Advancing Kidney Health
Through Optimal Medication Management

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CKD Treatment

Addressing Kidney and Cardiometabolic Outcomes Part 2: SGLT-2 Inhibitors

What We’re Going to Cover

- Why do SGLT-2is matter?
- The answer
- Case Scenario: SGLT-2i
- Key takeaways

Case Scenario: MR

Image is stock photo from Microsoft PowerPoint

- 68-year-old White female
- PMH = T2DM, HTN, dyslipidemia, CKD

Current Medications

- linagliptin 5 mg PO daily
- lisinopril 10 mg PO daily
- chlorthalidone 12.5 mg PO daily
- atorvastatin 40 mg PO daily
- ezetimibe 10 mg PO daily

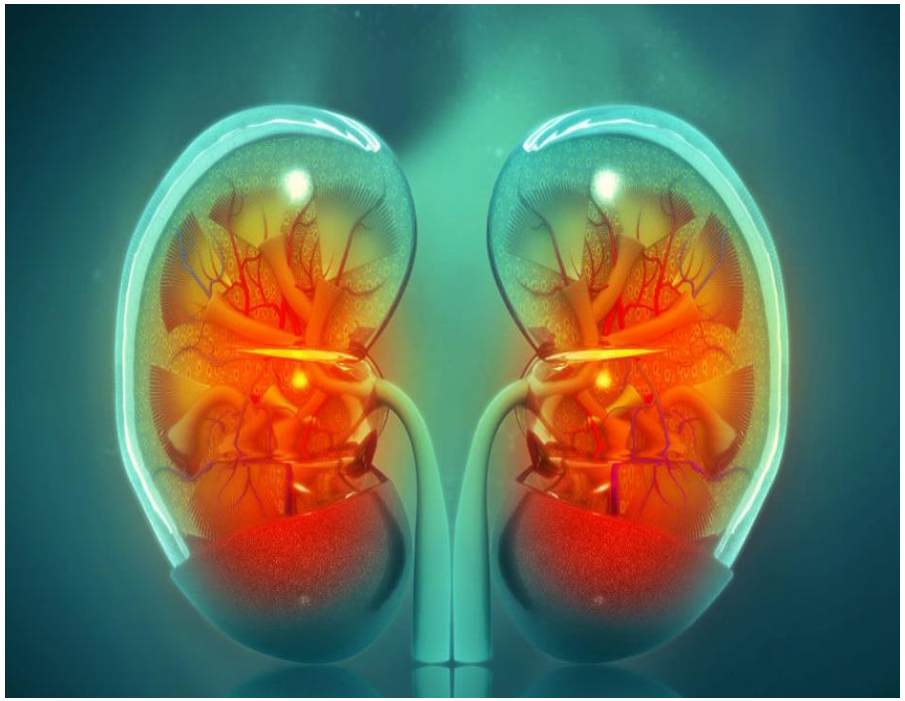
Labs & Physical Findings

- HbA1c = 6.9%
- BP = 118/70 mmHg
- eGFR (non-indexed)* = 22 mL/min
- eGFR (indexed)* = 17 mL/min/1.73m2
- UACR = 190 mg/g
- BMI 32 kg/m^2

*CKD-EPI_{Cr} 2021 non-race based eGFR

Why Do SGLT-2 Inhibitors Matter?

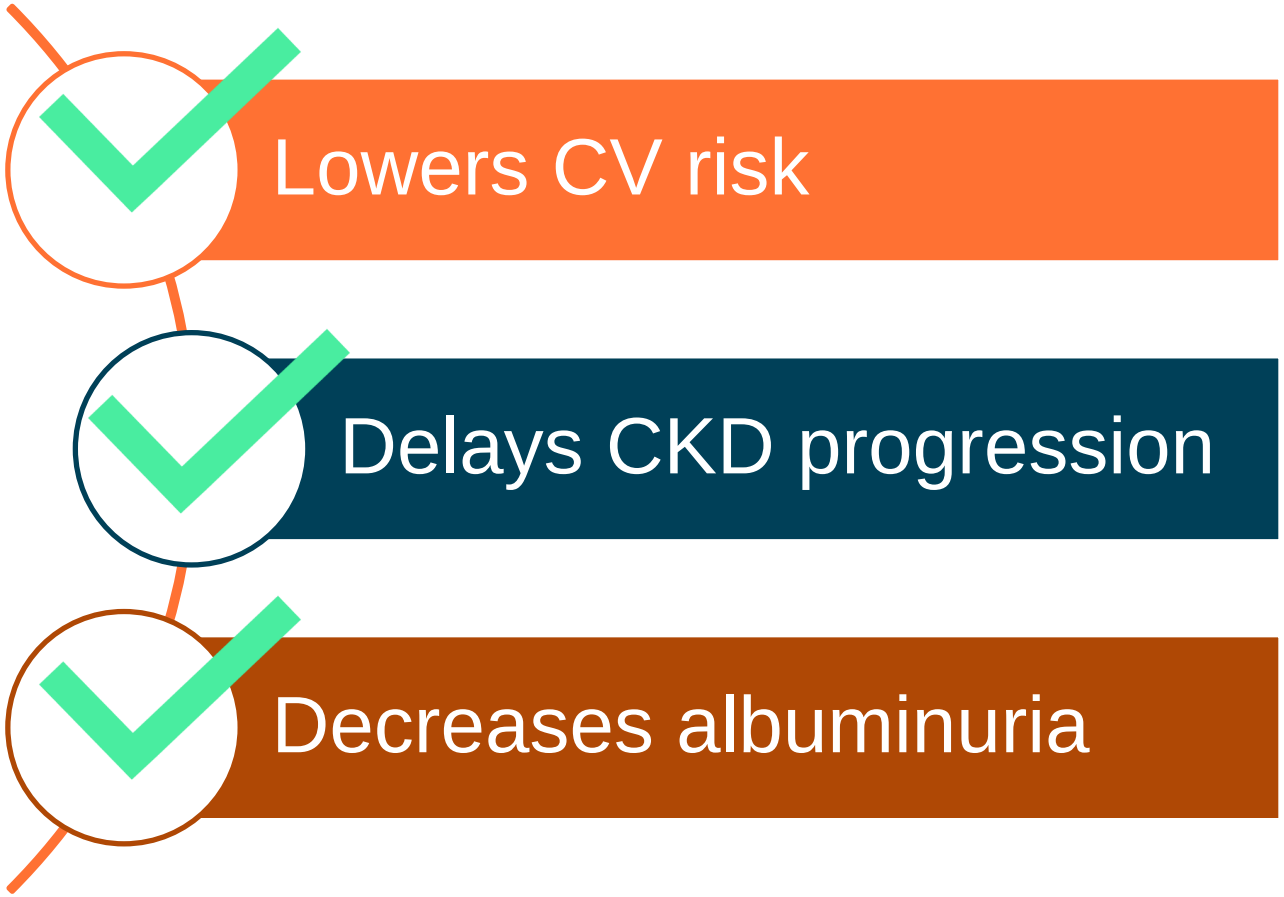
- Limited drugs specifically to delay or prevent CKD progression
- SGLT-2is initially approved for DM!
  - Diabetes is leading cause of CKD, ESKD
- DM trials showed CV, kidney benefits



The Solution

SGLT-2 inhibitors are cornerstone of optimal medication management in kidney disease

Irrespective of glycemic control, diabetes status!



