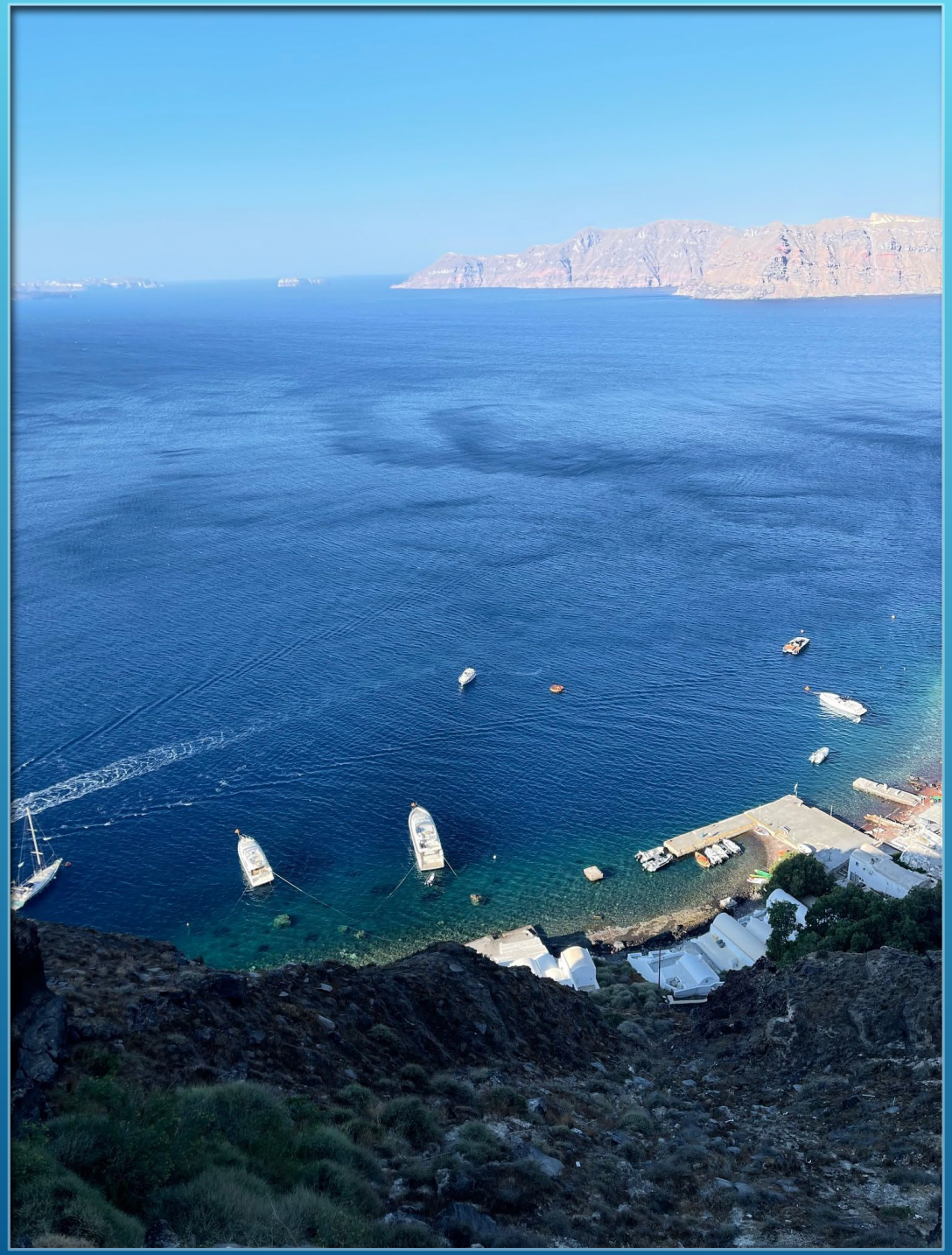


CKD UPDATE 2024

Christopher V. Poole, MD

ROADMAP

- GFR-What does it actually mean
- CKD Complications
- Albuminuria importance
- Risk assessment-KFRE
- ACEi/ARB still the BP meds of choice
- Finerenone-deployment and K management
- SGLT-2 Inhibitors-recommended for many
- GLP-1 agonist and CKD
- Medication safety in CKD
- Metformin-friend or foe
- Anemia/Acidosis management
- The Four Pillars or the Four Horsemen

CKD DEFINITION

- GFR <60mL/min/1.73m^2 for ≥ 3 months with or without kidney damage OR

- Kidney damage for ≥ 3 months with or without decreased GFR as evidenced by:

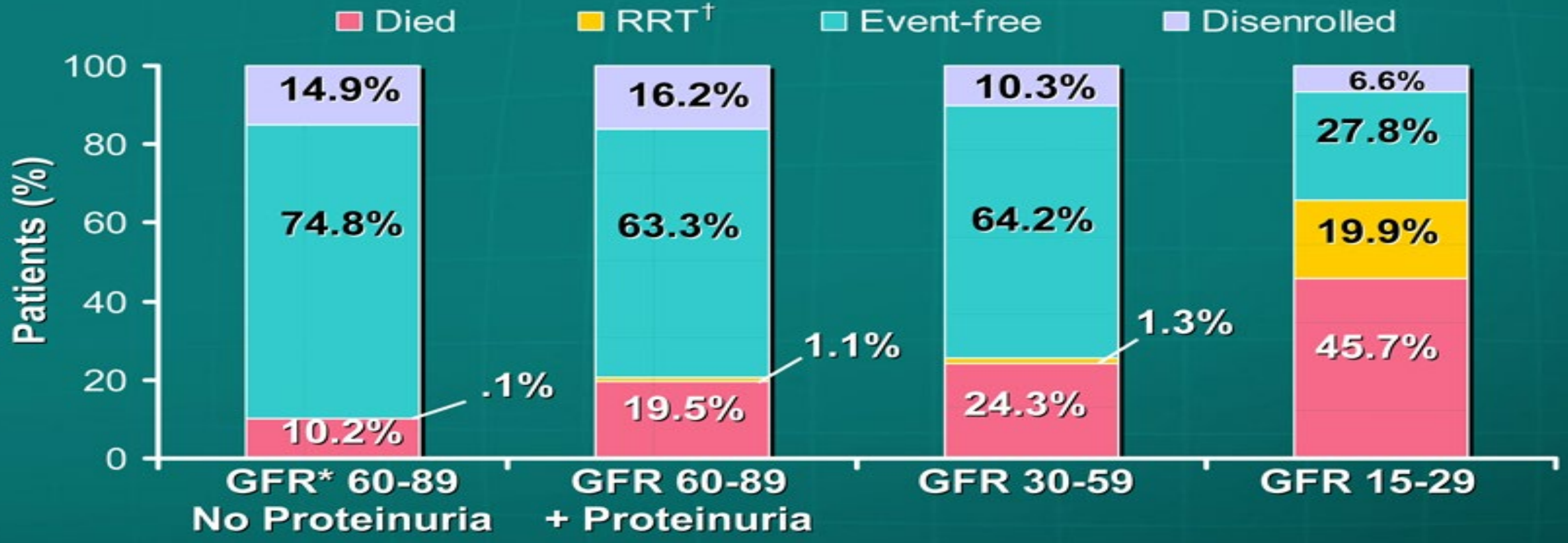
-Pathologic abnormalities or

-Markers of kidney damage, i.e., proteinuria

National Kidney Foundation. *AJKD* 2002;39(supp1):S1-S266

Death Is Recognized To Be a More Common Event Than Dialysis in CKD

5-Year Follow-Up



*GFR=mL/min/1.73 m²; †RRT=renal replacement therapy.
Patient population: health plan patients with estimated GFR* <90 followed up until RRT, death, or disenrollment from health plan. N=27,998.
Keith et al. *Arch Intern Med.* 2004;164:659-663.

CKD COMPLICATIONS

Age <65	ACR, mg/g				ACR, mg/g			
eGFRcr-cys	<10	10–29	30–299	300+	<10	10–29	30–299	300+
	All-cause mortality				Myocardial infarction			
105+	0.99	1.2	1.5	2.4	0.93	1.0	1.1	2.6
90–104	ref	1.3	1.5	2.5	ref	1.2	1.3	1.9
60–89	1.2	1.6	2.0	2.9	1.3	1.4	1.6	2.1
45–59	2.1	2.7	2.9	4.5	1.8	2.6	3.1	3.5
30–44	2.7	3.8	4.2	5.6	1.9	2.3	3.0	3.9
<30	5.2	4.0	7.1	8.6	4.1	3.6	4.7	5.8
	Cardiovascular mortality				Stroke			
105+	0.95	1.4	1.7	4	0.96	1.2	1.6	2.7
90–104	ref	1.6	1.8	3.5	ref	1.2	1.5	2.2
60–89	1.3	1.7	2.3	3.9	1.2	1.4	1.7	2.6
45–59	2.5	4.0	4.6	6.0	1.9	2.0	2.5	3.8
30–44	3.1	6.6	5.3	7.1	2.6	3.7	3.5	3.5
<30	6.0	5.5	9.4	12	2.6	2.9	5.1	5.1
	Kidney failure replacement therapy				Heart failure			
105+	0.57	0.77	2.3	12	0.86	1.1	1.7	3.4
90–104	ref	1.4	3.9	11	ref	1.3	1.5	3.0
60–89	1.9	3.7	8.3	33	1.2	1.7	2.1	3.6
45–59	7.0	16	28	100	1.7	3.3	3.4	5.3
30–44	22	34	109	210	3.5	4.3	6.8	5.7
<30	335	267	419	625	7.5	6.3	9.7	8.9
	Acute kidney injury				Atrial fibrillation			
105+	0.75	1.0	1.4	3.4	0.93	1.0	1.3	1.9
90–104	ref	1.2	1.8	2.6	ref	1.2	1.4	2.3
60–89	1.6	2.7	2.9	5.8	1.1	1.3	1.5	1.8
45–59	4.2	6.0	5.6	7.6	1.5	2.0	2.1	2.6
30–44	5.7	9.4	9.8	9.4	1.8	2.4	3.0	2.8
<30	15	14	14	13	3.7	2.9	4.3	5.4
	Hospitalization				Peripheral artery disease			
105+	1.0	1.1	1.1	1.5	0.93	1.9	1.5	2.6
90–104	ref	1.1	1.2	1.3	ref	1.8	2.1	3.9
60–89	1.1	1.2	1.3	1.6	1.2	2.1	2.2	5.4
45–59	1.3	1.7	1.5	2.0	3.2	7.3	3.4	8.4
30–44	1.5	1.8	1.6	2.1	6.5	9.1	6.6	13
<30	2.1	2.4	2.4	3.5	1.4	7.6	18	16

Age 65+	ACR, mg/g				ACR, mg/g			
eGFRcr-cys	<10	10–29	30–299	300+	<10	10–29	30–299	300+
	All-cause mortality				Myocardial infarction			
105+	1.2	1.4	1.9	3.5	0.97	1.4	2.0	19
90–104	ref	1.2	1.4	2.0	ref	1.2	1.1	1.9
60–89	1.2	1.5	1.8	2.3	1.1	1.4	1.5	1.9
45–59	1.6	2.0	2.4	2.9	1.6	1.9	2.3	3.4
30–44	2.0	2.4	3.2	4.1	2.1	2.6	3.1	3.8
<30	3.4	4.1	5.1	6.5	4.9	3.0	5.1	5.0
	Cardiovascular mortality				Stroke			
105+	1.1	1.5	2.0	12	1.2	1.3	1.5	3.3
90–104	ref	1.4	1.4	3.4	ref	1.3	1.3	2.8
60–89	1.2	1.7	2.2	3.1	1.1	1.4	1.8	2.5
45–59	1.7	2.4	3.0	4.3	1.5	1.7	2.0	2.3
30–44	2.4	3.1	4.5	5.8	1.5	2.0	2.1	2.3
<30	5.7	5.2	5.1	7.8	1.7	2.0	2.4	4.8
	Kidney failure replacement therapy				Heart failure			
105+	2.0	1.0	2.1		0.99	1.5	1.7	7.0
90–104	ref	1.9	4.7	10	ref	1.3	1.5	2.2
60–89	1.4	2.6	6.2	19	1.2	1.5	2.0	3.2
45–59	3.7	7.9	16	42	1.6	2.0	2.9	4.1
30–44	14	14	46	137	2.3	2.9	3.5	6.1
<30	87	364	241	406	4.4	4.1	5.5	7.2
	Acute kidney injury				Atrial fibrillation			
105+	0.91	1.1	1.3	1.9	0.95	1.1	1.0	3.7
90–104	ref	1.3	1.4	3.9	ref	1.2	1.3	2.4
60–89	1.5	2.1	2.7	4.7	1.1	1.2	1.5	2.0
45–59	3.6	4.3	5.1	7.3	1.2	1.4	1.7	1.9
30–44	5.7	5.9	7.2	9.8	1.5	1.8	2.0	2.2
<30	10	11	11	22	1.8	1.8	2.2	3.2
	Hospitalization				Peripheral artery disease			
105+	1.0	1.1	1.2	2.2	1.1	2.3	2.9	4.9
90–104	ref	1.1	1.3	1.4	ref	1.3	2.0	4.8
60–89	1.1	1.2	1.3	1.5	1.3	1.6	2.0	3.2
45–59	1.2	1.2	1.4	1.6	2.0	2.8	3.1	3.1
30–44	1.5	1.4	1.6	2.0	3.5	2.8	3.8	5.9
<30	1.9	1.9	2.0	2.6	8.4	4.1	5.9	10

