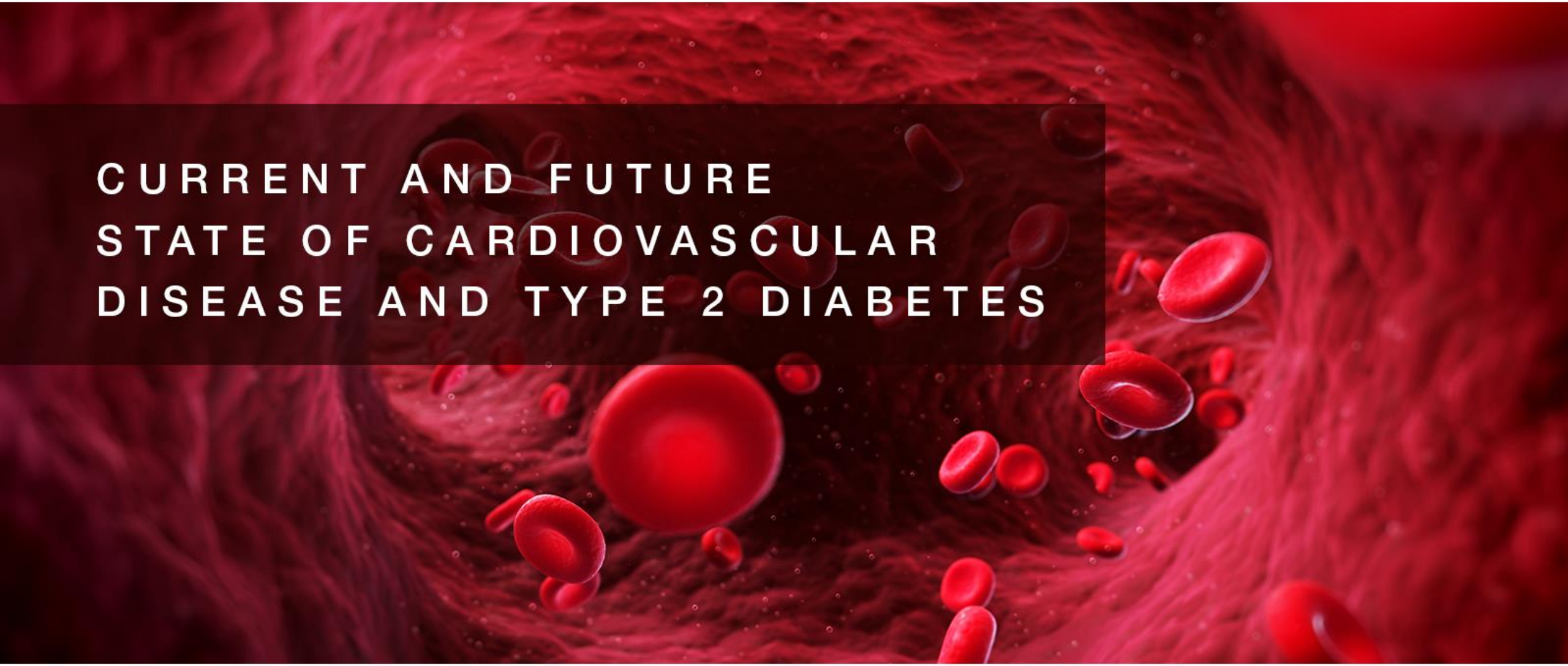

CURRENT AND FUTURE STATE OF CARDIOVASCULAR DISEASE AND TYPE 2 DIABETES

AAFP

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ENDOCRINE SOCIETY

Patient-Centered Management of Diabetes and Prevention of Cardiovascular Disease

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Cover from: *Clinical Diabetes.* December 2017, 35(5) Practical Information for Primary Care

Faculty

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Disclosures

Jonathan Purnell, MD

- *Novo Nordisk*: Consultant, Advisory Board

Angela Thompson, DNP

- *Novo Nordisk*: Consultant, Focus Group

Jeff Unger, MD, FAAFP, FACE

- *Novo Nordisk:* Consultant, Speaker, Advisory Board, Primary Investigator; *Abbott Diabetes:* Consultant, Advisory Board, Speaker; *Allergan:* Speaker

Jonathan Weber, MA, PA-C

- *Nothing to disclose*

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Accreditation Statements

- The AAFP has reviewed Current and Future State of Cardiovascular Disease and Type 2 Diabetes, and deemed it acceptable for AAFP credit. Term of approval is from 11/17/2020 to 11/16/2021. Credit approval includes the following session(s):
  - 1.00 Enduring Materials, Self-Study AAFP Prescribed Credit(s) - Case 2 - Patient-Centered Management of Diabetes and Prevention of Cardiovascular Disease.
- This activity is approved for 1.0 contact hour(s) of continuing education by the American Association of Nurse Practitioners. Activity ID# 20104590. This activity was planned in accordance with AANP Accreditation Standards and Policies.
- This activity has been reviewed by the AAPA Review Panel and is compliant with AAPA CME Criteria. This activity is designated for 1.0 AAPA Category 1 CME credits. PAs should only claim credit commensurate with the extent of their participation.
- The Endocrine Society designates this live activity for a maximum of 1.0 *AMA PRA Category 1 Credit*™ and 1.0 ABIM Medical Knowledge MOC point. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

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We thank Boehringer Ingelheim, Lilly USA, LLC and Novo Nordisk for generously supporting this program.

Learning Objectives

At the end of the learning session, the participant will be able to:

- Discuss prevalence and associations of diabetes, CVD, and DKD
- Recognize diabetes as a CVD equivalent and accelerator
- Review behavioral interventions for mitigating CVD and DKD risk in T2DM
- Distinguish major drug classes and outcomes from CVOTs related to impacts on glycemic control, CVD and DKD risk reduction in T2DM
- Develop clinical strategies using CVOT drug classes to optimize glycemic goals and reduce CVD and DKD risk for patients with T2DM
- Implement a team approach to diabetes care encouraging patient-centered diabetes self-management skills, education and support (DSMES)

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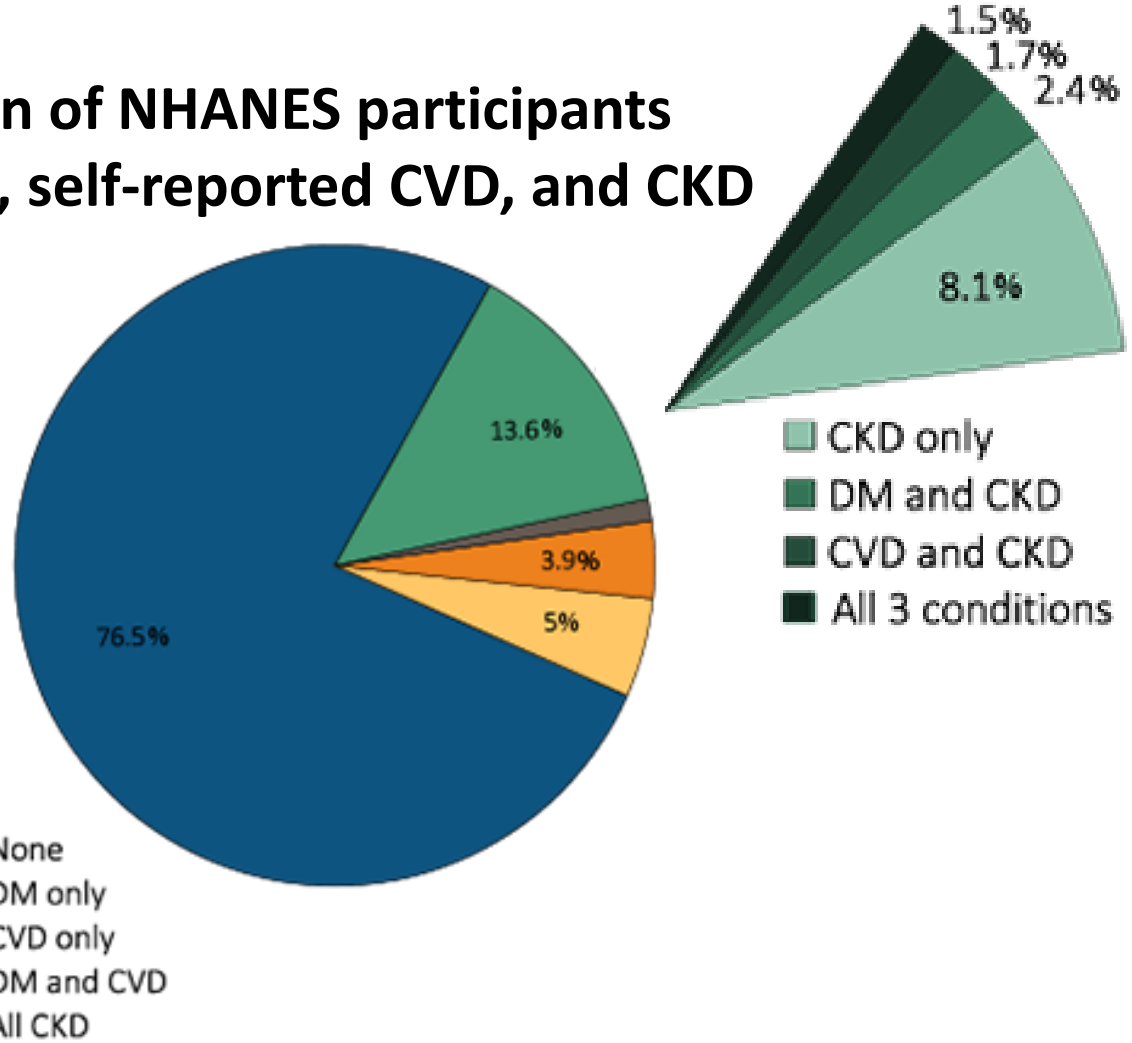
Diabetes, CKD & CVD in United States

Distribution of NHANES participants with diabetes, self-reported CVD, and CKD



NHANES (2007-2012)

Diabetes

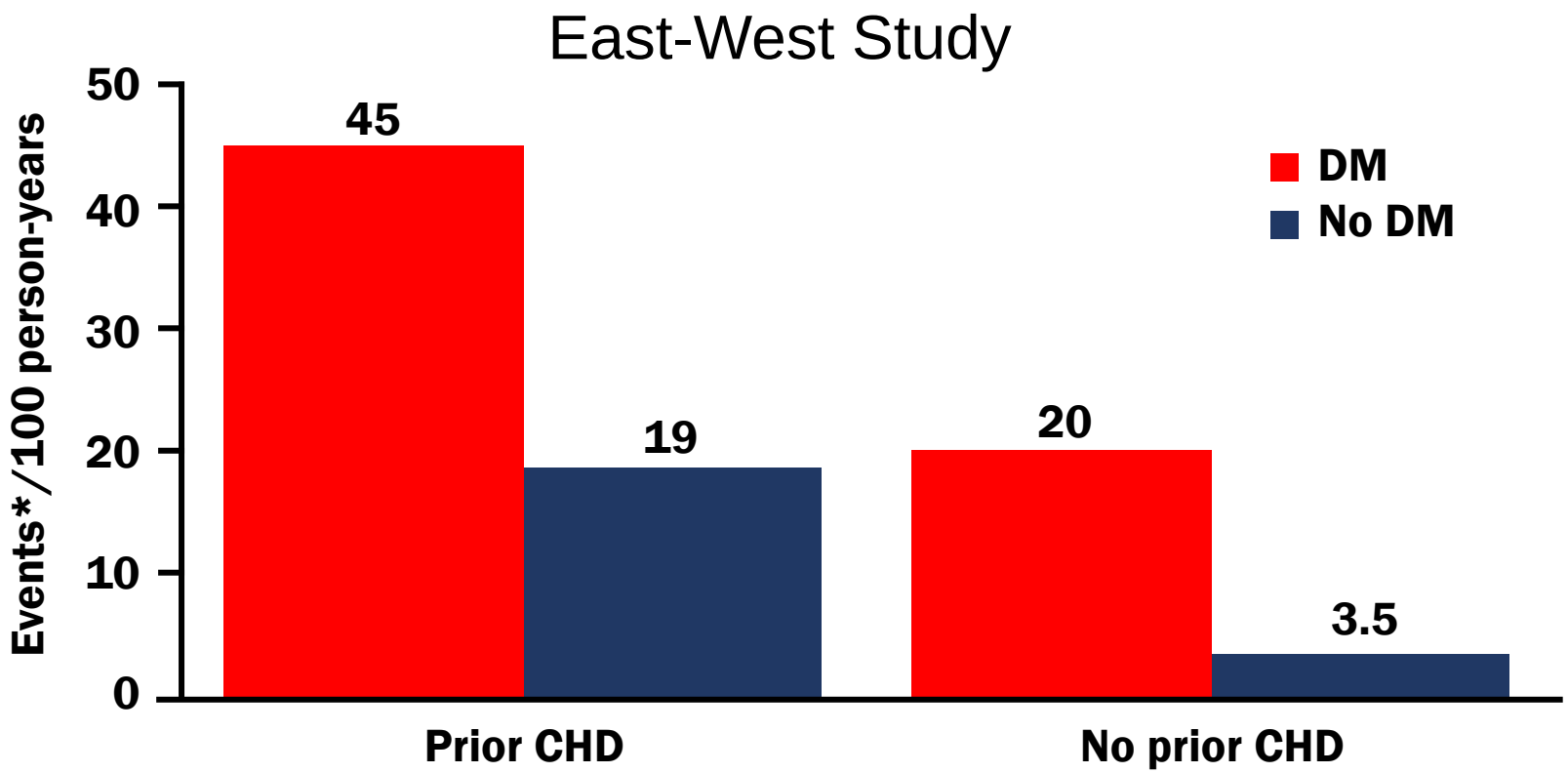
	26.0	diagnosed
	9.4	undiagnosed
+	91.8	pre-diabetes
	127.2	million

NIDDK Kidney Disease Statistics for the US. Available at https://www.niddk.nih.gov/health-information/health-statistics/kidney-disease

Virani SS, et al. *Circulation*. 2020;141:e139–e596.

