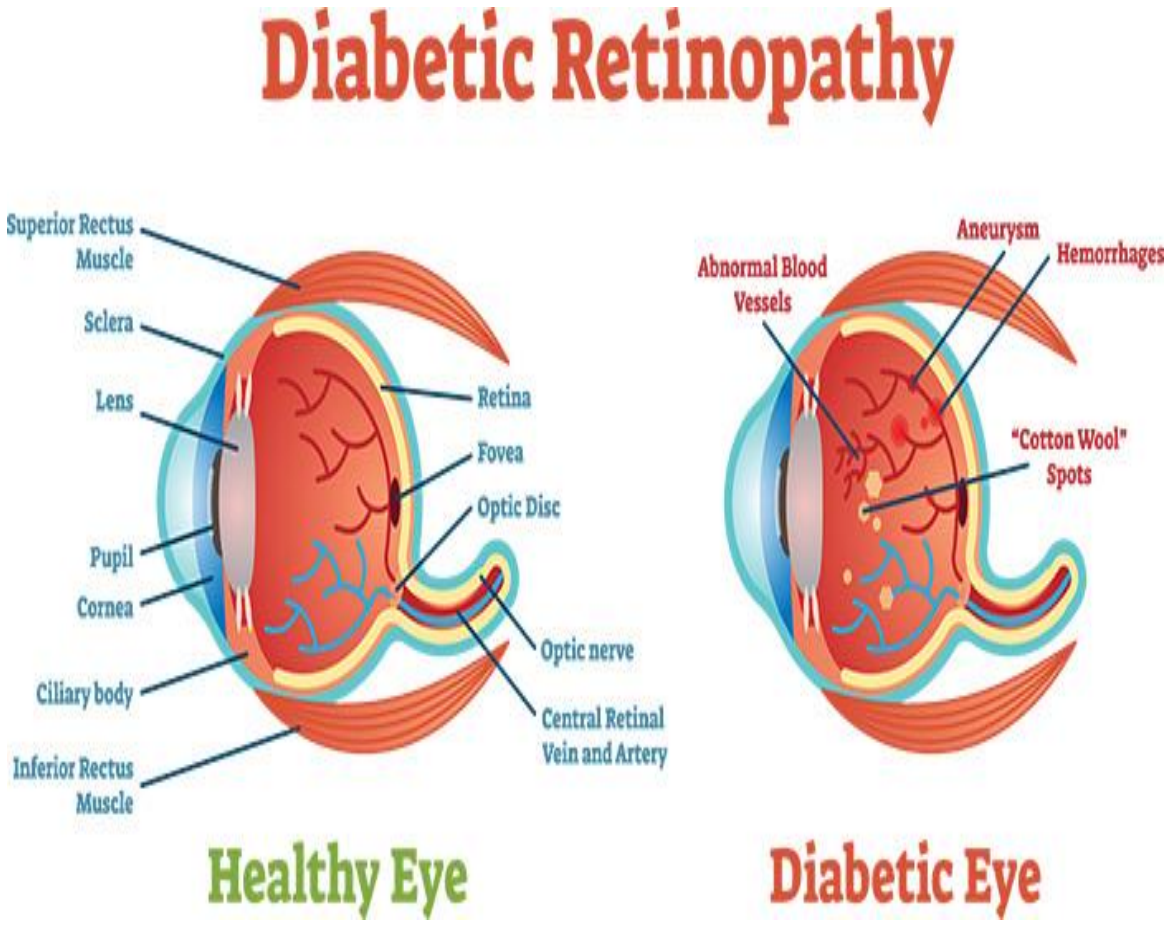
Cardiovascular Disease and Risk Management:
Standards of Care in Diabetes - 2024. *Diabetes Care* 2024;47(Suppl. 1):S179-S218

Recommendations Continued

- In adults with diabetes, continuing statin therapy in people age >75 who are currently on a statin is now recommended
- In adults >75, not on a statin, it may be reasonable to initiate moderate intensity statin, weighing the pros/cons.
- Main side effect to report: muscle aches/weakness in large muscles (not joints)

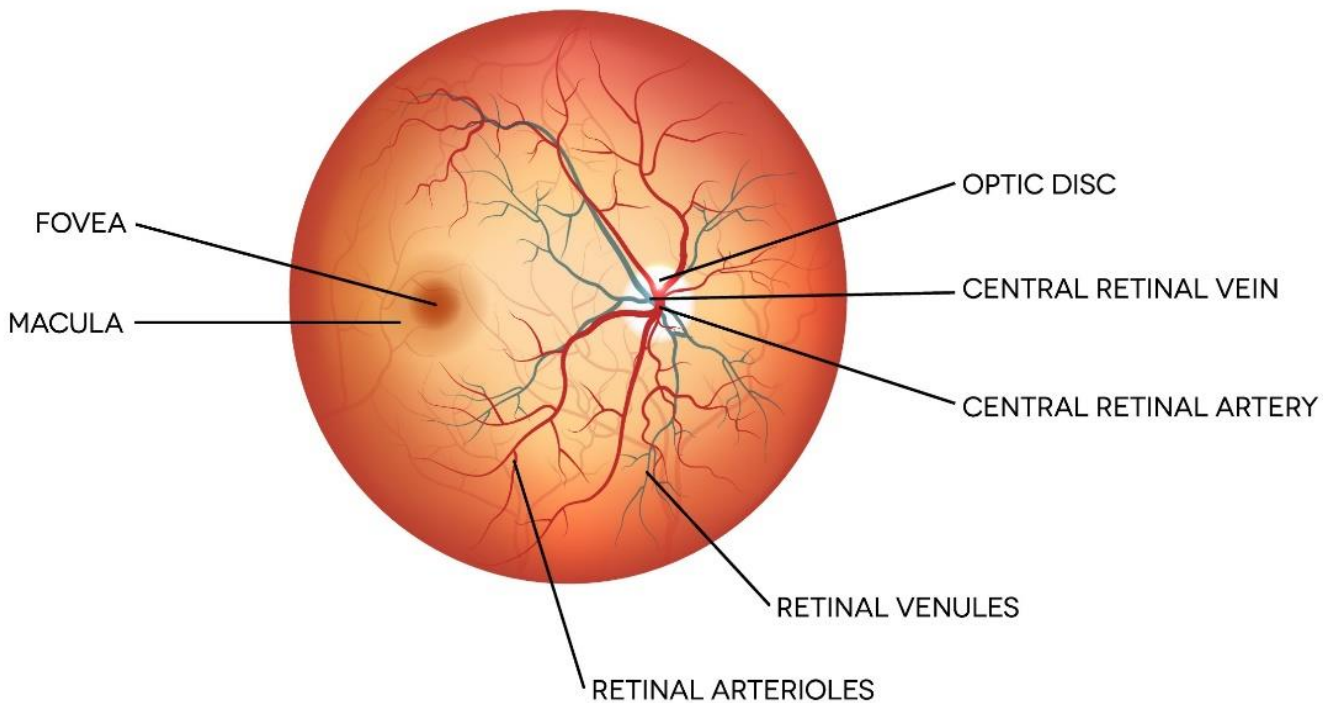
Retinopathy in Diabetes

- Leading cause of adult blindness in the US
- Best prevention: Dilated Eye Examination every year
  - Have good glucose control, so you can also read the eye chart for refraction evaluation.
- Non-midratic cameras are now available, so a dilated exam may not always be necessary
- Cataracts
  - People with diabetes tend to get them earlier, and they get worse faster, likely due to osmotic fluid shifts of glucose in the lens.

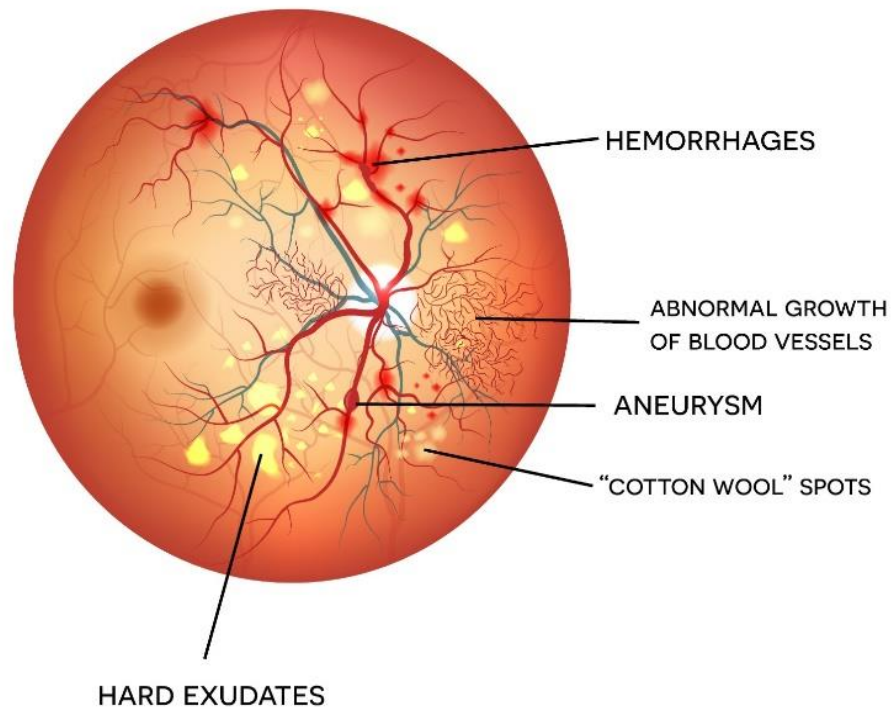


DIABETIC RETINOPATHY

NORMAL RETINA



DIABETIC RETINOPATHY



Diabetic Retinopathy—Screening

12.3 Adults with type 1 diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist within 5 years after the onset of diabetes. **B**

12.4 People with type 2 diabetes should have an initial dilated and comprehensive eye examination by an ophthalmologist or optometrist at the time of the diabetes diagnosis. **B**

12.5 If there is no evidence of retinopathy from one or more annual eye exams and glycemic indicators are within the goal range, then screening every 1–2 years may be considered. If any level of diabetic retinopathy is present, subsequent dilated retinal examinations should be repeated at least annually by an ophthalmologist or optometrist. If retinopathy is progressing or sight-threatening, examinations will be required more frequently. **B**

Diabetic Retinopathy—Screening (continued)

12.6 Programs that use retinal photography with remote reading or the use of U.S. Food and Drug Administration-approved artificial intelligence algorithms to improve access to diabetic retinopathy screening are appropriate screening strategies for diabetic retinopathy. Such programs need to provide pathways for timely referral for a comprehensive eye examination when indicated. **B**

12.7 Counsel individuals of childbearing potential with preexisting type 1 or type 2 diabetes who are planning pregnancy or who are pregnant on the risk of development and/or progression of diabetic retinopathy. **B**

12.8 Individuals with preexisting type 1 or type 2 diabetes should receive an eye exam before pregnancy and in the first trimester and should be monitored every trimester and for 1 year postpartum as indicated by the degree of retinopathy. **B**

Diabetic Retinopathy—Treatment

12.9 Promptly refer individuals with any level of diabetic macular edema, moderate or worse non-proliferative diabetic retinopathy (a precursor of proliferative diabetic retinopathy [PDR]), or any PDR to an ophthalmologist who is knowledgeable and experienced in the management of diabetic retinopathy. **A**

12.10 Panretinal laser photocoagulation therapy is indicated to reduce the risk of vision loss in individuals with high-risk PDR and, in some cases, severe non-proliferative diabetic retinopathy. **A**

12.11 Intravitreous injections of anti-vascular endothelial growth factor (anti-VEGF) are a reasonable alternative to traditional panretinal laser photocoagulation for some individuals with PDR and also reduce the risk of vision loss in these individuals. **A**