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CKD AND COMPLICATIONS

Overall	Urine albumin-creatinine ratio, mg/g					Urine albumin-creatinine ratio, mg/g				
eGFRcr	<10	10–29	30–299	300–999	1000+	<10	10–29	30–299	300–999	1000+
	All-cause mortality: 82 cohorts 26 444 384 participants; 2 604 028 events					Myocardial infarction: 64 cohorts 22 838 356 participants; 451 063 events				
105+	1.6	2.2	2.9	4.3	5.8	1.1	1.4	2.0	2.7	3.8
90–104	ref	1.3	1.8	2.6	3.1	ref	1.3	1.6	2.2	3.2
60–89	1.0	1.3	1.7	2.2	2.8	1.1	1.3	1.6	2.2	3.1
45–59	1.3	1.6	2.0	2.4	3.1	1.4	1.7	2.0	2.8	3.7
30–44	1.8	2.0	2.5	3.2	3.9	1.9	2.0	2.4	3.2	4.3
15–29	2.8	2.8	3.3	4.1	5.6	2.7	3.1	3.1	4.2	5.1
<15	4.6	5.0	5.3	6.0	7.0	4.6	5.6	4.8	6.0	6.0
	Cardiovascular mortality: 76 cohorts 26 022 346 participants; 776 441 events					Stroke: 68 cohorts 24 746 436 participants; 461 785 events				
105+	1.4	2.0	3.0	4.1	5.4	1.2	1.6	2.2	3.1	4.3
90–104	ref	1.3	1.9	2.7	3.6	ref	1.3	1.6	2.4	3.1
60–89	1.0	1.4	1.7	2.4	3.2	1.1	1.3	1.7	2.2	3.0
45–59	1.4	1.7	2.2	2.8	3.8	1.4	1.6	1.9	2.3	2.9
30–44	2.0	2.3	2.8	3.7	4.6	1.6	1.7	2.0	2.4	3.0
15–29	3.2	3.1	3.5	5.0	6.5	1.8	2.1	2.1	2.7	3.0
<15	6.1	6.4	6.4	7.3	8.2	3.2	2.8	2.9	3.2	3.8
	Kidney failure with replacement therapy: 57 cohorts 25 466 956 participants; 158 846 events					Heart failure: 61 cohorts 24 603 016 participants; 1 132 443 events				
105+	0.5	1.2	2.9	7.7	25	1.2	1.7	2.7	4.2	6.9
90–104	ref	1.8	4.3	12	43	ref	1.3	2.0	2.8	4.2
60–89	2.3	4.9	10	27	85	1.1	1.4	1.9	2.7	4.2
45–59	13	19	37	89	236	1.6	1.8	2.4	3.4	5.0
30–44	50	58	115	240	463	2.2	2.5	3.1	4.2	6.5
15–29	283	301	443	796	1253	3.6	3.5	4.1	5.8	8.1
<15	770	1040	1618	2297	2547	5.1	5.7	5.8	7.9	9.9
	Acute kidney injury: 49 cohorts 23 914 614 participants; 1 408 929 events					Atrial fibrillation: 50 cohorts 22 886 642 participants; 1 068 701 events				
105+	1.0	1.6	2.4	3.7	5.5	1.1	1.3	1.7	2.4	3.5
90–104	ref	1.4	2.1	3.2	5.0	ref	1.2	1.5	1.9	2.3
60–89	1.6	2.2	3.1	4.3	6.7	1.0	1.2	1.4	1.7	2.2
45–59	3.5	4.0	5.1	6.9	9.0	1.2	1.3	1.5	1.8	2.4
30–44	5.6	5.9	6.8	8.6	11	1.4	1.5	1.7	2.0	2.4
15–29	8.3	8.0	8.5	9.9	10	1.9	1.8	2.0	2.6	3.0
<15	8.5	11	7.9	5.5	5.7	2.6	2.5	3.1	3.6	4.2
	Hospitalization: 49 cohorts 25 426 722 participants; 8 398 637 events					Peripheral artery disease: 54 cohorts 24 830 794 participants; 378 924 events				
105+	1.4	1.7	2.1	2.1	2.3	0.9	1.4	1.9	2.8	5.0
90–104	ref	1.1	1.3	1.5	1.7	ref	1.3	1.9	2.8	4.3
60–89	1.0	1.1	1.3	1.5	1.8	1.0	1.3	1.8	2.5	3.8
45–59	1.3	1.3	1.5	1.7	2.1	1.5	1.7	2.1	2.9	4.2
30–44	1.5	1.5	1.6	1.9	2.3	2.0	1.9	2.5	3.6	5.0
15–29	1.8	1.8	1.9	2.4	2.8	3.3	3.3	3.8	5.7	8.1
<15	2.7	2.8	3.0	3.2	3.8	9.1	9.0	9.6	13	14

GFR-HOW ITS ESTIMATED

- The best we can do is estimate it
- Derived from a variety of equations
- Some or all are used as variables: SCr(or Cystatin C), gender, age, and weight
- MDRD equation remains most commonly used
- $eGFR=175x\ (Scr)^{-1.154}x(age)^{-0.203}x0.742$[if female)
- There was previously an adjustment factor for race of 1.212[if AA], now removed
- Still felt to be most accurate equation available
- But there are some issues

NKF, kidney.org

GFR-POINTS TO CONSIDER

- Creatinine not the most ideal filtration marker
- Generation-affected by muscle mass, protein intake, age
- Secretion-decreased by cephalosporins and AG abx, flucytosine, cisplatin, cimetidine, trimethoprim
- Limited utility in AKI due to non-steady state nature of the patient
- 24hr urine study for CrCl may still be useful, i.e., for potential transplant donors or very muscular patients
- Decreased accuracy at higher GFR levels
- Race component has been removed from eGFR equation
- Cystatin C based eGFR may be more useful in certain cases

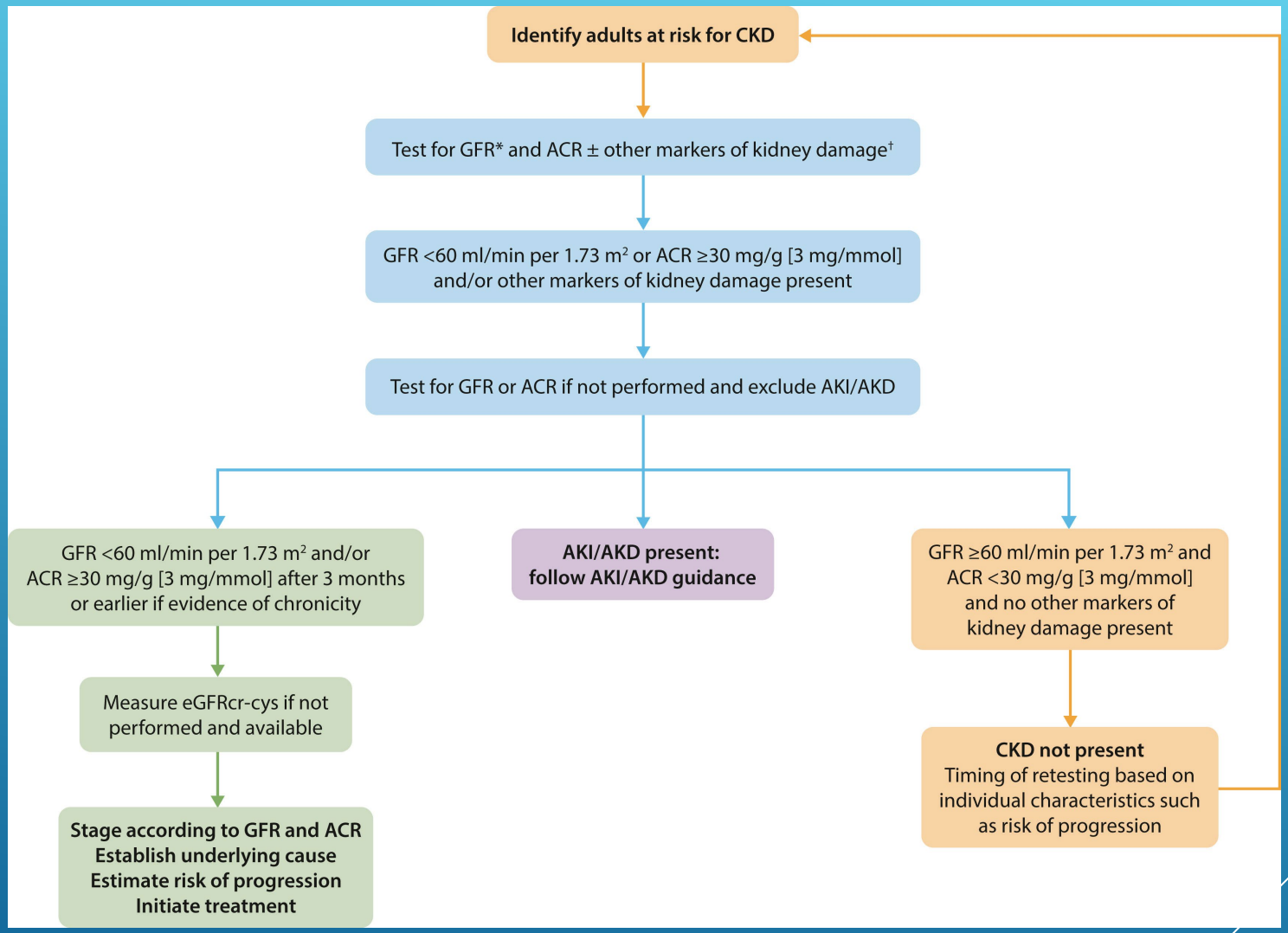
UNDERSTANDING ALBUMINURIA

- Albuminuria reflects kidney injury
- Refers to increased urinary excretion of albumin, which mots closely correlates with CKD and CVD risk
- Albuminuria sensitive for DM or HTN CKD
- Albuminuria-increased risk of HD, CVD and death

National Kidney Foundation. *AJKD* 2002;39(supp1):S1-S266

ASSESSING ALBUMINURIA-ACR

- Need to discern how much the patient is excreting in 24-hour period
- Spot albumin to creatinine ratio is an accurate way to assess protein excretion
- The ratio approximates the grams of albumin excreted per 24 hr period
- 200mg/dL albumin, 100mg/dL creatinine=2 grams albumin excretion per 24 hrs
- Eliminates need for 24-hour urine collection, on a routine basis
- Most accurate on early AM specimen



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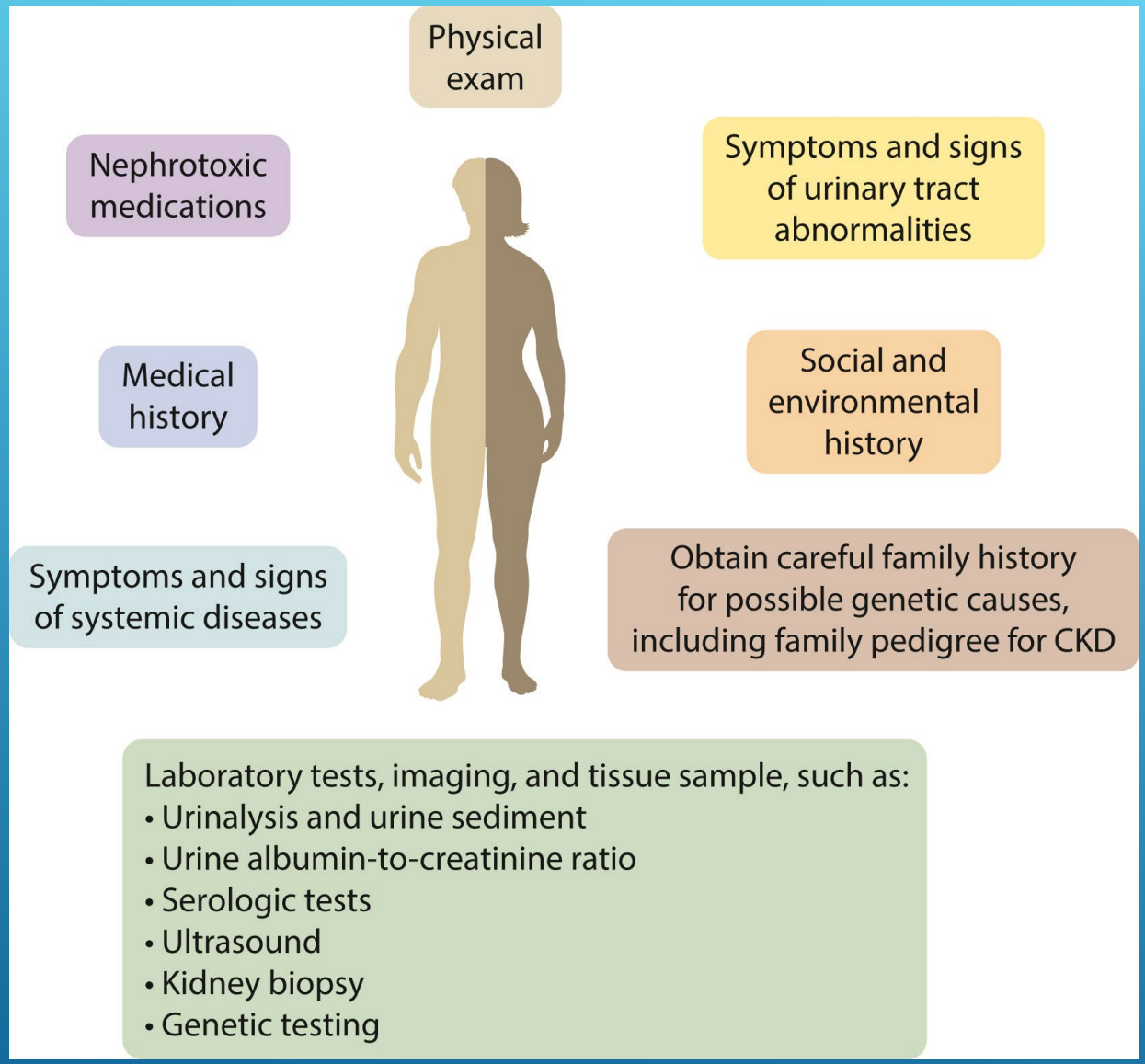