CKD = Chronic Kidney Disease
CVD = Cardiovascular Disease
DM = Diabetes Mellitus

Diabetes Mellitus: Myocardial Infarction Risk Equivalent



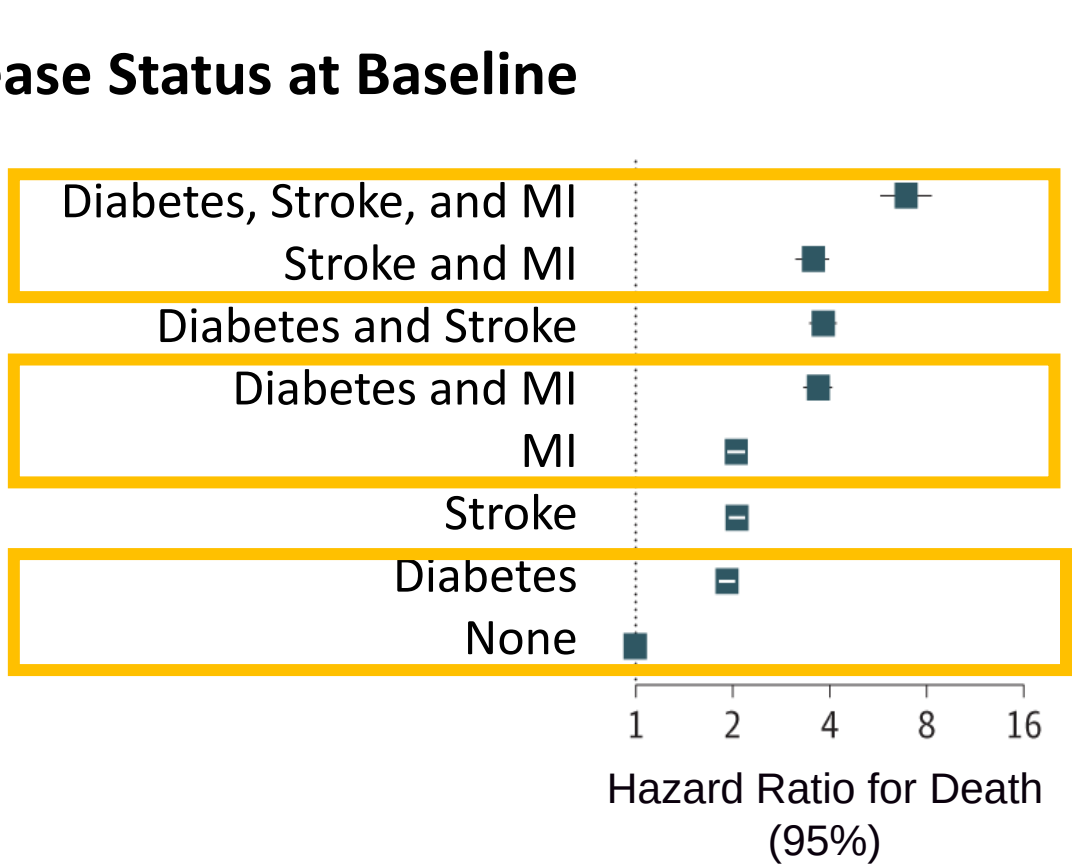
Patients with DM but no CHD experience a similar rate of MI* as patients without DM but with CHD

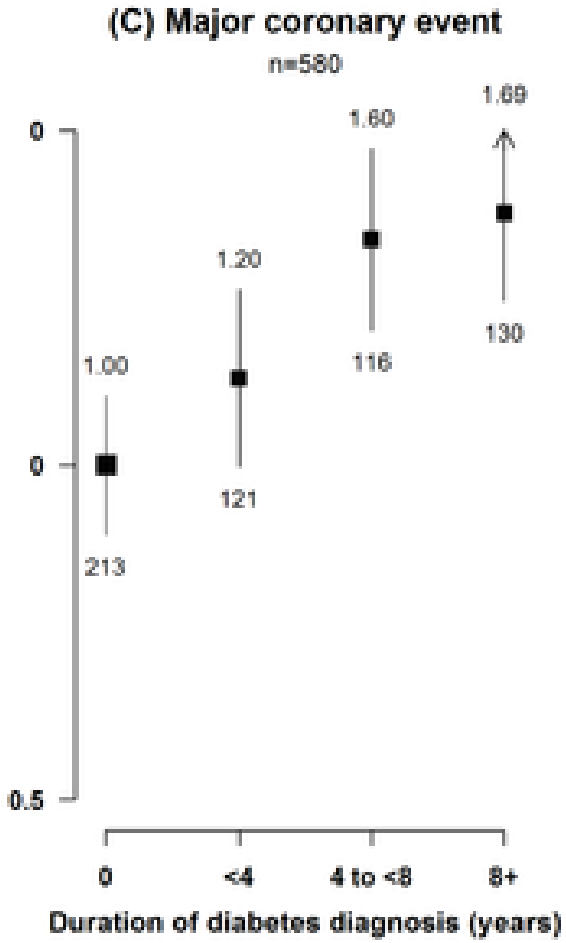
*Fatal or non-fatal MI

CHD = Coronary Heart Disease
DM = Diabetes Mellitus
MI = Myocardial Infarction

Haffner SM et al. *NEJM* 1998;339:229–234

Diabetes: An Atherosclerosis Risk Enhancer



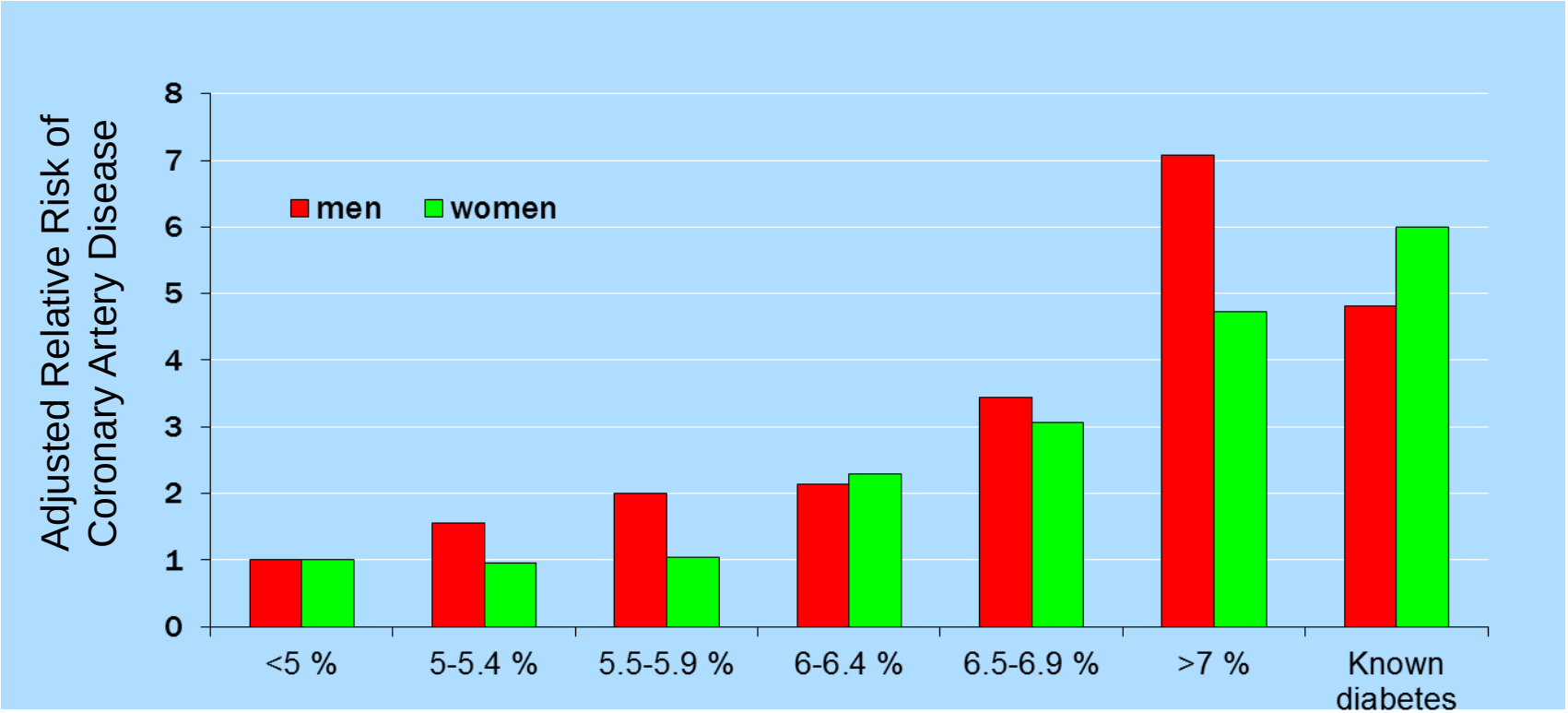


Adapted from Emerging Risk Factors Collaboration, Di Angelantonio E, et al. Association of Cardiometabolic Multimorbidity With Mortality. *JAMA.* 2015;314(1):52-60.

Bragg F, Li L, Yang L, Guo Y, Chen Y, et al. (2016) *Risks and Population Burden of Cardiovascular Diseases Associated with Diabetes in China:* A Prospective Study of 0.5 Million Adults. *PLoS Med*. 2016 13(7):e1002026. Open access article with unrestricted use.

Diabetes Mellitus: Impact of Glycemic Control on CV Risk

Prospective observational study of 10, 232 patients with DM aged 45-79 years

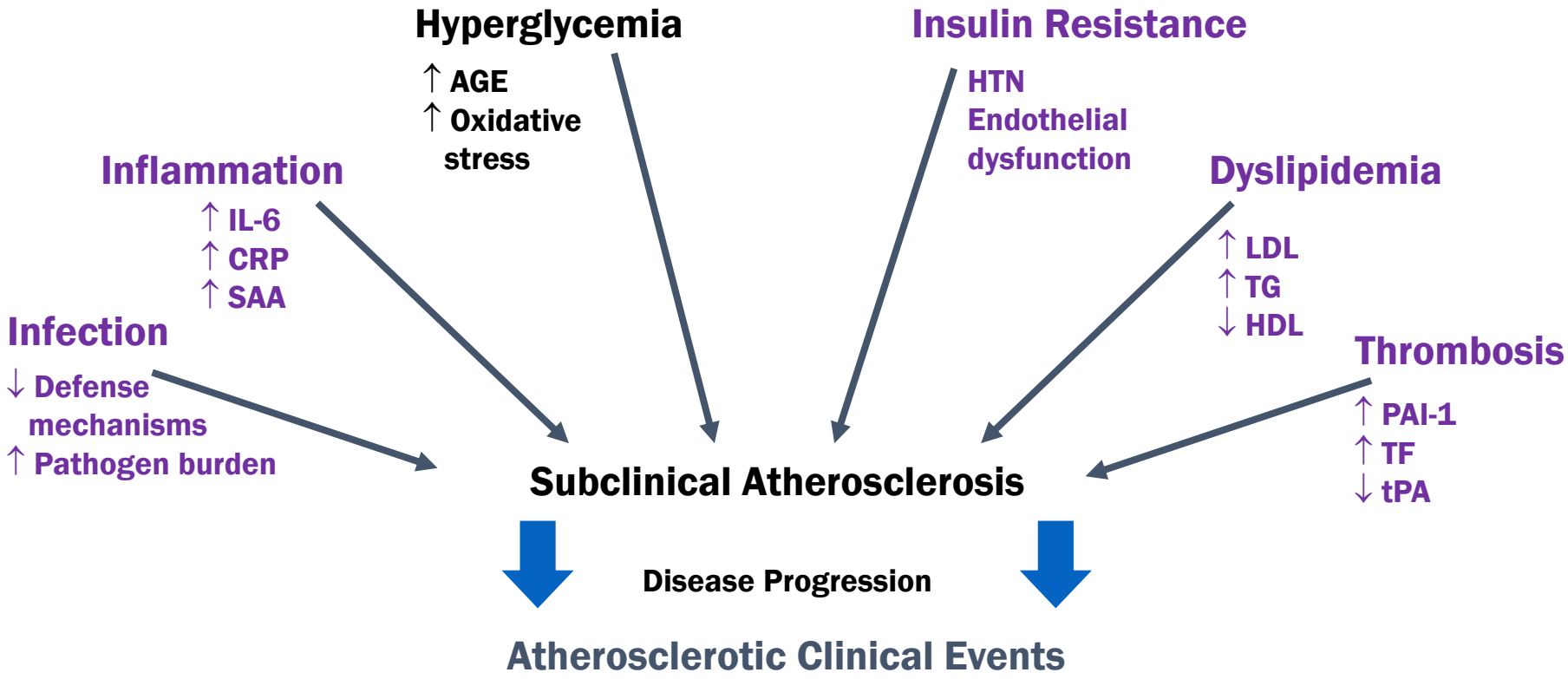


The risk of CV disease increases with increasing HbA_{1C}

Khaw KT et al. *Ann Intern Med* 2004;141:413-420

CV = Cardiovascular

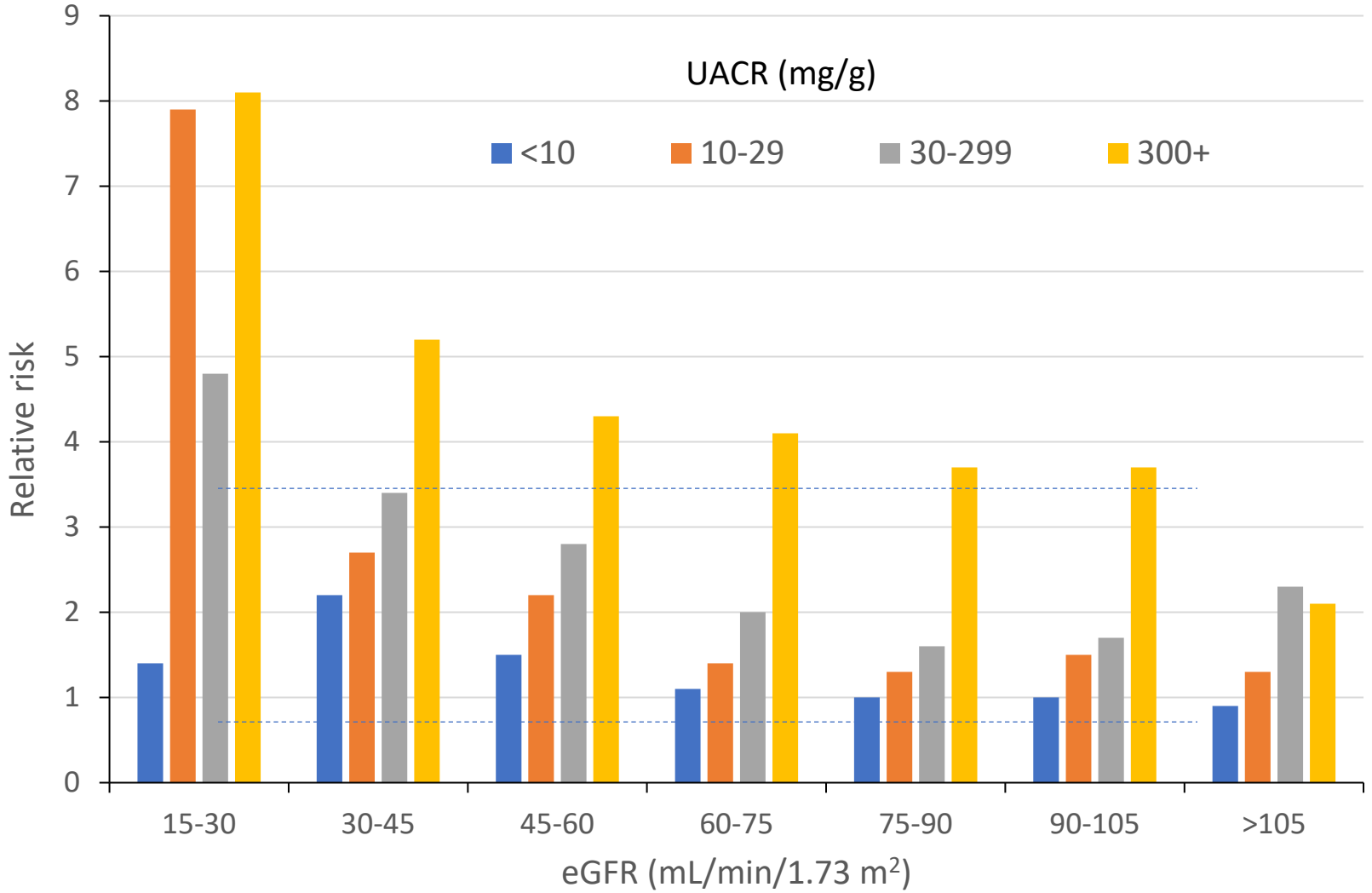
Mechanisms of Coronary Heart Disease in Diabetes: Much More Than Just Glucose