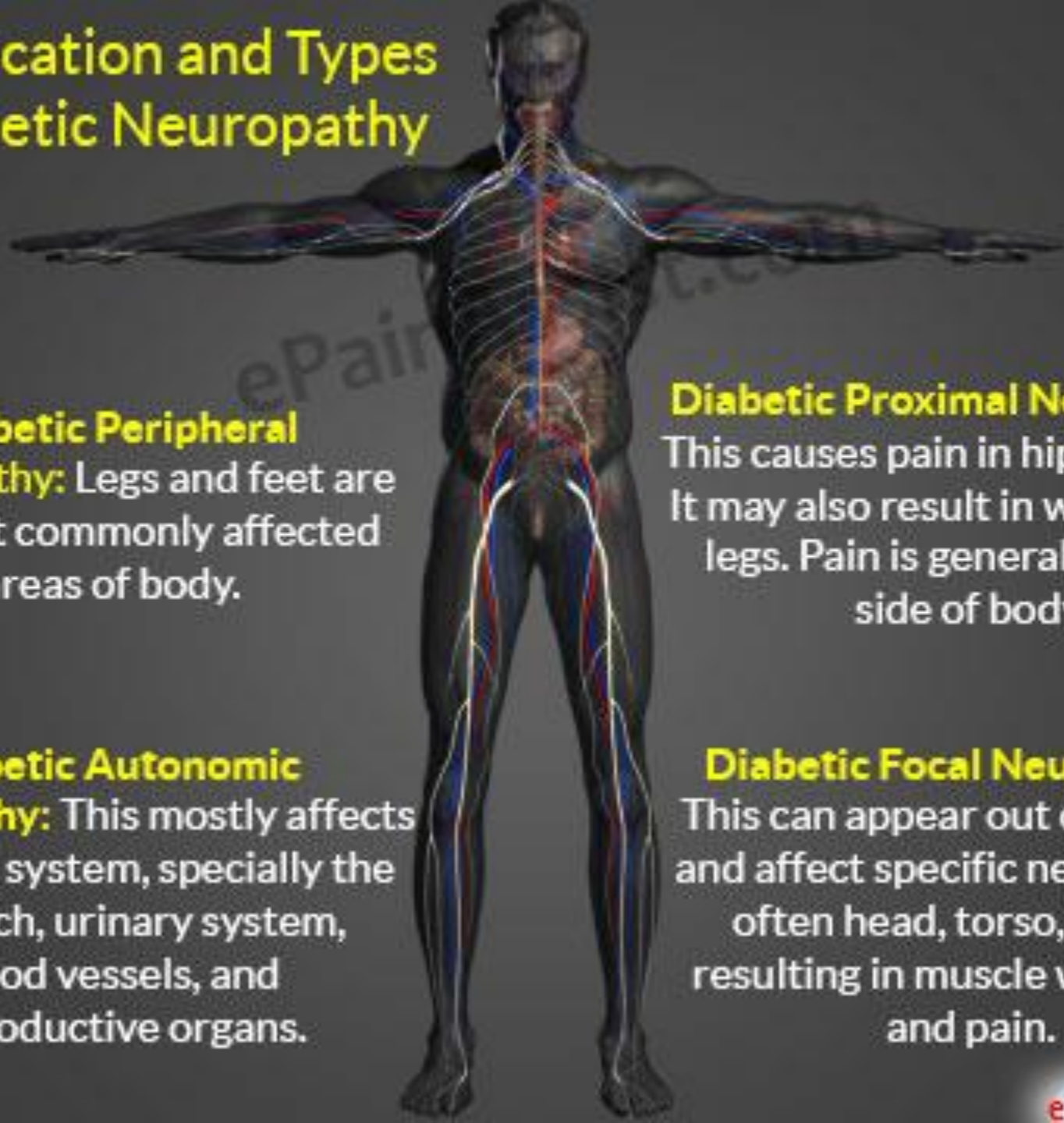
Diabetic Retinopathy—Treatment (continued)

12.12 Intravitreous injections of anti-VEGF are indicated as first-line treatment for most eyes with diabetic macular edema that involves the foveal center and impairs vision acuity. **A**

12.13 Macular focal/grid photocoagulation and intravitreal injections of corticosteroid are reasonable treatments in eyes with persistent diabetic macular edema despite previous anti-VEGF therapy or eyes that are not candidates or this first-line approach. **A**

12.14 The presence of retinopathy is not a contraindication to aspirin therapy for cardioprotection, as aspirin does not increase the risk of retinal hemorrhage. **A**

Classification and Types of Diabetic Neuropathy



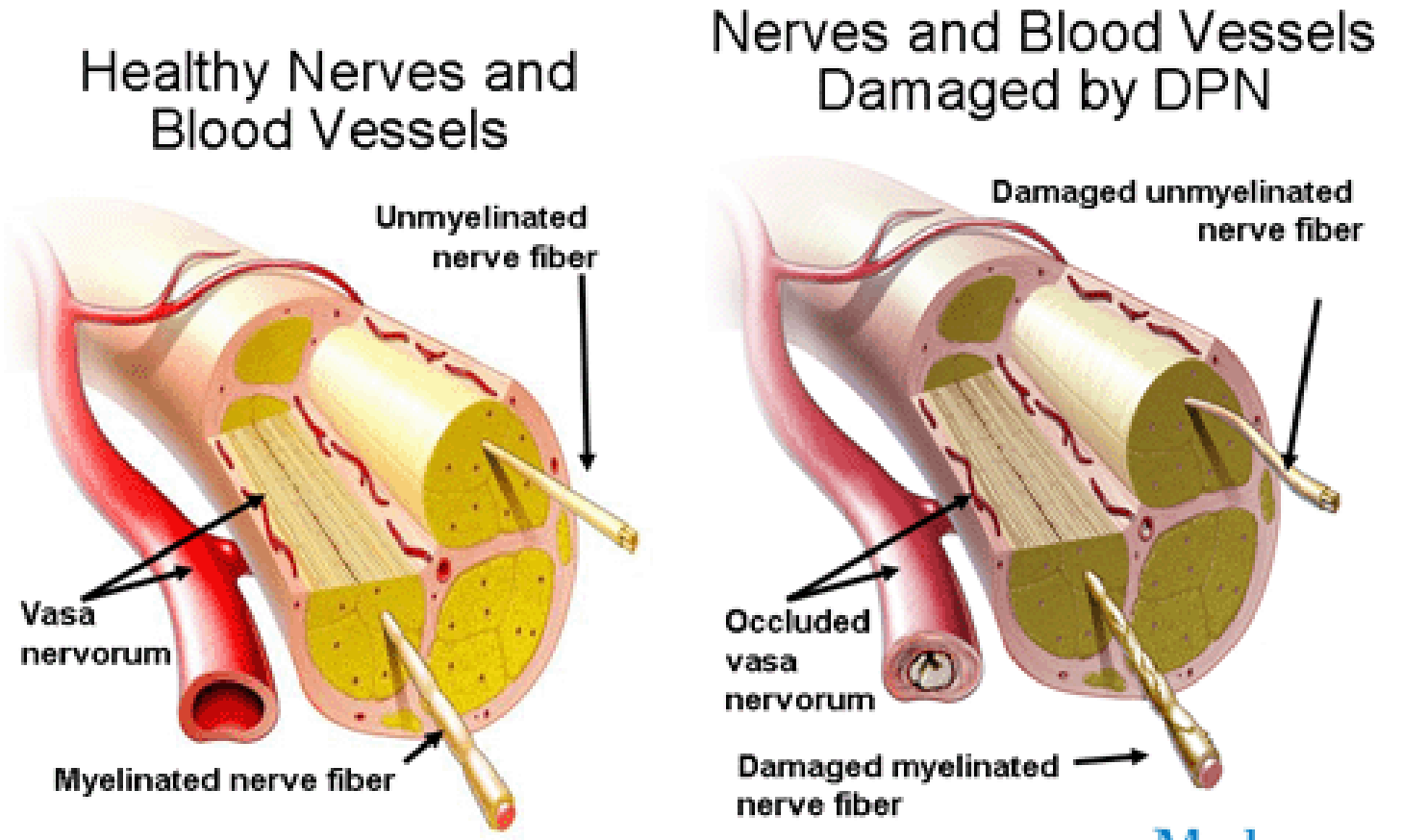
Diabetic Peripheral Neuropathy: Legs and feet are the most commonly affected areas of body.

Diabetic Autonomic Neuropathy: This mostly affects digestive system, specially the stomach, urinary system, blood vessels, and reproductive organs.

Diabetic Proximal Neuropathy: This causes pain in hips or thighs. It may also result in weakness of legs. Pain is generally on one side of body.

Diabetic Focal Neuropathy: This can appear out of the blue and affect specific nerves, most often head, torso, and leg resulting in muscle weakness and pain.

Diabetic Peripheral Neuropathy



Vinik AI. *Diabetic Microvascular Complications Today*. 2006;3:23-26.

Symptoms: vary based on sensory fibers involved

Painful diabetic peripheral neuropathy

- Numbness or insensitivity to pain or temperature
- Tingling, burning, or prickling sensation
- Sharp pains or cramps
- Extreme sensitivity to touch, even light touch
- Loss of balance and co-ordination
- Muscle weakness and loss of reflexes
- Symptoms are often worse at night

National Institute of Diabetes and Digestive and Kidney Diseases. *Diabetic Neuropathies: The Nerve Damage of Diabetes*. Available at: http://diabetes.niddk.nih.gov/dm/pubs/neuropathies/. Accessed 18 Oct 2011.

Diabetes is most common cause of neuropathy

- **Neuropathy** is the most common complication of diabetes

How to diagnose? A diagnosis of Exclusion

- History of symptoms
- Physical exam: muscle weakness, numbness, and impaired motor fx
- Labs: vitamin deficiencies, check underlying disease that can affect nerve function (B1, B6, B12, niacin)
- Electromyogram (EMG) and nerve conduction studies (NCS) tests (pinpoint the abnormal nerves and where it is coming from)
- MRI (tumors/nerve compression)
- Nerve and muscle biopsies

Neuropathy

Causes:

- *60% to 70% of neuropathy due to diabetes.*
- *30% to 40% of people who receive chemotherapy to treat cancer get neuropathy.*
- *Frostbite*
- *Can be caused by other meds too.*
- *Autoimmune disorders*
- *Trauma- nerve compression, repetitive motion*

Autonomic Neuropathy can impact:

- Bladder: Neurogenic bladder.
  - Crede maneuver may be necessary
- Eyes- pupils. Don’t dilate and constrict
- Digestion: Gastroparesis
  - Gastric Emptying study notoriously unreliable
  - GLP’s *may* have a trial with very low doses
  - Meal time insulin may need to be given after the meal. Or use Regular, instead of Rapid Acting – LisPro or Aspart
  - Consult with RD. Soft foods, low fiber, low fat, well cooked vegetables & fruit
- Heart & Blood vessels
  - Fixed heart rate
- Sexual function

Neuropathy Treatment

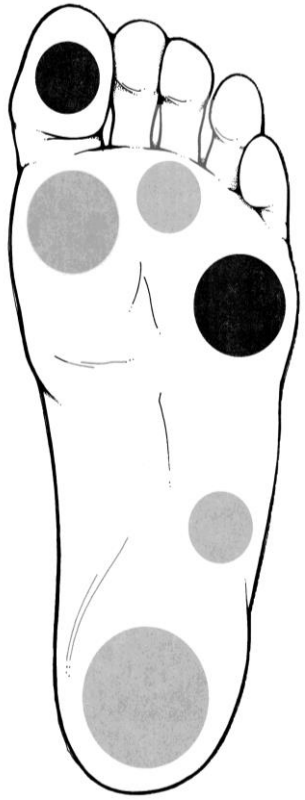
- Optimize blood sugar control- to prevent, delay, or slow progression
- Vitamin therapy if deficient and an improved diet
- Avoiding alcohol
- Medication: Gabapentin (Neurontin), Cymbalta (Duloxetine), Lyrica (Pregabalin), Topical patches (Lidocaine), creams (Capsaicin & Rx Capsaicin (Qutenza)). Tegratol or Alpha Lipoic Acid may also be effective. Metanx: B6, B12, Folic Acid. Pain and nerve regeneration.
- Physical Therapy (to help with balance)
- Surgery (if something needs to be fixed: herniated disc/ carpal tunnel)
- Mechanical aids (braces, shoes, canes)
- TENs units (electrical nerve stimulation)
- Other: Acupuncture, meditation, behavioral therapy

Exercise Safety: adjust activity for diabetes complications

- Cardiac Autonomic neuropathy:
  - Heart rate is unreliable for gauging exercise intensity
  - Extended warm up and cool down
  - Maintain hydration (thirst signals may be impaired)
  - Avoid extreme weather
    - People with heart disease: consult cardiologist
    - Avoid low blood sugar- can increase stress hormones and the workload on the heart
- Peripheral Neuropathy:
  - Low and non impact activity
  - May need activity with feet fixed if proprioception altered with loss of sensation. Exercise bike, rowing machine, indoor mall walking maybe
  - Avoid overstretching, pain signals are diminished.
  - Proper footwear/ inspect feet
  - Foot complications: non-weight bearing exercise
- Proliferative retinopathy:
  - Avoid sudden changes in direction
  - Don’t hold breath when lifting- no straining
  - Steady paced exercise
  - Keep head above heart