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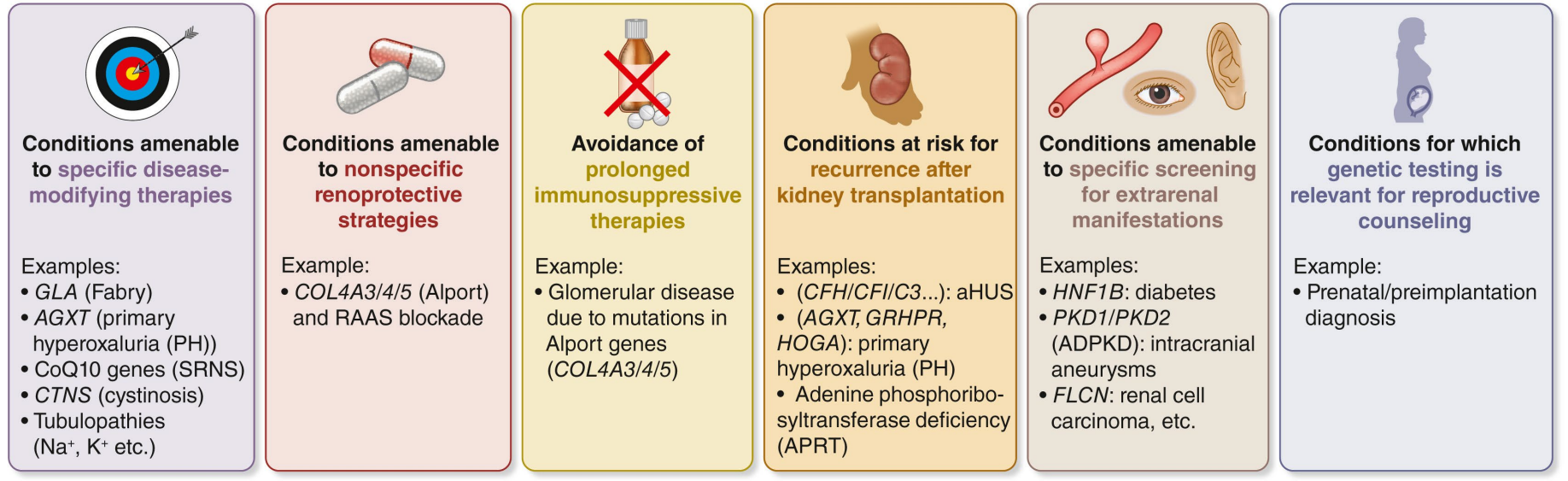
ROLE OF GENETIC TESTING



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ASSESSING RISK

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 3
	G2	Mildly decreased	60–89	Screen 1	Treat 1	Treat 3
	G3a	Mildly to moderately decreased	45–59	Treat 1	Treat 2	Treat 3
	G3b	Moderately to severely decreased	30–44	Treat 2	Treat 3	Treat 3
	G4	Severely decreased	15–29	Treat* 3	Treat* 3	Treat 4+
	G5	Kidney failure	<15	Treat 4+	Treat 4+	Treat 4+

Low risk (if no other markers of kidney disease, no CKD)
Moderately increased risk
High risk
Very high risk

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KIDNEY RISK FACTOR EQUATION

Use the Kidney Failure Risk Equation to determine 2 and 5 year probability of treated kidney failure (dialysis or transplantation) for a patient with CKD Stage 3 to 5.

Age (yrs)	76	
Sex	Male	
GFR (ml/min/1.73m^2)	28	
Urine Albumin:Creatinine Ratio	900	(•) mg/g ( ) mg/mmol
Calcium	9	(•) mg/dL ( ) mmol/L
Phosphorus	4.5	(•) mg/dL ( ) mmol/L
Albumin	3.4	(•) g/dL ( ) g/L
Bicarbonate (mmol/L)	22	

Submit

KFRE ACCURACY

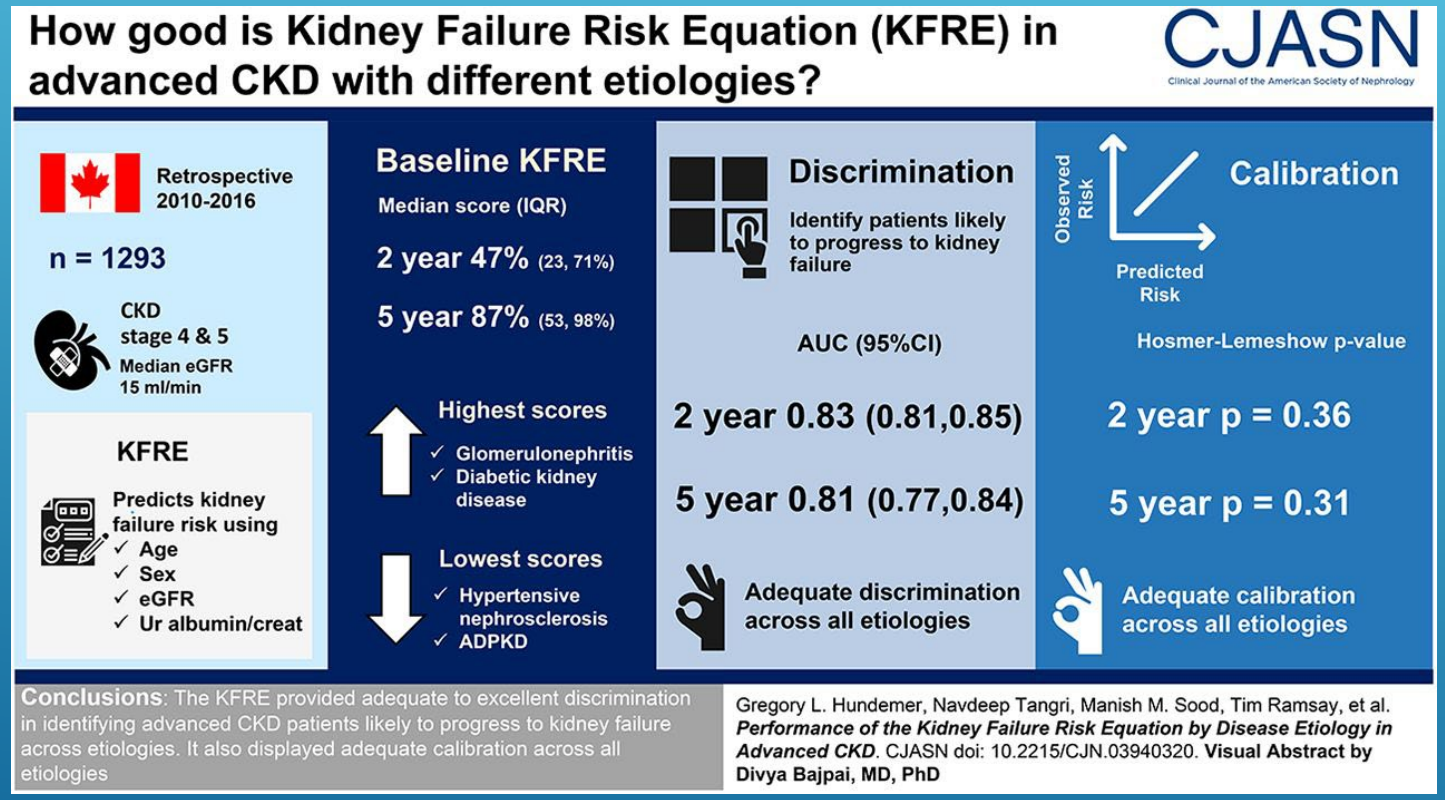

Figure 14

USING KFRE

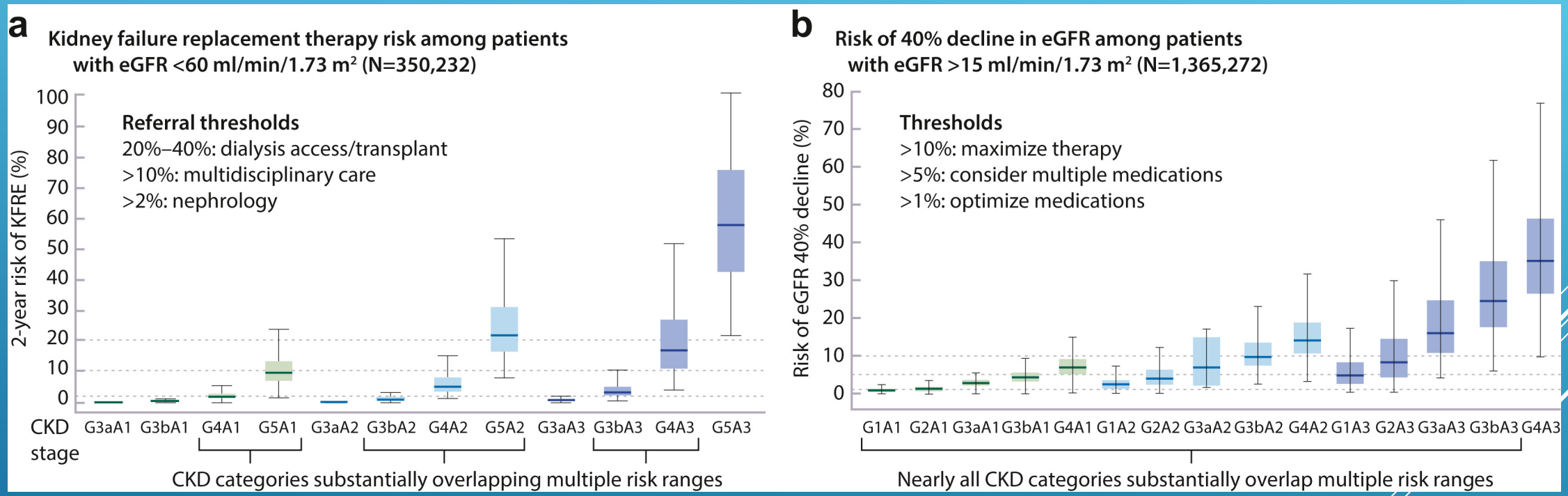

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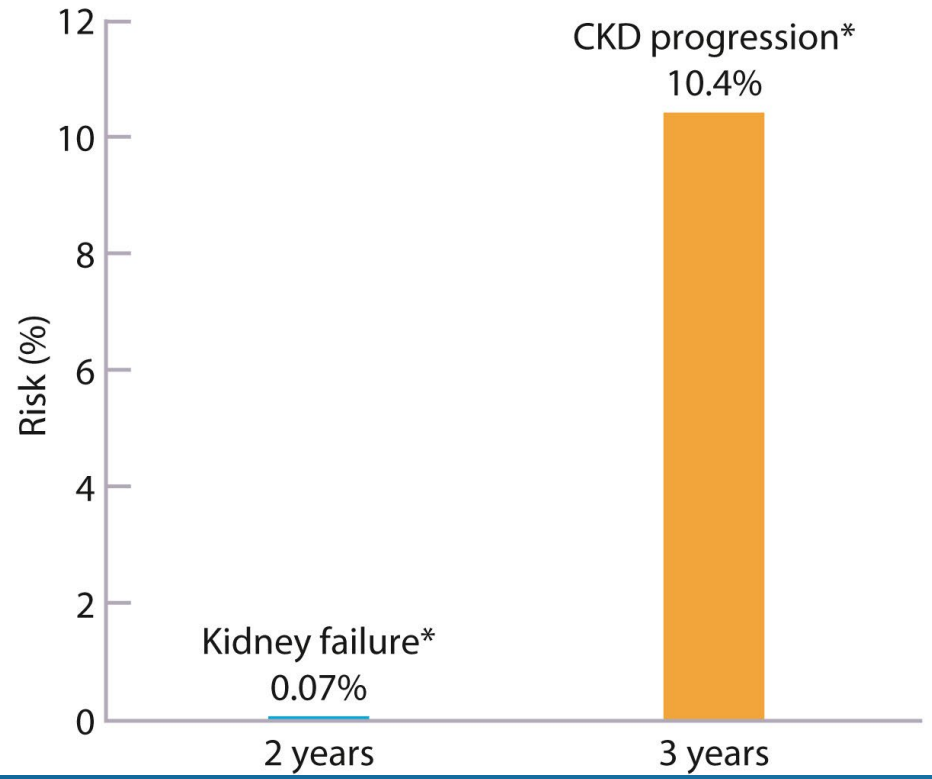
Figure 16