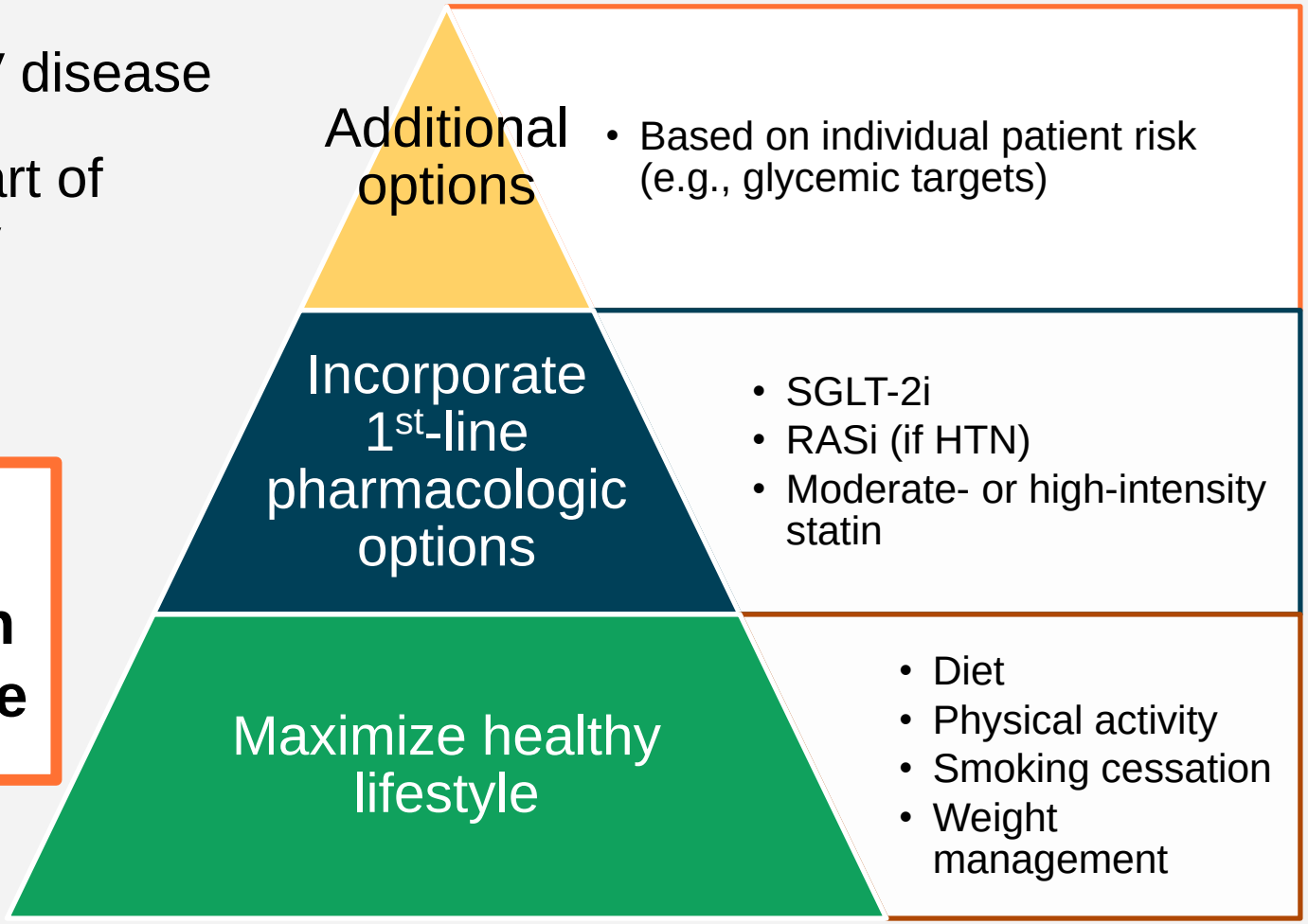
What is the “?” symbol?

- On slides with the orange question mark, select the “I” button for more information.
- When you are done reviewing the material, press the “X” to return to the video.
- You may need to press the “PLAY” key to resume watching the module.

What Do the Guidelines Say?

- CKD = high risk of CV disease
- Glycemic control is part of management strategy

SGLT-2 inhibitors are 1st-line drug therapy in diabetic kidney disease



de Boer IH et al. *Diabetes Care.* 2022;45(12):3075-3090
ADA Standards of Medical Care in Diabetes - 2023. *Diabetes Care* 2023; 46,S1-S4.

What Do the Guidelines Say?

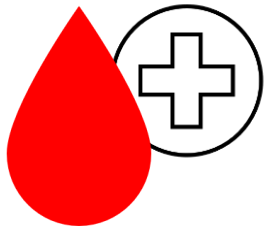
- SGLT-2 inhibitors should be used to prevent heart failure hospitalizations in T2DM + established CVD (or high CV risk)

- Irrespective of diabetes, SGLT-2 inhibitors are GDMT for:
  - HFpEF
  - HFmrEF
  - HFrEF

SGLT-2 inhibitors are backbone of therapy for management and prevention of heart failure

Heidenreich PA et al. Circulation. 2022;145:e895-e1032.

Let's Bring It Together



Diabetes

Heart Failure

SGLT-2 inhibitors are cornerstone of optimal medication management in **kidney disease**…

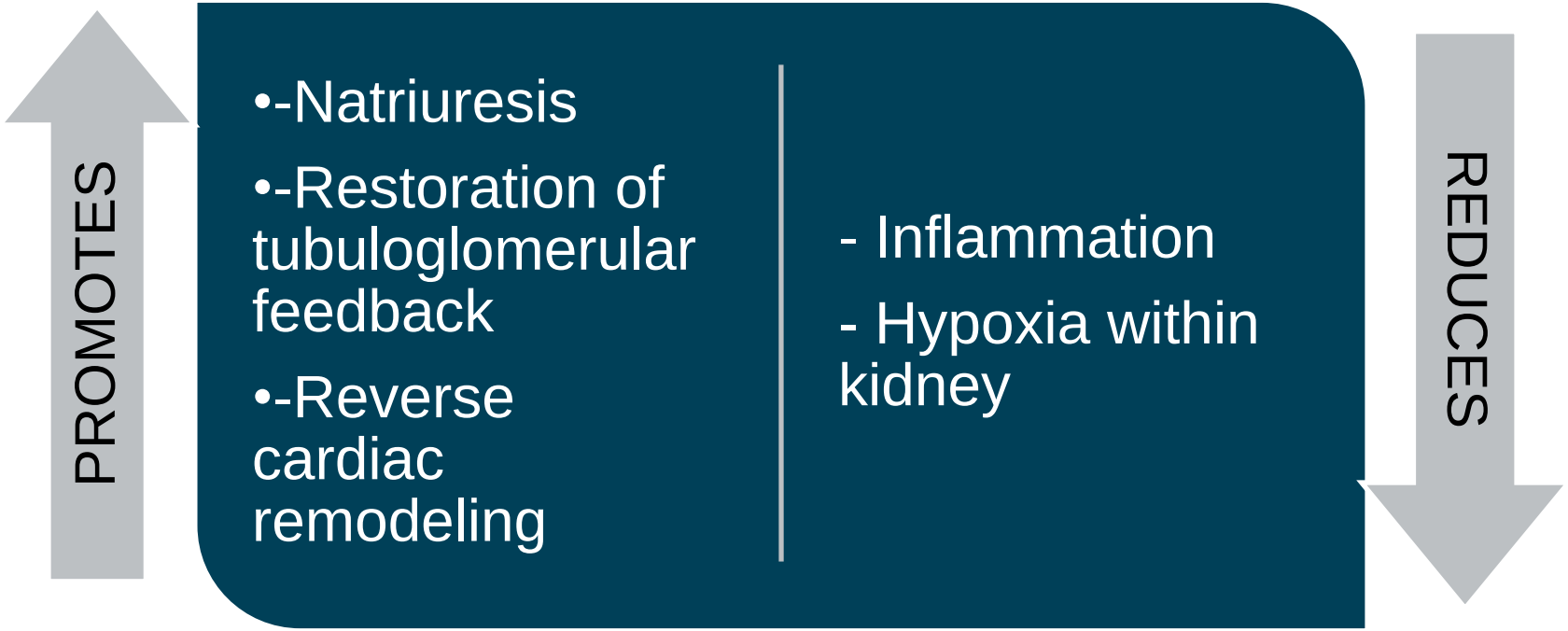
- WITH or WITHOUT diabetes
- WITH or WITHOUT heart failure

Assuming no other notable findings, which of the following individuals is NOT a candidate for an SGLT-2 inhibitor?