Foot Care

- **Test for sensation using monofilament foot exam at least once yearly**
- **Should Include one other test:**
  - **Vibratory, pin prick**
- **Have MA ask pts to take off shoes when waiting in the exam room**
- **Avoid heating pads, hot water bottles, etc**
- **Avoid going barefoot indoors and outdoors**
- **Put sunscreen on tops of feet (and other exposed skin)**



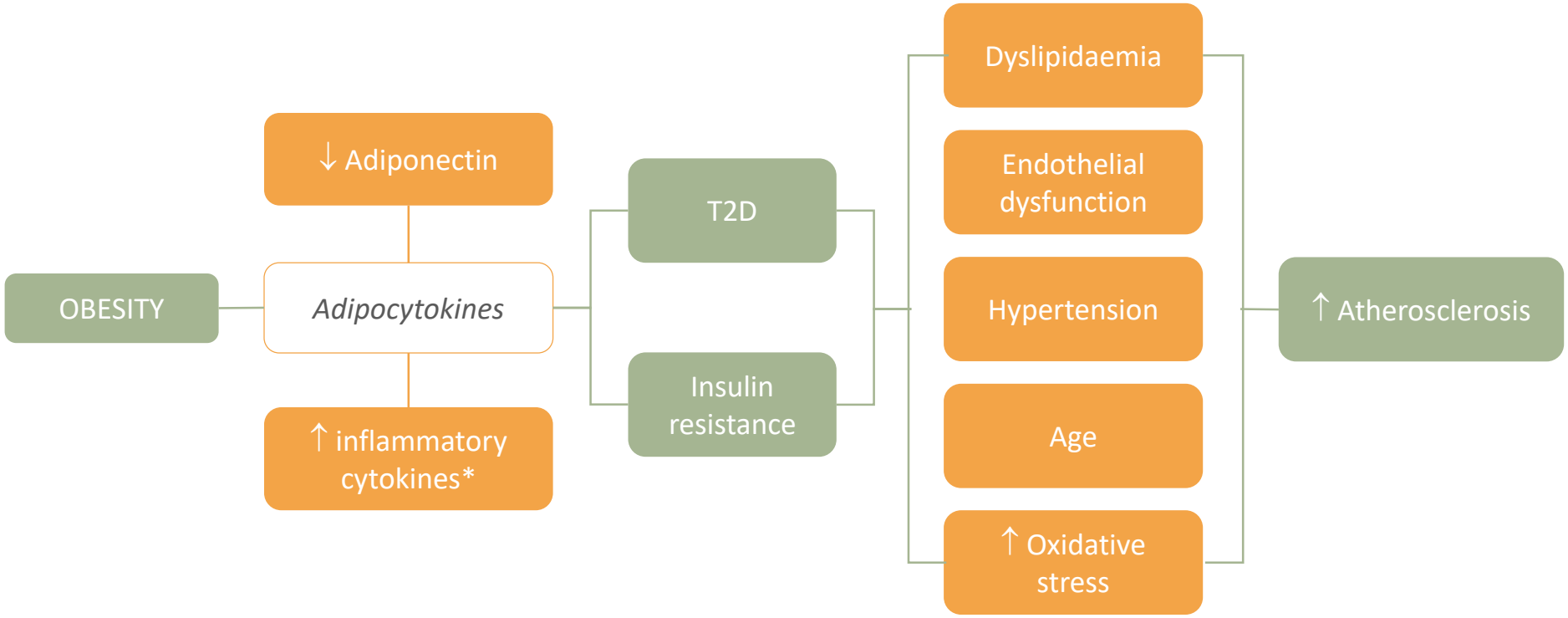
Peripheral Artery Disease (PAD)

- PAD can build up over a lifetime, and symptoms may not appear until later in life
  - Cramping in legs or hips with activity
  - Discomfort goes away with rest
  - Reduced pulses in feet
  - Cold feet
  - Sores that don’t heal
  - Discoloration- dark red (rubor) or purple/blue (dusky)

- **Peripheral Arterial Disease**
- Diabetes increases the incidence and severity of limb ischemia approximately 2- to 4-fold.
- Data from the Framingham cohort and Rotterdam studies show increased rates of absent pedal pulses, femoral bruits, and diminished ankle-brachial indices.
- Diabetic peripheral arterial disease often affects distal limb vessels, such as the tibial and peroneal arteries, limiting the potential for collateral vessel development and reducing options for revascularization.
- As such, patients with diabetes are more likely to develop symptomatic forms of the disease, such as intermittent claudication and critical limb ischemia, and undergo amputation.

Visceral adiposity is related to inflammation, insulin resistance, dyslipidaemia and atherosclerosis

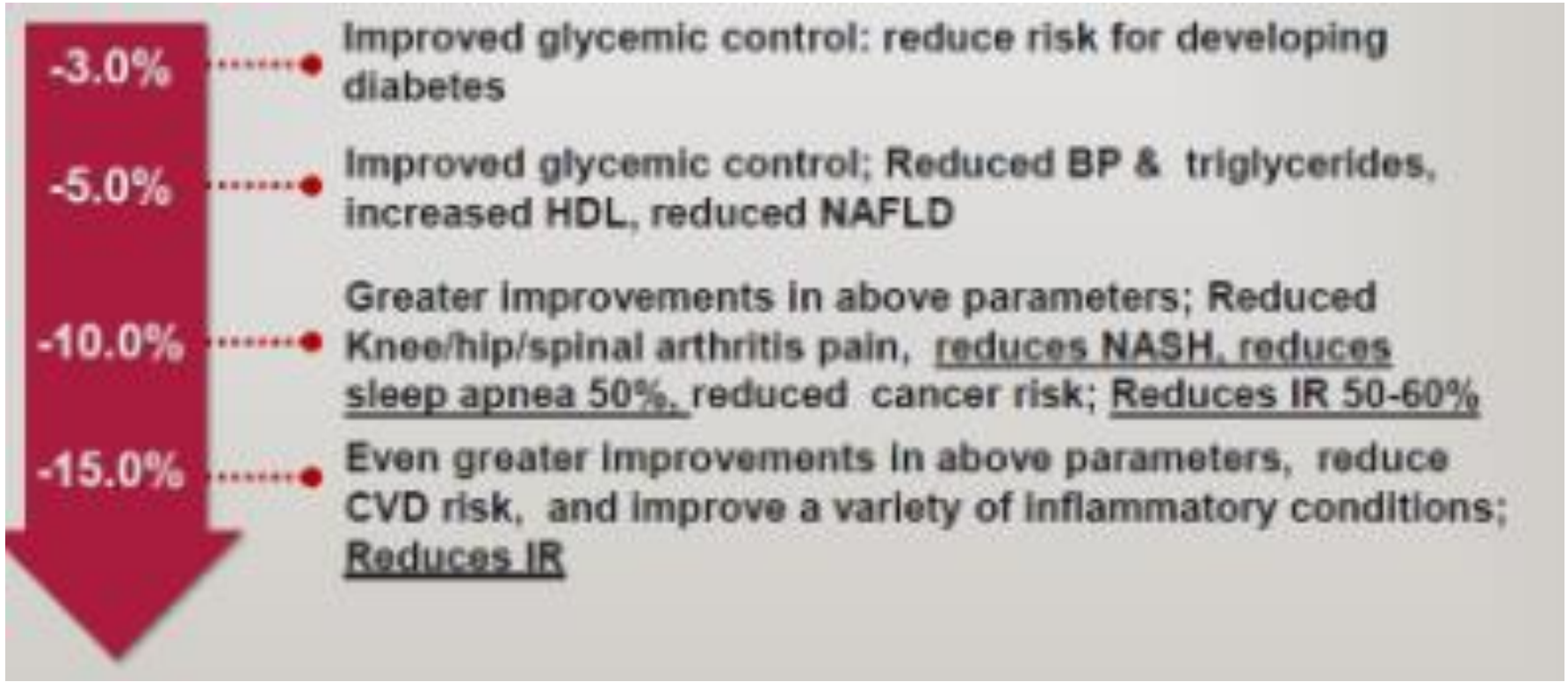
Interactions are complex, inter-related and not necessarily causal



*including: TNFα, IL-6, resistin, PAI-1, angiotensinogen

Lau et al. Am J Physiol Heart Circ Physiol 2005;288:H2031–41.

Metabolic Benefits of Percent of Body Weight Loss



Jensen, MD et al. J AM Coll Cardiol. 2014;63 (25)

Weight Loss Strategies and Interventions

- **Lifestyle interventions**
  - Targeted diets and eating plans
  - Increased activity
  - Psychotherapy---behavior changes
- **Approved Anti-obesity medications**
  - Phentermine
  - Orlistat
  - Naltrexone HCL-Buproprion HCL (*Contrave*)
  - Phentermine-topiramate ER (*Qsymia*)
  - Liraglutide 3 mg (*Saxenda*)
  - Semaglutide 2.4 mg (Wegovy)
  - *Tirzepatide (Mounjaro) not approved*

Gastric & Endoscopic interventions

Hydrogels (Plenity)
Intragastic balloons
Endoscopic sleeve gastroplasty
(Refer to GI for this)

Metabolic & Bariatric surgery (MBS)

Adjustable Gastric Band
Sleeve Gastrectomy
Gastric bypass (RYGB)
Duodenal switch
(Refer to bariatric surgeon)

Non Alcoholic Fatty Liver Disease

Non Alcoholic Fatty Liver Disease (NAFLD)

- Is Liver fat greater than 5% in those without excessive alcohol use
- Prevalence: NAFLD is the most common chronic liver condition in the US. About **25 percent of adults** have NAFLD. It is often underdiagnosed.
- 22% of people with Type 1 diabetes have NAFLD.
- >68% of people with Type2 diabetes have NAFLD.
- It is not a given that people with type 2 diabetes will automatically develop fatty liver disease, but obesity, insulin resistance and elevated triglycerides increase the risk.

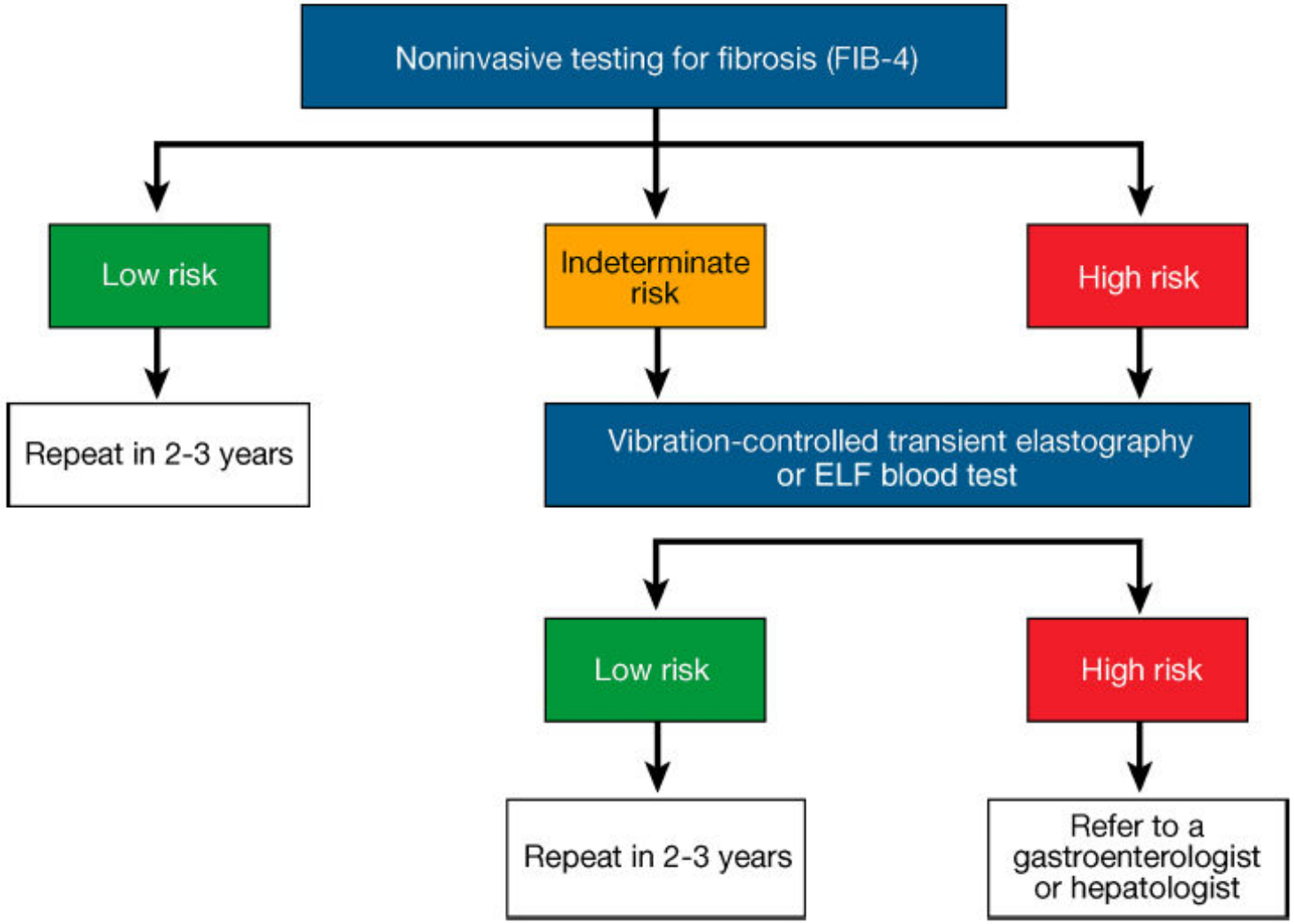
Nonalcoholic Fatty Liver Disease and Nonalcoholic Steatohepatitis (continued)