AGE=Advanced glycation end products, CRP=C-reactive protein, HDL=High-density lipoprotein, HTN=Hypertension, IL-6=Interleukin-6, LDL=Low-density lipoprotein, PAI-1=Plasminogen activator inhibitor-1, SAA=Serum amyloid A protein, TF=Tissue factor, TG=Triglycerides, tPA=Tissue plasminogen activator

Biondi-Zoccai GGL et al. *JACC* 2003;41:1071-1077

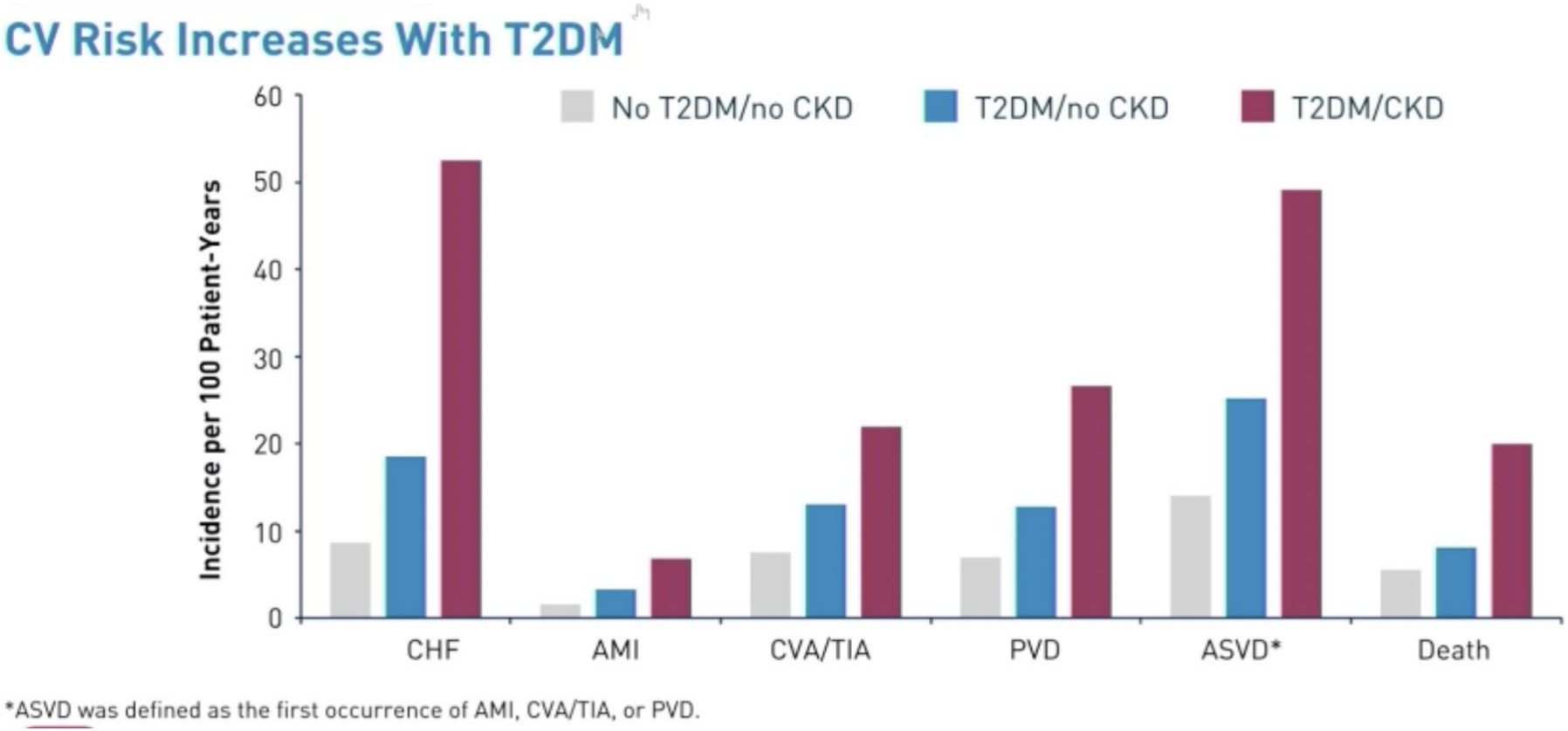
Cardiovascular Mortality Based on eGFR and UACR



KDIGO. *Kidney Int Suppl (2011)*. 2013;3(1):19-62.

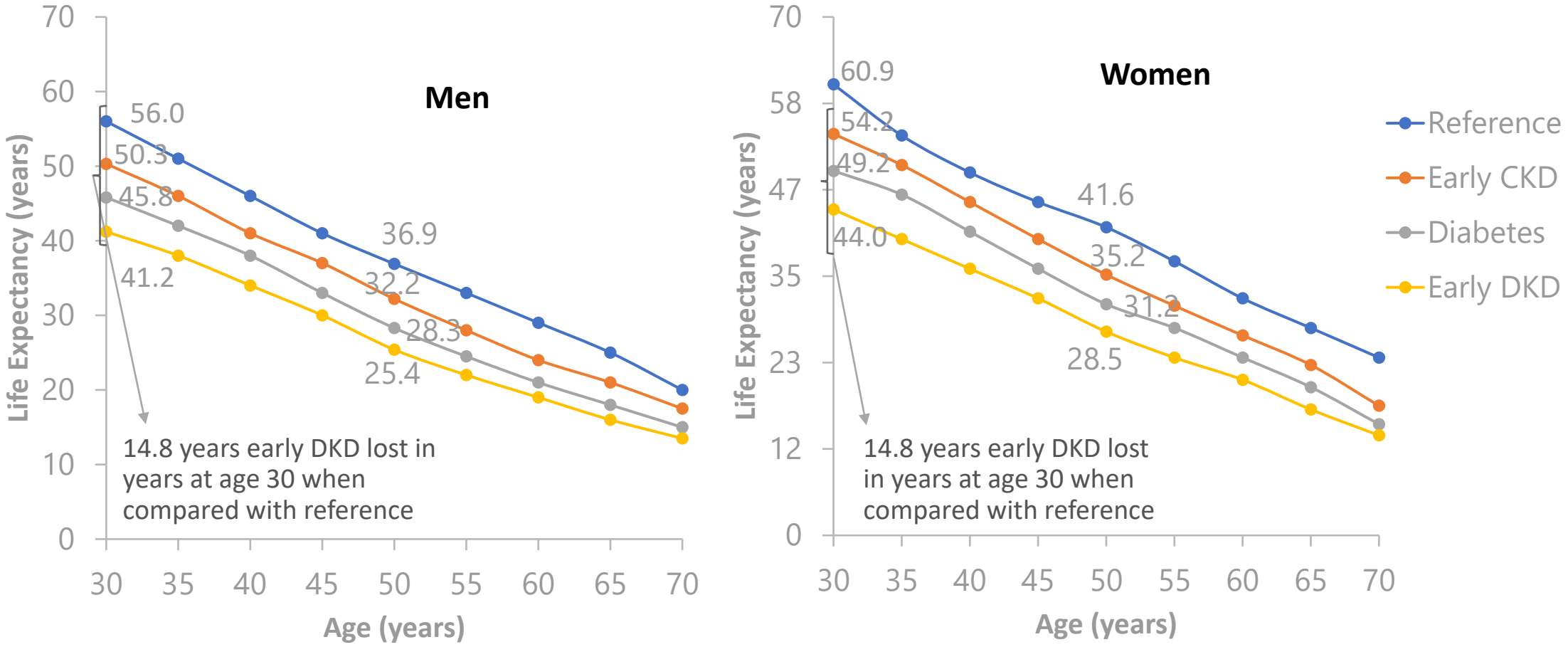
UACR = Urine Albumin-to-Creatinine Ratio

T2DM & Associated Risks of CVD, CKD & Death



Adapted from Foley et al. *American Journal of Nephrology*. 2005.

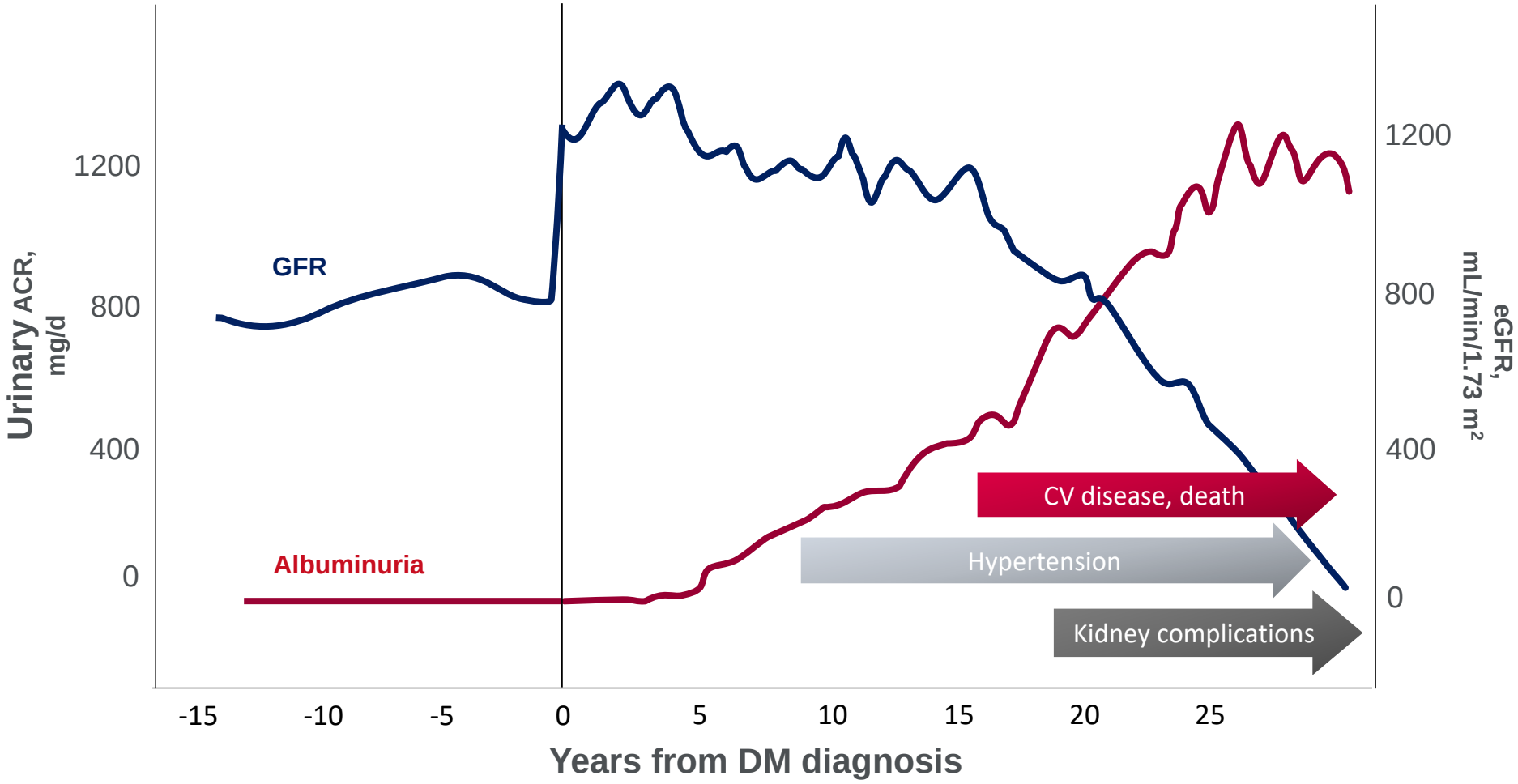
DKD and Life Expectancy



Life span loss (16 years) with early DKD is much worse than with early CKD (6 years) or diabetes (10 years)

Wen CP, et al. *Kidney Int.* 2017;92(2):388-396.

Albuminuria Can Occur Long Before eGFR Declines in DKD



Alicic RZ, et al. *Clin J Am Soc Nephrol*. 2017;12:2032-2045;
Afkarian M. *Pediatr Nephrol*. 2015;30:65-74.