KFRE CASE STUDY

Patient profile:
50-year-old male with diabetes, eGFR 80 ml/min per 1.73 m^2, urine ACR 1 g/g
Kidney failure risk: 0.07% over 2 years, 0.23% over 5 years
CKD progression risk: 10.4% over 3 years



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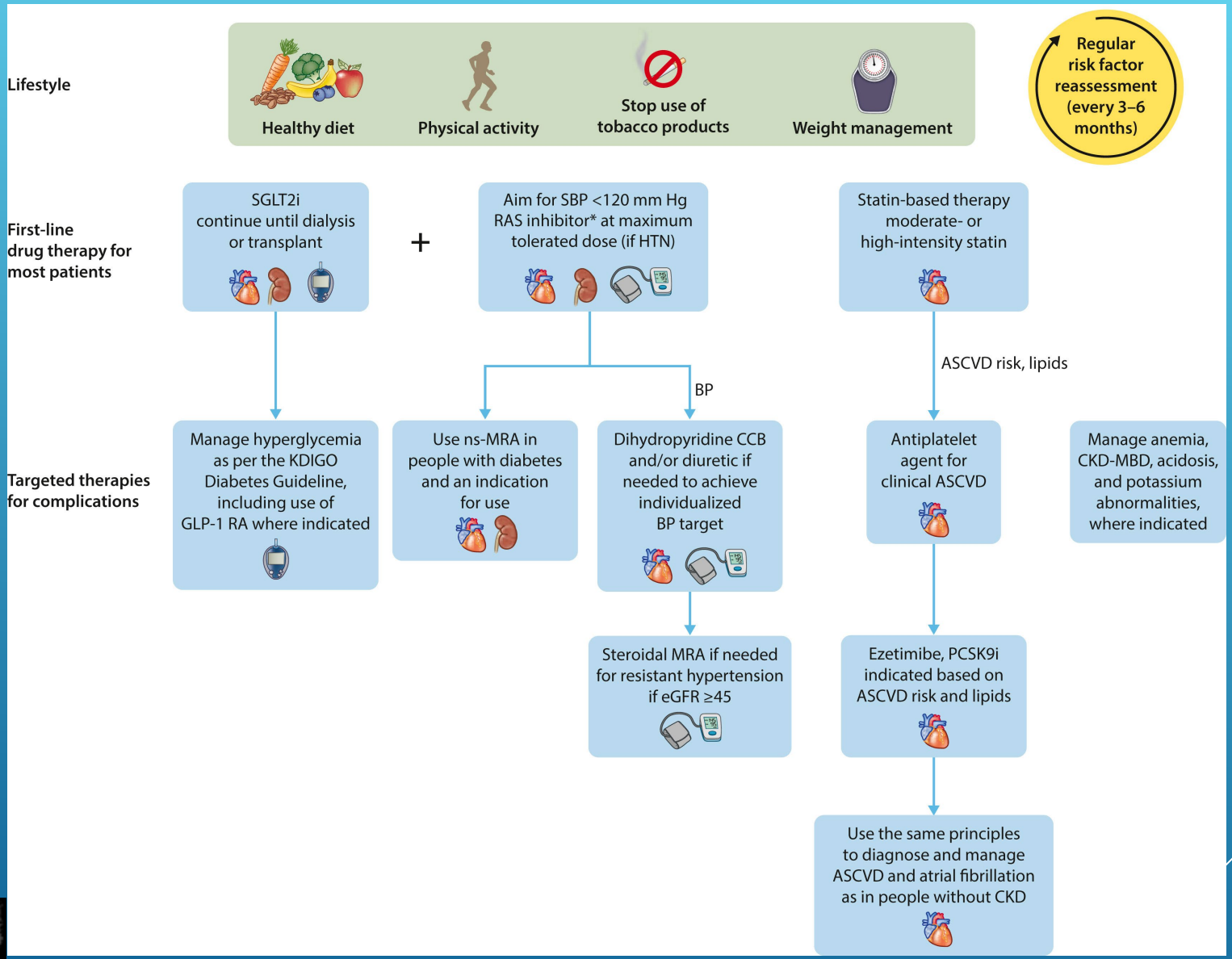
USING KFRE TO GUIDE REFERRAL

- What is the patient's GFR trajectory?
- What is their risk of kidney failure on a 5-year timeline?
- If that risk is 3% or greater, the patient would benefit from nephrology referral
- Risk>10%- needs CKD education, dietary education
- Risk >40%-needs preparation for RRT

WHEN TO REFER

- eGFR <30cc/min, eGFR <60cc/min if deemed higher risk of progression
- Proteinuria >500mg/day
- Resistant HTN
- Decrease in GFR >30% in 4-month period
- Persistent hyperkalemia(more options to treat this now)

OVERALL GAMEPLAN



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DIETARY PROTEIN INTAKE

Body weight (kg)	35	40	50	55	60	65	70	75	80	85	90	95	100
Grams of protein per day (wt × 0.8 g/kg)	28	32	40	44	48	52	56	60	64	68	72	76	80

- Maintaining protein intake of 0.8g/kg for adults in CKD G3-G5
- This is only a 2C recommendation
- This is at the level of "we suggest" with "low evidence of certainty"
- Reasonable to avoid high protein diets in these patients and have a renal dietician involved if intake higher than 1.3g/kg being considered

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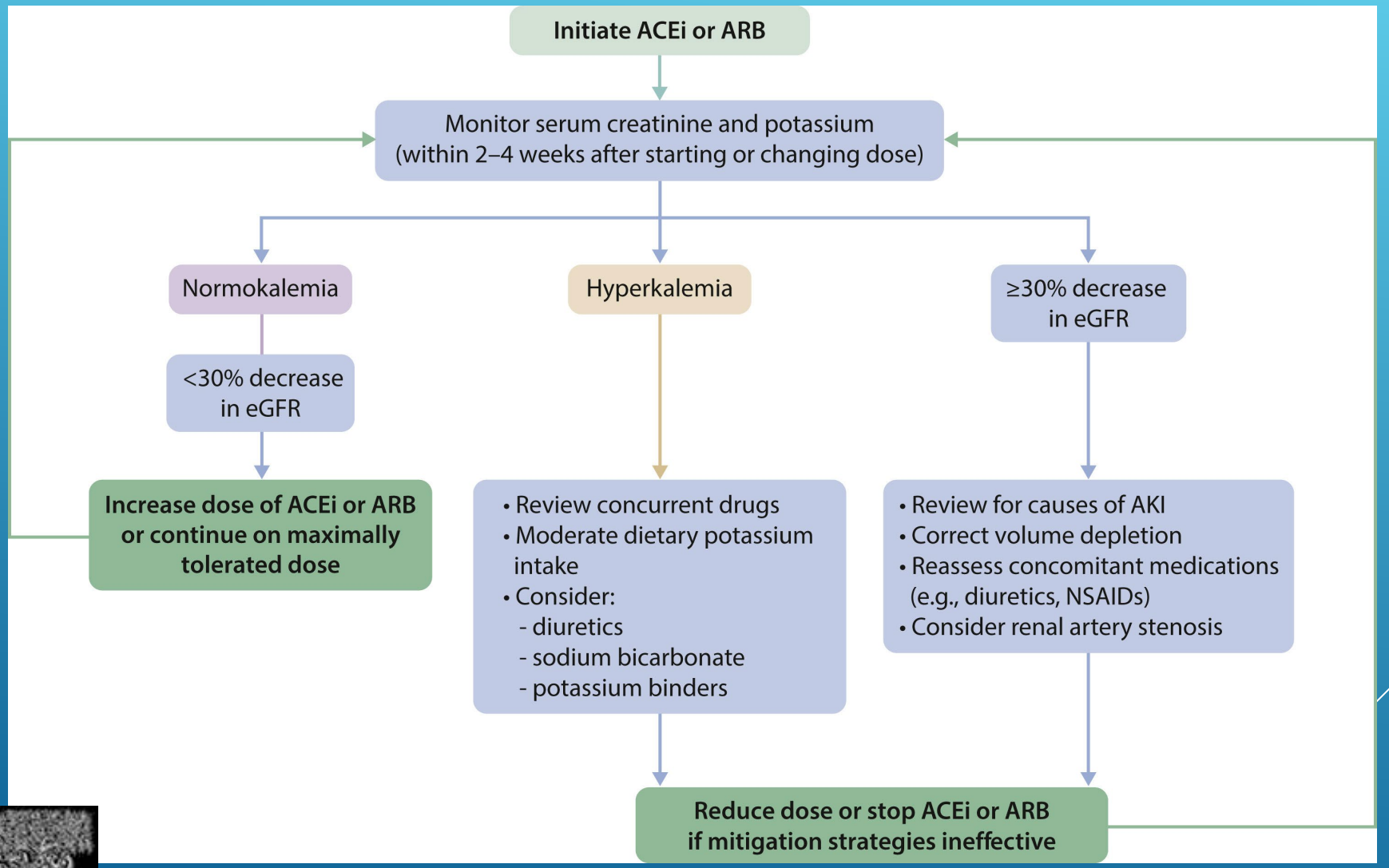
BP CONTROL

- SBP goal of <120mmHg is a 2B level recommendation
- Suggestion with moderate certainty of evidence
- Most of the benefit is derived from lower CVD risk
- Those with frailty should have somewhat higher target

Figure 21

ACE/ARB INITIATION



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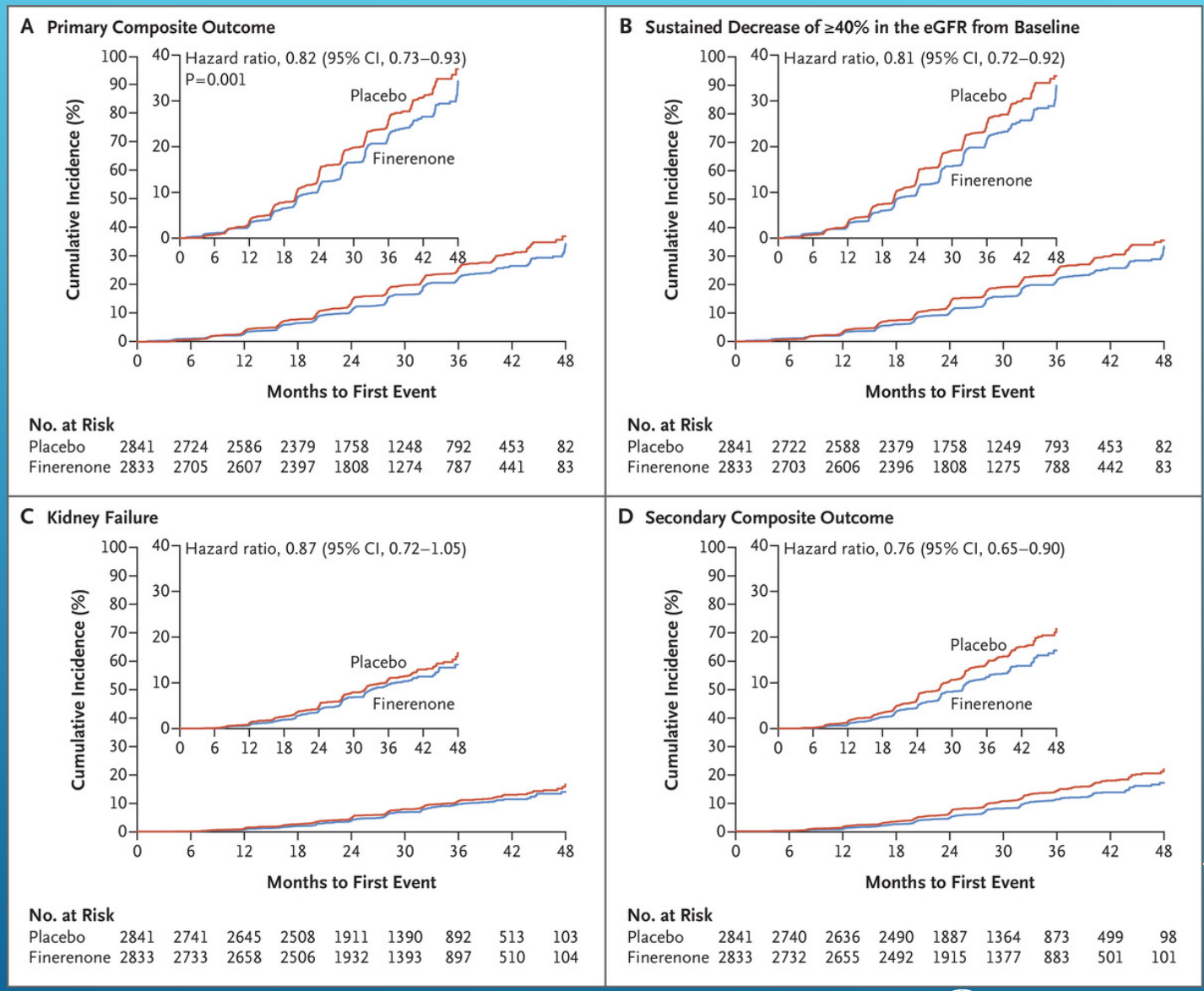
MINERALOCORTICOID RECEPTOR ANTAGONISTS