4.27 Adults with type 2 diabetes or prediabetes, particularly with overweight or obesity, with nonalcoholic fatty liver disease (NAFLD) should be recommended lifestyle changes that promote weight loss, ideally within a structured nutrition plan and physical activity program for cardiometabolic benefits B and histological improvement. **C**

4.28 For adults with type 2 diabetes, particularly with overweight or obesity, with NAFLD, consider using a glucagon-like peptide 1 (GLP-1) receptor agonist with demonstrated benefits in nonalcoholic steatohepatitis (NASH) as an adjunctive therapy to lifestyle interventions for weight loss. **B**

4.29 Pioglitazone or GLP-1 receptor agonists are the preferred agents for the treatment of hyperglycemia in adults with type 2 diabetes with biopsy-proven NASH or those at high risk with clinically significant liver fibrosis using noninvasive tests. A

COMPREHENSIVE MEDICAL EVALUATION AND ASSESSMENT OF COMORBIDITIES



Comprehensive Medical Evaluation and Assessment of Comorbidities:
Standards of Care in Diabetes - 2024. *Diabetes Care* 2024;47(Suppl. 1):S52-S76

FIB-4
To assess risk for advanced liver fibrosis

- Laboratory measures (AST, ALT, platelet count)
- In combination with patient age
  - Low risk (<1·30),
  - indeterminate (1·30–2·67),
  - high (>2·67) risk of fibrosis
- ADA: screen if elevated liver enzymes or fatty liver on imaging
- sequential measurements (every 1-3 years) should indicate evolving risk of severe events, fibrosis, CV and all cause mortality

Anstee et al https://www.thelancet.com/journals/lanepe/issue/vol36nonull/PIIS2666-7762(23)X0011-8 12-23.

NAFLD as a complication of type 2 diabetes

- (Newer) Metabolic dysfunction-Associated Steatotic Liver Disease (MASLD).
- Benefits in the liver after just a 5-10% weight loss
- Recent studies show: many approved oral and injectable diabetes medications hold promise as a treatment for fatty liver disease (pioglitazone & GLP1s. ADA ‘24)
- Fatty liver usually has no symptoms
  - Fatty Liver raises your risk of developing liver inflammation or scarring (cirrhosis).
  - Fibrosis- 4 (FIB-4 calculator)- formula to calculate risk
  - ALT/AST- But blood tests do not always pick up NAFLD. It may also be spotted during an ultrasound/ MRI of your abdomen.

VACCINE RECOMMENDATIONS FOR PERSONS WITH DIABETES MELLITUS

CDC IMMUNIZATION RECOMMENDATIONS FOR PERSONS WITH DIABETES MELLITUS[1]

VACCINE	RECOMMENDATION
Age-appropriate vaccines	All persons should receive according to the CDC/ACIP immunization schedules.
COVID-19	Primary series and booster per current CDC recommendations and FDA approvals
Flu	Annually
HepB	All adults ≤59 years Based on risk and quality of immune response for adults ≥60 years
PCV	Adults with DM ages ≥19 years 1 dose PCV15 followed by PPSV23 at ≥1 year (or ≥8 weeks for adults who are immunocompromised) OR 1 dose PCV20 See also current CDC recommendations for details.
RZV	All adults ≥50 years
Tdap	Every 10 years following completion of the primary series

ACIP = Advisory Committee on Immunization Practices; **CDC** = Centers for Disease Control and Prevention; **COVID-19** = coronavirus disease 2019; **DM** = diabetes mellitus; **FDA** = Food and Drug Administration; **HepB** = hepatitis B; **PCV** = pneumococcal conjugate vaccine; **PPSV23** = pneumococcal polysaccharide vaccine; **RZV** = recombinant zoster vaccine; **TDAP** = tetanus, diphtheria, acellular pertussis

[1]https://www.cdc.gov/vaccines/schedules/index.html

For child/adolescent specific recommendations, see https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html

CDC STANDARDS FOR ADULT IMMUNIZATION PRACTICE

ASSESS	Assess immunization status of all individuals at every encounter. • Incorporate into workflow. • Stay up to date on the latest recommendations of the CDC Advisory Committee on Immunization Practices. Updated immunization schedules are released annually.
RECOMMEND	**STRONGLY** recommend vaccines based on age/risk factors. • Address questions and concerns. • Highlight positive experiences and benefits of vaccines.
ADMINISTER/ REFER	Administer or refer patients for immunization. • Stock routine vaccines or know your local vaccine providers for referral.
DOCUMENT	Document receipt of vaccine in state immunization registry and electronic health record. https://www.cdc.gov/vaccines/hcp/adults/for-practice/standards/index.html

Endocrine Practice 2023 29305-340DOI: (10.1016/j.eprac.2023.02.001

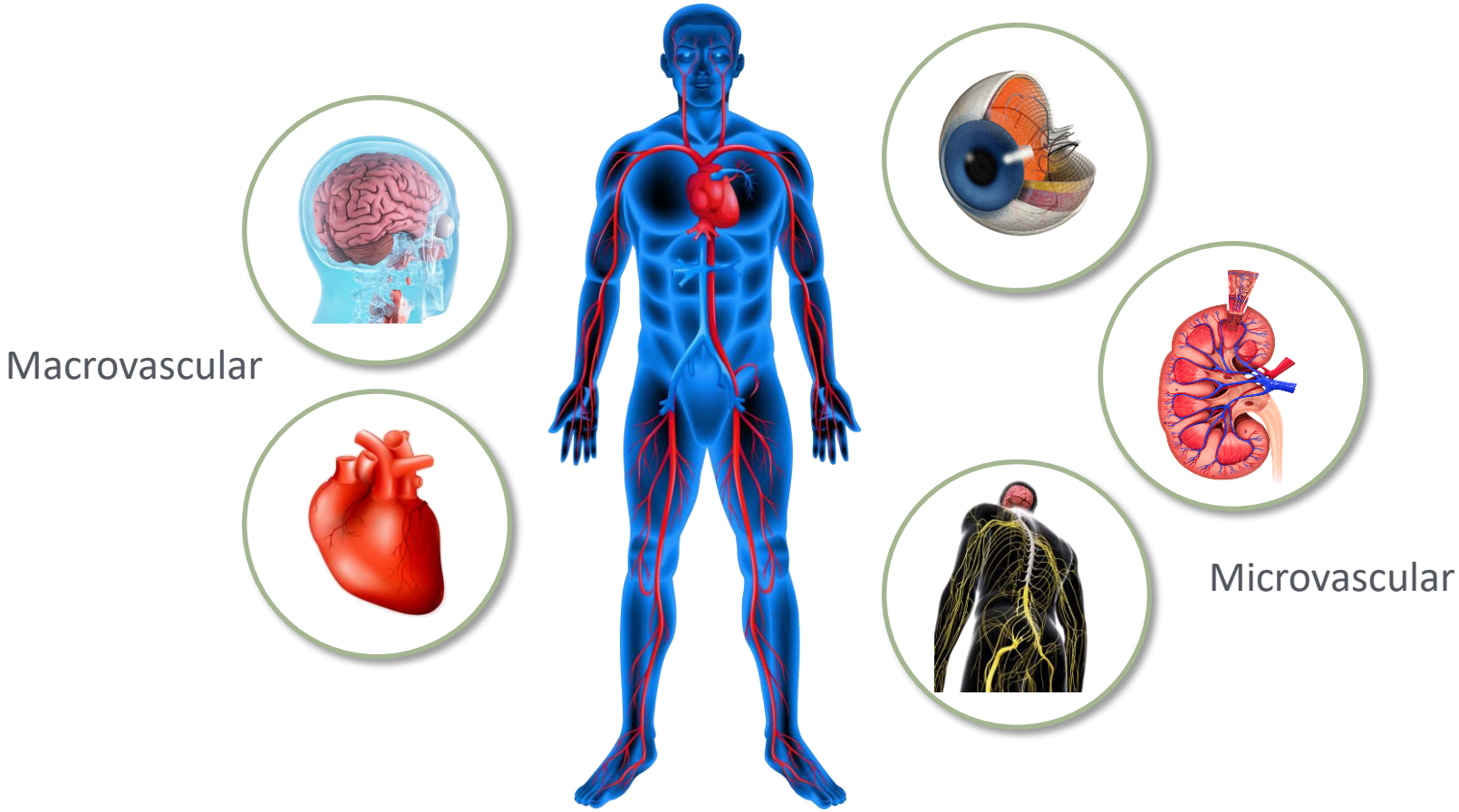
Patient Friendly Slides

to help teach Complications

Are Complications Inevitable? NO!

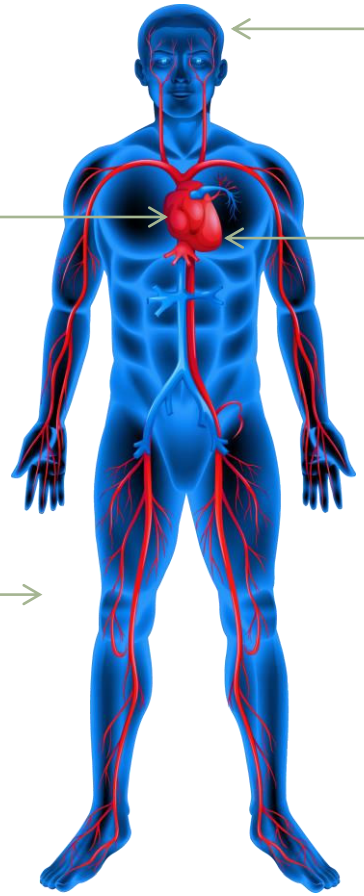
- Major studies (DCCT and UKPDS) show improved glucose control (A1c 7% or below) reduces risk of complications in micro and macro vessel.
- Studies show that newest classes of the diabetes medications (SGLT2s and GLPs) reduce cardiovascular (heart) and kidney complications
- BUT, What are you up against?