DIABETIC KIDNEY DISEASE

ALBUMIN:CREATININE RATIO

>300MG/G

ALBUMIN:CREATININE RATIO 30-299MG/G

RETINOPATHY

OR

T1DM >10 YRS

National Kidney Foundation: www.kidney.org

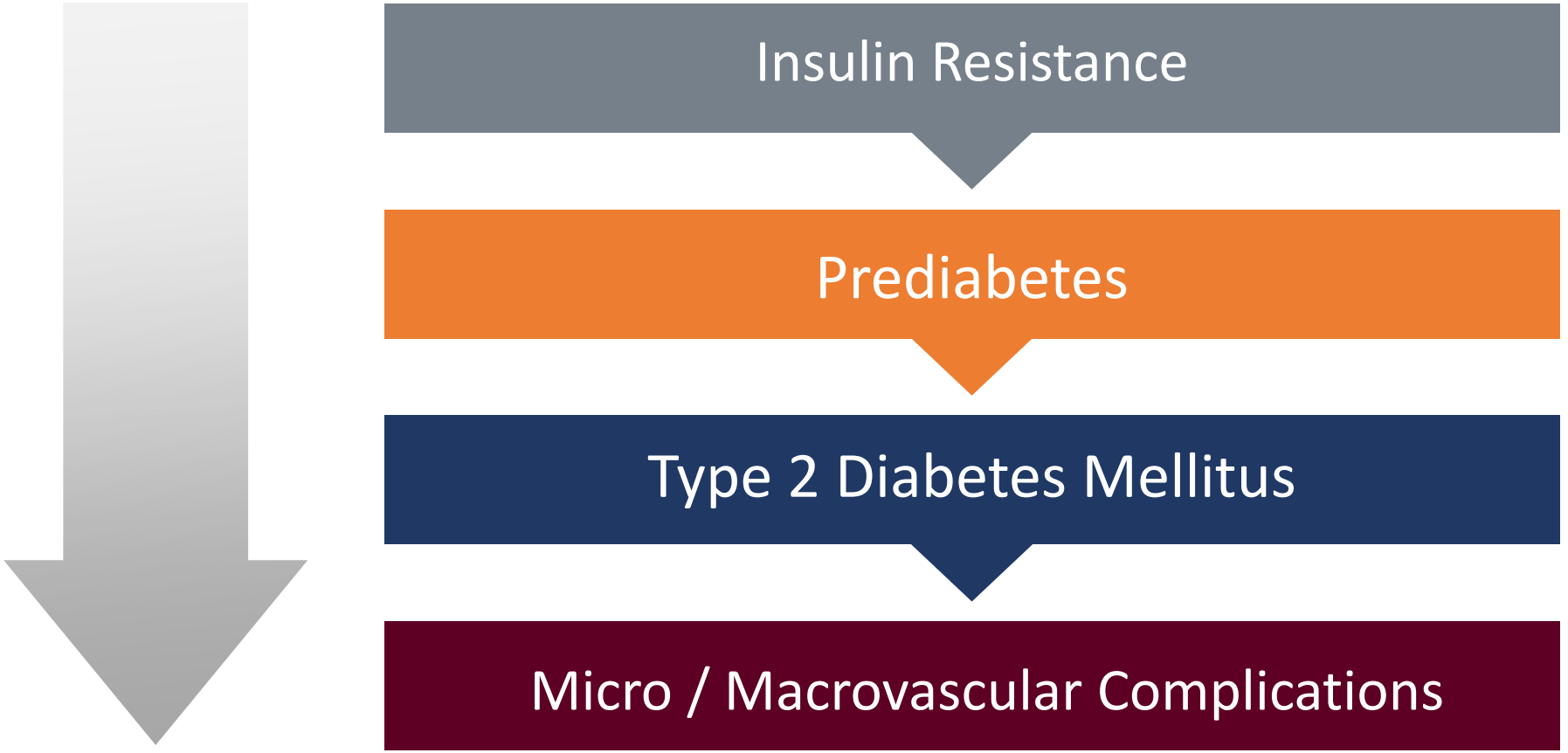
CKD Progression Risk as function of GFR & ACR

Green = Low Risk Yellow = Moderately Increased Risk Orange = High Risk Red = Very High Risk (Numbers = numbers of visits per year)				**Persistent Albuminuria Categories**		
				A1	**A2**	**A3**
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3mg/mmol	30-299 mg/g 3-29 mg/mmol	>300 mg/g >30 mg/mmol
GFR Categories (mL/min/1.73m^2) Description and range	**G1**	Normal or High	≥90	**1 if CKD**	**Treat 1**	**Refer 2**
	G2	Mildly decreased	60-89	**1 if CKD**	**Treat 1**	**Refer 2**
	G3a	Mildly or moderately decreased	45-59	**Treat 1**	**Treat 2**	**Refer 3**
	G3b	Moderately to severely decrease	30-44	**Treat 2**	**Refer 3**	**Refer 3**
	G4	Severely decreased	15-29	**Refer 3**	**Refer 3**	**Refer 4+**
	G5	Kidney failure	<15	**Refer 4+**	**Refer 4+**	**Refer 4+**

Adapted from KDIGO CKD Work Group. *Kidney Int Suppl.* 2013;3:1-150.

GFR = Glomerular Filtration Rate
ACR = Albumin Creatinine Ration

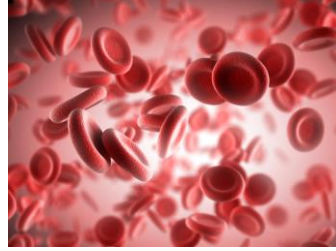
Making the Connection



Patient Case: Meet Les

- 67-year-old African American male
- Type 2 diabetes for 12 years
- Hyperlipidemia, hypertension, and CKD stage G2A2 (eGFR= 66 mL/min/1.73 m^2)
- Does not always refill medications on time- forgets- sometimes out of meds for 3-5 days before gets filled
- Commercial coverage with high deductible
- Testing his glucose levels a few times a week
- Medications
  - Losartan 50 mg QD
  - Atorvastatin 20 mg QD
  - Metformin 500 mg BID
  - Sitagliptin 100 mg QD
  - Aspirin 81 mg QD

Les' Physical and Labs



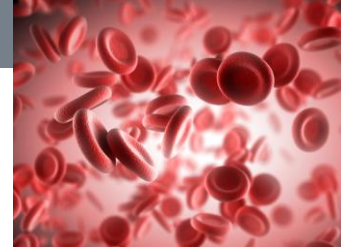
Physical

- Blood pressure: 150/94 mm Hg
- BMI: 32 kg/m^2 Waist circ: 43 in
- Pertinent physical findings
  - Loss of leg hair
  - LE skin discoloration

Labs

A1C	8.4% (elevated)
eGFR/ACR	66 mL/min/? m^2 (low) ACR= 120 mg/G (high)
LDL	124 mg/dL (elevated)
HDL	33 mg/dL (low)
TG	324 mg/dL (elevated)

BMI = body mass index;
HDL = high-density lipoprotein;
LDL =low-density lipoprotein; TG = triglycerides.



Les' Lifestyle

- Exercise – Golf and walks his dog once a day
- Diet – Dine out at restaurants 3-4 times a week and with work travel, eats 2 meals a day
- Employment – Trucking company executive; frequent domestic travel
- Alcohol Use – on the weekends consumes 5-6 beers when golfing
- Tobacco Use – quit 15 years ago
- Sleep Schedule – 6-7 hours a night
- Not filling medications regularly

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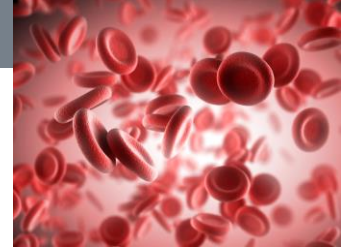

Patient Case: Faculty Discussion

What are your primary treatment considerations for Les?

How would you address lifestyle interventions?

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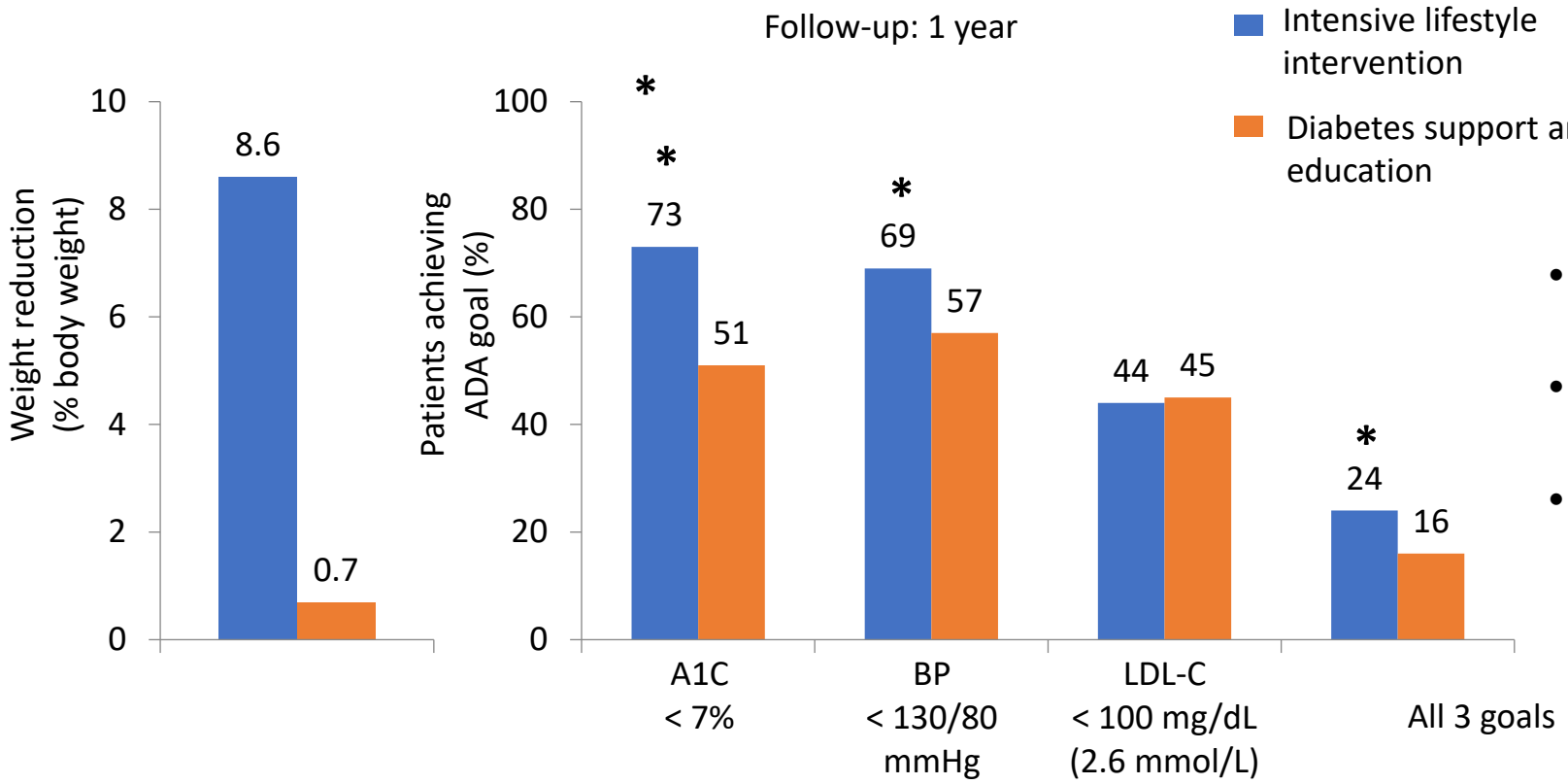
Goals Of Diabetes Management

- Define & achieve glycemic targets to reduce both microvascular and macrovascular CVD events
  - A1C targets
  - Ambulatory Glucose Profile targets
    - SMBG - Fasting & postprandial glycemia goals
    - CGM – "Time in Range" & glucose variability goals
- Consider T2DM therapies in view of pathogenesis (ominous octet)
  - Lifestyle Interventions
  - Pharmacologic interventions aimed at:
    - Minimizing hypoglycemia
    - Controlling glycemic variability to maximize "Time in Range"
- Consider therapies for prevention or management of comorbidities
  - CVD, HTN, CHF – aspirin, anti-platelet, antihypertensive agents
  - DKD – RAAS agents
  - Dyslipidemia – statins, ezetimibe, fibrates, fenofibrates, Icosapent ethyl, PCSK9 inhibitors

SMBG = Self-Monitoring of Blood Glucose
CGM = Continuous Glucose Monitoring
RAAS = Renin-Angiotensin-Aldosterone System

Standards of Medical Care in Diabetes - 2020. *Diabetes Care 2020;43*(Suppl. 1):S37-S47

Lifestyle Interventions for T2DM: Short-Term Benefits



- Annual hospitalizations ↓ 11% ($P = 0.004$)
- Annual hospital days ↓ 15% ($P = 0.01$)
- Number of medications ↓ 6% ($P < 0.001$)

*p < 0.001 vs diabetes support and education.

Look AHEAD Research Group. *Diabetes Care 2007*;30:1374–83.
Gregg EW, et al. *JAMA*. 2012;308(23):2489-2496.
Espland MA, et al. *Diabetes Care 2014*;37:2548–2556

Healthy Eating/Medical Nutrition Therapy

General	Don’t skip meals and keep serving sizes consistent Portion control is the key
Carbohydrates	Emphasize nutrient dense-carbohydrates that are minimally processed and high in fiber (fresh fruits/vegetables, legumes, whole grains) Reduce overall carbohydrate intake
Fats	Emphasize consumption of mono & polyunsaturated fats (avocados, certain plant oils, fish) Limit saturated fats (butter, fatty red meats, tropical plant oils, fast foods) & trans fat Choose fat-free or low-fat dairy products
Proteins	Consume protein foods with low saturated fats (fish, egg whites, beans) Limit processed meats
Micronutrients	Routine supplementation is not necessary There is no clear evidence that vitamins, supplements or herbs/spices can improve glucose control in people with diabetes (Chromium; Vitamin D, cinnamon, aloe vera)

Grams J, et al. *Curr Obes Rep*. 2015 Jun;4(2):287-302. doi: 10.1007/s13679-015-0155-x

Activity and Exercise Recommendations

- Most adults should engage in 150 minutes of moderate- to vigorous-intensity aerobic activity per week, spread over at least 3 days/week, with no more than 2 consecutive days without activity
- Shorter durations (minimum 75 min/week) of vigorous-intensity or interval training may be sufficient for younger and more physically fit individuals
- 2-3 days of resistance training/week (non-consecutive days)
- Reduce sedentary time
- Flexibility training and balance training are recommended 2–3 times/week for older adults with diabetes
- Yoga and tai chi may be included based on individual preferences to increase flexibility, muscular strength, and balance

Diabetes Care 2020 Jan; 43(Supplement 1): S48-S65. https://doi.org/10.2337/dc20-S005

Lifestyle & Behavioral Change

Lifestyle

- Collaborate on a realistic activity plan tailored to patient
- Identify simple changes in diet/meal plan that facilitate weight loss and healthy eating habits
- Reduce alcohol consumption
- Encourage appropriate sleep hygiene
- Select technology (s) most appropriate for evaluating behavior change
  - BGM
  - CGM
  - Apps
  - Online portals

Behavioral

- Avoid the use of fear or intimidation tactics
- Provide encouragement
- Evaluate patient goals/health outcomes for treatment
- Identify biggest challenge/barrier to diabetes self-care
  - Common obstacles include knowledge deficit, cost, stress, family, social support, competing priorities
- Develop strategy for dealing with challenges and potential set-backs
- Consider DSME referral

Adherence in Patients With Diabetes

Disease State	Nonadherence Rate
Coronary heart disease	40%-50%
Hypertension	16%-22%
Oral diabetes medications	**7%-64%**
Insulin therapy	**43%**
HIV	13%
Asthma	25%-75%
Major depression	51%-69%

"Drugs don't work if you don't take them."
C. Everett Koop, MD

Image from Dartmouth Geisel School of Medicine

Consequences of Poor Medication Adherence

1-point drop in self-reported medication adherence (MMAS) is associated with[1]:

- ↑ 0.21% HbA1c
- ↑ 4.6% Physician visits
- ↑ 20.4% ER visits
- ↑ 20.9% Hospital visits

Poor medication adherence → **Missed clinical appointments**

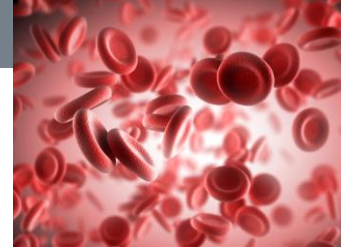
↑ **1.6×** all-cause mortality[2]

DiBonaventura M, et al. The association between nonadherence and glycated hemoglobin among type 2 diabetes patients using basal insulin analogs. *Patient Prefer Adherence*. 2014;8:873-882.

