

Metabolic Disease in CKM Syndrome: Clinical Case Studies

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Objectives

1. Assess the current therapy and determine the severity of metabolic disease in patients with or at risk for CKM syndrome.
2. Apply evidence-based guidelines and primary literature to develop comprehensive treatment plans encompassing both pharmacological and non-pharmacological interventions for patients with metabolic disease in CKM syndrome.

Abbreviations

- ACEi: angiotensin converting enzyme inhibitor
- ARB: angiotensin receptor blocker
- ASCVD: atherosclerotic cardiovascular disease
- BMP: basic metabolic panel
- BP: blood pressure
- CAC: coronary artery calcium
- CKD: chronic kidney disease
- CKM Syndrome: cardiovascular kidney metabolic syndrome
- CVD: cardiovascular disease
- GLP-1 RA: glucagon like peptide 1 receptor agonist
- HF: heart failure
- MACE: major adverse cardiovascular events
- PCSK9i: proprotein convertase subtilisin/kexin type 9 inhibitor
- SDOH: social determinants of health
- SGLT2i: sodium glucose cotransporter 2 inhibitors
- TG: triglycerides
- UACR: urine albumin to creatinine ratio

Clinical Case Part 1 - MW

MW is a 40-year-old African-American male presenting to his primary care clinic for his annual exam.

- PMH: major depressive disorder, obesity, chronic low back pain, type 2 diabetes
- Social History:
 - Divorced, single father to 2 small children
 - Works full time as a server at a restaurant, taking college classes at night
 - Current smoker (1 ppd)
 - No alcohol or illegal drug use
 - Minimal physical activity
 - Diet: frozen TV dinners, take-out

Clinical Case Part 1 - MW

MW is a 40-year-old African-American male presenting to his primary care clinic for his annual exam.

- Current Medications:

- Acetaminophen 1,000 po BID prn
- Atorvastatin 40mg po daily
- Citalopram 20mg po daily
- Lidocaine patches 5% applied to back daily prn
- Metformin XR 1,000mg po BID

- Vitals:

BP	122/76 mmHg
HR	76 bpm
Weight	223 lb
Height	5' 5"
BMI	37 kg/m ²
Waist circumference	130 cm

- Pertinent Labs (obtained before clinic):

- Lipid panel:

TC: 170 mg/dL

HDL: 35 mg/dL

LDL-C: 102 mg/dL

TG: 160 mg/dL

- BMP:

140	100	14	165
4.1	24	0.9	

eGFR: 111 mL/min/1.73m²

Albumin/creatinine ratio: 23 mg/g

- A1C: 8.3%

CKM Risk Assessment and Staging

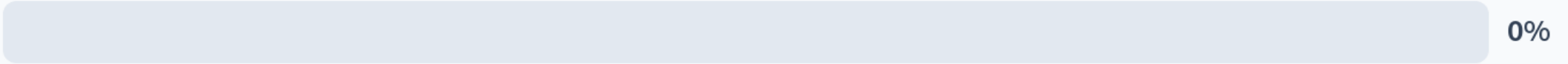


Screening for CKM Risk

- Life's Essential 8:
 1. Dietary patterns
 2. Physical activity
 3. Sleep duration and quality
 4. Nicotine exposure
 5. BMI
 6. Blood pressure
 7. Blood sugar
 8. Cholesterol

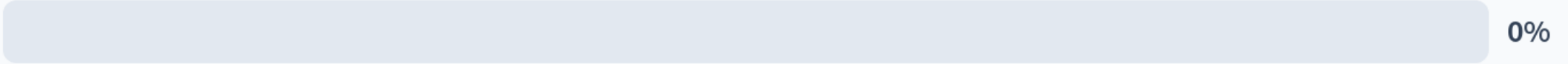
How many modifiable CKM risk factors from Life's Essential 8 can you identify for MW?