T2D out of control is a major and independent risk factor for both microvascular and macrovascular complications



1. World Health Organization. http://www.who.int/diabetes/action_online/basics/en/index3.html

Types of CV disease



Stroke

Caused by disruption of blood supply to the brain[1]

Coronary heart disease

Disease of blood vessels supplying heart muscle[1]

Heart failure

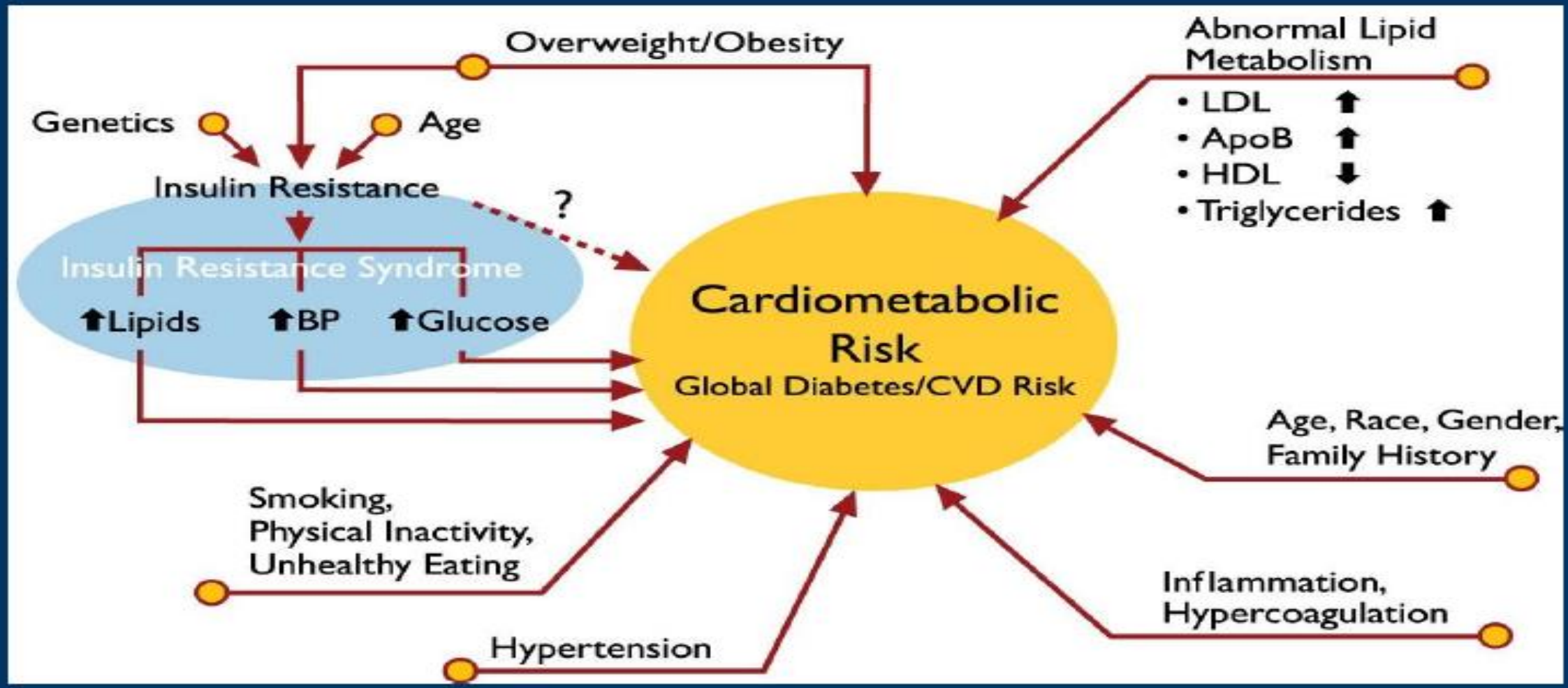
Failure of the heart to pump blood with normal efficiency (**sometimes called congestive heart failure**)[2]

Peripheral arterial disease

Disease of blood vessels supplying arms and legs[1]

1. World Health Organization 2015: http://www.who.int/cardiovascular_diseases/en/cvd_atlas_01_types.pdf?ua=1
2. http://www.heart.org/HEARTORG/Caregiver/Resources/WhatisCardiovascularDisease/What-is-Cardiovascular-Disease_UCM_301852_Article.jsp#

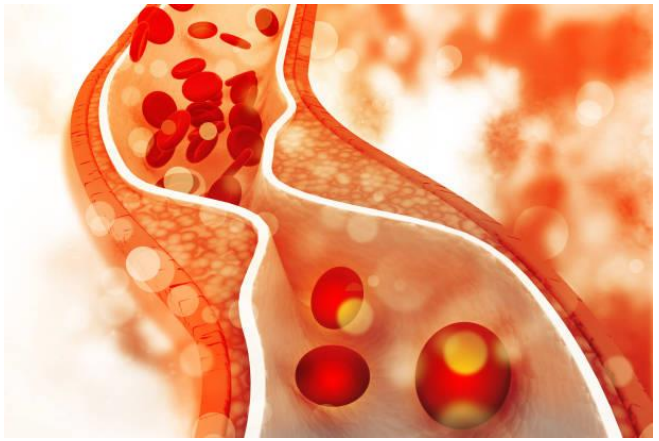
Cardiometabolic Risk



Large Vessel Disease

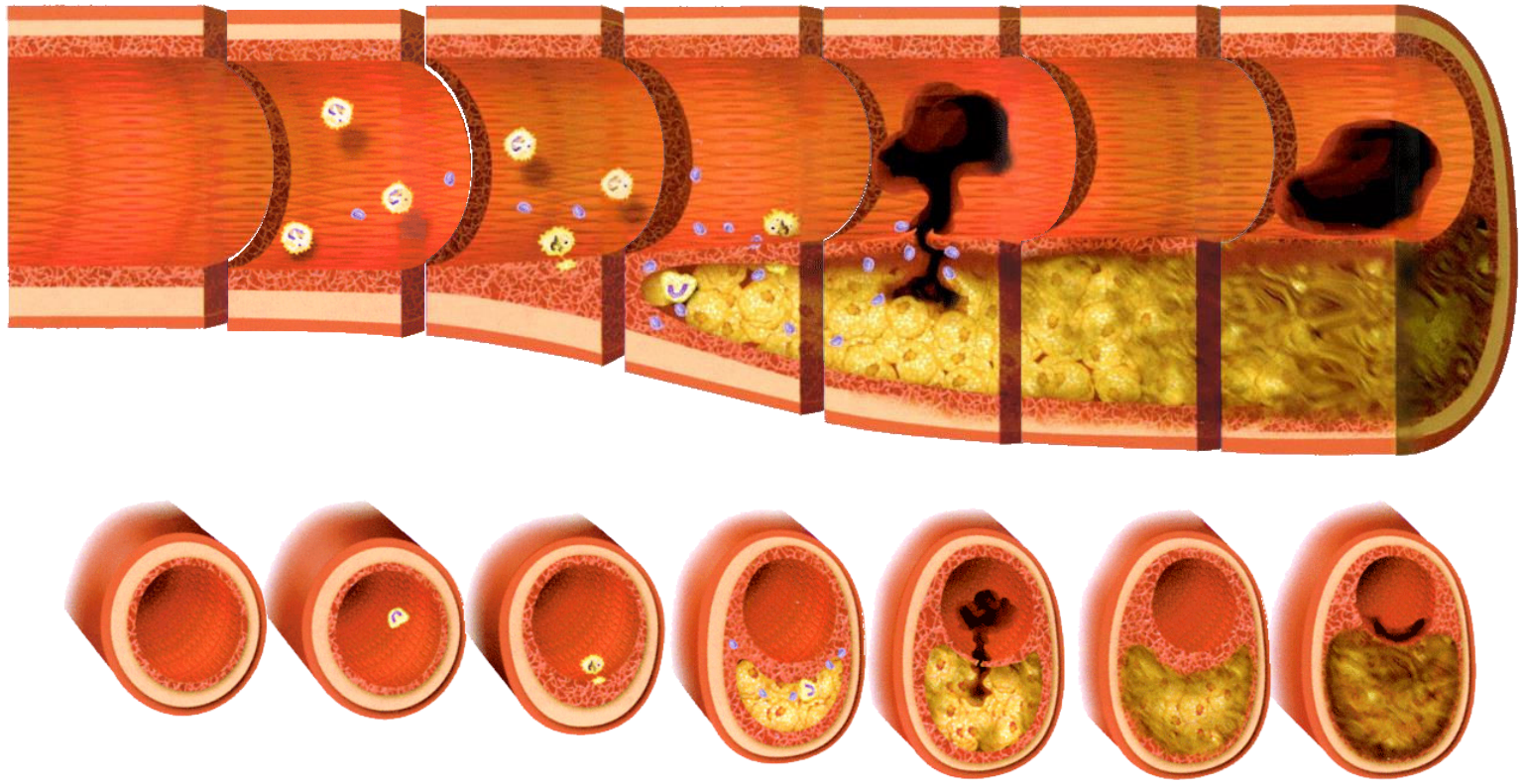
- Inflammation in the arteries
- Blocked or reduced circulation in arteries (to brain, heart, and legs)

Can cause:



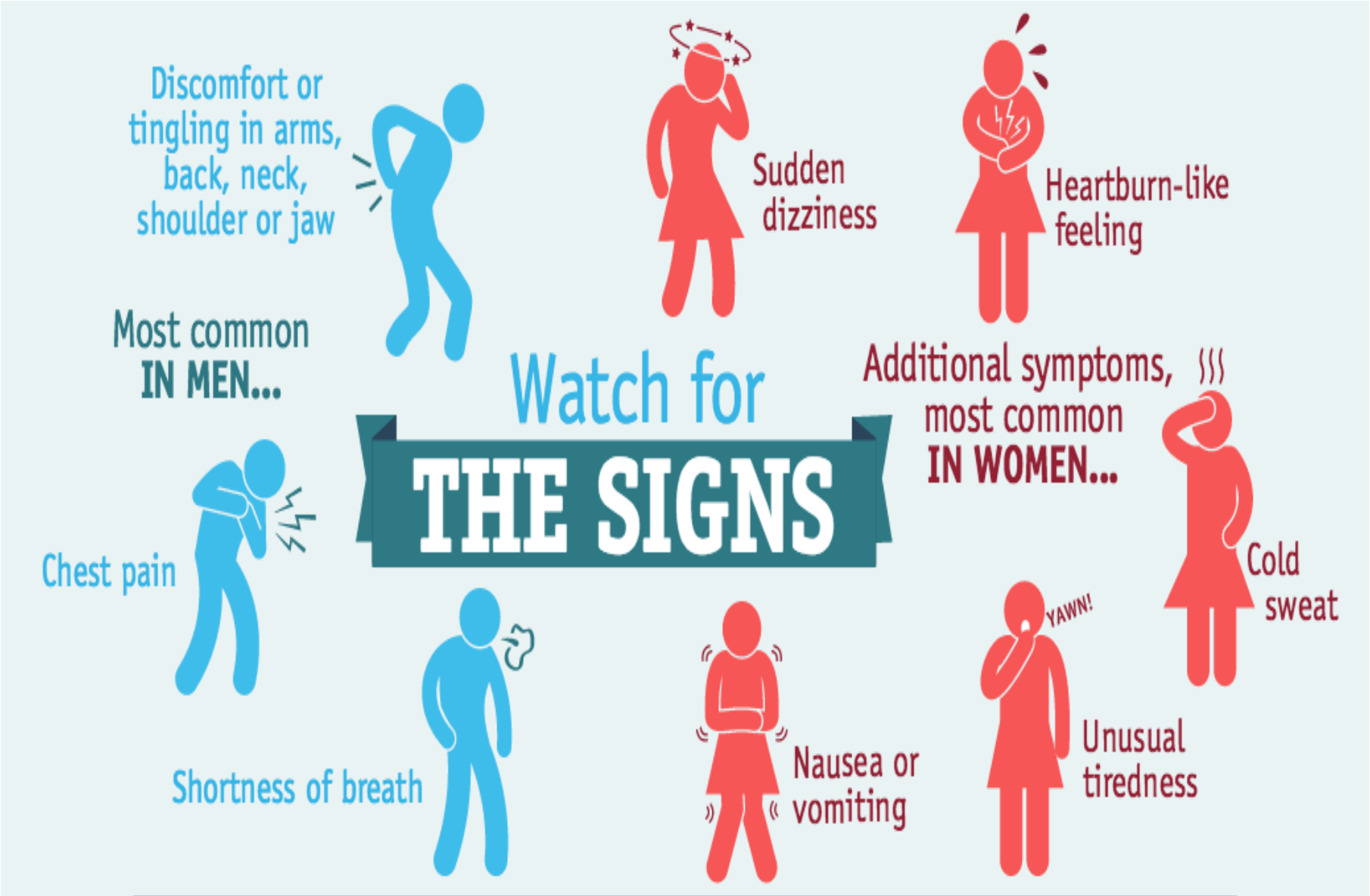
- Heart Attack
- Heart Failure
- Stroke
- Peripheral Arterial Disease (PAD)
- Lowering glucose appears to promote some beneficial long-term effects
- CGM monitoring devices have revealed that post meal spikes of high blood sugar occur frequently, and may be important in CVD risk in increasing atherosclerosis.