Option		Feedback / Rationale
A.	63-year-old male with CKD and diabetes (A1c is above goal).	Incorrect. SGLT-2 inhibitors are recommended in diabetes.
B.	79-year-old male with CKD and HFpEF.	Incorrect. SGLT-2 inhibitors are recommended in heart failure.
C.	48-year-old female with CKD.	Incorrect. SGLT-2 inhibitors are recommended in CKD, *regardless* of concomitant diabetes and/or heart failure.
D.	All of the above are candidates for an SGLT-2 inhibitor.	**Correct!** SGLT-2 inhibitors are recommended in people living with diabetes and heart failure as well as those living with CKD.

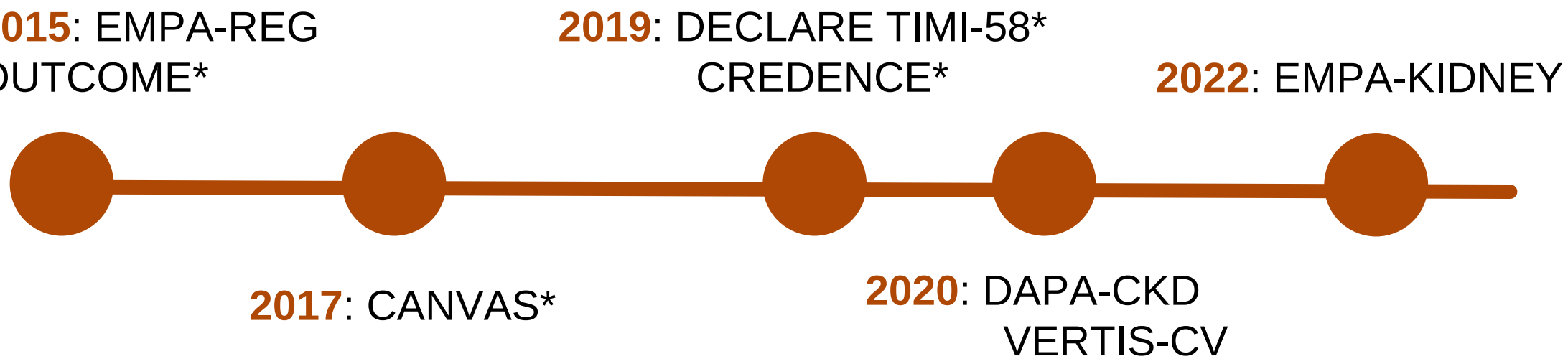
How Do SGLT-2 Inhibitors Help the Heart & Kidneys?

CV, renal benefits appear independent of glycemic control!



Cowie MR, Fisher M. Nat Rev Cardiol. 2020;17:761:772.

At-A-Glance: SGLT-2i Clinical Trials



*all enrolled subjects had diabetes

Selected SGLT-2 T2DM Trials: Summary

	EMPA-REG OUTCOME	CANVAS	DECLARE TIMI-58
Drug	empagliflozin	canagliflozin	dapagliflozin
T2DM; CVD	100%; 99%	100%; ~65%	100%; ~40%
Primary (1°) Outcome	3-pt MACE: 0.86 (0.74-0.99) •CVD 0.62 (0.49-0.77) •MI 0.87 (0.70-1.09) •Stroke 1.24 (0.92-1.67)	3-pt MACE: 0.86 (0.75-0.97) •CVD 0.87 (0.72-1.06) •MI 0.85 (0.69-1.05) •Stroke 0.90 (0.71-1.15)	3-pt MACE: 0.93 (0.84-1.03) •CVD 0.98 (0.82-1.17) •MI 0.89 (0.77-1.01) •Stroke 1.01 (0.84-1.21
Secondary (2°) Renal*	2°: 0.50 (0.32-0.77)	2°: 0.60 (0.47-0.77) Albuminuria: 0.73 (0.67-0.79)	2°: 0.53 (0.43-0.66)
Conclusion	**Empagliflozin, canagliflozin, and dapagliflozin** have additional CV and nephroprotective benefits in individuals with Type 2 diabetes mellitus.		

MACE, major adverse cardiovascular event; CVD, CV death; MI, myocardial infarction
*renal outcomes varied by trial

Zinman et al. NEJM. 2015; 373:2117-2128.
Anker et al. NEJM. 2021; 385:1451-1461.
Wanner et al. NEJ M. 2016; 375:323-334.
Wiviott et al. NEJM. 2019; 380:347-357.

Selected SGLT-2 Inhibitor Cardiovascular Outcome Trials

	EMPEROR-R	EMPEROR-P	CANVAS	VERTIS-CV	DAPA-HF
Drug	empagliflozin	empagliflozin	canagliflozin	ertugliflozin	dapagliflozin
T2DM; CVD	50%; 100%	49%; 100%	100%; ~65%	100%; 23%	42%; 100%
eGFR for Inclusion	≥ 20	≥ 20	≥ 30	≥ 30	≥ 30
Mean eGFR	61.8	61	76	76	66
eGFR < 60	48%	50%	20%	22%	7.4%
1° Outcome	CVD or HFH: 0.75 (0.65-0.86) • CVD 0.92 (0.75-1.12) • HHF 0.69 (0.59-0.81)	CVD or HFH: 0.79 (0.69-0.90) • CVD 0.91 (0.76-1.09) • HHF 0.71 (0.60-0.83)	3-pt MACE: 0.86 (0.75-0.97) • CVD 0.87 (0.72-1.06) • MI 0.85 (0.69-1.05) • Stroke 0.90 (0.71-1.15)	3-pt MACE: 0.97 (0.85-1.11)	4-pt MACE: 0.74 (0.65-0.85) • CVD 0.82 (0.69-0.98) • HHF 0.70 (0.59-0.83) • UHFV 0.43 (0.20-0.90 • HHF or UHFV 0.70 (0.59-0.83)
2° Renal*	0.50 (0.32-0.77)	Not significant	0.60 (0.47-0.77)	Not significant	Not significant
T2DM Subgroup	0.75 (0.60-0.87) vs 0.78 (0.64-0.97)	0.79 (0.67-0.94) vs 0.78 (0.64-0.95)	N/A	N/A	0.75 (0.63-0.90) vs 0.73 (0.60-0.88)
FDA CV Indication?	YES	YES	YES – in T2DM only	NO	YES

Conclusion **Empagliflozin, canagliflozin, and dapagliflozin** have additional CV indications for use in select populations.

MACE, major adverse cardiovascular event; CVD, CV death; HHF, hospitalization for HF; UHFV, urgent HF visit.
*renal outcomes varied by trial

Neal et al. NEJM. 2017; 377(7):644-657.
Packer et al. NEJM. 2020; 383:1413-1424.
Anker et al. NEJM. 2021; 385:1451-1461.
Cannon et al. NEJM. 2020; 383:1425-1435.
McMurray et al. NEJM. 2019;381:1995-2008

Baseline Kidney Function in SGLT-2i Trials

Prognosis of CKD by GFR and Albuminuria Categories

GFR categories (ml/min/1.73 m²) Description and range				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
	G1	Normal or high	≥90			
	G2	Mildly decreased	60-90			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.
KDIGO 2012

- Earlier trials included *only* those living with diabetes
  - Albuminuria at baseline varied
- In kidney outcomes trials, some included those *without* diabetes
  - Baseline albuminuria varied