2 risk factors



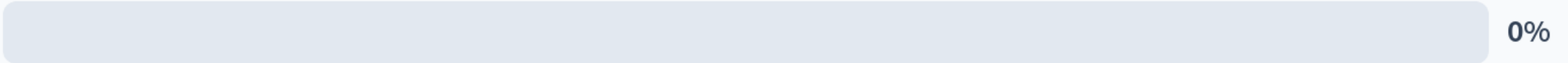
0%

4 risk factors



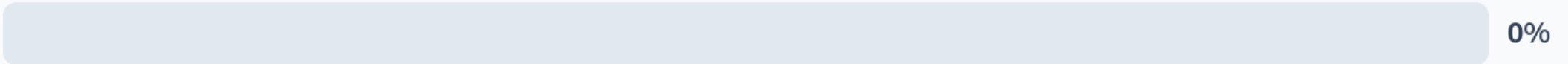
0%

6 risk factors




0%

8 risk factors



0%

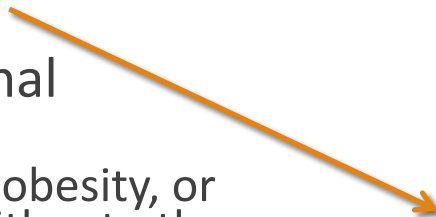


Social Determinants of Health (SDOH)

- SDOH: economic, social, environmental, and psychosocial factors that impact health outcomes throughout life
- Influence CKD development, diagnosis, and outcomes
- Adverse SDOH have downstream consequences for CV events and CV and all-cause mortality
- Several screening tools exist to survey individual social needs
- Highlights the importance of interdisciplinary care


CKM Staging

- Stage 0: No CKM risk factors
- Stage 1: Excess or dysfunctional adiposity
 - Overweight/obese, abdominal obesity, or dysfunctional adipose tissue without other metabolic risk factors or CKD
- Stage 2: Metabolic risk factors and CKD
- Stage 3: Subclinical CVD in CKM
 - Subclinical ASCVD or subclinical HF with excess/dysfunctional adiposity, other metabolic risk factors, or CKD
- Stage 4: Clinical CVD in CKM
 - 4a: no kidney failure
 - 4b: kidney failure

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- Normal BMI and waist circumference
 - Normoglycemia
 - Normotension
 - Normal lipid panel
 - No evidence of CKD or subclinical/clinical CVD

CKM Staging

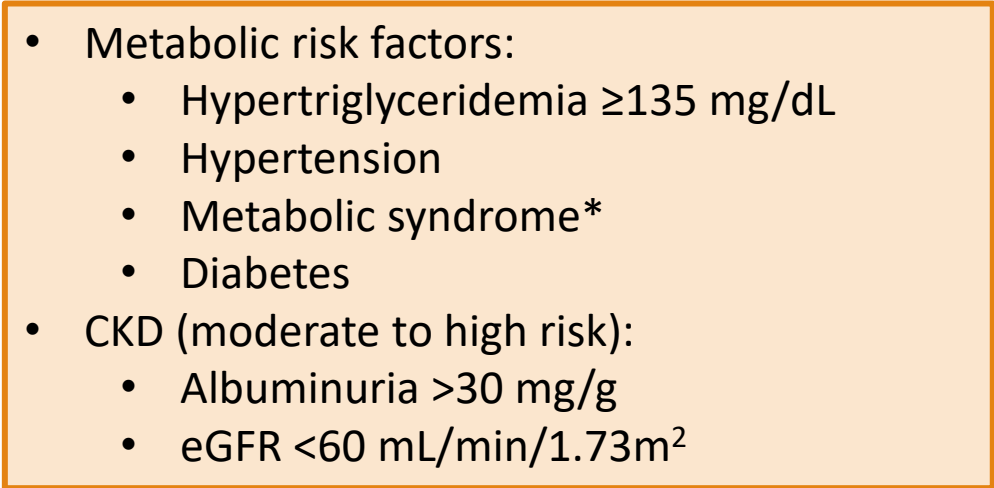
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- BMI ≥ 25 kg/m²*
 - Waist circumference $\geq 88/102$ cm women/men*
 - Fasting blood glucose $\geq 100-124$ mg/dL
 - HbA1c 5.7-6.4%