Diabetes out of control drives atherosclerotic progression



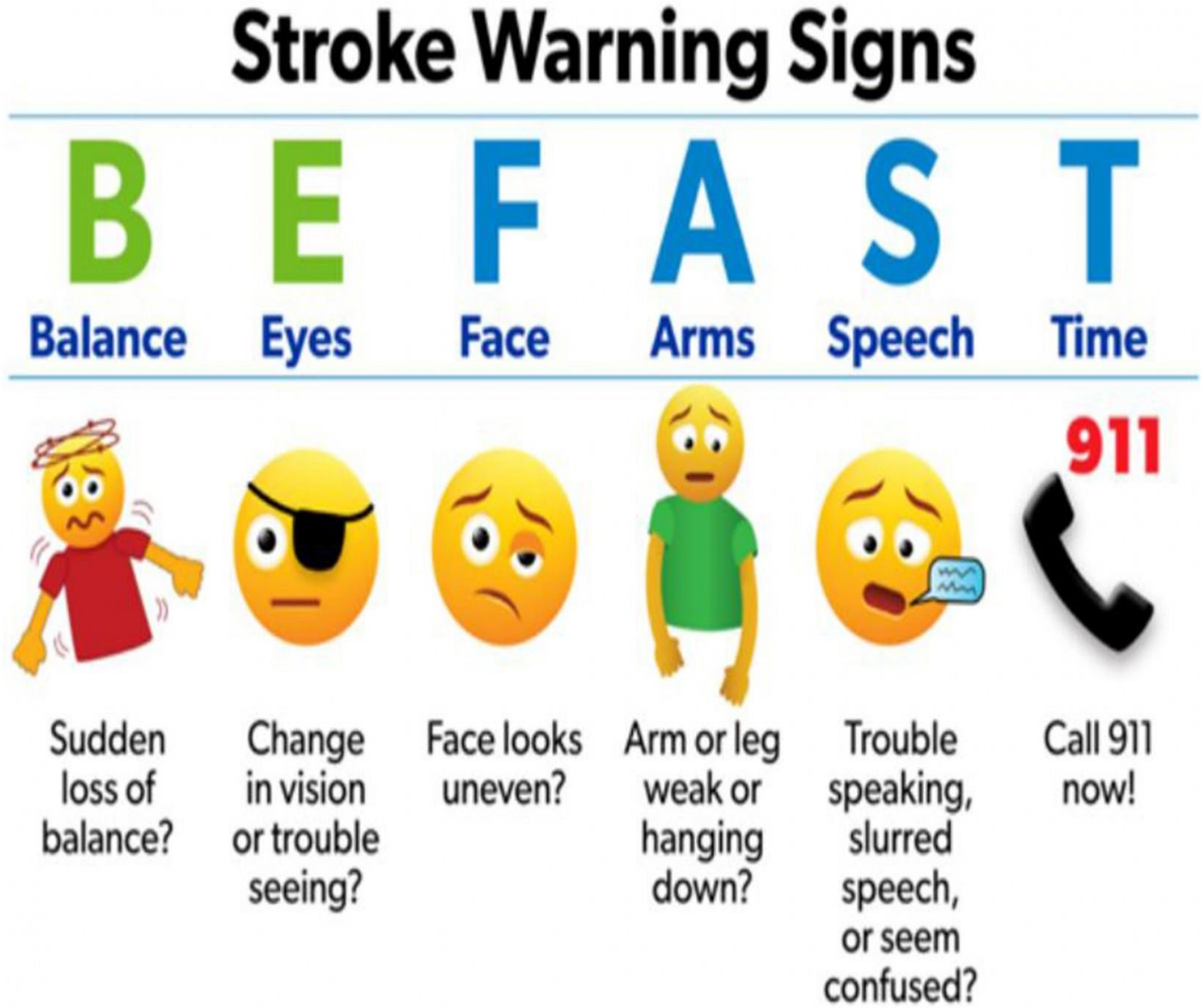
Atherosclerosis is accelerated in T2D by hyperglycaemia, insulin resistance, inflammation and diabetic dyslipidaemia

Figure adapted from Libby. Circulation 2001;104:365–72.
Zeadin et al. Can J Diabetes 2013;37:345e350.



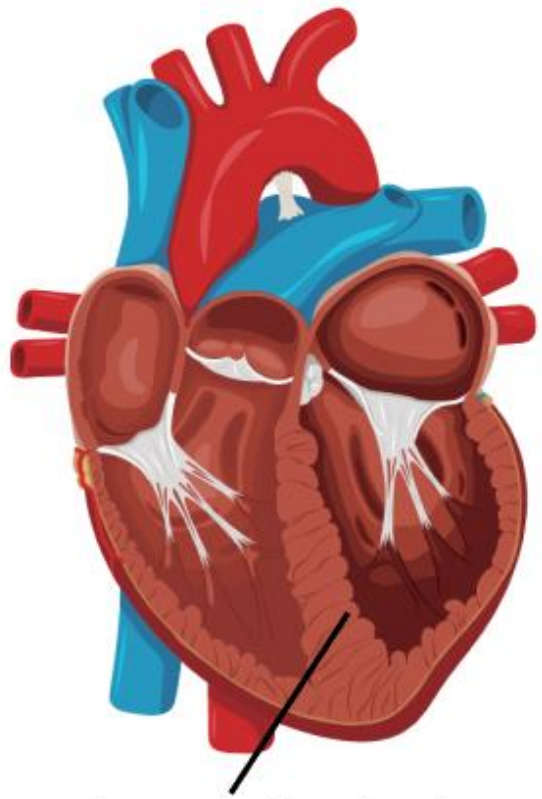
Symptoms of a Heart Attack-call 911

Signs and symptoms of stroke



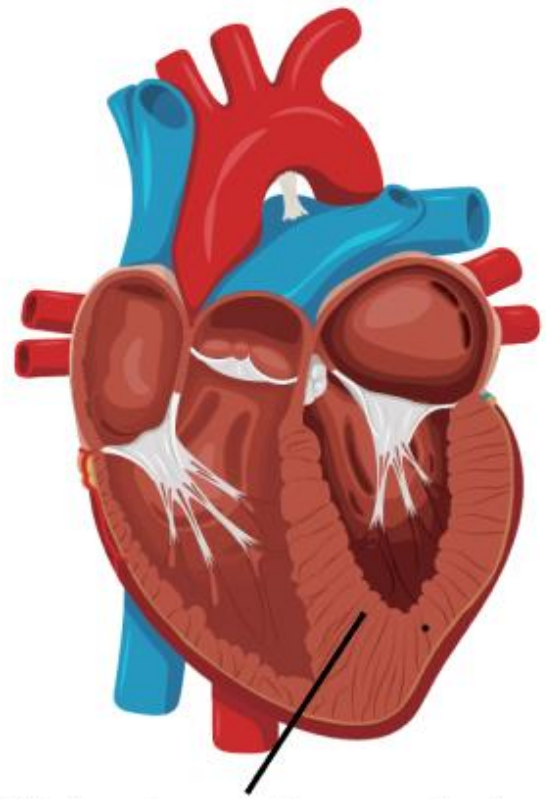
Normal vs. Congestive Heart

Normal heart



Normal ventricular chambers

Congestive heart



Thickening of the ventricular chambers and smaller filling capacity and ejection of blood

CHF- What is Heart Failure?

- Changes in the shape of the heart due to uncontrolled blood pressure/blood sugar
- Reduced pumping and filling of heart
- Breathing problems, swelling in feet, decreased activity levels
- Can lead to rhythm problems (atrial fibrillation, irregular beats)
- High BP is often a precursor to CHF
- Patients with poorly controlled diabetes were more likely to advance to symptomatic heart failure faster than those in good control. J Am Coll Cardiol. 2022 Jun, 79 (23) 2285–2293

What you can do to Reduce Lipids & Heart Health

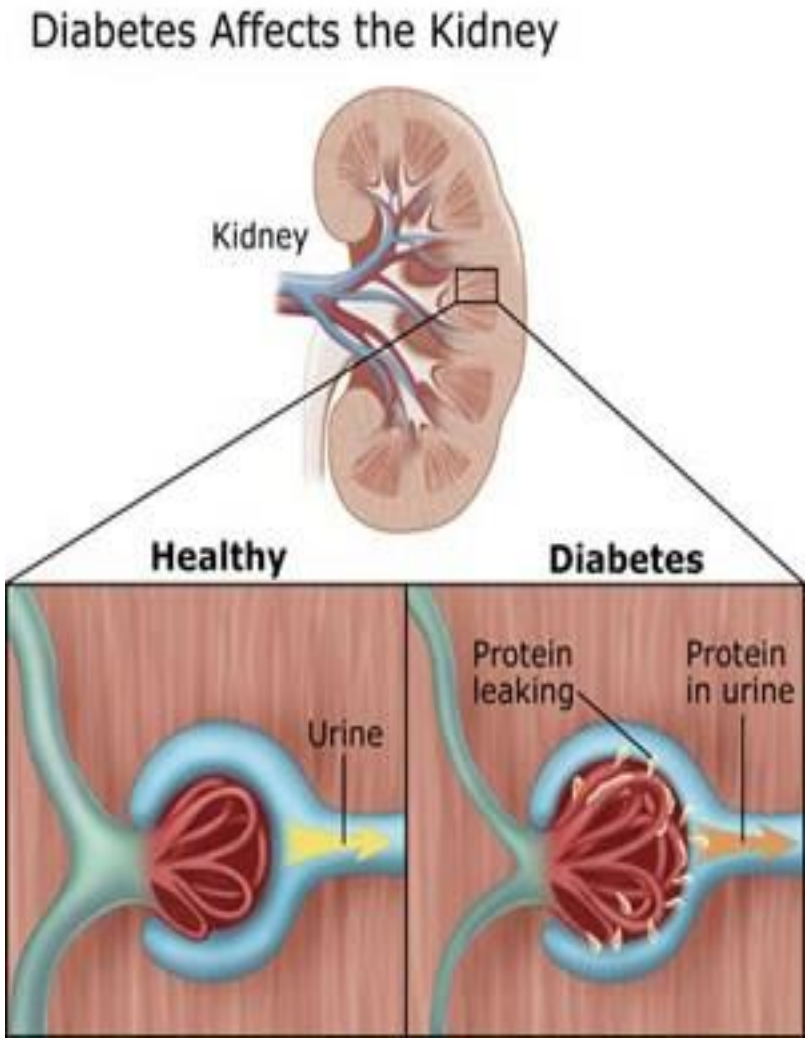
- Lifestyle modification (Mediterranean or DASH diet)
- Reducing saturated fat/ trans fat/ fried foods
- Increasing plant based foods/ fiber
- Choose healthier fats like olive oil,

  canola oil, nuts, fish, avocado
- Increasing physical activity
- Weight loss
- Stop or reduce nicotine use (smoking) http://coquitline.org

Your Provider will likely prescribe a ***Statin*** to reduce/prevent Heart Attack and Stroke

- Statins work in 3 ways:
  - 70% works in the liver to decrease production of cholesterol
  - 30% decreases inflammation in the arteries
  - To stabilize the plaque
- Zocor **(Simvastatin)** ↓ LDL 37 %
- Lipitor **(Atorvastatin)** ↓ LDL 50 %
- Crestor **(Rosuvastatin)** ↓ LDL 63 % plus ↓ Triglycerides
- Other cholesterol lowering meds: PCSK9 inhibitors (like Repatha & Praluent)monoclonal antibodies (help your liver clear bad cholesterol and ↓ LDL. Heat seeking missles)

Diabetic Nephropathy



- TESTS to do Annually:
- **(UACR) Microalbumin or random Albumin to Creatinine Ratio.**
  - **URINE test** done once yearly
  - UACR- if > 30, retest;
  - if persistently 30-299;
  - recommended treatment with ACEI/"pril" or ARB/ "sartan"
  - Watch for dry cough, w ACEI
- Creatinine/ **eGFR** –blood work) yearly
- BP goal < 130/80

Kidney Protection Meds

- ACE inhibitor meds (Lisinopril)
- ARBs (Losartan, Valsartan)
- Finerenone (Kerendia) in Chronic Kidney Disease- it is in a class of medications **mineralocorticoid receptor (MR) antagonists -**works by blocking the activity of certain steroids made in the body that can damage the heart and kidney and helps decrease kidney decline

- SGLT-2 diabetes meds & GLP-1 diabetes meds
  - Benefits beyond A1c reductions…weight loss, decreases protein in urine, decreases blood pressure
- Type2 diabetes & kidney disease, use of SGLT2 is recommended to reduce progression