Blue = EMPA-REG OUTCOME; CANVAS; DECLARE TIMI-58; VERTIS CV

Green = CREDENCE

Purple = DAPA-CKD

Dashed line = EMPA-KIDNEY

☆ Stars represent average study participant

KDIGO 2012 CPG for E&M of CKD. Kidney Int. 2013;3:1

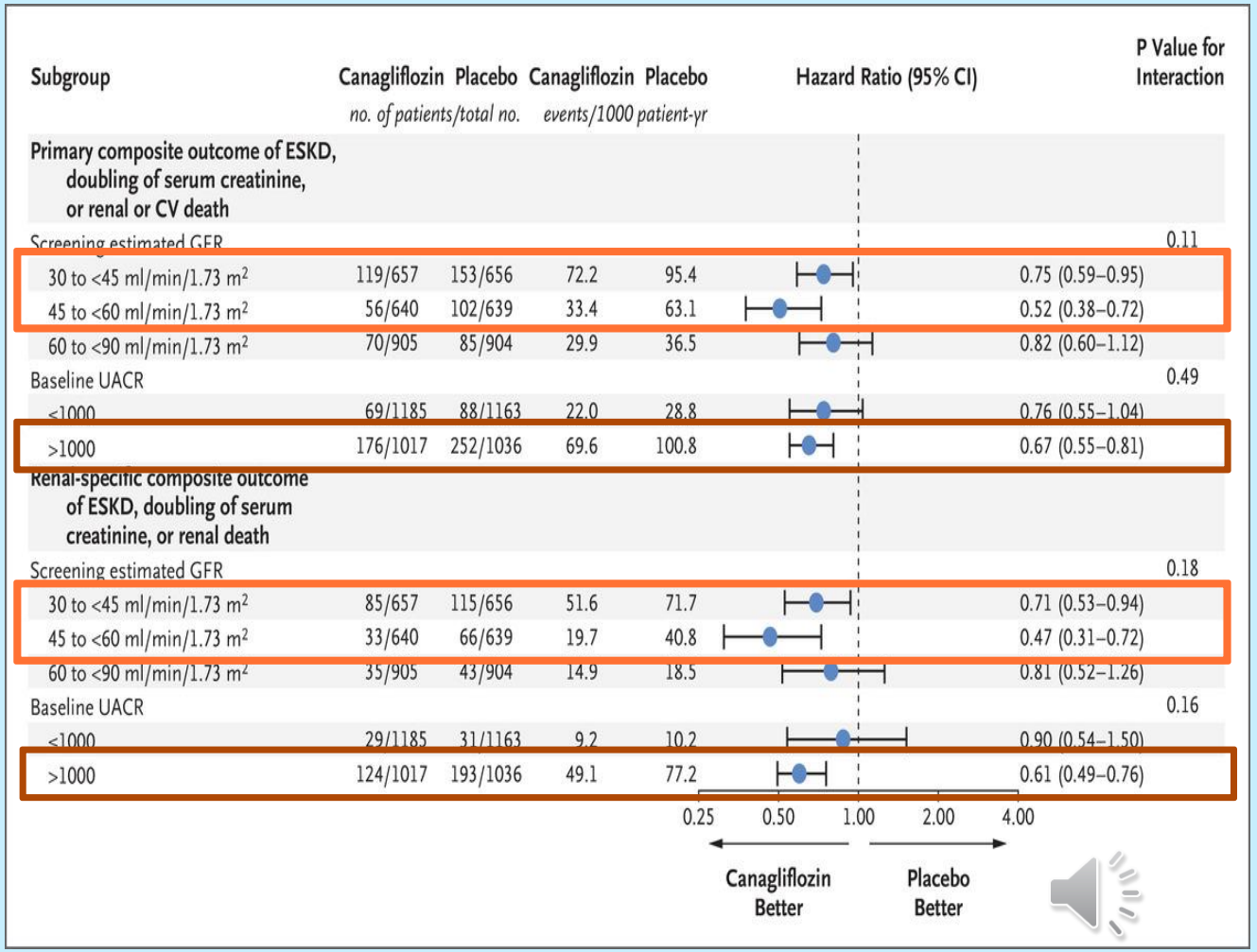
Selected SGLT-2i CKD Trials: CREDENCE

Drug	canagliflozin
T2DM; CVD	100%; 50%
eGFR for Inclusion	30-90 (+UACR > 300 mg/g)
Mean eGFR	56 mL/min/1.73m^2 *(Note: 26% eGFR < 60)*
1° Outcome	4-pt composite: 0.70 (0.59-0.82) •2x SCr 0.60 (0.48-0.76) •ESKD 0.68 (0.54-0.86) •Renal death NS •CV death 0.78 (0.61-1.00) NNT = 22
Renal Outcome	0.66 (0.53-0.82)
Conclusion	**Canagliflozin improves kidney outcomes in T2DM + UACR > 300 mg/g**

Perkovic et al. NEJM. 2019;380:2295-2306.

CREDENCE Sub-Group Analysis

- Primary outcome significant:
  - eGFR < 60 mL/min/1.73m^2
  - Baseline UACR > 1000 mg/g
- Renal-specific outcome similar



Perkovic et al. NEJM. 2019;380:2295-2306.

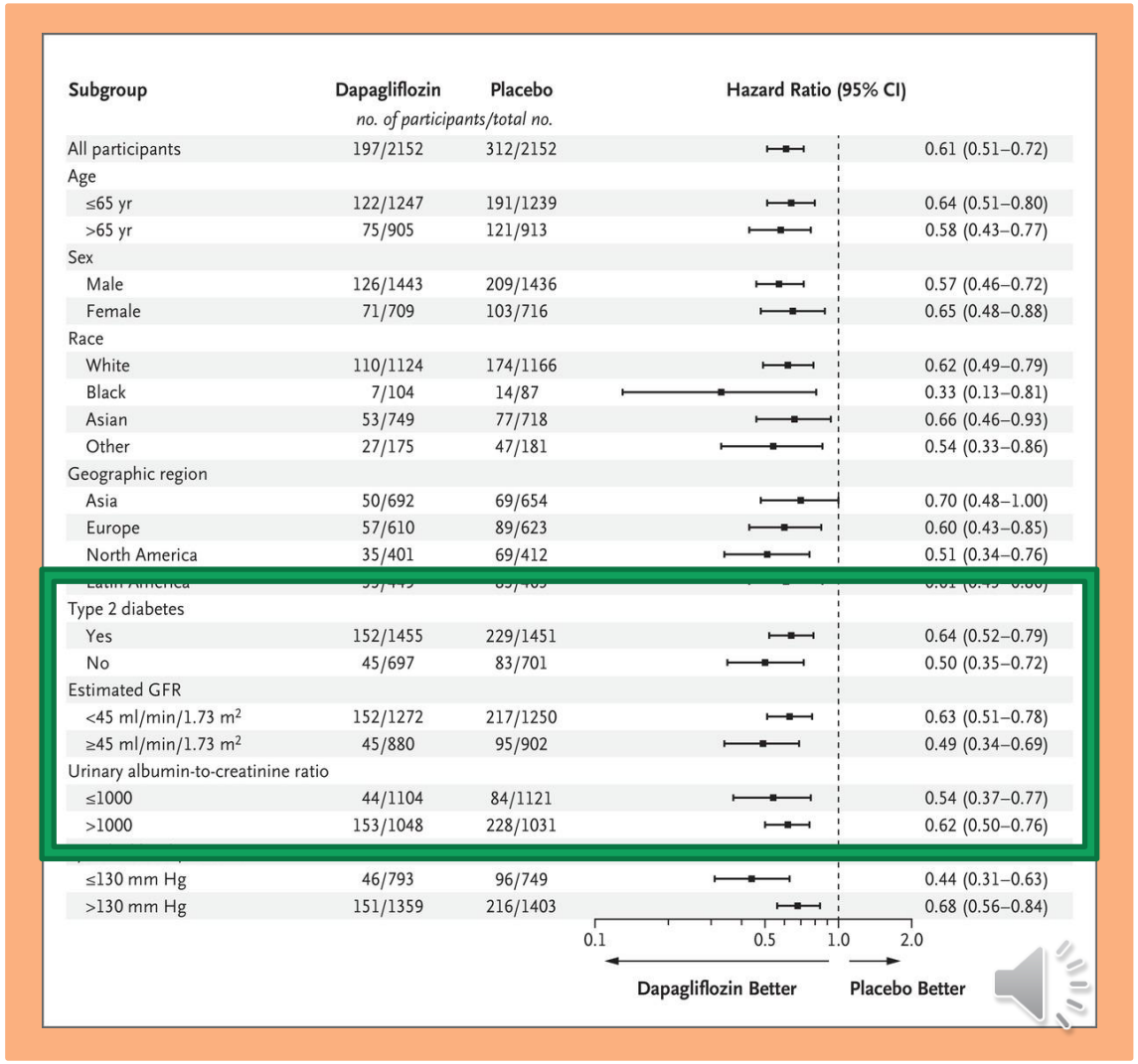
Selected SGLT-2i CKD Trials: DAPA-CKD

Drug	dapagliflozin
T2DM; CVD	67%; 37%
eGFR for Inclusion	25-75 (+ UACR ≥ 200 mg/g)
Mean eGFR	43 (Note: 14.5% eGFR < 30)
1° Outcome	4-pt composite: 0.61 (0.51-0.72) •↓ eGFR ≥ 50% 0.53 (0.42-0.67) •ESKD 0.64 (0.50-0.82) •Renal death NS •CV death 0.81 (0.58-1.12) NNT = 19
Renal Outcome	0.56 (0.45-0.68)
Conclusion	**Dapagliflozin improves kidney outcomes in those with CKD at risk of progression, regardless of diabetes.**

Heerspink et al. NEJM. 2020;383:1436-1446.