*reduced cutoff values for patients of Asian ancestry

CKM Staging

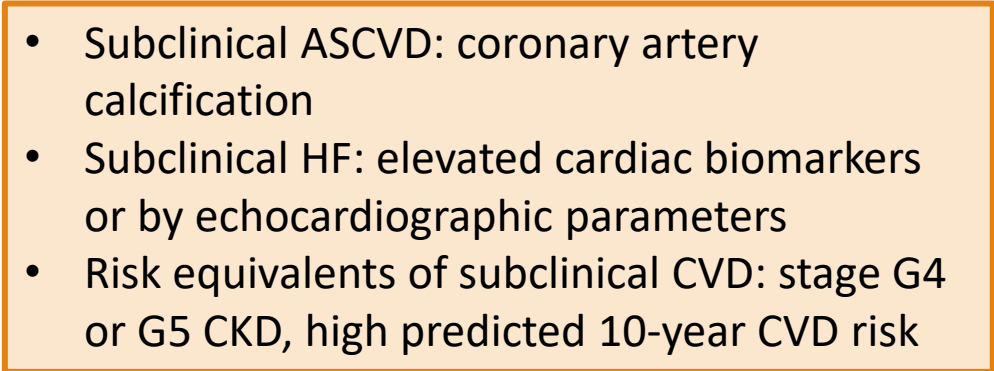
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- Metabolic risk factors:
 - Hypertriglyceridemia ≥ 135 mg/dL
 - Hypertension
 - Metabolic syndrome*
 - Diabetes
 - CKD (moderate to high risk):
 - Albuminuria >30 mg/g
 - eGFR <60 mL/min/1.73m²

*Presence of 3 or more of the following: (1) waist circumference $\geq 88/102$ cm women/men; (2) HDL $<40/50$ mg/dL men/women; (3) TG ≥ 150 mg/dL; (4) BP $\geq 130/80$ or on antihypertensives; (5) fasting blood glucose 100mg/dL


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- Subclinical ASCVD: coronary artery calcification
 - Subclinical HF: elevated cardiac biomarkers or by echocardiographic parameters
 - Risk equivalents of subclinical CVD: stage G4 or G5 CKD, high predicted 10-year CVD risk

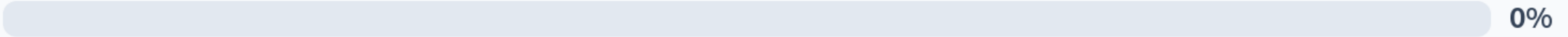
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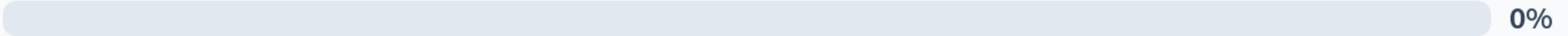
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- Clinical CVD (CAD, HF, stroke, peripheral artery disease, atrial fibrillation) in individuals with excess/dysfunctional adiposity or other CKM risk factors or CKD

What stage of CKM syndrome would you classify MW?

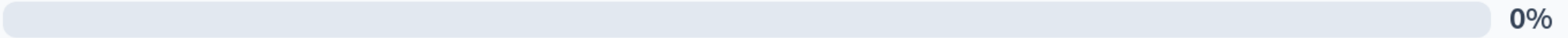
Stage 0



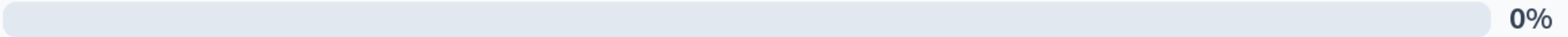
Stage 1



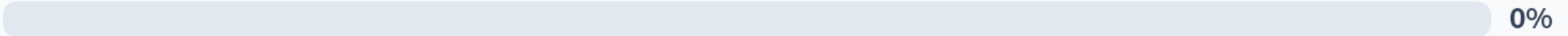
Stage 2



Stage 3



Stage 4



CKM Management



Considerations for All Stages



Promotion of cardiovascular health: Emphasis on Life's Essential 8 framework



Systematic screening for SDOH using validated tools



Interdisciplinary care



Stage 1: Excess or Dysfunctional Adiposity

- Focus on weight loss: STOP obesity alliance toolkit
- Weight loss support with an integrated team
 - Intensive lifestyle intervention
 - Pharmacotherapies BMI ≥ 30 kg/m² (without comorbidities)
 - Bariatric surgery BMI ≥ 40 kg/m² (without comorbidities)
- Persistent/progressive impaired glucose tolerance – consider metformin



Stage 2: Established CKM Risk Factors

Hypertriglyceridemia			
<ul style="list-style-type: none">• Maximize statin therapy• Fibrates for TG $\geq 500\text{mg/dL}$• Icosapent ethyl for TG 135-499 mg/dL with risk factors			



Stage 3: Subclinical CVD in CKM Syndrome

Subclinical Atherosclerosis

- CAC >0 favors statin use in intermediate risk
- CAC >100 favors aspirin use (low bleeding risk)
- Consider other agents for ASCVD risk reduction



Which of the following would you recommend for MW's cholesterol management?