Currie CJ, et al. The impact of treatment noncompliance on mortality in people with type 2 diabetes. *Diabetes Care*. 2012;35:1279-1284.

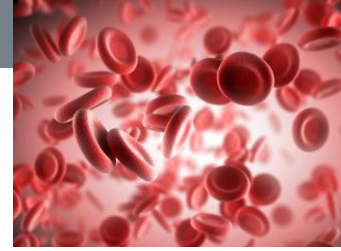
MMAS = Morisky Medication Adherence Scale

Lifestyle/Behavioral- Les



• Exercise – Golf on weekends and walking his dog once a day	• Walk the golf course rather than use cart, take dog out twice a day
• Diet – Dine out at restaurants 3-4 times a week, eats 2 meals a day	• Drink big glass water before eating, select baked/steamed or grilled items, order sauces/dressing on the side
• Alcohol Use – on the weekends consumes 5-6 beers when golfing	• Reduce alcohol- 1 to 2 beers a day
• Not refilling medications regularly	• Prescribe 90 day supply of medications

Patient Case: Faculty Discussion



What pharmacological options would you consider for Les?

What tools would you use to evaluate the response to the treatment plan?

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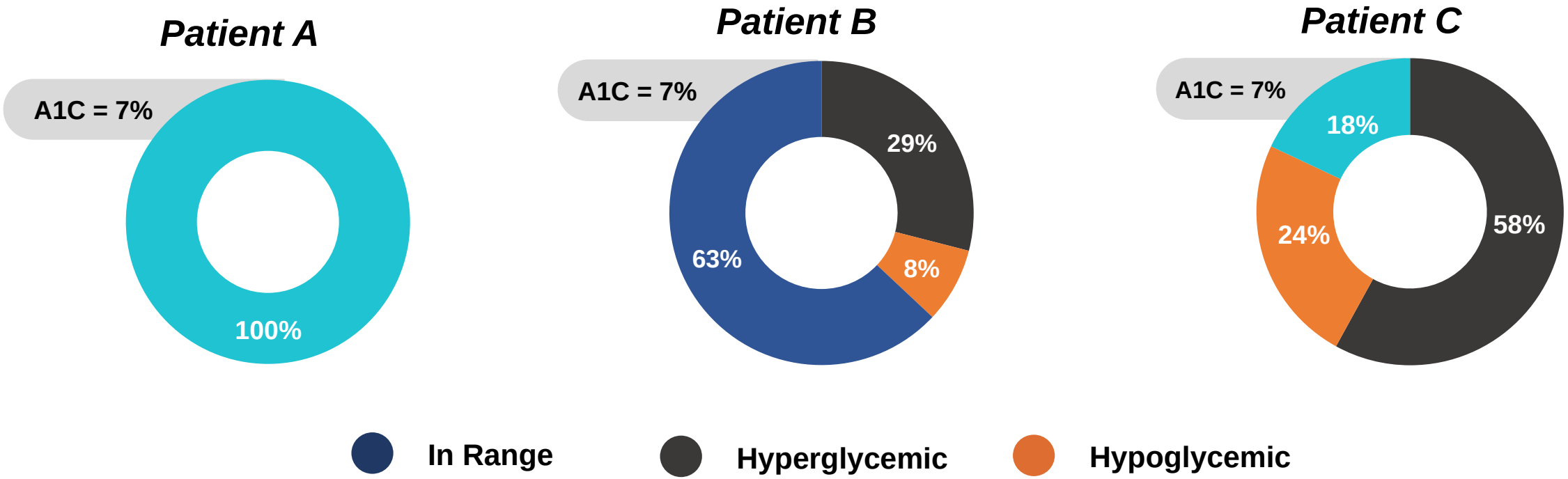
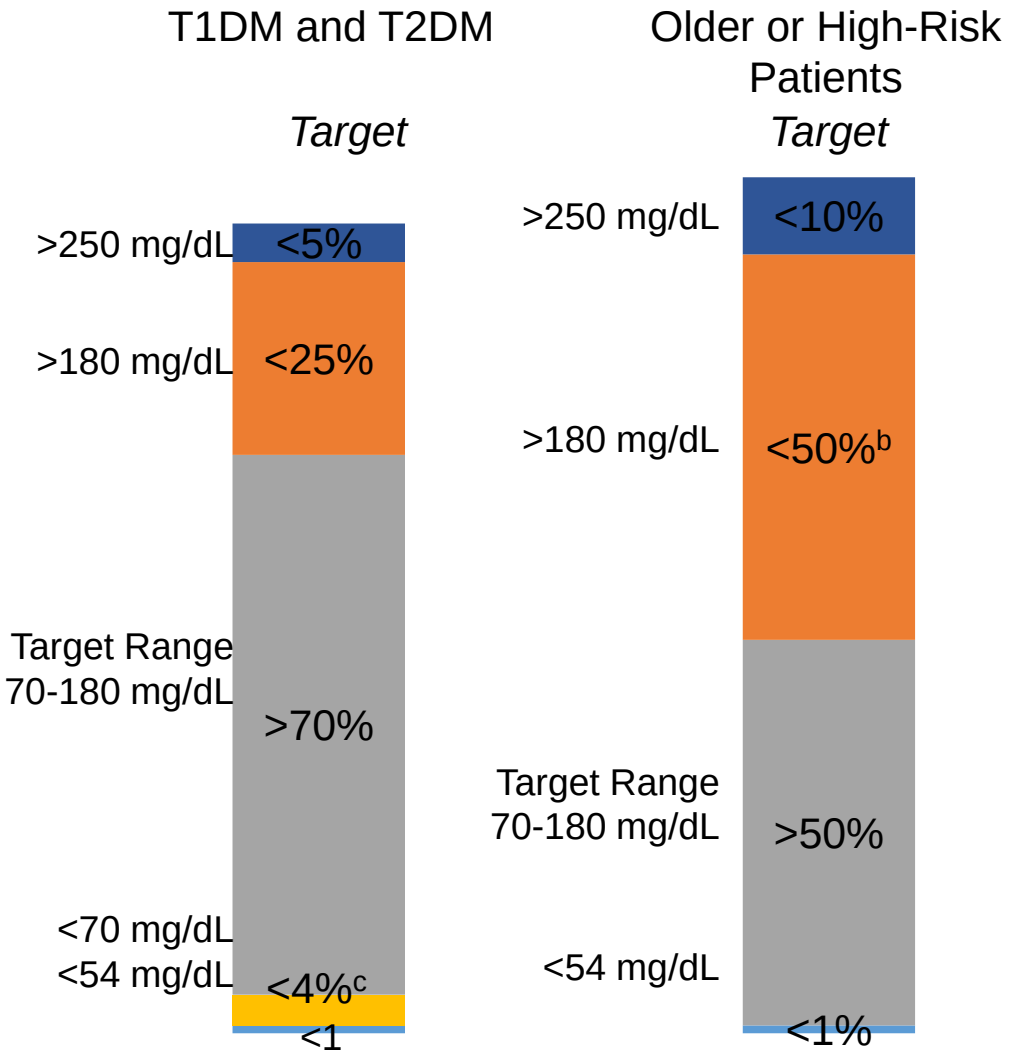
Goals of Management- Glycemic Targets



Correlation of glucose regulation and hemoglobin AIc in diabetes mellitus. *N Engl J Med*. 1976 Aug 19;295(8):417-20

Ambulatory Glucose Profile

- Identify and minimize hypoglycemic events
  - Target nocturnal hypoglycemia
- Reduce postprandial hyperglycemia
- Reduce glycemic variability, which increases oxidative stress and risk of long-term complications
- Improve time in range (70-180 mg/dL)
  - Every 10% increase in time in range = ~0.5%-0.8% HbA1c reduction
  - Each 5% increase is clinically beneficial

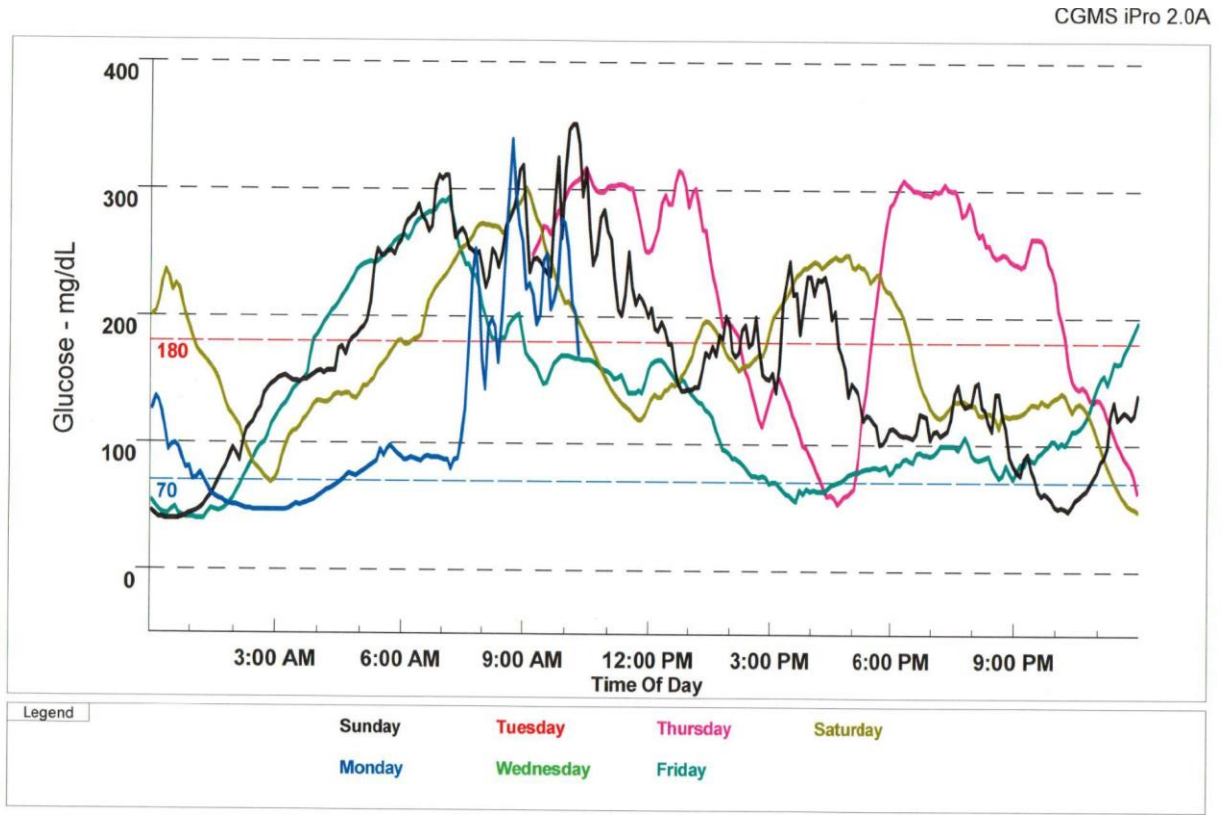


Battelino T, et al. *Diabetes Care 2019* Jun; dci190028

CGM = Continuous Glucose Monitoring

Glucose Fingersticks VS CGM

	Fasting	Prelunch	Predinner	Bedtime
Sunday	248	101	144	136
Monday	210	147	55	318
Tuesday	239	157	83	180
Wednesday	159	130	126	116
Thursday	183	128	103	101
Friday	289	173		



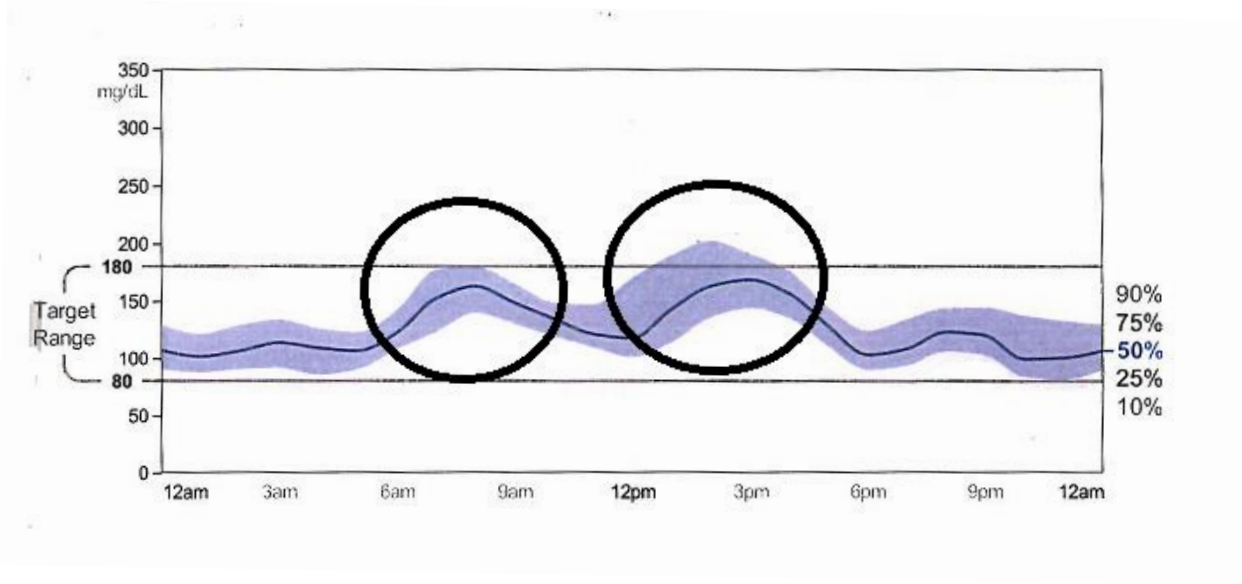
Professional CGM

- Inserted and download at an outpatient office visit
- Conducted for up to 14 days with patient blinded to the readings
- Food, exercise, and medication logs completed by the patient
- Sensor data downloaded in the office (7 and/or 14 day)
- Billable service