- Nonsteroidal MRA-Finerenone
- Steroidal MRAs-spironolactone/eplerenone
- nsMRA-showed benefit in heart failure hospitalizations as an add on to maximal dose RASi
- Treatment withdrawal in studies 1.7% for hyperkalemia

FINERENONE-FIDELIO-DKD

- Nonsteroidal selective MRA (more selective than eplerenone)
- 5734 patients with 1:1 finerenone:placebo
- Type II DM with GFR 25-60cc/min, 30-300mg ACR with DM retinopathy OR
- Type II DM with 300-5000mg ACR with GFR 25-75cc/min
- All on RAS agents
- Primary composite outcome-loss of 40% GFR, renal failure or death from renal causes
- $680/month vs $30/month for eplerenone

Kidney Outcomes.



GL Bakris et al. N Engl J Med 2020;383:2219-2229.

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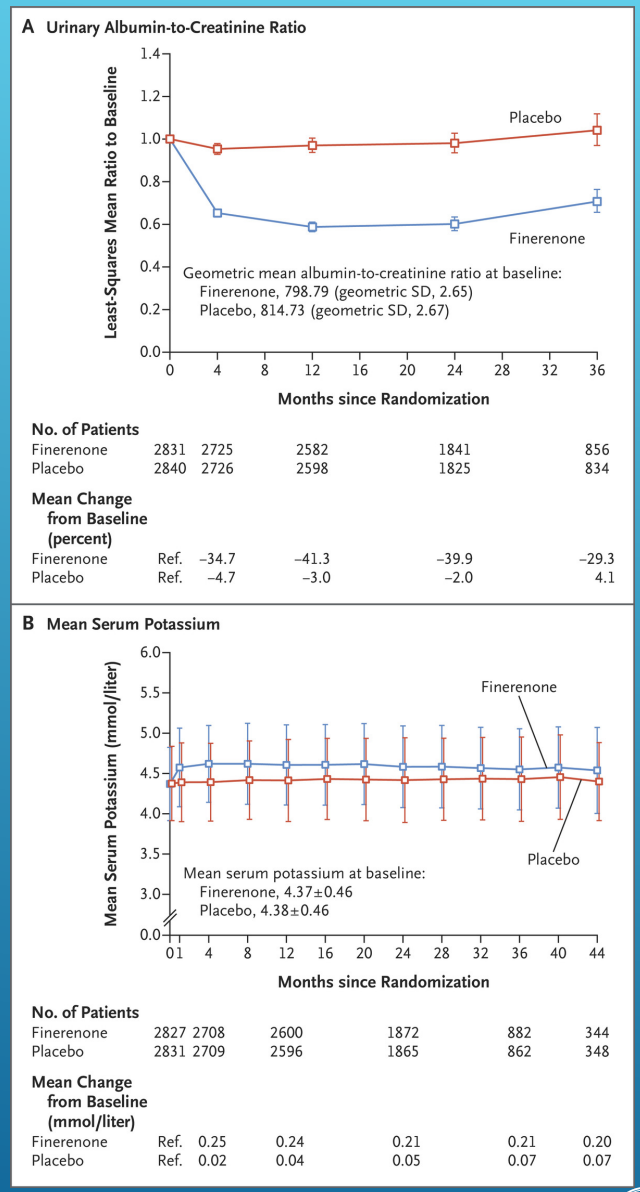
Effects on Albuminuria and Serum Potassium over Time.



GL Bakris et al. N Engl J Med 2020;383:2219-2229.

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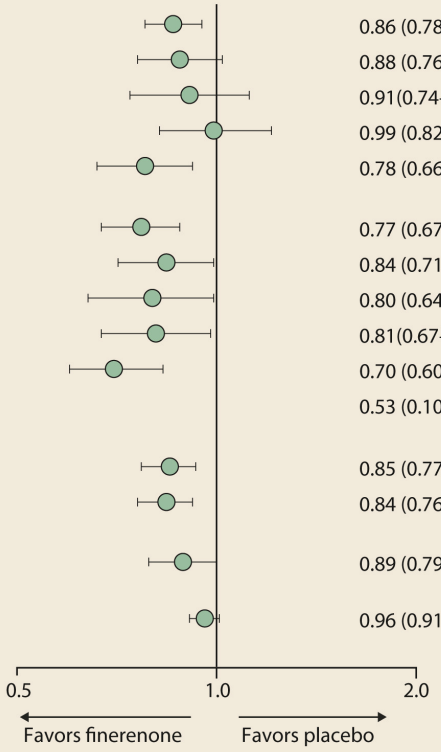
Figure 27

FINERENONE TRIAL DATA

Outcome	Finerenone (n = 6519)		Placebo (n = 6507)		Hazard ratio (95% CI)	*P* value[a]
	Number of patients with event (%)	Number of patients with event per 100 patient-years	Number of patients with event (%)	Number of patients with event per 100 patient-years		
Composite cardiovascular outcome[b]	825 (12.7)	4.34	939 (14.4)	5.01	0.86 (0.78–0.95)	0.0018
Death from cardiovascular causes	322 (4.9)	1.61	364 (5.6)	1.84	0.88 (0.76–1.02)	0.092
Nonfatal myocardial infarction	173 (2.7)	0.88	189 (2.9)	0.97	0.91(0.74–1.12)	0.36
Nonfatal stroke	198 (3.0)	1.01	198 (3.0)	1.02	0.99 (0.82–1.21)	0.95
Hospitalization for heart failure	256 (3.9)	1.31	325 (5.0)	1.68	0.78 (0.66–0.92)	0.0030
eGFR ≥57% composite kidney outcome[c]	360 (5.5)	1.96	465 (7.1)	2.55	0.77 (0.67–0.88)	0.0002
Kidney failure	254 (3.9)	1.38	297 (4.6)	1.62	0.84 (0.71–0.99)	0.039
End-stage kidney disease[d]	151 (2.3)	0.76	188 (2.9)	0.96	0.80 (0.64–0.99)	0.040[e]
Sustained decrease in eGFR to <15 ml/min/1.73 m^2	195 (3.0)	1.06	237 (3.6)	1.29	0.81(0.67–0.98)	0.026[e]
Sustained ≥57% decrease in eGFR from baseline	257 (3.9)	1.40	361 (5.5)	4.03	0.70 (0.60–0.83)	<0.0001
Renal death	2 (<0.1)	0.01	4 (<0.1)	0.02	0.53 (0.10–2.91)	0.46[e]
eGFR ≥40% composite kidney outcome[f]	854 (13.1)	4.81	995 (15.3)	5.64	0.85 (0.77–0.93)	0.0004
Sustained ≥40% decrease in eGFR from baseline	817 (12.5)	4.60	962 (14.8)	5.45	0.84 (0.76–0.92)	0.0002
Death from any cause	552 (8.5)	2.76	614 (9.4)	3.10	0.89 (0.79–>1.00[g])	0.051[e]
Hospitalization for any cause	2836 (43.5)	19.04	2926 (45.0)	19.91	0.96 (0.91–1.01)	0.087[e]



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HYPERKALEMIA

1st line: **Address correctable factors**	• Review non-RASi medications (e.g. NSAIDs, trimethoprim) • Assess dietary potassium intake (dietary referral) and consider appropriate moderation of dietary potassium intake
2nd line: **Medications**	Consider: • Appropriate use of diuretics • Optimize serum bicarbonate levels • Licensed potassium exchange agents
3rd line: **Last resort**	• Reduce dose or discontinue RASi/MRA (Discontinuation is associated with increased cardiovascular events. Review and restart RASi or MRA at a later date if patient condition allows.)

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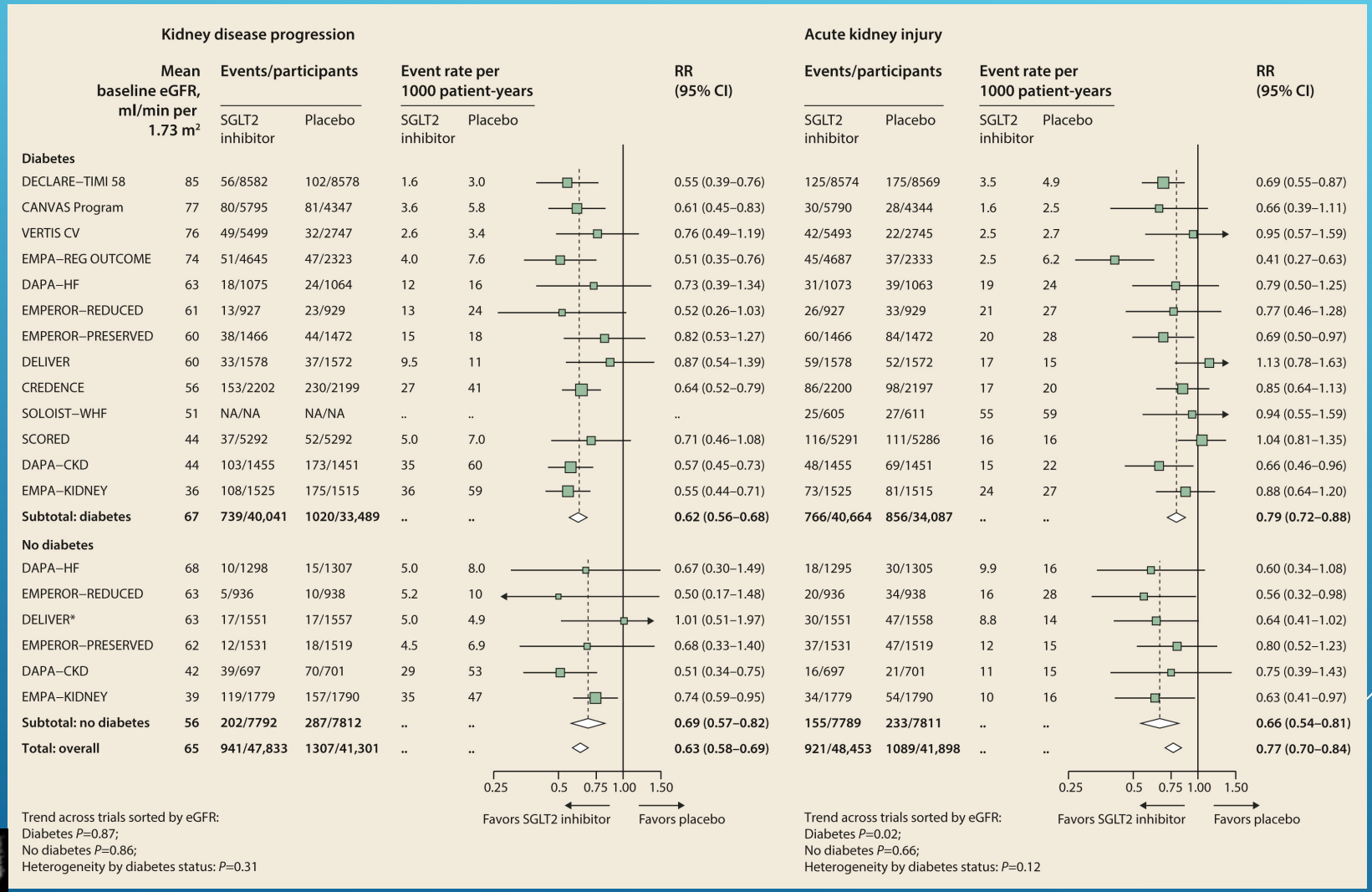
HYPERKALEMIA

- Follow up labs are vital
- Options to treat this but they are quite expensive
- Patiromer-8.4g dose~ $35
- Sodium zirconium cyclosilicate-10g dose~ $27
- Sodium polystyrene sulfonate-15g dose~ $2.00, if you can find it and it gets poor patient reviews