DAPA-CKD Sub-Group Analysis

- Primary outcome significant across subgroups
  - Diabetes status
  - Baseline eGFR
  - Baseline albuminuria



Heerspink et al. NEJM. 2020;383:1436-1446.

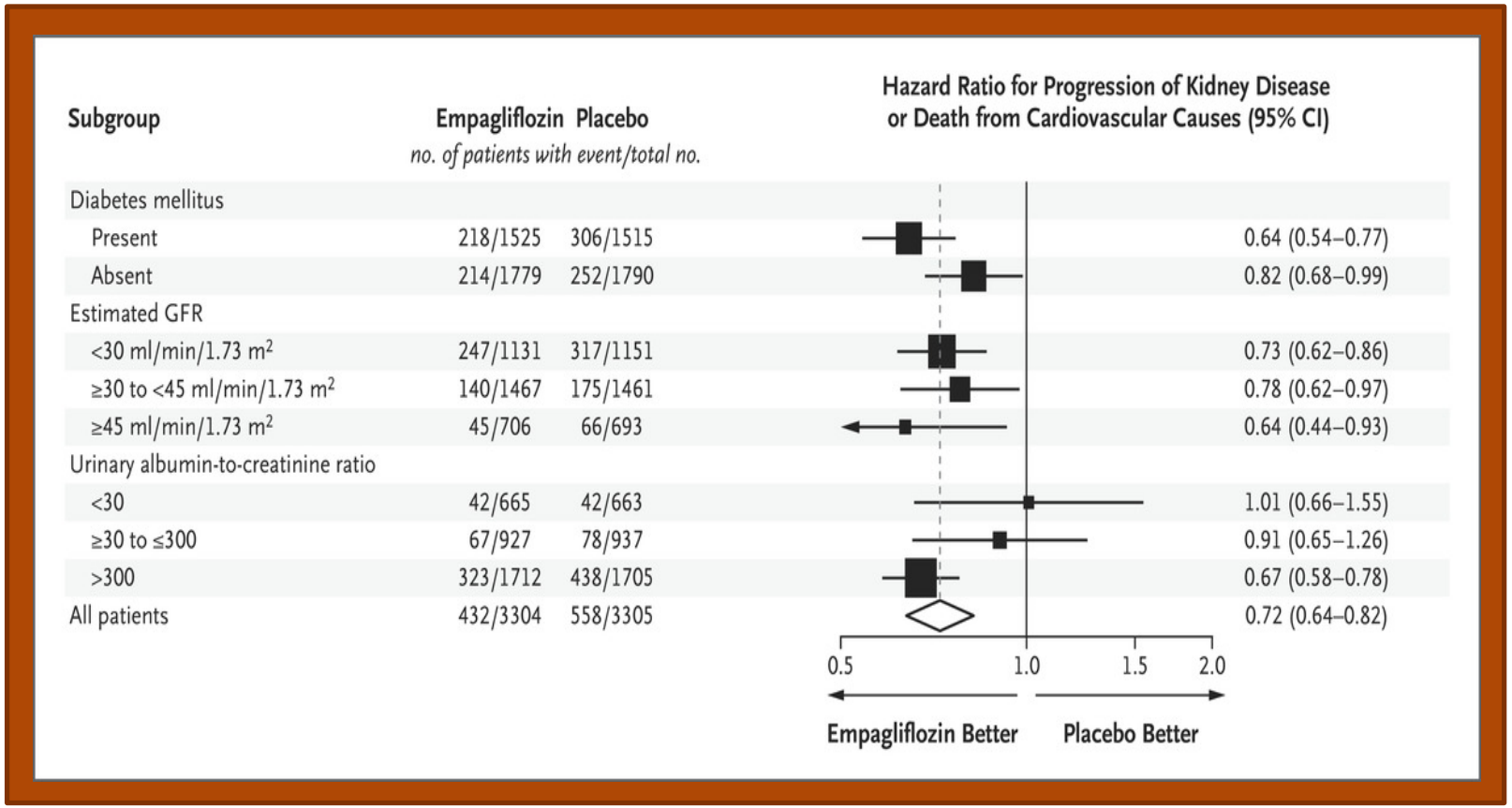
Selected SGLT-2i CKD Trials: EMPA-KIDNEY

Drug	empagliflozin
T2DM; CVD	46%; 26%
eGFR for Inclusion	20-44 *or* 45-89 (+UACR ≥ 200 mg/g)
Mean eGFR	37 (Note: 34.5% eGFR < 30)
1° Outcome	5-pt composite: 0.72 (0.64-0.82) • ↓ eGFR ≥ 40% 0.70 0.61-0.81 • Sustained eGFR < 10 (0.69 0.54-0.87) • ESKD 0.67 (0.52-0.85) • Renal death 0.90 (0.22-3.66) • CVD 0.81 (0.60-1.19)
Renal Outcome	0.71 (0.62-0.81)
Conclusion	**Empagliflozin reduces the risk of CKD progression in those with CKD.**

The EMPA-KIDNEY Collaborative Group. NEJM. 2022. DOI:10.1056/NEJMoa2204233

EMPA-KIDNEY Sub-Group Analysis

- Benefit persists across subgroups
  - Diabetes status
  - Baseline eGFR
- Benefit greater in higher baseline UACR



The EMPA-KIDNEY Collaborative Group. NEJM. 2022. DOI:10.1056/NEJMoa2204233

Selected SGLT-2 CKD Trials: Summary

- Canagliflozin, dapagliflozin, empagliflozin reduce risk of composite kidney endpoint in those with CKD
  - With or without diabetes
  - With or without heart failure
- Endpoints driven by reduction in progression of kidney disease
  - Mortality outcomes not significant

Perkovic et al. NEJM. 2019;380:2295-2306.
Heerspink et al. NEJM. 2020;383:1436-1446.
The EMPA-KIDNEY Collaborative Group. NEJM. 2022. DOI:10.1056/NEJMoa2204233

Which of the following SGLT-2 inhibitors has demonstrated kidney benefits in CKD?

Option		Feedback / Rationale
A.	Dapagliflozin	**Correct!** Dapagliflozin is one of the SGLT-2 inhibitors with demonstrated cardiovascular and kidney protective benefits in CKD.
B.	Ertugliflozin	Incorrect. Ertugliflozin does NOT have evidence demonstrating cardiovascular or kidney protective benefits in CKD.
C.	Sotagliflozin	Incorrect. Sotagliflozin does NOT have evidence demonstrating cardiovascular or kidney protective benefits in CKD.
D.	All of the above have demonstrated kidney benefits in CKD.	Incorrect. Of the choices above, only dapagliflozin is correct. The two other SGLT-2 inhibitors with demonstrated cardiovascular and kidney benefits are: canagliflozin and empagliflozin.