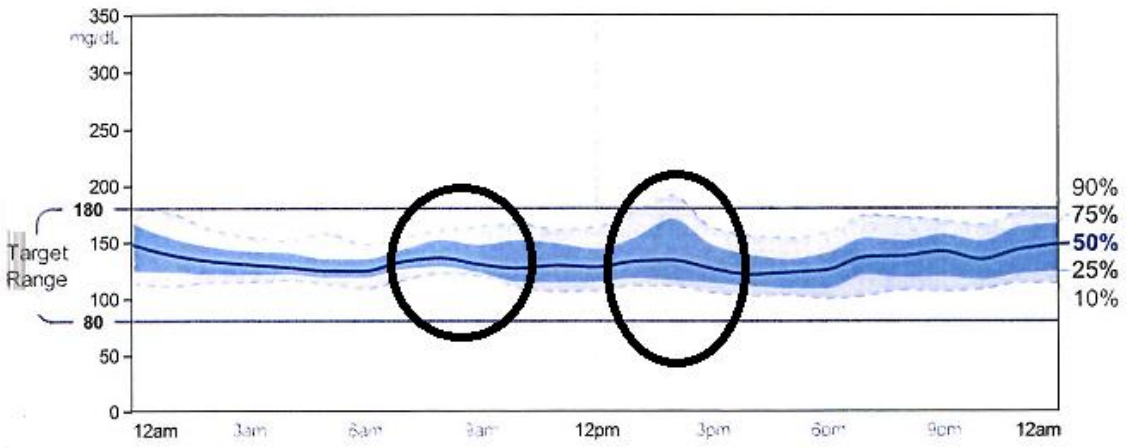
Codes	Billed by	Fee Schedule* (Private payer)
CPT 95250 (Do not bill more than 1x/mo)	Any qualified staff under the direct supervision of a MD, PA or NP	$305
CPT 95251 (Do not bill more than 1x/mo)	MD, PA, NP	$90

CGM Application

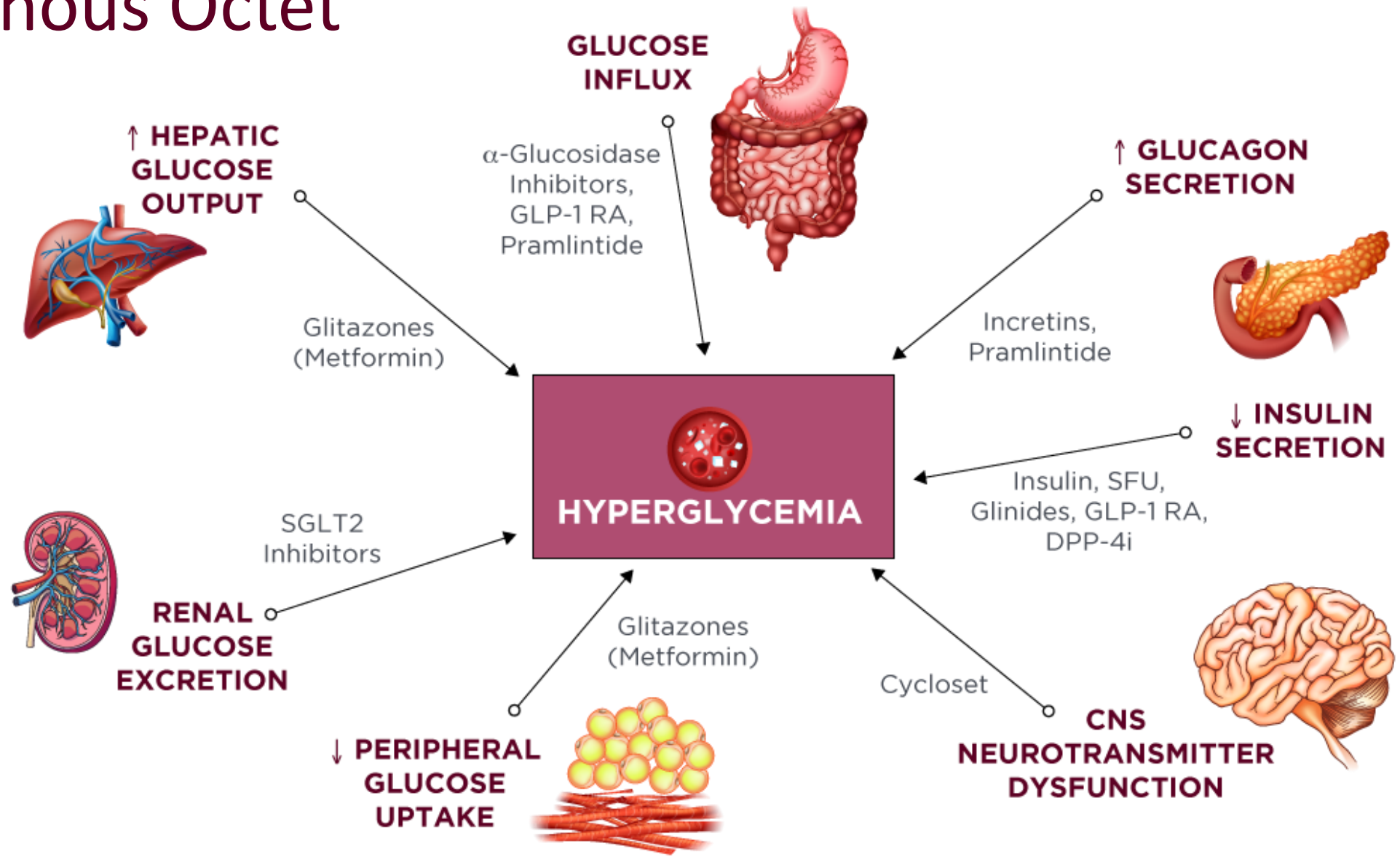
Week 1



Week 2



Ominous Octet



Adapted from Cavaiola TS, Pettus JH. Management Of Type 2 Diabetes: Selecting Amongst Available Pharmacological Agents. https://www.ncbi.nlm.nih.gov/books/NBK425702/

CNS = Central Nervous System
SFU = Sulfonylureas

Cardiovascular Outcomes Trials (CVOTs)

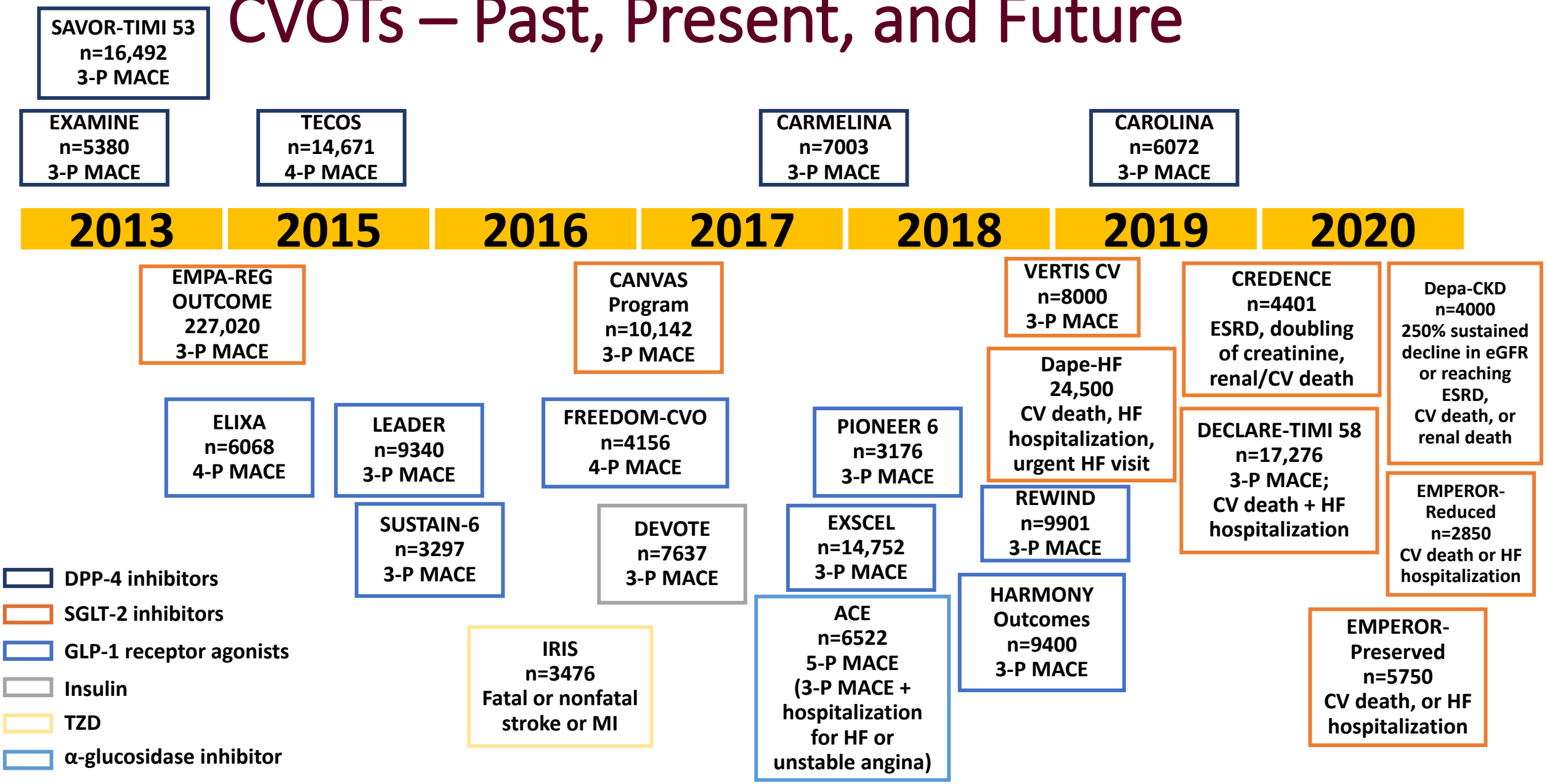
- Since FDA issued guidance >25 CVOTs have launched
- Primary endpoint: major adverse cardiac events (MACE)
  - 3-point MACE = cardiovascular death, nonfatal myocardial infarction, nonfatal stroke
  - 4-point MACE = 3-point MACE + additional CV endpoint (acute coronary syndrome or hospitalization for heart failure or unstable angina)

Major Drug Classes Studied

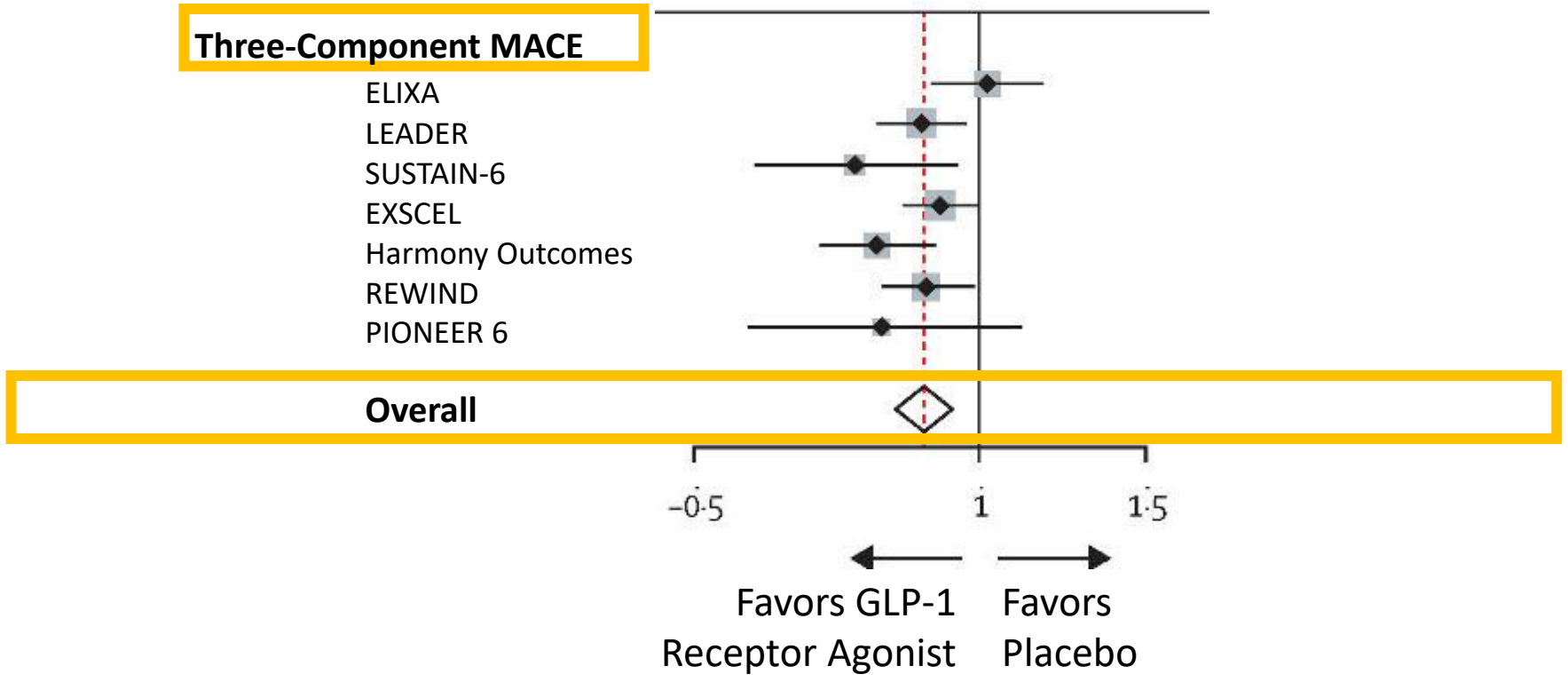
DPP-4 Inhibitors	GLP-1 Receptor Agonists	SGLT2 Inhibitors
• Alogliptin • Linagliptin • Saxagliptin • Sitagliptin	• Albiglutide • Dulaglutide • Exenatide • Lixisenatide • Liraglutide • Semaglutide	• Canagliflozin • Dapagliflozin • Empagliflozin • Ertugliflozin

- DPP-4 inhibitors: Increase incretin levels, reducing release of glucagon and increasing insulin secretion
- GLP-1 receptor agonists: Stimulate glucose-dependent insulin release and inhibit glucagon secretion
- SGLT2 inhibitors: Interfere with glucose reabsorption and prevent renal reuptake of glucose from the glomerular filtrate