SGLT2 INHIBITORS

- Recommended at Level 1A for Type 2 DM with eGFR>20cc/min
- Recommended with High certainty of evidence
- Plethora of data for improvement in kidney survival, CV death, and heart failure hospitalizations
- Recommended at 1A for any CKD with eGFR >20cc/min and ACR >200mg/g or heart failure irrespective of level of albuminuria
- Recommended 2B(suggestion with moderate certainty) for CKD eGFR 20-45cc/min with ACR<200mg/g

SGLT KIDNEY OUTCOMES DM/NON-DM



Kidney disease progression

	Mean baseline eGFR, ml/min per 1.73 m²	Events/participants		Event rate per 1000 patient-years		RR (95% CI)
		SGLT2 inhibitor	Placebo	SGLT2 inhibitor	Placebo	
Diabetes						
DECLARE–TIMI 58	85	56/8582	102/8578	1.6	3.0	0.55 (0.39–0.76)
CANVAS Program	77	80/5795	81/4347	3.6	5.8	0.61 (0.45–0.83)
VERTIS CV	76	49/5499	32/2747	2.6	3.4	0.76 (0.49–1.19)
EMPA–REG OUTCOME	74	51/4645	47/2323	4.0	7.6	0.51 (0.35–0.76)
DAPA–HF	63	18/1075	24/1064	12	16	0.73 (0.39–1.34)
EMPEROR–REDUCED	61	13/927	23/929	13	24	0.52 (0.26–1.03)
EMPEROR–PRESERVED	60	38/1466	44/1472	15	18	0.82 (0.53–1.27)
DELIVER	60	33/1578	37/1572	9.5	11	0.87 (0.54–1.39)
CREDENCE	56	153/2202	230/2199	27	41	0.64 (0.52–0.79)
SOLOIST–WHF	51	NA/NA	NA/NA	..	..	..
SCORED	44	37/5292	52/5292	5.0	7.0	0.71 (0.46–1.08)
DAPA–CKD	44	103/1455	173/1451	35	60	0.57 (0.45–0.73)
EMPA–KIDNEY	36	108/1525	175/1515	36	59	0.55 (0.44–0.71)
Subtotal: diabetes	**67**	**739/40,041**	**1020/33,489**	..	..	**0.62 (0.56–0.68)**
No diabetes						
DAPA–HF	68	10/1298	15/1307	5.0	8.0	0.67 (0.30–1.49)
EMPEROR–REDUCED	63	5/936	10/938	5.2	10	0.50 (0.17–1.48)
DELIVER*	63	17/1551	17/1557	5.0	4.9	1.01 (0.51–1.97)
EMPEROR–PRESERVED	62	12/1531	18/1519	4.5	6.9	0.68 (0.33–1.40)
DAPA–CKD	42	39/697	70/701	29	53	0.51 (0.34–0.75)
EMPA–KIDNEY	39	119/1779	157/1790	35	47	0.74 (0.59–0.95)
Subtotal: no diabetes	**56**	**202/7792**	**287/7812**	..	..	**0.69 (0.57–0.82)**
Total: overall	**65**	**941/47,833**	**1307/41,301**	..	..	**0.63 (0.58–0.69)**

0.25 0.5 0.75 1.00 1.50

Favors SGLT2 inhibitor Favors placebo

Trend across trials sorted by eGFR:
Diabetes *P*=0.87;
No diabetes *P*=0.86;
Heterogeneity by diabetes status: *P*=0.31

Acute kidney injury

	Events/participants		Event rate per 1000 patient-years		RR (95% CI)
	SGLT2 inhibitor	Placebo	SGLT2 inhibitor	Placebo	
DECLARE–TIMI 58	125/8574	175/8569	3.5	4.9	0.69 (0.55–0.87)
CANVAS Program	30/5790	28/4344	1.6	2.5	0.66 (0.39–1.11)
VERTIS CV	42/5493	22/2745	2.5	2.7	0.95 (0.57–1.59)
EMPA–REG OUTCOME	45/4687	37/2333	2.5	6.2	0.41 (0.27–0.63)
DAPA–HF	31/1073	39/1063	19	24	0.79 (0.50–1.25)
EMPEROR–REDUCED	26/927	33/929	21	27	0.77 (0.46–1.28)
EMPEROR–PRESERVED	60/1466	84/1472	20	28	0.69 (0.50–0.97)
DELIVER	59/1578	52/1572	17	15	1.13 (0.78–1.63)
CREDENCE	86/2200	98/2197	17	20	0.85 (0.64–1.13)
SOLOIST–WHF	25/605	27/611	55	59	0.94 (0.55–1.59)
SCORED	116/5291	111/5286	16	16	1.04 (0.81–1.35)
DAPA–CKD	48/1455	69/1451	15	22	0.66 (0.46–0.96)
EMPA–KIDNEY	73/1525	81/1515	24	27	0.88 (0.64–1.20)
Subtotal: diabetes	**766/40,664**	**856/34,087**	..	..	**0.79 (0.72–0.88)**
DAPA–HF	18/1295	30/1305	9.9	16	0.60 (0.34–1.08)
EMPEROR–REDUCED	20/936	34/938	16	28	0.56 (0.32–0.98)
DELIVER*	30/1551	47/1558	8.8	14	0.64 (0.41–1.02)
EMPEROR–PRESERVED	37/1531	47/1519	12	15	0.80 (0.52–1.23)
DAPA–CKD	16/697	21/701	11	15	0.75 (0.39–1.43)
EMPA–KIDNEY	34/1779	54/1790	10	16	0.63 (0.41–0.97)
Subtotal: no diabetes	**155/7789**	**233/7811**	..	..	**0.66 (0.54–0.81)**
Total: overall	**921/48,453**	**1089/41,898**	..	..	**0.77 (0.70–0.84)**

0.25 0.5 0.75 1.00 1.50

Favors SGLT2 inhibitor Favors placebo

Trend across trials sorted by eGFR:
Diabetes *P*=0.02;
No diabetes *P*=0.66;
Heterogeneity by diabetes status: *P*=0.12

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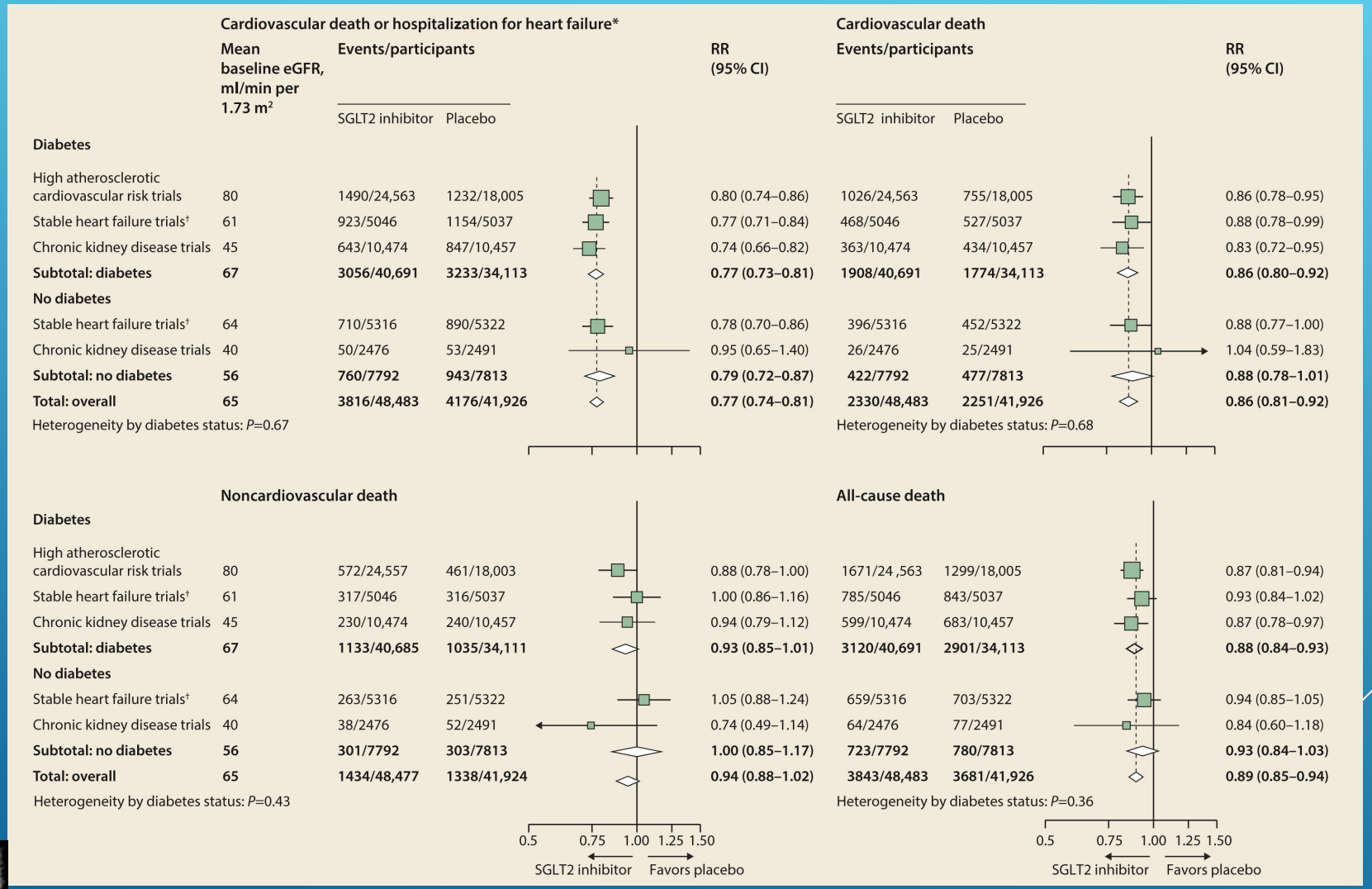
SGLT2 AND CV OUTCOMES



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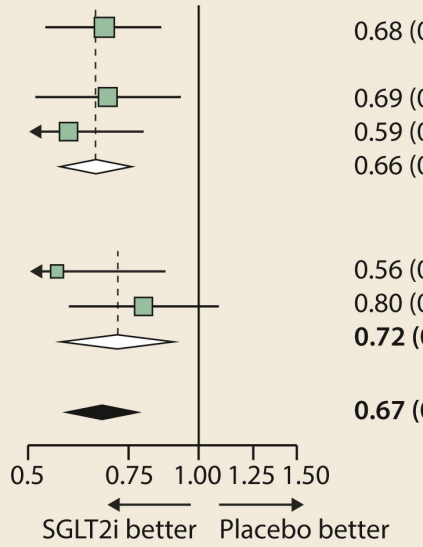
SGLT2 EFFECT ON KIDNEY FAILURE

	Mean baseline eGFR (ml/min/1.73 m²)	Events/participants		Rate per 1000 patient-years		Relative risk (95% CI)	Trend across trials sorted by eGFR
		SGLT2i	Placebo	SGLT2i	Placebo		
Diabetes							
CREDENCE	56	116/2202	165/2199	20	29	0.68 (0.54, 0.86)	
SCORED	44	NA/NA	NA/NA	26	37		
DAPA-CKD	44	77/1455	109/1451	24	39	0.69 (0.51, 0.92)	*P*=0.48
EMPA-KIDNEY	36	74/1525	116/1515			0.59 (0.44, 0.79)	
Subtotal: DIABETES	**47**	**267/5182**	**390/5165**			0.66 (0.56, 0.77)	
No diabetes							
DAPA-CKD	42	32/697	52/701	24	39	0.56 (0.36, 0.87)	*P*=0.19
EMPA-KIDNEY	39	83/1779	105/1790	25	31	0.80 (0.60, 1.07)	
Subtotal: NO DIABETES	**40**	**115/2476**	**157/2491**			**0.72 (0.56, 0.91)**	
TOTAL: OVERALL	**45**	**382/7658**	**547/7656**			**0.67 (0.59, 0.77)**	