Pros & Cons of SGLT-2 Inhibitors

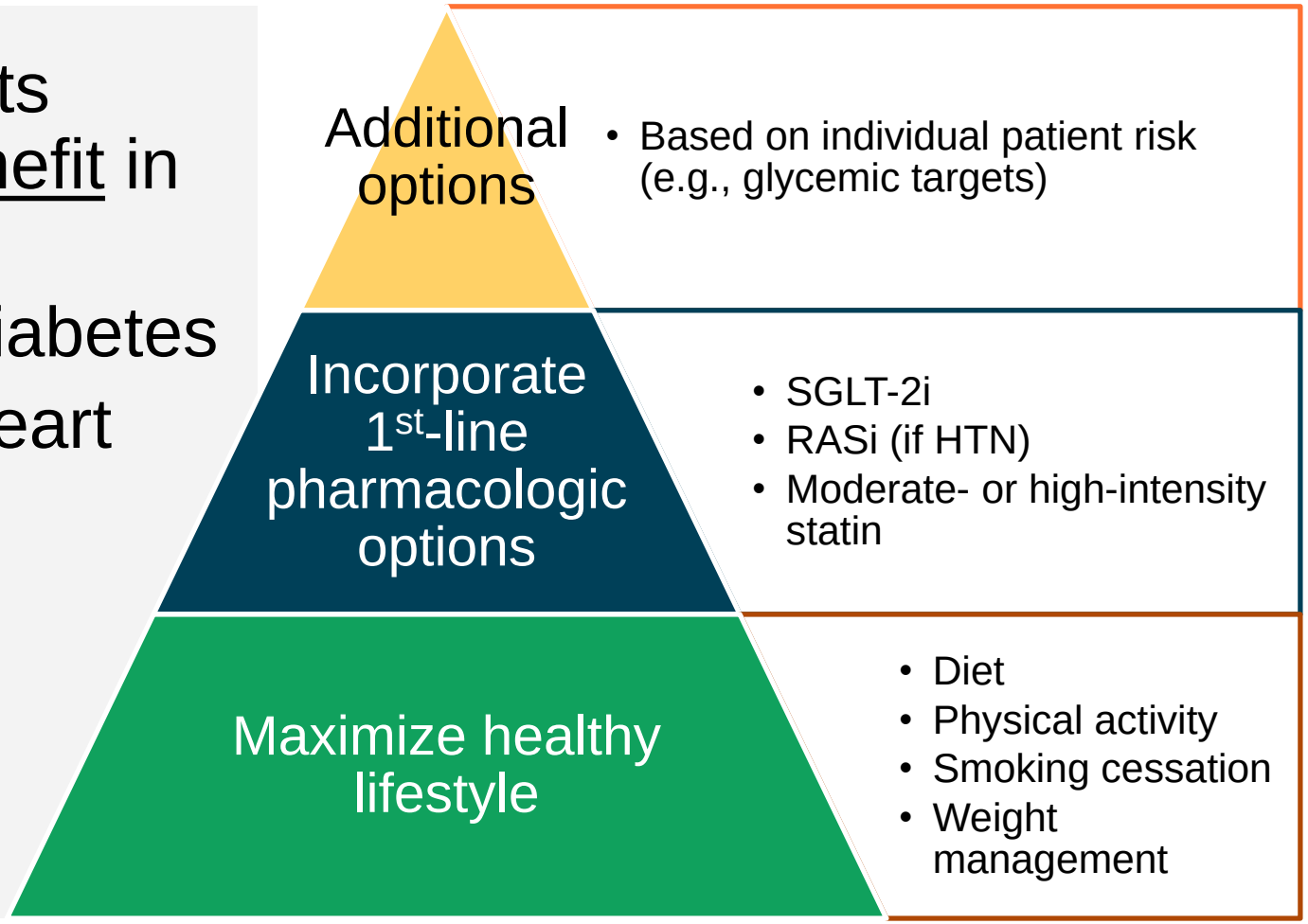
- Beneficial CV, kidney effects
- Low hypoglycemia risk
- Weight loss
- Oral agent
- No need for dose escalation

- High cost
- Intermediate glycemic lowering efficacy
- Diminishing glycemic lowering at lower eGFRs
- Potential volume depletion, genitourinary infection
- Euglycemic DKA

ADA Standards of Medical Care in Diabetes - 2023. *Diabetes Care* 2023; 46,S1-S4.

Where's the place for SGLT-2 Inhibitors in CKD?

- Clinical evidence supports SGLT-2i with proven benefit in CKD:
  - WITH or WITHOUT diabetes
  - WITH or WITHOUT heart failure
- In conjunction with other evidence-based treatments



de Boer IH et al. Diabetes Care. 2022;45(12):3075-3090

Dosing in CKD

eGFR 30-44*

- Canagliflozin 100 mg PO daily
- Dapagliflozin 10 mg PO daily
- Empagliflozin 10 mg PO daily
- **NO** ertugliflozin at eGFR < 45

eGFR 15-29*

- **DO NOT START** canagliflozin
- *If eGFR < 25,* **DO NOT START** dapagliflozin
- *If eGFR < 20,* **DO NOT START** empagliflozin

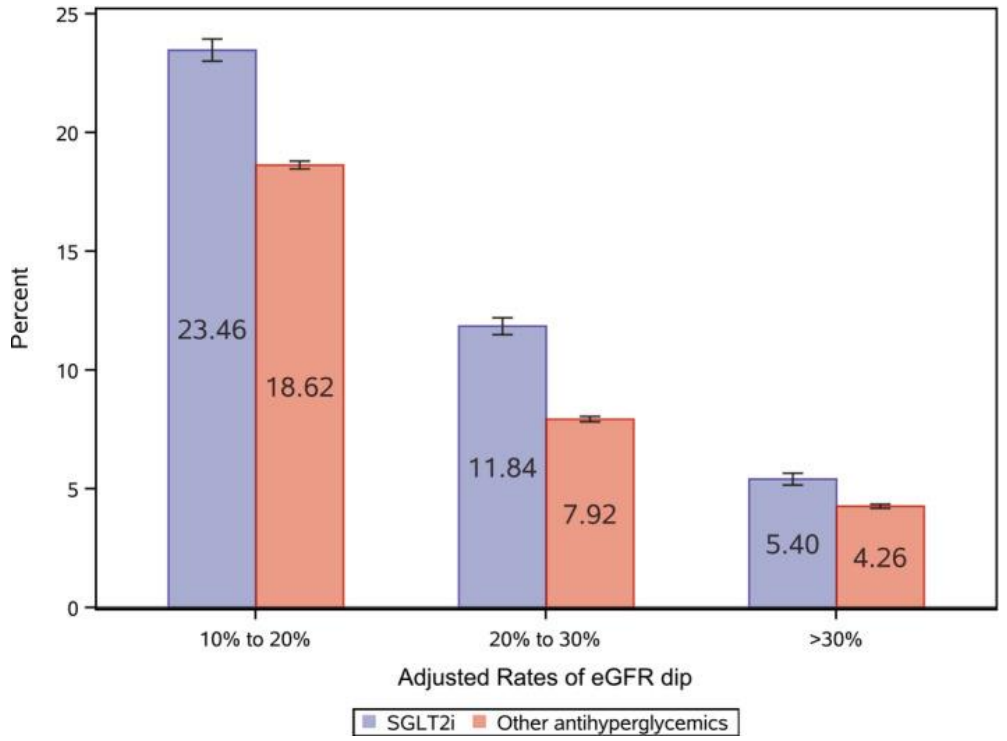
* mL/min/1.73m^2

- No need to escalate/titrate doses
- Current eGFR cutoffs for initiation
  - Continue until dialysis!
  - Expect initial “dip” in eGFR

de Boer IH, et al. Kidney Int. 2022;102(5):974-989.

What do you mean by “initial dip”?

- **Initial eGFR decline <u>is expected</u>** **(**~3-5 mL/min/1.73m^2)
  - eGFR decline > 30% is rare
- Partial eGFR recovery after 12 weeks
- CV, kidney benefits persist *regardless* of degree of eGFR dip
- SGLT-2i attenuates rate of eGFR decline over time
  - <u>Alone, eGFR dip may **NOT** warrant SGLT-2 inhibitor discontinuation!</u>



Meraz-Munoz AY et al. *Kidney360.* 2021;2(6):1042-1047.
Xie Y, et al. *J Am Heart Assoc.* 2021;10(11):e020237.
Heerspink HJL and Cherney DZI. *CJASN.* 2021;16(8):1278-1280.