CVOTs – Past, Present, and Future

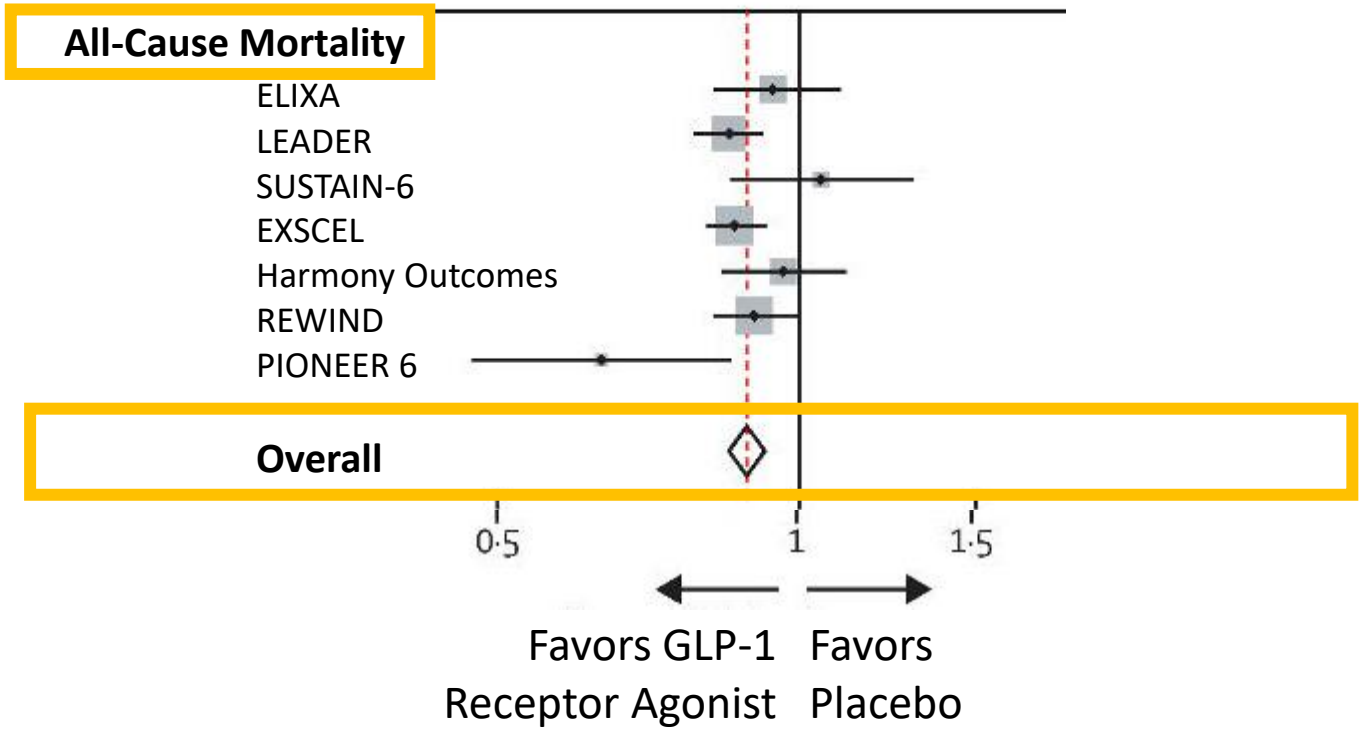


Cardiovascular Outcomes: GLP-1 Receptor Agonists in Patients with Type 2 Diabetes: A systematic review & meta-analysis of CVOT



Adapted from Kristensen SL, et al *Lancet Diabetes Endocrinol*. 2019; 7: 776–85

Renal, Heart Failure, and Mortality Outcomes with GLP-1 Receptor Agonists in Patients With Type 2 Diabetes: A systematic review & meta-analysis of CVOT



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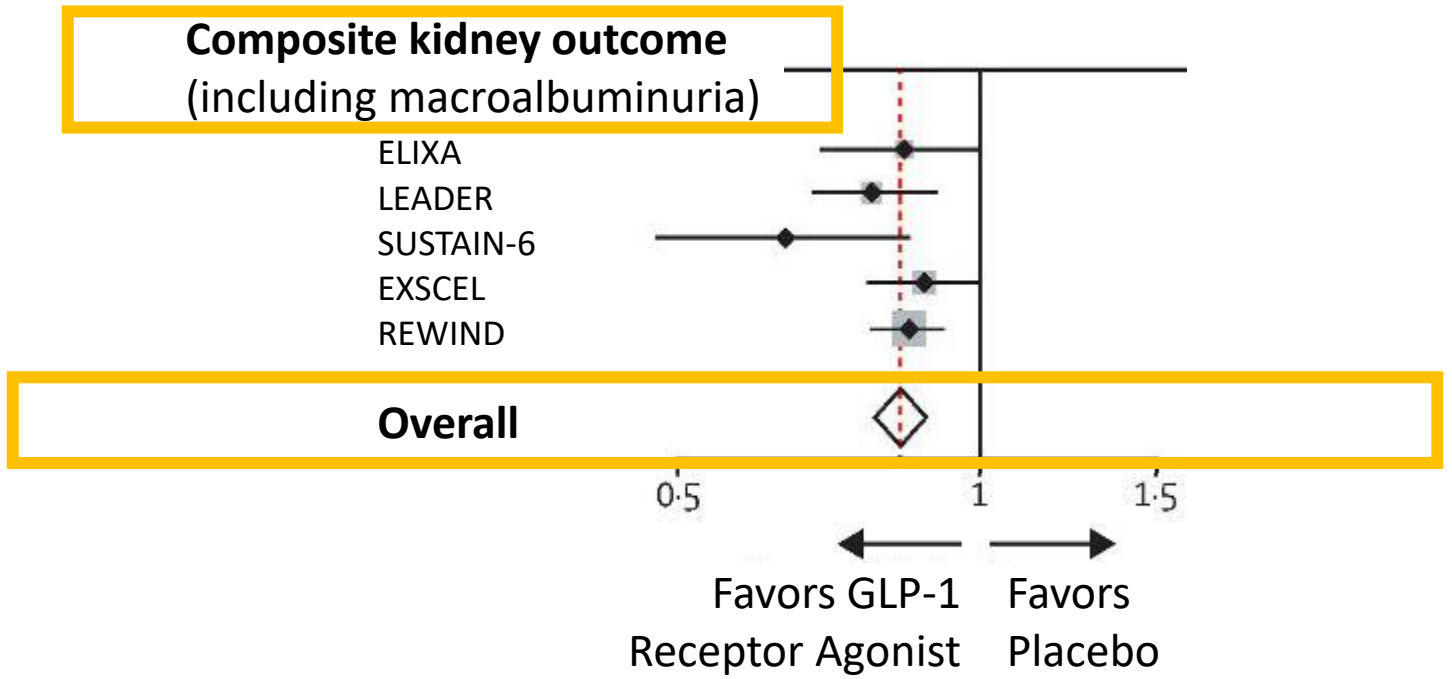
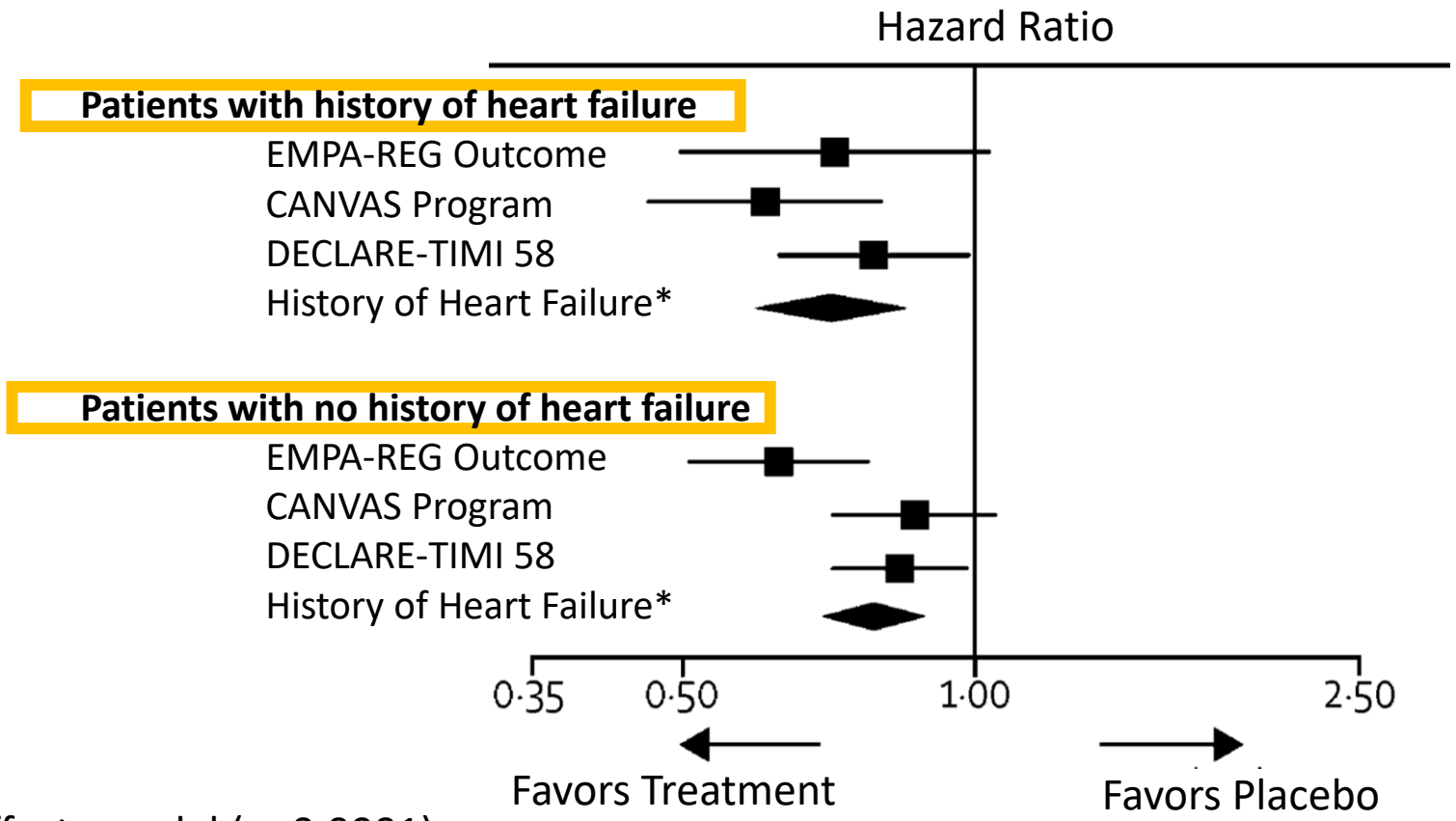


Adapted from Kristensen SL, et al *Lancet Diabetes Endocrinol*. 2019; 7: 776–85

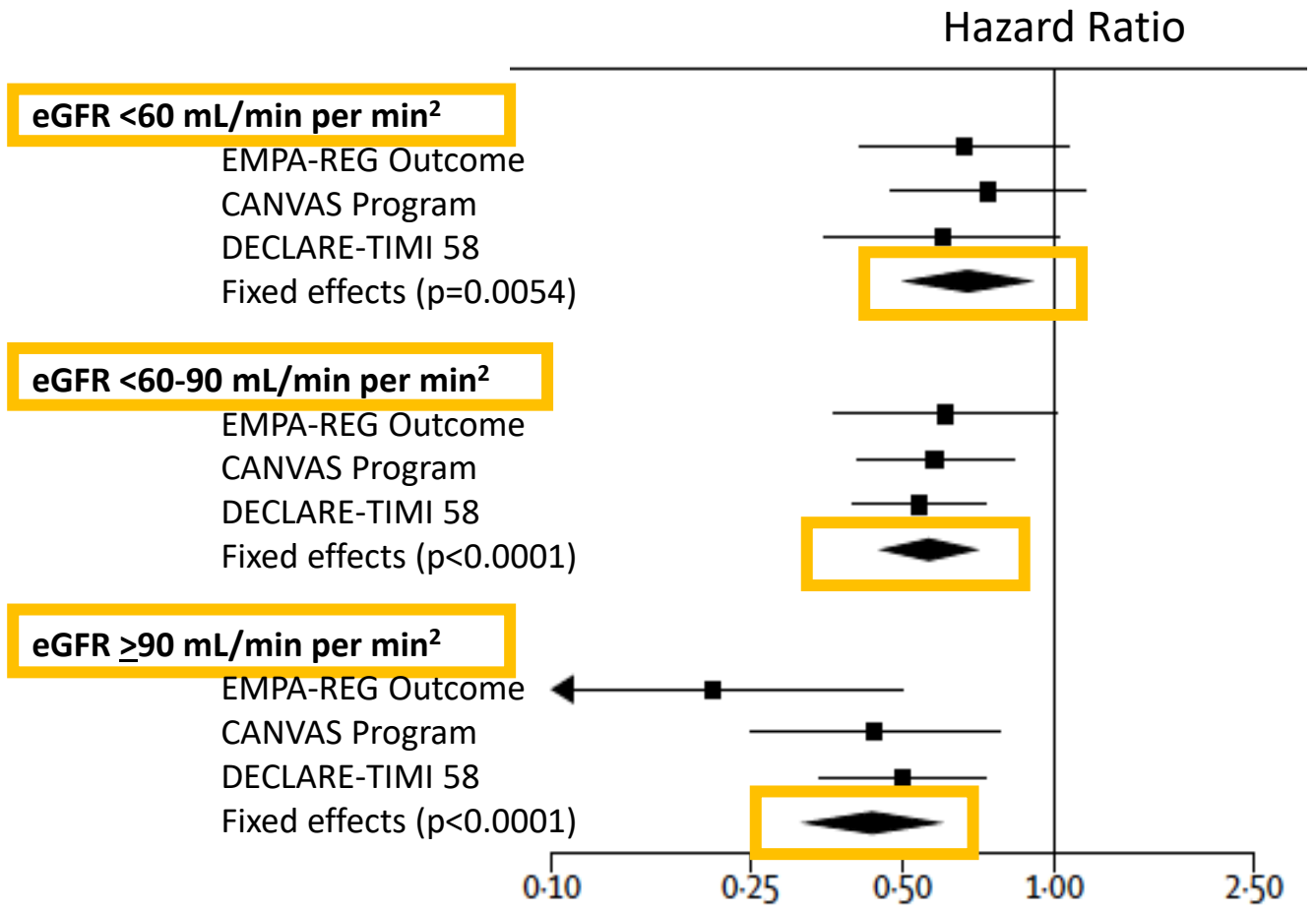
Meta-analysis of SGLT2i Trials Stratified by eGFR Levels: Class Benefit on Hospitalization for Heart Failure and CV Death



*Fixed effects model (p<0.0001)

Adapted from Zelniker TA et al *Lancet*. 2019; 393: 31–39

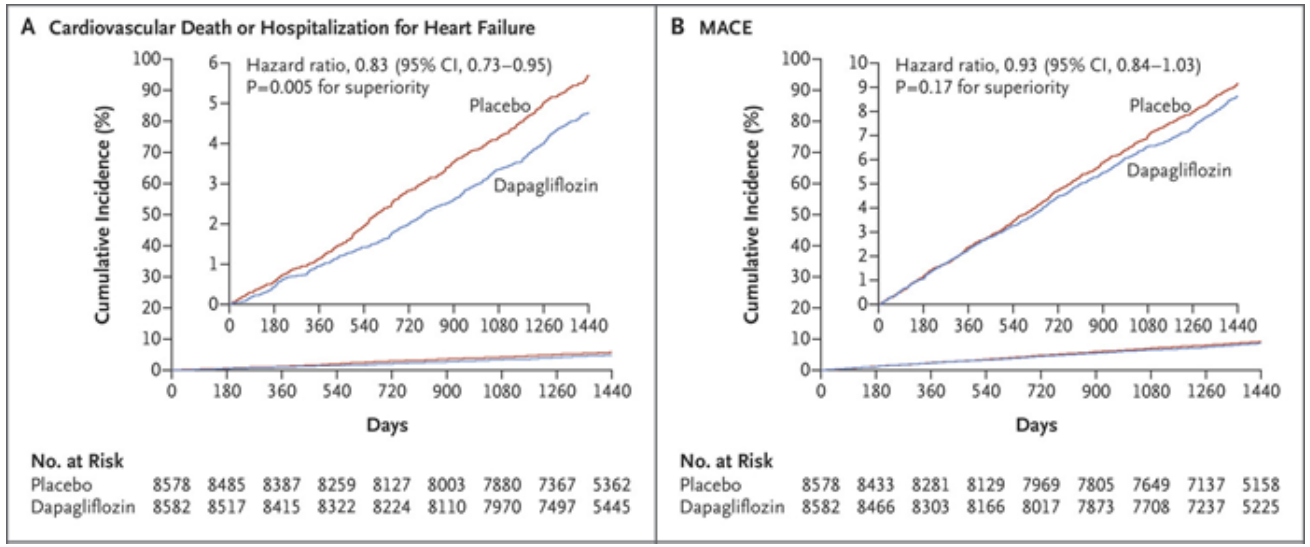
Meta-analysis of SGLT2i Trials Stratified by eGFR Levels: Class Benefit on Composite of Worsening of Renal Function, End-stage Renal Disease, or Renal Death