Increase dose of atorvastatin

0%

Start ezetimibe

0%

Start icosapent ethyl

0%

Start fenofibrate

0%



MW's Cholesterol Management

LDL-C is not at goal

- ADA goal for primary prevention: LDL-C <70mg/dL
- ACC/AHA goal for primary prevention and diabetes: 30-49% LDL-C lowering from baseline or <100mg/dL

First consider statin intensification

Ezetimibe should be considered if LDL-C still not at goal after statin intensification

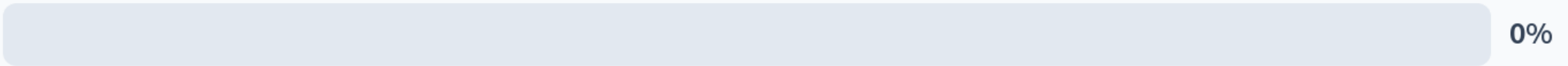
Icosapent ethyl could be considered

- TG \geq 135 mg/dL
- Current smoker
- HDL <40 mg/dL
- <50 years old

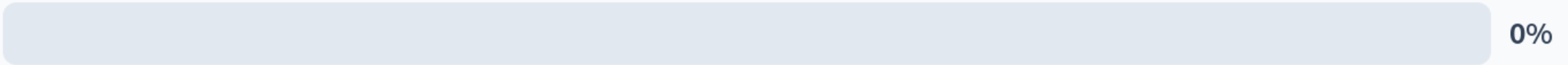
Fibrate not yet indicated

Which of the following would you recommend for MW's diabetes management?

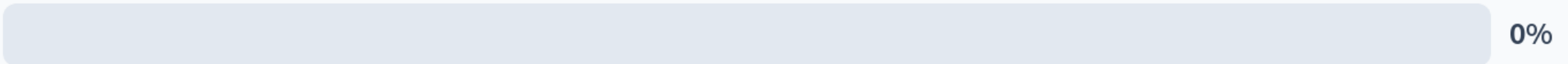
Discontinue metformin, start SGLT2i



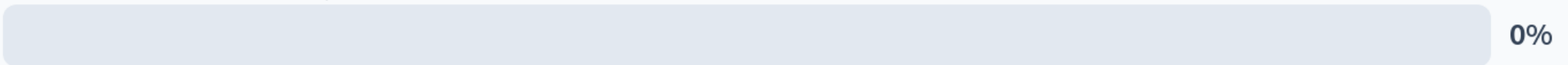
Continue metformin, start GLP1-RA



Continue metformin, start SGLT2i

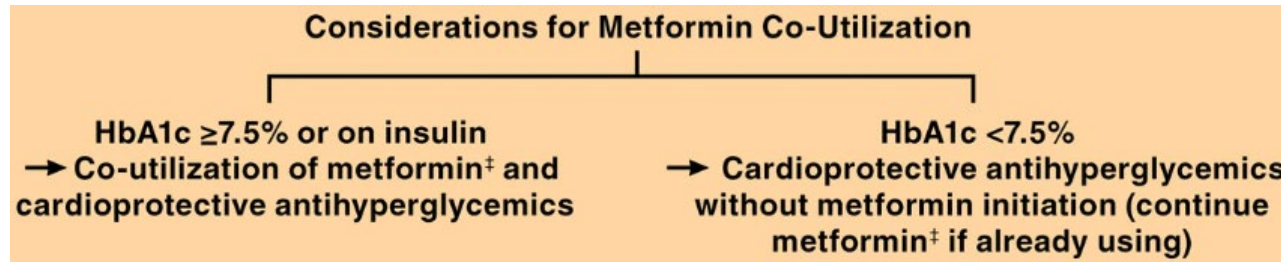


Discontinue metformin, start GLP1-RA



MW's Diabetes Management

- A1C goal <7%
- Metformin use:



Adapted from Figure 3. CKM Health: A Presidential Advisor From the American Heart Association

- BMI ≥ 35 kg/m²
 - Start GLP1-RA
 - Examples: Semaglutide (SQ), dulaglutide, liraglutide
- CKD not currently present – SGLT2i may be considered in the future



Clinical Case Part 2 – MW

MW is now 52 years old. He is presenting to his primary care clinic for his annual exam. He was hospitalized 2 months ago for an NSTEMI and his diabetes continues to worsen. He has now developed complications from his diabetes.