Clinical Considerations

I'm worried about…	Consider…
↓ eGFR, ↑ sCr	• An initial, small change is expected! • Ensuring appropriate lab monitoring, medication counseling • Assess volume status

Dehydration due to illness	• Empower your patients
	  • Facilitate medication education
	  • "Sick day" protocols

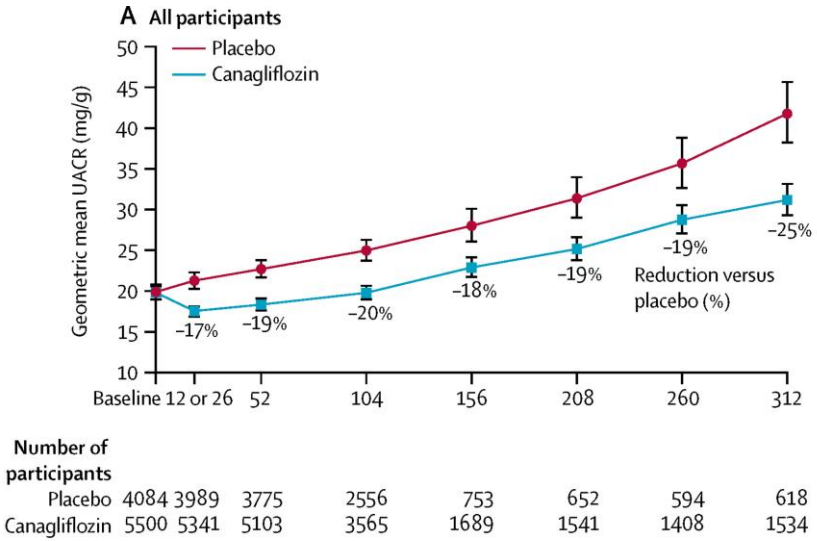
Concomitant antidiabetic drugs	• Low hypoglycemia risk
	  • Consider decreasing insulin doses by ~10-20%
	  • Consider tapering off or stopping insulin secretagogues
	• Discuss hypoglycemia management, recognition of signs & symptoms

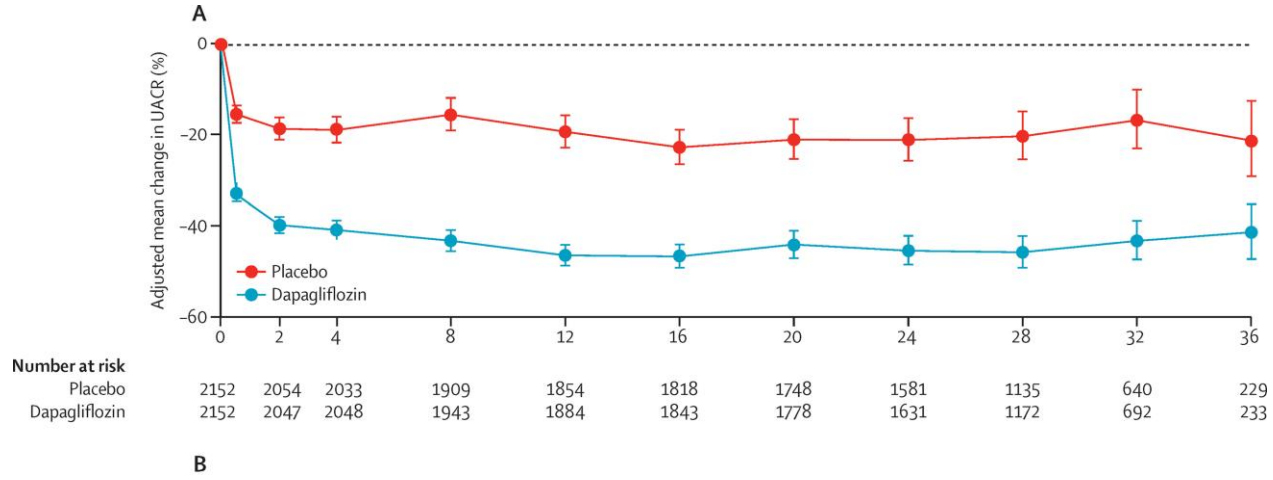
Concomitant diuretics	• Do NOT start if hypovolemic, hypotensive • May need to reduce dose or stop if euvolemic/normotensive

Meraz-Munoz AY, Weinstein J, Wald R. *Kidney360.* 2021;2(6):1042-1047.
Lam D, Shaikh A. *Kidney360.* 2021;2(4):742-746.
Das SR *et al. J Am Coll Cardiol*. 2020;76(9):1117-1145.

Clinical Consideration: Albuminuria

- **SGLT-2 inhibitors improve albuminuria** *<u>regardless of ΔHbA1c</u>*
  - Effect appears after weeks (dapagliflozin) to months (canagliflozin)
    - Reduction in albuminuria sustained
- Consider appropriate guidelines – may inform your decision to add other guideline-recommended agents (e.g., finerenone)





Perkovic V *et al. Lancet Diabetes & Endocrinol*. 2018;6(9):691-704.
Jongs N *et al.Lancet Diabetes & Endocrinol.* 2021;9(11):755-766.

Case Scenario: MR

Image is stock photo from Microsoft PowerPoint

- 68-year-old White female
- PMH = T2DM, HTN, dyslipidemia, CKD

Current Medications

- linagliptin 5 mg PO daily
- lisinopril 10 mg PO daily
- chlorthalidone 25 mg PO daily
- atorvastatin 40 mg PO daily
- ezetimibe 10 mg PO daily

Labs & Physical Findings

- HbA1c = 6.9%
- BP = 118/70 mmHg
- eGFR (non-indexed)* = 22 mL/min
- eGFR (indexed)* = 17 mL/min/1.73m2
- UACR = 190 mg/g
- BMI 32 kg/m^2

*CKD-EPI$_{Cr}$ 2021 non-race based eGFR

MR is currently managed with linagliptin. Which of the following is the best evidence-based practice recommendation for her glucose-lowering therapy?

Option		Feedback / Rationale
A.	Metformin	Incorrect. Metformin should be avoided given her eGFR < 30 mL/min/1.73m^2.
B.	SGLT-2 inhibitor	**Correct!** SGLT-2 inhibitors are preferred in people with T2DM and CKD with an eGFR ≥ 20 mL/min/1.73m^2 for their cardio- and nephroprotective benefits.
C.	GLP-1 receptor agonist	Incorrect. An evidence-based GLP-1 receptor agonist may be considered if needed to achieve individualized glycemic target despite use of 1st-line treatments (i.e., SGLT-2i ± metformin).
D.	No changes since HbA1c is at goal.	Incorrect. ADA/KDIGO recommends use of SGLT-2 inhibitors as a 1st-line agent regardless of need to achieve glycemic goals. Furthermore, cardiorenal benefits have been observed in clinical trials irrespective of diabetes status and baseline A1c, and the risk of hypoglycemia is low.

Based on current ADA/KDIGO recommendations, which of the following SGLT-2 inhibitors would you initiate for MR?

Option		Feedback / Rationale
A.	ertugliflozin 5 mg PO daily	Incorrect. Nephroprotective benefits have not been demonstrated with ertugliflozin, and it should not be initiated if eGFR < 45 mL/min/1.73m^2.
B.	dapagliflozin 10 mg PO daily	Incorrect. Dapagliflozin should not be initiated if eGFR < 25 mL/min/1.73m^2.
C.	canagliflozin 100 mg PO daily	Incorrect. Canagliflozin should not be initiated if eGFR < 30 mL/min/1.73m^2.
D.	empagliflozin 10 mg PO daily	**Correct!** In addition to the CV and kidney benefits observed with empagliflozin, it can be used since MR's current eGFR of 22 is greater than the cutoff for initiation of empagliflozin (i.e., ≥ 20 mL/min/1.73m^2).

MR is to begin empagliflozin 10 mg PO daily today. Which of the following may be a reasonable adjustment and follow-up plan for her current medications?