Kidney Protection Habits

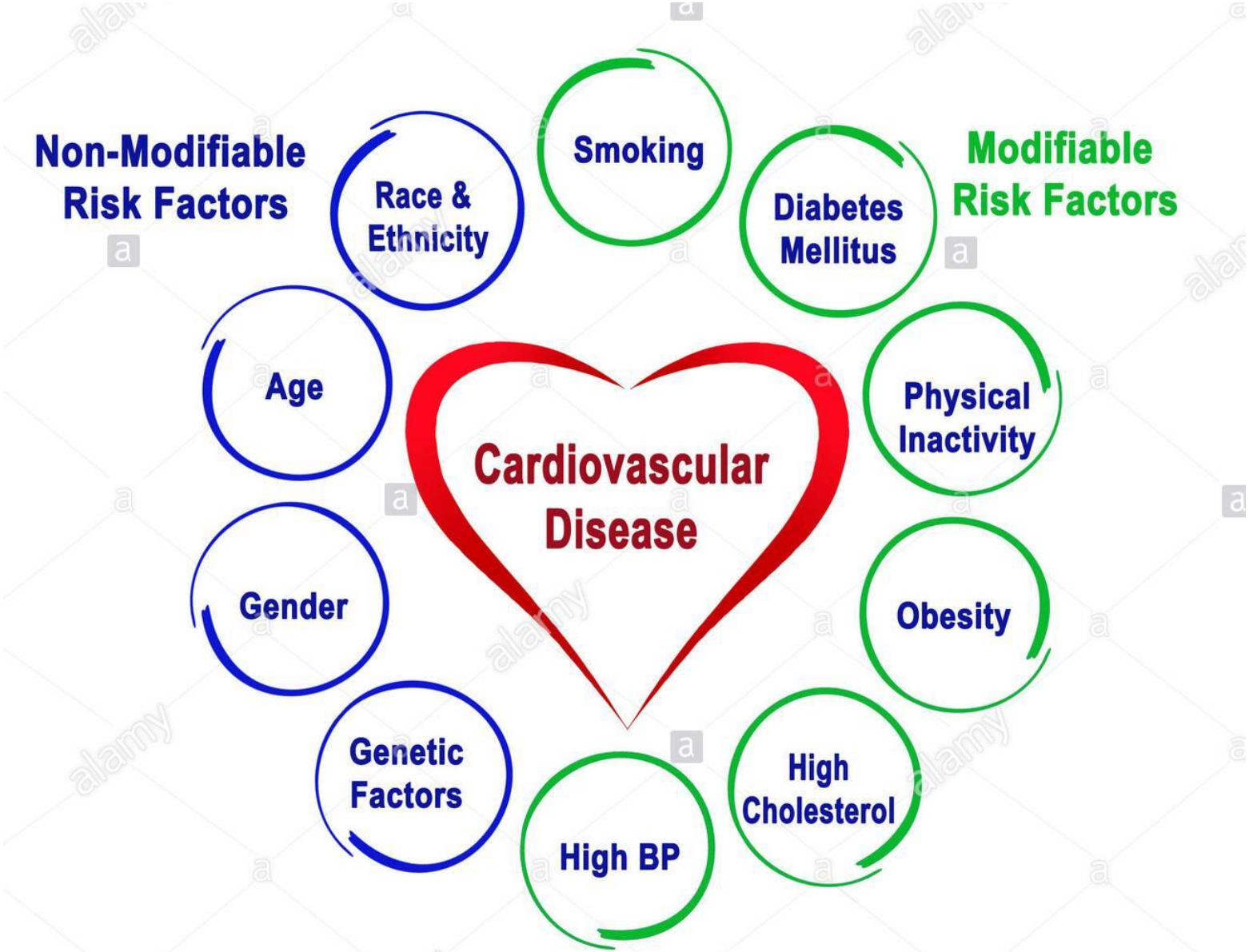
- Control Diabetes
- Control Blood Pressure
- Adequate hydration- Water/Fluid intake
- Avoid certain over the counter meds (NSAIDS)
- Stop or reduce nicotine use
- Avoid alcohol
- Eat healthy and maintain a healthy weight
- Reduce Salt intake
- Get routine lab work: uMA/ Creatinine & eGFR

You should know,

Your Provider may prescribe: Heart Protective Meds

- Statin medications/ Some kinds of non-statin lipid meds
- Blood pressure meds that are cardio protective- ACE inhibitors/ ARBs
- Aspirin (for some people only!)
- SGLT-2 diabetes meds
- GLP-1 diabetes meds
- Metformin

Heart Disease Risk Factors



High Blood Pressure

- *BP should be measured at every visit. Make sure blood pressure is measured accurately!*

- After 5 minutes of rest
- Don't Have a Conversation.
- Support Back in chair.
- Appropriate cuff size/ Cuff on Bare Arm not over clothes
- Support Arm at Heart Level.
- Empty Bladder.
- Keep Legs Uncrossed.
- Support Feet (on the floor).

Lowering Blood Pressure

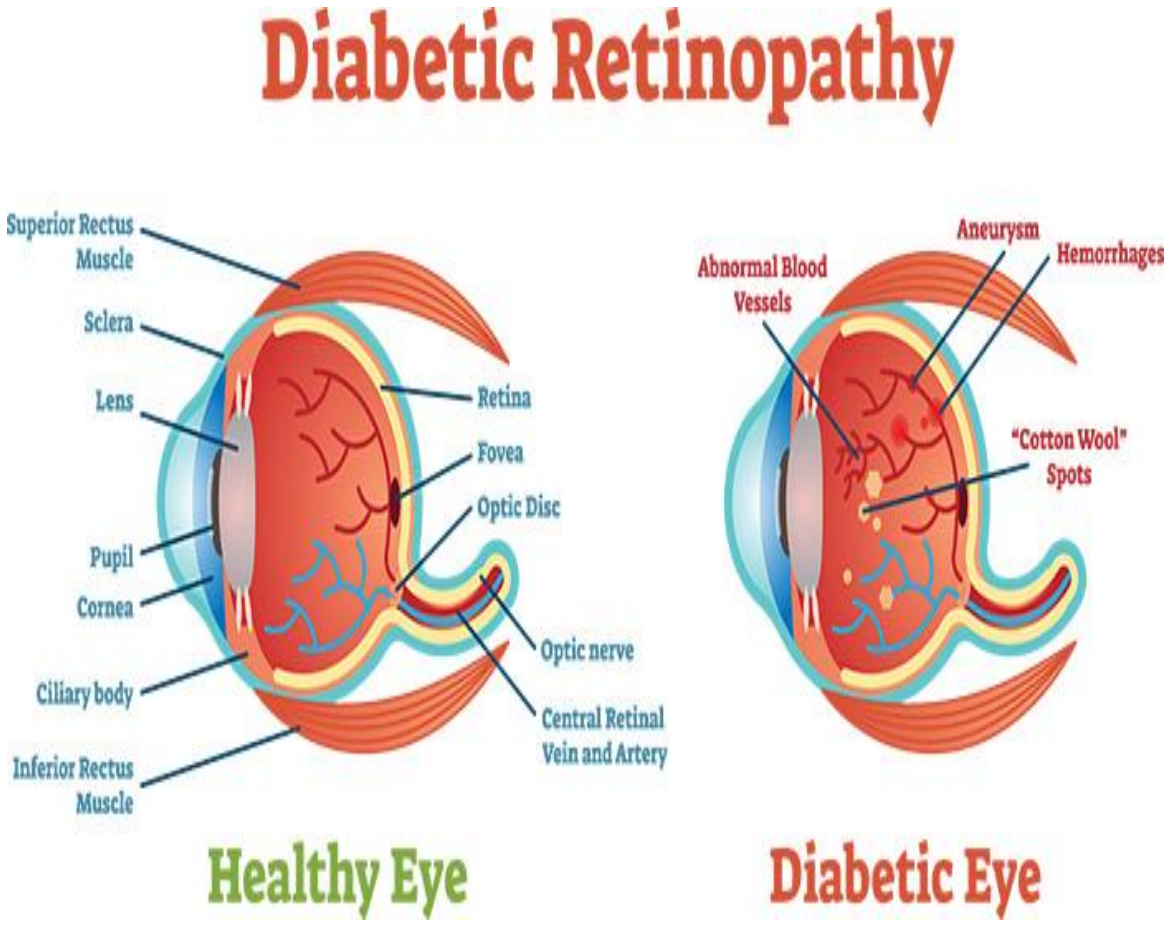
- Exercise/ increase physical activity
- Lose weight
- Eat well -Mediterranean or DASH diet

(Dietary Approaches to Stop Hypertension diet) More fresh fruits and vegetables and whole grain (more fiber)

  - limits foods that are high in saturated fat
- Cut down on salt
- Decrease alcohol
- Stop or cut back on nicotine (smoking, chew)
- Decrease stress
- Medications (it may take several in combination)

Retinopathy in Diabetes

- Leading cause of adult blindness in the US
- Best prevention: Dilated Eye Examination every year
  - Have good glucose control, so you can also read the eye chart for refraction evaluation.
- Non-midratic cameras are now available, so a dilated exam may not always be necessary
- Cataracts
  - People with diabetes tend to get them earlier, and they get worse faster, likely due to osmotic fluid shifts of glucose in the lens.

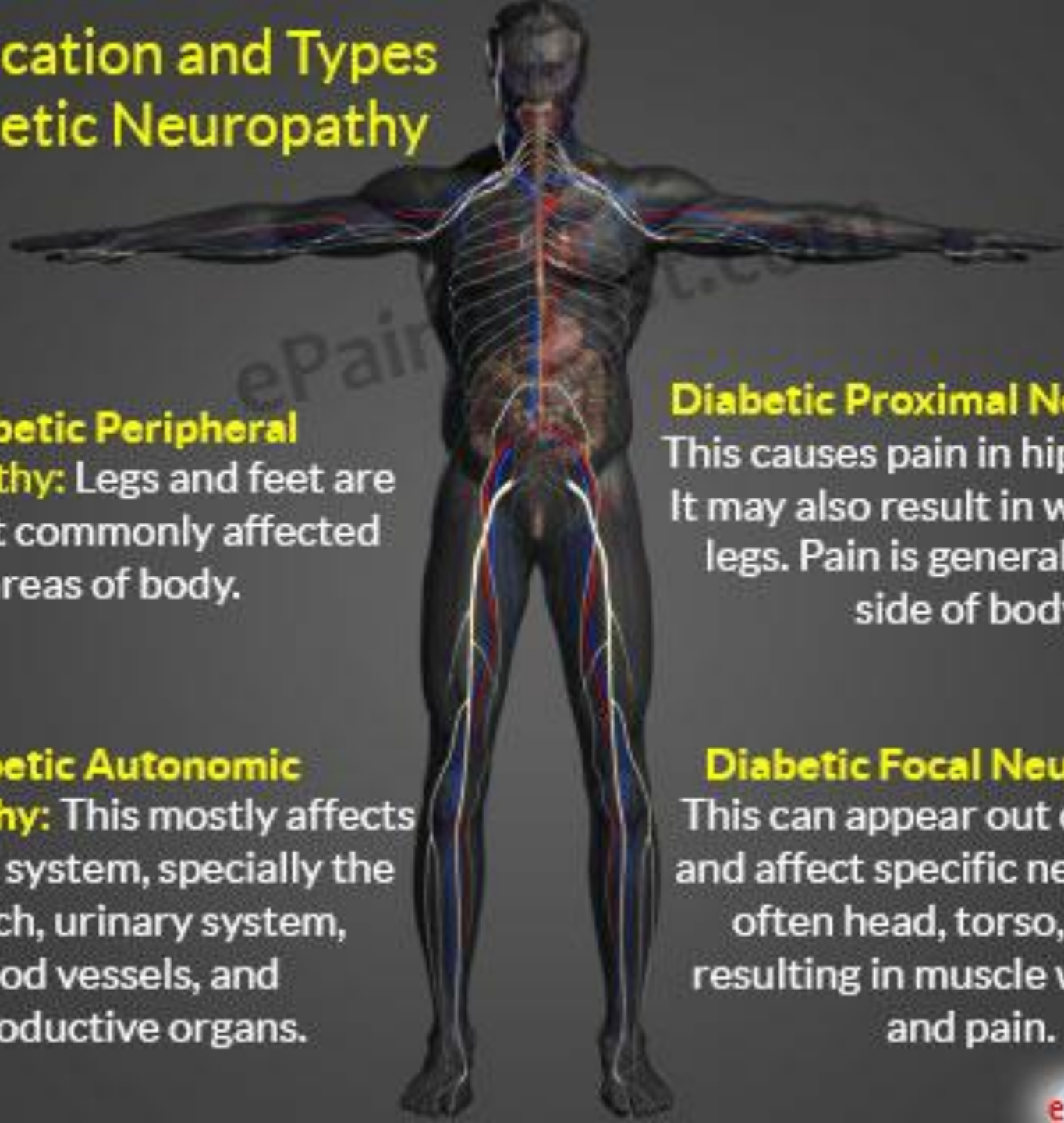


Advanced Retinopathy Treatment

While treatment can slow or stop the progression of retinopathy, it's not a cure

- Photocoagulation
  - Laser treatment that can stop or slow the leakage of blood vessels and fluid in the eye
  - Panretinal photocoagulation: Scatter laser. Cause tiny new blood vessels to shrink & scar
- Anti-VEGF (vascular endothelial growth factor inhibitors)
  - A group of medicines injected into the vitreous that decrease new blood vessel growth and swelling/ fluid buildup
  - Macular edema

Classification and Types of Diabetic Neuropathy



Diabetic Peripheral Neuropathy: Legs and feet are the most commonly affected areas of body.