Heterogeneity by diabetes status: *P*=0.54

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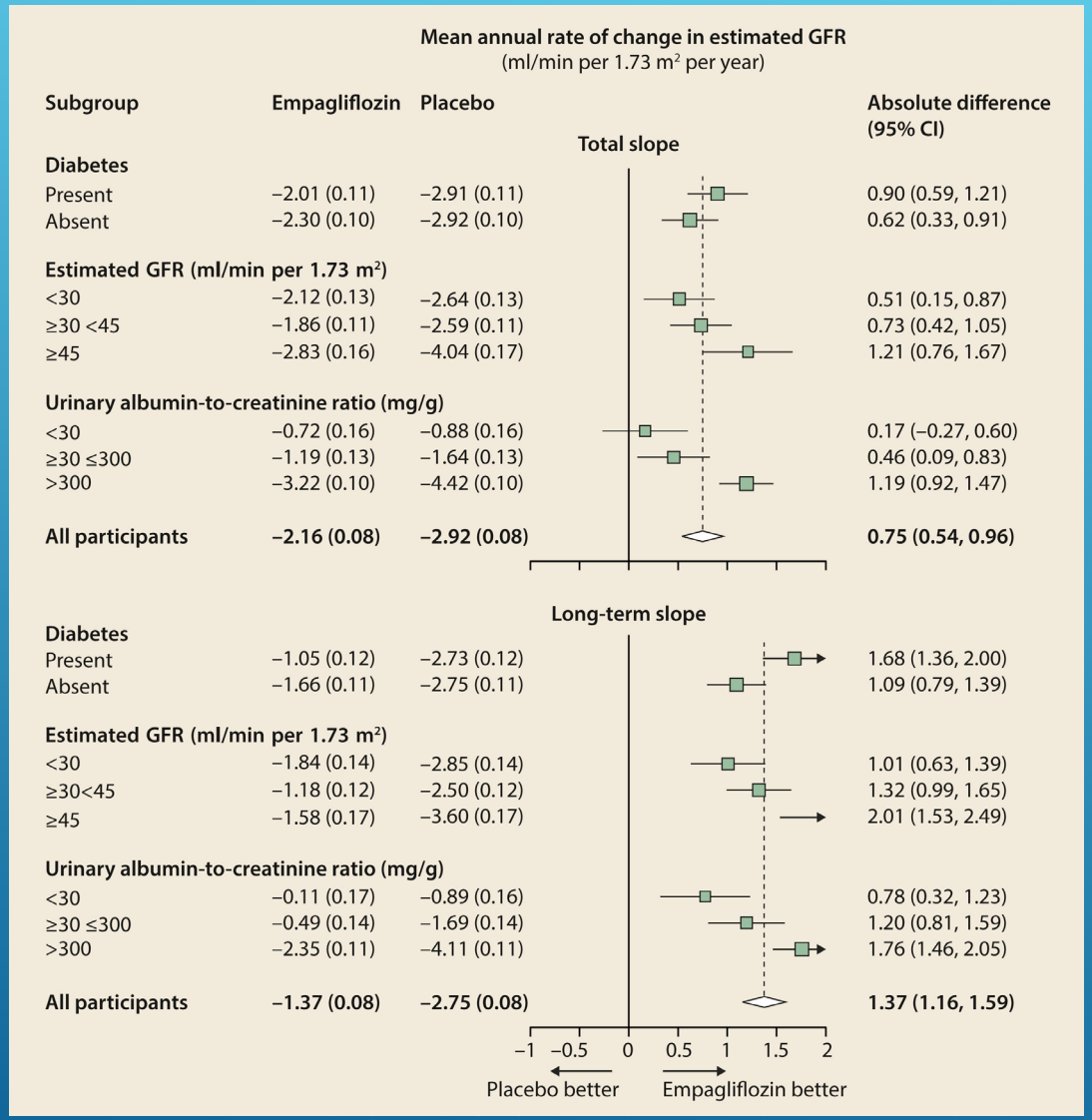
SGLT2 EFFECT ON GFR CHANGE



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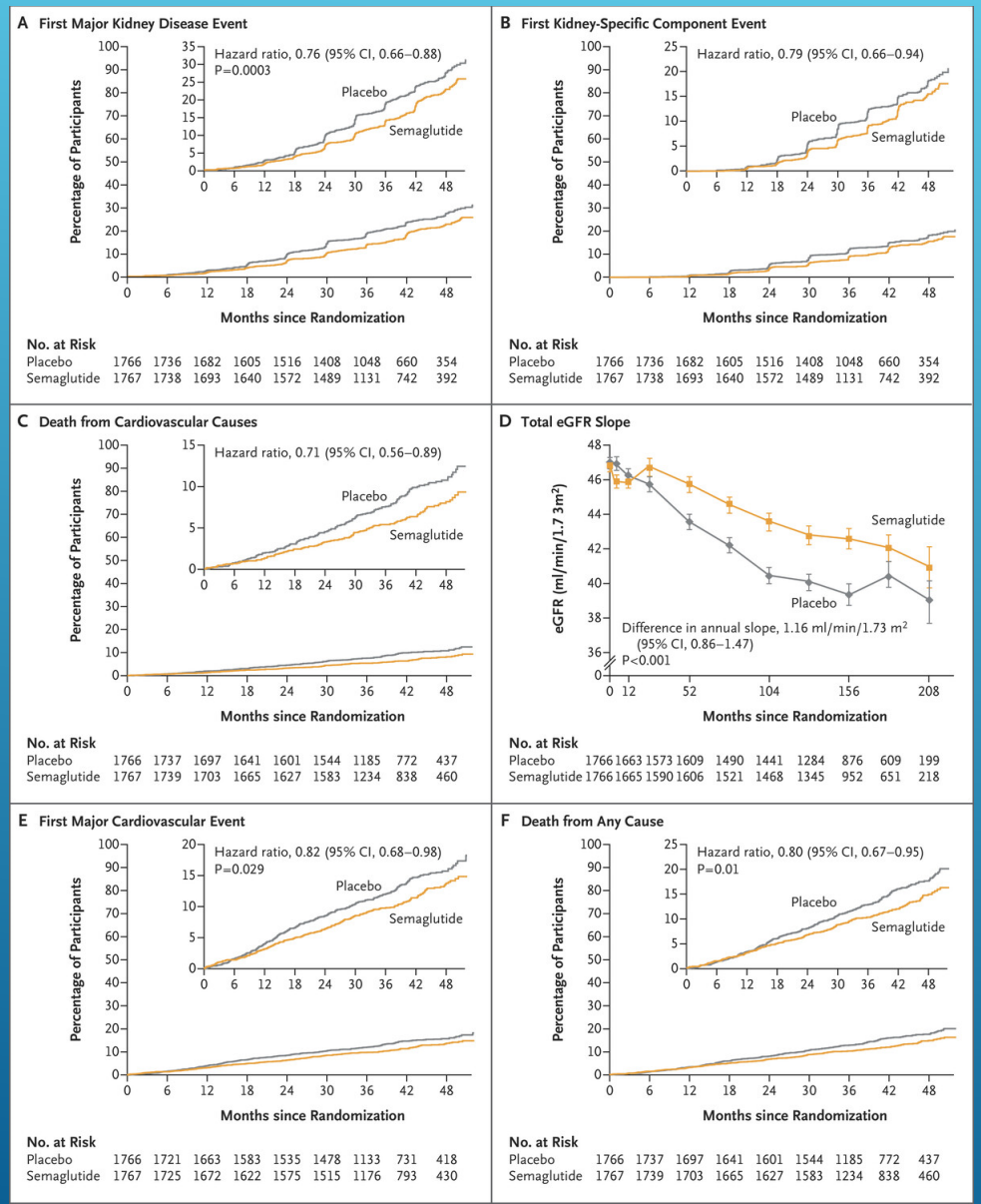
SGLT-2 INHIBITORS

- Appears to be another weapon in the fight on Type 2 DM
- Initiate with GFR >20cc/min, but this may be in evolution
- Adverse reactions to watch for:
  - Yeast infections>>>Fournier's gangrene
  - UTIs
  - DKA w/o hyperglycemia-not to be used in the critically ill
  - Amputations/fracture risk, though not seen in study
  - AKI-guidelines don't suggest repeat labs, but I would

FLOW STUDY

- CKD pts with eGFR 50-75cc/min and ACR 30mg to 5000mg and CKD pts with eGFR 20-50cc/min and ACR 100mg to 5000mg
- Given 1mg weekly of semaglutide or placebo
- Looked at major kidney disease events or death from kidney-related or cardiovascular causes
- Showed a 24% risk reduction in major kidney disease events

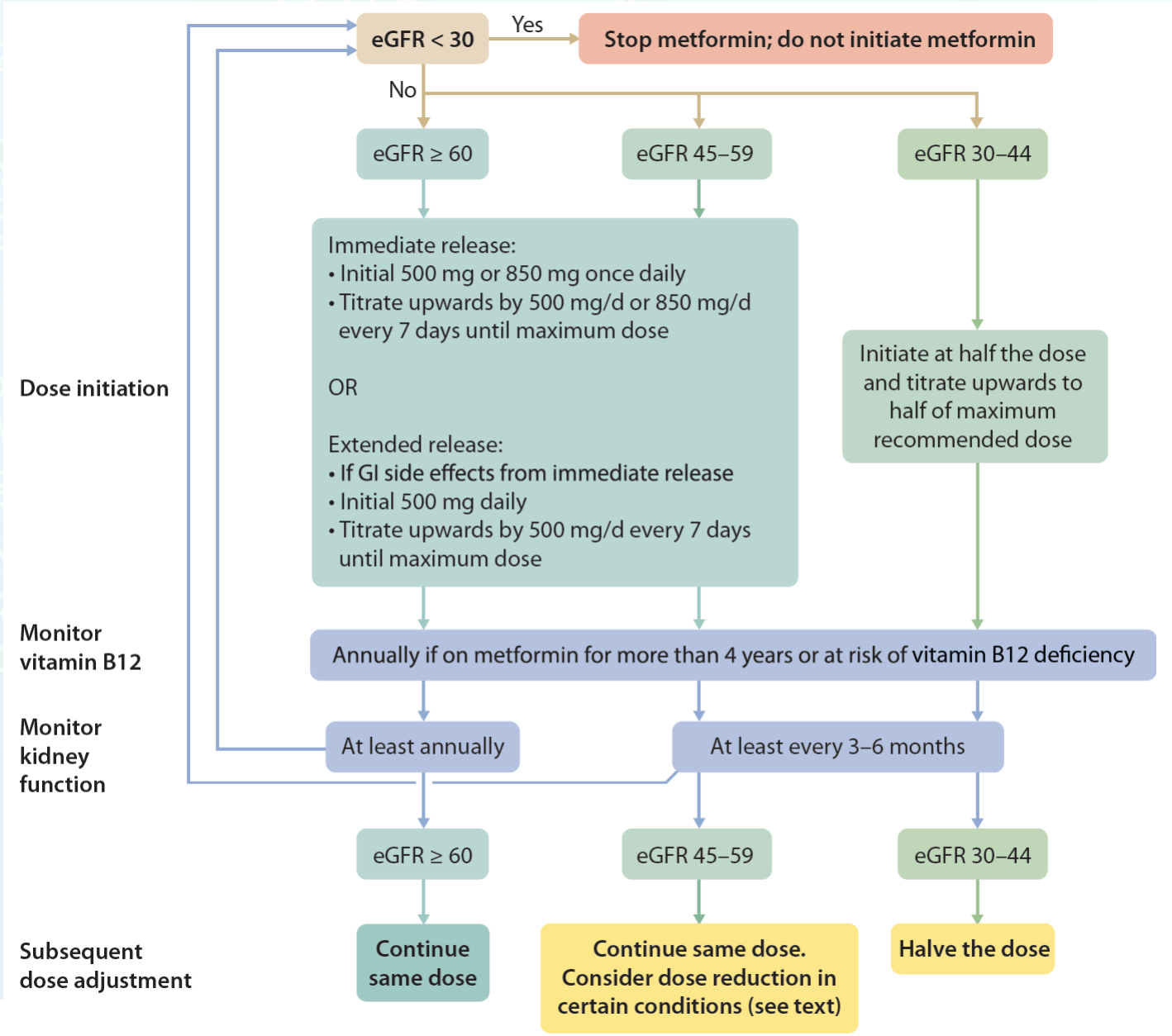
SEMAGLUTIDE IN CKD



METFORMIN-SAFETY IN NUMBERS

- Metformin-Does not cause kidney damage
- Initial limitations were-Scr 1.5 for men, Scr 1.2 for women
- Changed to GFR>30cc/min if stable and on therapy, caution to start if GFR<45cc/min
- Risk of lactic acidosis-Rare but does exist
- CKD stage 3 patients-less CV risk in metformin users in TREAT study
- 2 episodes of lactic acidosis in 591 patients

FIGURE 22. SUGGESTED APPROACH IN DOSING METFORMIN BASED ON THE LEVEL OF KIDNEY FUNCTION



ESA USE TODAY

- Check iron stores first and check for blood loss
- Discuss with patient risks/benefits
- Keep Hgb between 10-11
- Don’t start most people until their Hgb is close to 9.0
- BP must be well controlled as well
- This paradigm has also extended to the ESRD world
- New KDIGO guideline to come out later in 2024

METABOLIC ACIDOSIS

- Another abnormal lab value in a sea of abnormal labs in a CKD patient
- Concern in ESRD patients due in part to bone loss
- Slow downward creep in bicarbonate levels with CKD
- Does it really matter? Recent studies did not show much benefit in treatment
- Consider treatment when serum bicarbonate <18mmol/L

STATIN THERAPY IN CKD

- Recommended at 1A level for patients >50 with eGFR <60cc/min, not on dialysis or with renal transplant
- Recommended at 2A for those 18-49 with CKD and with comorbid conditions(CAD, DM, CVA)
- Risk of these agents remain low in numerous studies