Option		Feedback / Rationale
A.	Decrease or discontinue chlorthalidone. Recheck BP, BMP in 2-4 weeks.	**Correct!** In normotensive/euvolemic patients, you may need to reduce or discontinue background diuretics and appropriate lab monitoring should be ordered.
B.	Discontinue lisinopril. Recheck BP, BMP in 2-4 weeks.	Incorrect. It is not necessary to discontinue RAS inhibitor therapy.
C.	Discontinue linagliptin. Recheck A1c in 3 months.	Incorrect. It is not necessary to modify all other antidiabetic drugs when initiating an SGLT-2 inhibitor. However, a reduction in insulin or insulin secretagogue doses (i.e., sulfonylureas, meglitinides) may be considered.
D.	Discontinue atorvastatin. Recheck FLP in 4-12 weeks.	Incorrect. It is not necessary to discontinue statin therapy.

Case Scenario: MR – 2 weeks later

- 68-year-old White female
- PMH = T2DM, HTN, dyslipidemia, CKD

Current Medications

- linagliptin 5 mg PO daily
- empagliflozin 10 mg PO daily
- lisinopril 10 mg PO daily
- chlorthalidone 12.5 mg PO daily
- atorvastatin 40 mg PO daily
- ezetimibe 10 mg PO daily

Labs & Physical Findings

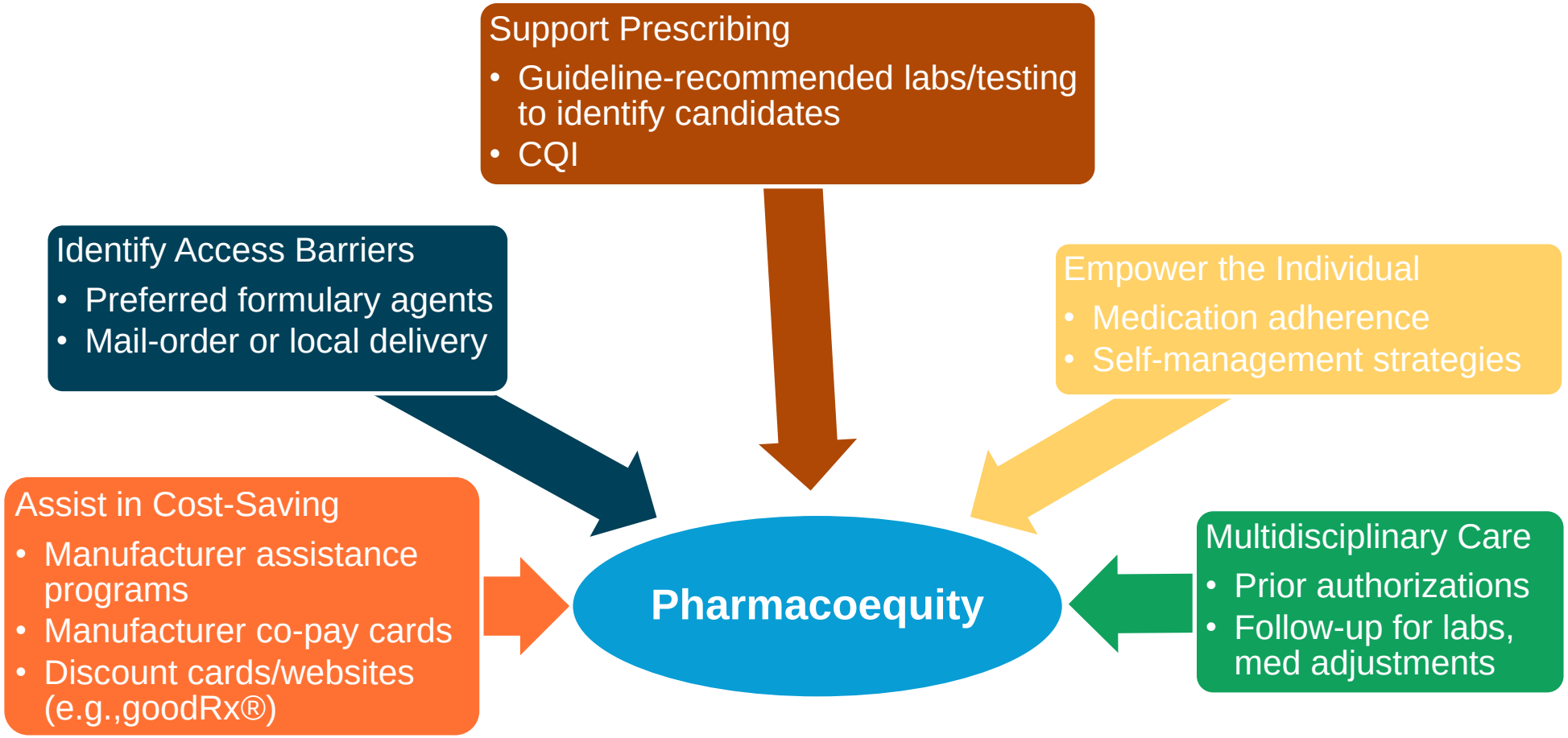
	Today	2 Weeks Ago
BP (mmHg)	124/76	118/70
eGFR (mL/min)*	19	22
BUN	36	32
sCr (mg/dL)	2.3	2.0
FBG (mg/dL)	128	115

*CKD-EPI$_{Cr}$ 2021 non-race based non-indexed eGFR

Based on MR's labs and physical findings today, what changes would you make to her current medication regimen?

Option		Feedback / Rationale
A.	Increase empagliflozin from 10 mg to 25 mg PO daily.	Incorrect. It is not necessary to increase empagliflozin.
B.	Discontinue empagliflozin. Recheck BMP in 2-4 weeks.	Incorrect. The initial changes to sCr, eGFR are expected, and SGLT-2 inhibitors should be continued until dialysis.
C.	No changes to her medications at this time.	Correct! Nothing suggests that she is hypoglycemic or that she is not normotensive or euvolemic. Additionally, BMP is stable and reflects anticipated changes post-SGLT-2 inhibitor start. Thus, her SGLT-2 inhibitor and all other medications should be continued.
D.	Increase chlorthalidone from 12.5 to 25 mg PO daily.	Incorrect. It is not necessary to increase chlorthalidone.

Supporting SGLT-2 Inhibitor Pharmacoequity



Essien UR, Dusetzina SB, Gellad WF. JAMA. 2021;326(18):1793:1794.

Summary

SGLT-2 inhibitors improve cardiometabolic and kidney outcomes, regardless of diabetes or heart failure

SGLT-2 inhibitors are evidence-based 1st-line medications for CKD

Initial eGFR “dip” is expected with SGLT-2i start

SGLT-2 inhibitor selection, dosing, and education should be individualized and include appropriate follow-up

Advancing Kidney Health

Through Optimal Medication Management

Thank you!

Additional Helpful References

- United States Renal Data System. 2022 *USRDS Annual Data Report: Epidemiology of kidney disease in the United States.* National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2022.
- KDIGO Guidelines (https://kdigo.org/guidelines/).
- American Journal of Kidney Diseases blog (https://ajkdblog.org/)
- Association of Diabetes Care & Education Specialists (https://www.diabeteseducator.org/)

Glossary of Terms

- **ADA** = American Diabetes Association
- **BMI** = body mass index
- **BP** = blood pressure
- **CKD** = chronic kidney disease
- **CV** = cardiovascular
- **CVD** = cardiovascular death
- **eGFR** = estimated glomerular filtration rate
- **ESKD** = end-stage kidney disease
- **GLP-1** = glucagon-like peptide-1
- **HbA1c** = hemoglobin A1c
- **HFmrEF** = heart failure with mildly reduced ejection fraction
- **HFpEF** = heart failure with preserved ejection fraction
- **HFrEF** = heart failure with reduced ejection fraction
- **HHF** = hospitalization for heart failure
- **HTN** = hypertension
- **KDIGO** = Kidney Disease: Improving Global Outcomes
- **MACE** = major adverse cardiovascular event
- **MI** = myocardial infarction
- **NS** = not significant
- **PMH** = past medical history
- **PO** = by mouth
- **sCr** = serum creatinine
- **SGLT-2i** = sodium glucose co-transporter type-2 inhibitor
- **T2DM** = Type 2 diabetes mellitus
- **UACR** = urinary albumin-to-creatinine ratio