- PMH: NSTEMI, HTN, major depressive disorder, obesity, chronic low back pain, type 2 diabetes, CKD

- Current Medications:

- Aspirin 81mg po daily

- Atorvastatin 80mg po daily

- Citalopram 20mg po daily

- Clopidogrel 75mg po daily

- Dulaglutide 3mg SQ once weekly

- Lisinopril 20mg po daily

- Metoprolol succinate 50mg po daily

- Lidocaine patches 5% applied to back daily prn

- Metformin XR 1,000mg po BID

Clinical Case Part 2 – MW

- Vitals:

BP	118/66 mmHg
HR	64 bpm
Weight	198 lb
Height	5' 5"
BMI	33 kg/m ²
Waist circumference	112 cm

- Pertinent Labs (obtained before clinic):

- Lipid panel:

TC: 150 mg/dL

HDL: 38 mg/dL

LDL-C: 84 mg/dL

TG: 142 mg/dL

- BMP:

137	105	14	186
4.5	22	1.6	

eGFR: 52 mL/min/1.73m²

Albumin/creatinine ratio: 367 mg/g

- A1C: 9.1%

Stage 4: Patient with CKM Syndrome with Existing CVD

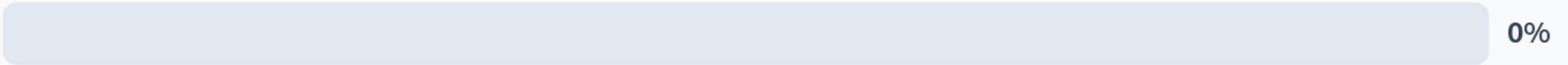
ASCVD

- Aspirin and high intensity statin
- Consider addition of ezetimibe and PCSK9i based on LDL-C level/goals

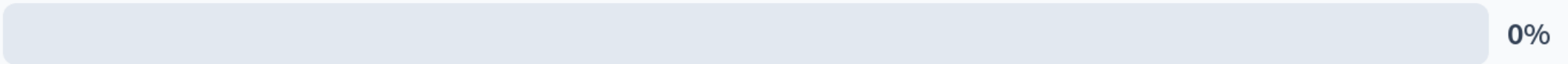


What recommendation would be appropriate to optimize MW's ASCVD management?

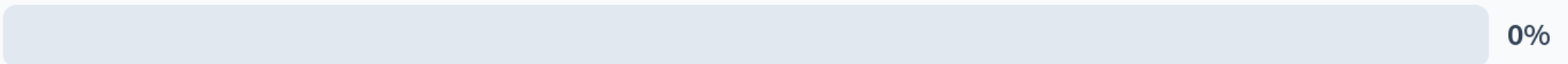
Switch to rosuvastatin at a high intensity dose



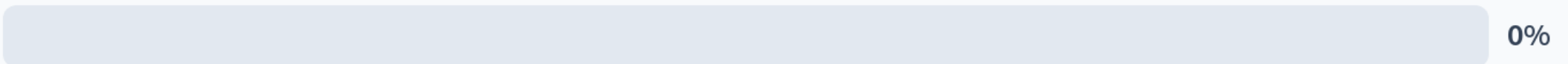
Add on ezetimibe



Add on a PCSK9i



Add on both ezetimibe and a PCSK9i



MW's ASCVD Management

- LDL-C goal – secondary prevention
 - <55 mg/dL (2024 ADA Standards of care)
 - <70 mg/dL (2018 ACC/AHA Cholesterol guidelines)
- High intensity statin
- Adjunct therapy to achieve LDL-C goals:
 - Ezetimibe first
 - PCSK9i if still above goal

What would be the most appropriate recommendation for management of MW's CKD and diabetes?

Add on an SGLT2i and decrease metformin dose

0%

Add on finerenone

0%

Add on an SGLT2i and increase dose of dulaglutide

0%

Increase dose of lisinopril and dulaglutide

0%



MW's CKD and Diabetes Management

- SGLT2i would provide several benefits:
 - ASCVD risk reduction
 - Slowing progression of CKD
 - Antihyperglycemic
- Metformin dose appropriate
 - Consider dose reduction when eGFR <45 mL/min/1.73m²
- Increase dulaglutide dose:
 - Additional blood glucose lowering and weight loss
- Finerenone could be considered for CKD

Take Home Points

- Regardless of CKM stage, a patient's care should include assessment of SDOH, interdisciplinary care, and Life's Essential 8 framework to ensure optimal outcomes
- Cardiovascular, renal, and metabolic risk factors must be evaluated together to optimize management and reduce risk for ASCVD
- SGLT2 inhibitors and GLP1-RA are the cornerstone medications used for diabetes management given their benefits for CVD and CKD

Questions?

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