Adapted from Zelniker TA et al *Lancet*. 2019; 393: 31–39

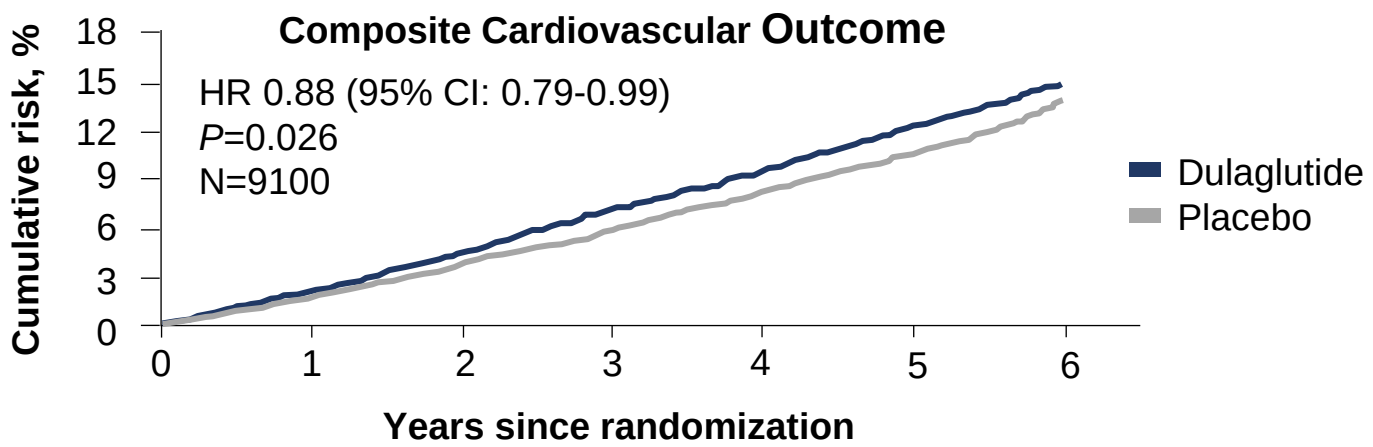
Recent News: Dapagliflozin and Dulaglutide

DECLARE TIMI-58
Dapagliflozin[1]



P<0.001 for noninferiority

REWIND: Dulaglutide[2]



- 66 % were primary prevention and 34 % had established disease.
- 12 % reduction in MACE vs PBO
- Renal function preservation

Permissions purchased from Wiviott SD, et al. *N Engl J Med* 2019; 380:347-357
Gerstein HC, et al. *Lancet*. 2019 Jul 13;394(10193):121-130

Renal Outcomes in CVOTs

- **SGLT2 Inhibitors**
  - Benefits demonstrated on renal outcomes as a class effect
  - Not recommended below eGFR < 45 ml/min per 1.73 m^2
- **GLP-1 Receptor Agonists**
  - Benefits demonstrated on renal outcomes as a class effect
  - Okay to use in all stages of renal disease
- **DPP-4 Inhibitors**
  - Inconsistent results on renal outcomes
  - Most produced no significant differences in prespecified endpoints, but some reduced UACR

SGLT2 = Sodium/Glucose Co-Transporter 2
GLP-1 = Glucagon-Like Peptide-1
DPP-4 = Dipeptidyl Peptidase 4

SGLT2 Inhibitors and GLP-1 Receptor Agonists

Monotherapy

Lifestyle Management + Metformin

Initiate metformin if no contraindications

If A1C not at target, consider dual therapy

Dual Therapy

With indicators of high-risk or established ASCVD, CKD, or HF

Consider independently of baseline A1C or individualized A1C target

ASCVD Predominates

PREFERABLY

- **GLP-1 receptor agonist** with proven CVD benefit* **OR**
- **SGLT2 inhibitor** with proven CVD benefit (if eGFR adequate)*

HF or CKD Predominate

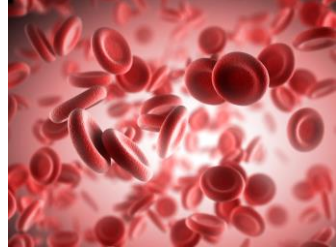
PREFERABLY

- **SGLT2 inhibitor** with evidence of reducing HF and/or CKD in CVOTs if eGFR adequate† **OR**
- If SGLT2 inhibitor not tolerated or contraindicated or if eGFR less than adequate, add **GLP-1 receptor agonist** with proven CVD benefit*

***Proven CVD benefit** = label indication of reducing CVD events (canagliflozin, empagliflozin, liraglutide; dapagliflozin for HHF)

†Evidence from CVOTs = empagliflozin, canagliflozin, and dapagliflozin have shown ↓ HF and CKD progression

Adapted from ADA. *Diabetes Care*. 2020;43:S98-S110.



Treatment Intensification- Les

Pharmacologic

- **Increase Metformin** to 1000 mg BID
- Stop Sitagliptin
- **Consider adding GLP1-RA :**
  - **Semaglutide, Dulaglutide** or **Liraglutide**
- **Consider adding an SGLT-2i:**
  - **Erutgliflozin, dapagliflozin, empaglifloxin, or canagliflozin**

- Review safety considerations/potential side effects
- Provide instruction on administration, titration, storage, and site selection for GLP1-RA
- Provide discount/savings cards to help offset cost (high deductible)

Safety Considerations

GLP-1 RA

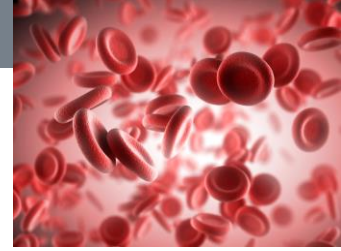
- Black Box Warning – thyroid C-cell tumors (liraglutide, dulaglutide, exenatide extended release)
- Gastrointestinal side effects common (nausea, vomiting, diarrhea)
- Injection-site reactions
- Acute pancreatitis risk (?)

SGLT-2i

- Canagliflozin Black Box Warning (BBW) – risk of amputation
- Canagliflozin – risk of bone fractures
- Diabetic ketoacidosis (T1D)
- Genitourinary infections
- Risk of volume depletion, hypotension
- Increased LDL
- Risk of Fournier's gangrene

RA = Receptor Agonist
i = Inhibitor

Patient Case: Faculty Discussion



What additional therapy changes would you recommend to manage comorbidities for Les?

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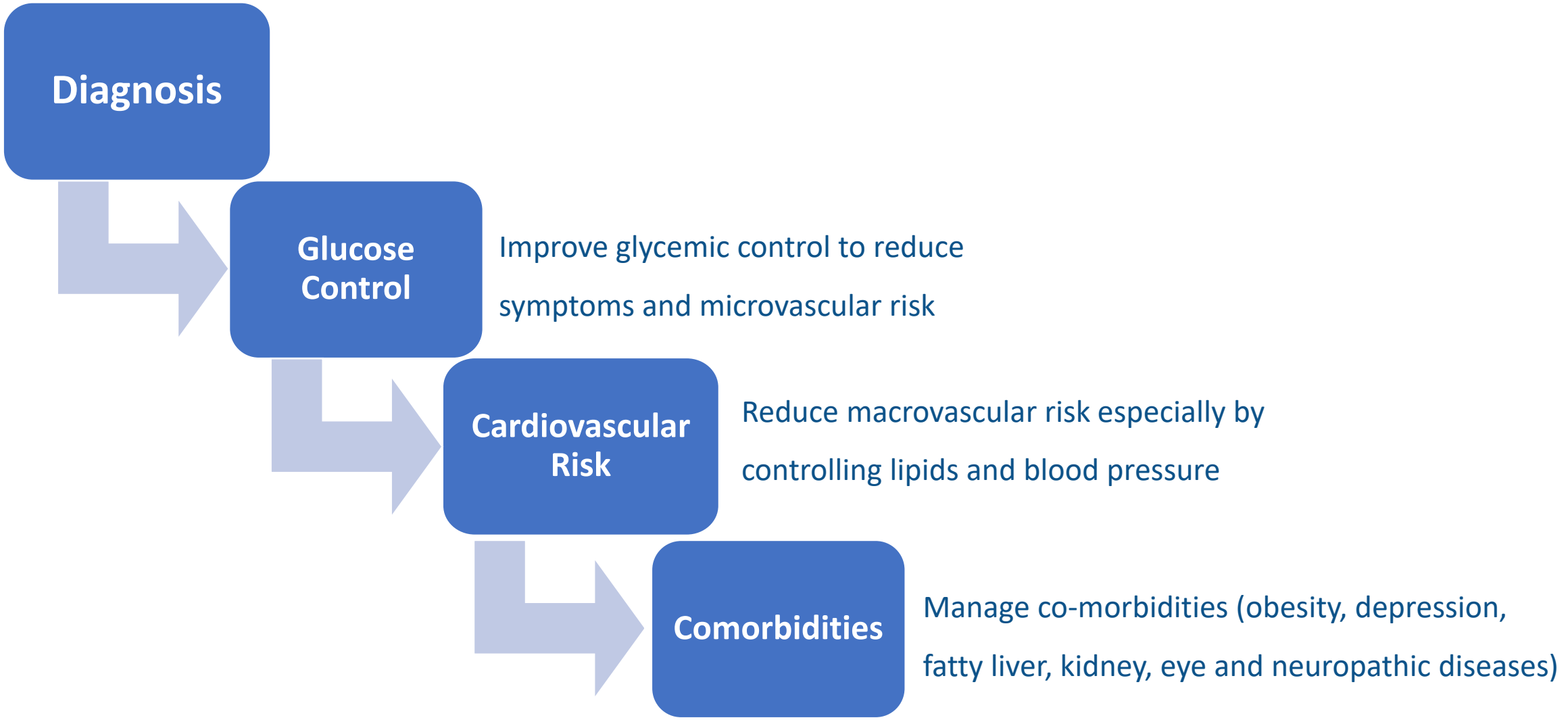
Proactive Management of Type 2 Diabetes



Goals of Diabetes Management: Beyond Glucose Control

	AACE[1]	ADA[2]
A1C %	≤6.5	≤7.0
Fasting/pre-meal BG, mg/dL	<110	80-130
Postprandial, mg/dL	<140[a]	<180[b]
Blood pressure, mm Hg	< 130/80	<140/90
LDL-C, mg/dL	<100 (<70) (<55)[c]	Based on risk

[a]2-hr postmeal; [b]Peak; [c]Lower goals recommended for high-risk/CVD

1. Garber AJ, et al. *Endocr Pract*. 2018;24(1):91-120;
2. ADA. *Diabetes Care* 2018; 41(Supplement 1):S86-S104.

BG = Blood Glucose
AACE = American Association of Clinical Endocrinologists
ADA = American Diabetes Association

ADA Recommendations to Screen and Treat CHD in Patients with Diabetes Mellitus

Primary and Secondary Prevention

- In asymptomatic patients, evaluate risk factors to stratify patients by 10-year risk, and treat risk factors accordingly
- In patients with known CV disease, an ACE inhibitor, aspirin, and statin therapy (if not contraindicated) should be used to reduce the risk of CV events
- In patients with a prior MI, beta-blockers should be continued for at least 2 years after the event.

American Diabetes Association. *Diabetes Care* 2010;33:S11-61

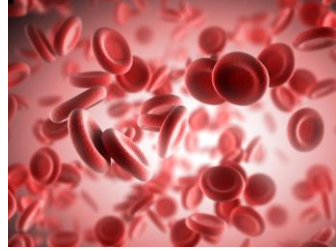
ACE = Angiotensin Converting Enzyme

Proven ASCVD Prevention/Treatment in Diabetes

2018 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic CV Risk

- Smoking cessation
- Reduce LDL cholesterol:
  - Statins
  - PCSK9 inhibitors
- Manage hypertension
  - ACEI / ARB (also good for microalbuminuria)
- Baby aspirin
- Icosapent Ethyl (EPA 4 g/day) when TG > 150 mg/dL
- Weight loss following bariatric surgery
- Glucose control

ARB = Angiotensin II receptor blockers
PCSK9 = Proprotein convertase subtilisin/kexin type 9

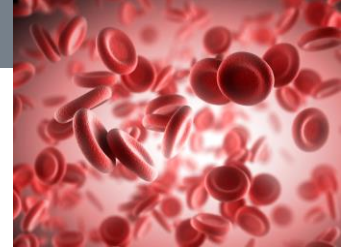


Les' Labs

	Results	Target
A1C	8.4% (elevated)	< 7.0%
eGFR/ACR	66 mL/min/? m^2 (low) ACR= 120 mg/G (high)	
LDL	124 mg/dL (elevated)	< 100
HDL	33 mg/dL (low)	
TG	324 mg/dL (elevated)	
BP	150/94 mm Hg	<130/80

Current Medications:

- Losartan 50 mg QD
- Atorvastatin 20 mg QD
- Aspirin 81 mg QD



Treatment Intensification- Les

- Intensifying dose of ARB
- Titrate statin to high-intensity dose
- Consider adding icosapent ethyl
- Continue aspirin
- Review goals for blood pressure and other lab parameter goals
- Have patient check BP at home routinely
- Consider adding a PCSK9i if LDL goals not met at follow-up

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Conclusions

- The landscape of diabetes management has changed from a gluco-centric approach to one targeting **customized** patient metabolic targets.
- Clinicians should **intensify** management of diabetes based on the presence of coronary artery disease, heart failure, diabetic kidney disease, obesity, hypoglycemia risk, and financial concerns.
- **GLP-1 RAs** reduce 3-point MACE, have modest weight loss, slow progression of DKD, with less improvements on CHF. No renal threshold for use.
- **SGLT-2is** reduce 3-point MACE, reduces CHF, slow progression of DKD, but less weight loss. Not recommended eGFR < 45 ml/min per 1.73 m^2.
- Don't forget about **treating to targets** for LDL and blood pressure.
- Implement **team-approach DSMES proven interventions** for improving patient adherence.

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