Diabetic Autonomic Neuropathy: This mostly affects digestive system, specially the stomach, urinary system, blood vessels, and reproductive organs.

Diabetic Proximal Neuropathy: This causes pain in hips or thighs. It may also result in weakness of legs. Pain is generally on one side of body.

Diabetic Focal Neuropathy: This can appear out of the blue and affect specific nerves, most often head, torso, and leg resulting in muscle weakness and pain.

Symptoms: vary based on sensory fibers involved

Painful diabetic peripheral neuropathy

- Numbness or insensitivity to pain or temperature
- Tingling, burning, or prickling sensation
- Sharp pains or cramps
- Extreme sensitivity to touch, even light touch
- Loss of balance and co-ordination
- Muscle weakness and loss of reflexes
- Symptoms are often worse at night

National Institute of Diabetes and Digestive and Kidney Diseases. *Diabetic Neuropathies: The Nerve Damage of Diabetes*. Available at: http://diabetes.niddk.nih.gov/dm/pubs/neuropathies/. Accessed 18 Oct 2011.

Diabetes is most common cause of neuropathy

- **Neuropathy** is the most common complication of diabetes

How to diagnose? A diagnosis of Exclusion

- History of symptoms
- Physical exam: muscle weakness, numbness, and impaired motor fx
- Labs: vitamin deficiencies, check underlying disease that can affect nerve function (B1, B6, B12, niacin)
- Electromyogram (EMG) and nerve conduction studies (NCS) tests (pinpoint the abnormal nerves and where it is coming from)
- MRI (tumors/nerve compression)
- Nerve and muscle biopsies

Neuropathy

Causes:

- *60% to 70% of neuropathy due to diabetes.*
- *30% to 40% of people who receive chemotherapy to treat cancer get neuropathy.*
- *Frostbite*
- *Can be caused by other meds too.*
- *Autoimmune disorders*
- *Trauma- nerve compression, repetitive motion*

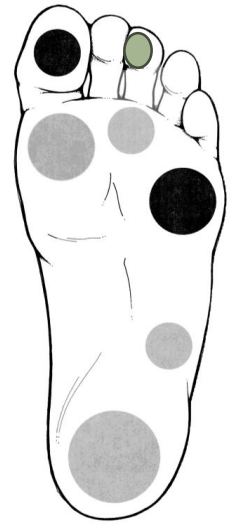
Neuropathy Treatment

- **Optimize blood sugar control-** to prevent, delay, or slow progression
- **Pain Medication**: Gabapentin (Neurontin), Cymbalta (Duloxetine), Lyrica (Pregabalin), Topical patches (Lidocaine), creams (Capsaicin & Rx Capsaicin (Qutenza)). Tegratol or Alpha Lipoic Acid may also be effective. Metanx: B6, B12, Folic Acid. Pain and nerve regeneration.
- Also: Vitamin therapy if deficient and an improved diet
- Avoiding alcohol
- Physical Therapy (to help with balance)
- Surgery (if something needs to be fixed: herniated disc/ carpal tunnel)
- Mechanical aids (braces, shoes, canes)
- TENs units (electrical nerve stimulation)
- Other: Acupuncture, meditation, behavioral therapy

Preventive Care: Foot Care

Especially if you have lost some sensation in your feet

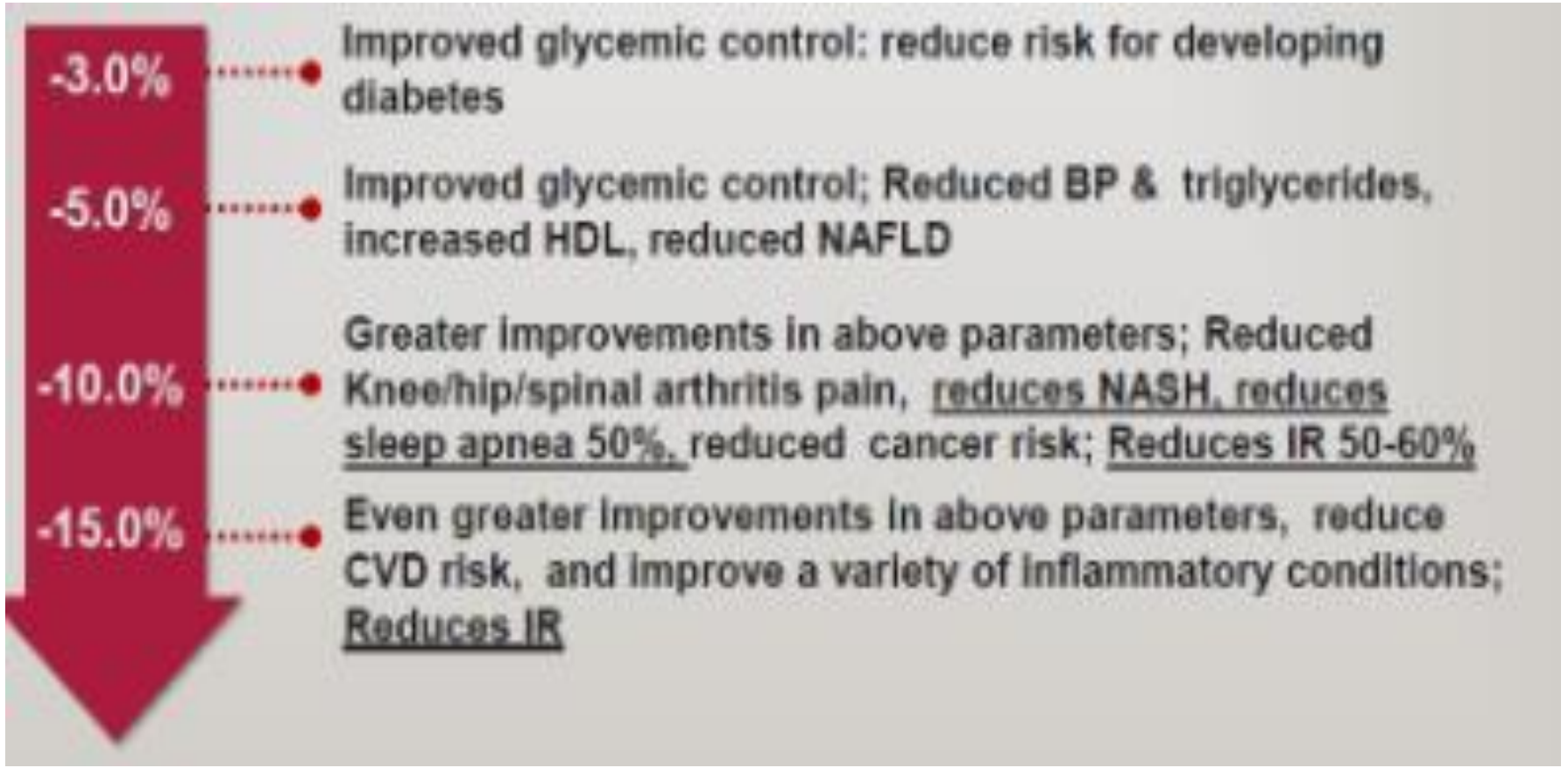
- **Check your feet EVERY Day. Look for cuts, infection, callus**
- **Avoid heating pads, hot water bottles, and microwavable warmers**
- **Avoid going barefoot indoors and outdoors**
- **Put sunscreen on tops of feet (and other exposed skin)**
- **Ask for a test for sensation using monofilament foot exam at least once yearly**
- **So, take off your shoes when you are waiting.**
- **The exam should include one other test:**
  - **Vibratory, pin prick**



Peripheral Artery Disease (PAD)

- PAD can build up over a lifetime, and symptoms may not appear until later in life
  - Cramping in legs or hips with activity
  - Discomfort goes away with rest
  - Reduced pulses in feet
  - Cold feet
  - Sores that don’t heal
  - Discoloration- dark red (rubor) or purple/blue (dusky)

Are you overweight?
Metabolic Benefits of Modest Weight Loss



Jensen, MD et al. J AM Coll Cardiol. 2014;63 (25)

Weight Loss Strategies and Interventions

- **Lifestyle interventions**
  - Targeted diets and eating plans
  - Increased activity
  - Psychotherapy---behavior changes
- **Approved Anti-obesity medications**
  - Phentermine
  - Orlistat
  - Naltrexone HCL-Buproprion HCL (*Contrave*)
  - Phentermine-topiramate ER (*Qsymia*)
  - Liraglutide 3 mg (*Saxenda*)
  - Semaglutide 2.4 mg (Wegovy)
  - *Tirzepatide (Mounjaro) not approved*

Gastric & Endoscopic interventions

Hydrogels (Plenity)
Intragastic balloons
Endoscopic sleeve gastroplasty
(Refer to GI for this)

Metabolic & Bariatric surgery (MBS)

Adjustable Gastric Band
Sleeve Gastrectomy
Gastric bypass (RYGB)
Duodenal switch
(Refer to bariatric surgeon)

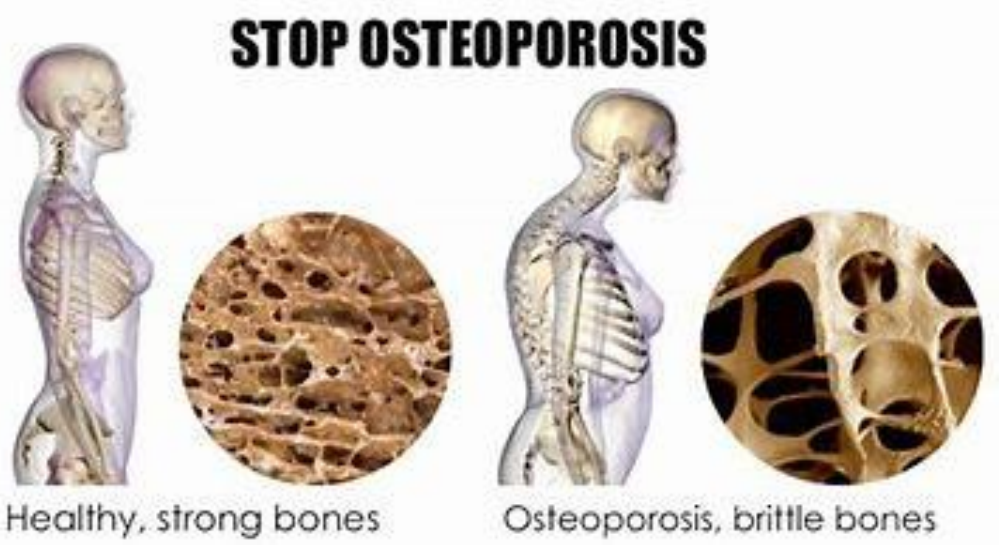
Non Alcoholic Fatty Liver Disease (NAFLD)

NAFLD may be a complication of type 2 diabetes

- You may even see benefits in the liver after just a 5-10% weight loss
- Recent studies show: many approved oral and injectable diabetes medications hold promise as a treatment for fatty liver disease (pioglitazone & GLP1s. ADA ‘24)
- Fatty liver usually has no symptoms
  - Fatty Liver raises your risk of developing liver inflammation or scarring (cirrhosis).
  - Fibrosis- 4 (FIB-4 calculator)- formula can calculate risk
  - Liver blood tests: ALT/AST- do not always pick up NAFLD. It may also be spotted during an ultrasound/ MRI of your abdomen.

Osteoporosis

- Having type 1 or type 2 diabetes may increase the risk of developing an osteoporosis-related bone fracture.
- Increased glucose in the urine causes increased excretion of calcium and magnesium
- ↑osteclasts (Break down) and
  ↓ osteoblasts (Bone formation)
- Appropriate weight bearing exercise help
- Calcium containing foods help
- Have Vit D level checked
- Calcium citrate supplements **with** Vit D or supplement
- Vit D only if recommended by your PCP
- Get Screening/ Bone density scanning-DEXA



Dental Care and Diabetes

- People with diabetes who have higher blood sugars, are at increased risks for infection, reduced wound healing and less saliva which can contribute to:
  - Dry mouth
  - Periodontal disease
  - Gingivitis (gum inflammation)
  - Periodontal abscess
  - Tooth loss

Prevention of Complications: What can you do?

- Lead a healthy lifestyle
- Optimal Blood sugar control
- Optimal BP control
- Healthy Eating
- Exercise
- Stop smoking
- Adequate sleep/ Check for sleep apnea (up to 23% with Type 2 diabetes)
- No unplanned pregnancies
- Get your “To Do”(Standards of Care) list checked out EVERY Year