OAC IN CKD FOR AFIB

a

eCrCl (ml/min)[a]	Warfarin	Apixaban[b]	Dabigatran	Edoxaban[c]	Rivaroxaban
>95	Adjusted dose (INR 2–3)	5 mg b.i.d.	150 mg b.i.d.	60 mg QD[d]	20 mg QD
51–95	Adjusted dose (INR 2–3)	5 mg b.i.d.	150 mg b.i.d.	60 mg QD	20 mg QD
31–50	Adjusted dose (INR 2–3)	5 mg b.i.d. (eCrCl cut off 25 ml/min)	150 mg b.i.d. or 110 mg b.i.d.[e]	30 mg QD	15 mg QD

b

eCrCl (ml/min)[a]	Warfarin	Apixaban[b]	Dabigatran	Edoxaban	Rivaroxaban
15–30	Adjusted dose for INR 2–3 could be considered	2.5 mg PO b.i.d. could be considered	Unknown (75 mg PO b.i.d.)[f,g]	30 mg QD[h] could be considered	15 mg QD could be considered
<15 not on dialysis	Equipoise based on observational data and meta-analysis	Unknown (2.5 mg PO b.i.d.)[f]	Not recommended	Not recommended	Unknown (15 mg QD)[f]
<15 on dialysis	Equipoise based on observational data and meta-analysis	Unknown (2.5 mg PO b.i.d.)[f]	Not recommended	Not recommended	Unknown (15 mg QD)[f]

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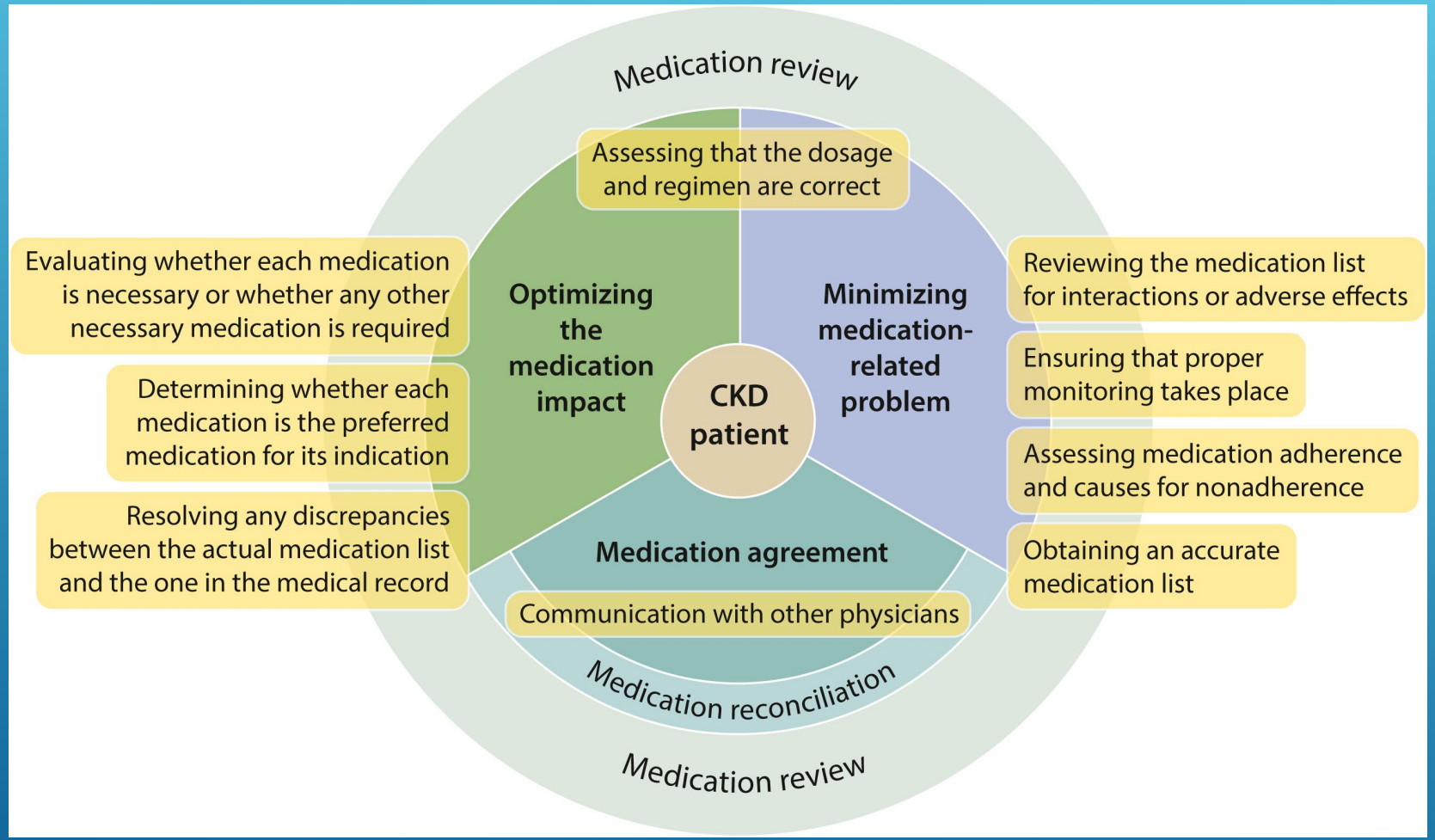
AVOIDING HARM



Valacyclovir/Acyclovir

Gabapentin

Opiates

Too much GDMT at once

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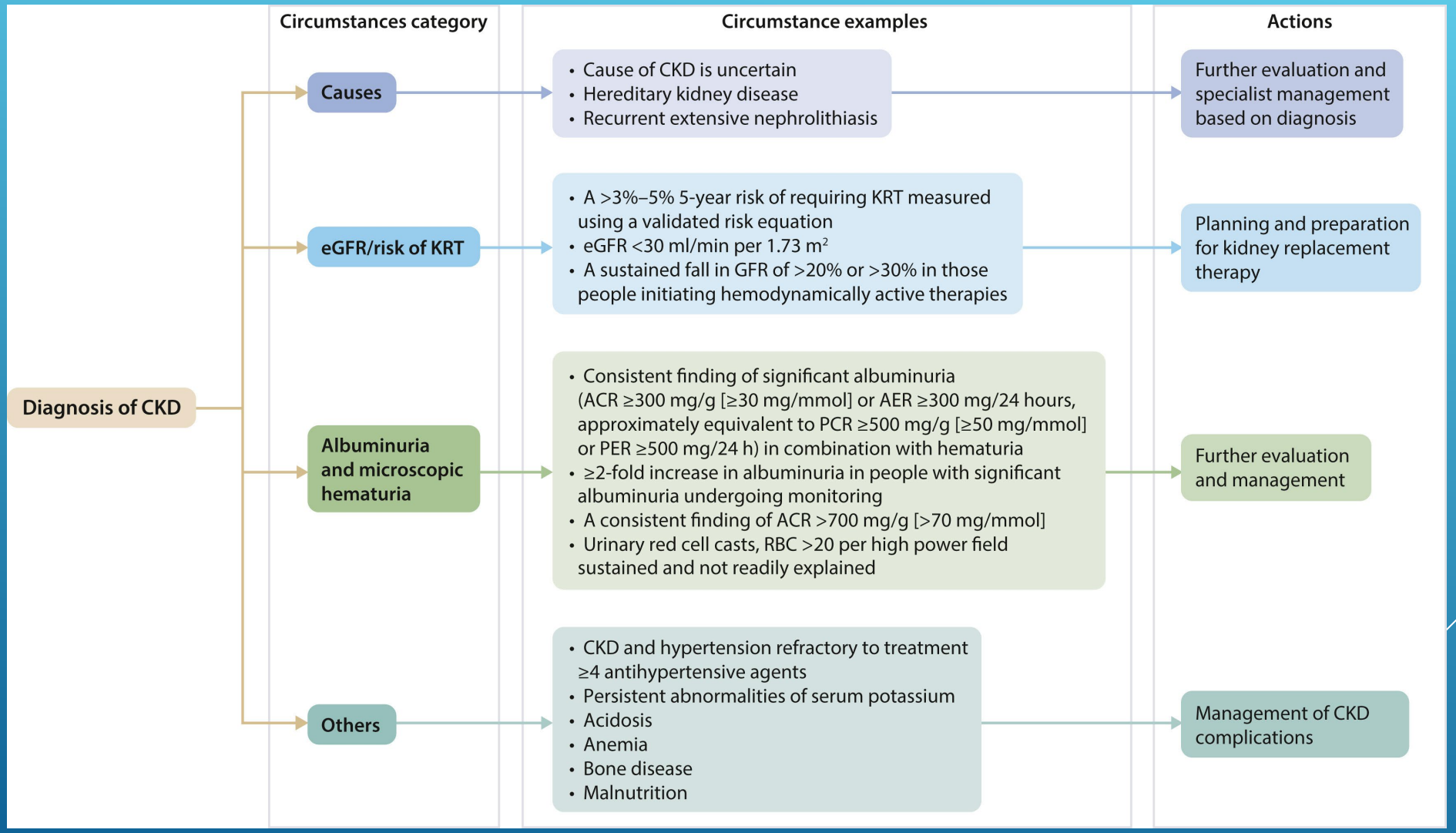
CKD WORKFLOW



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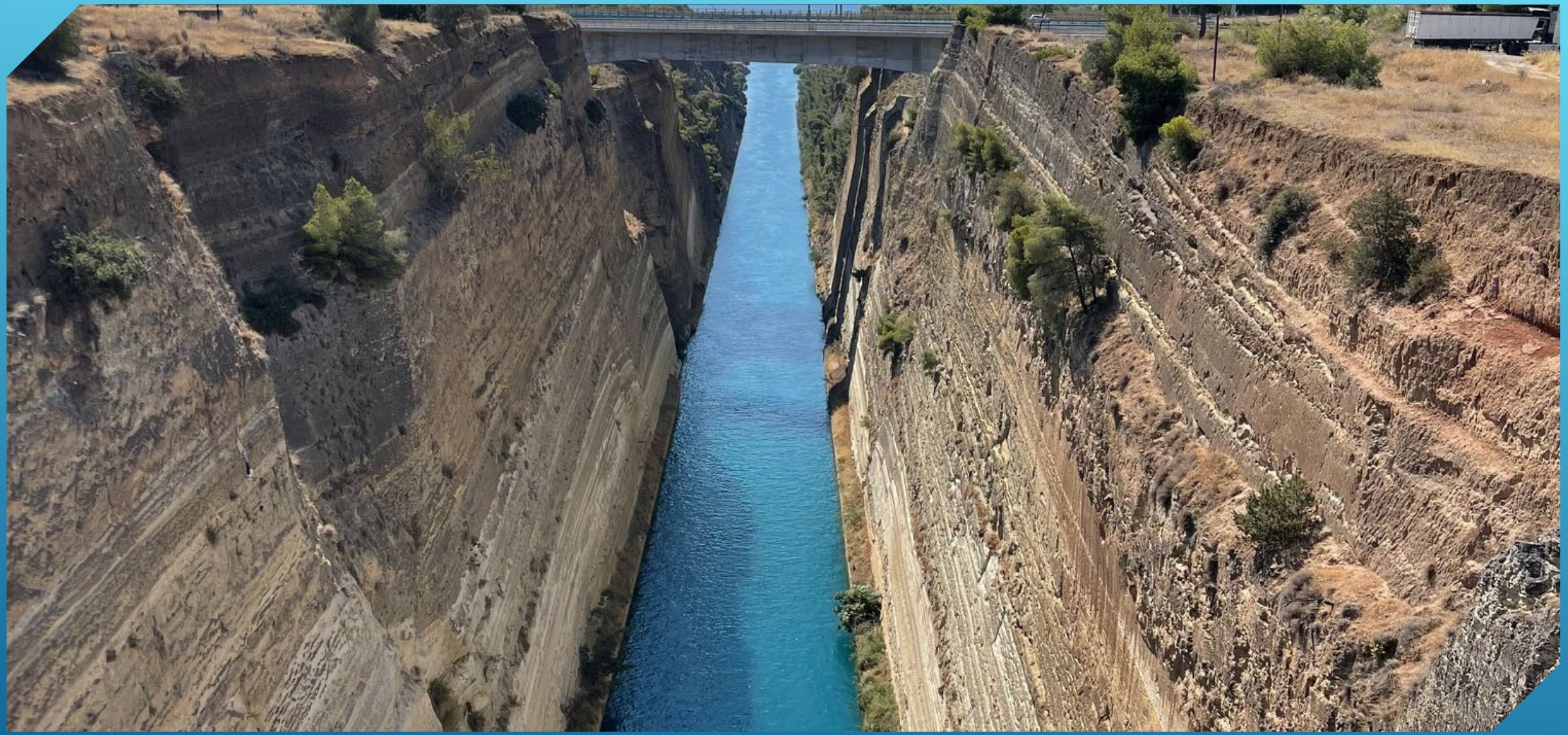
FOUR PILLARS OF DM-CKD THERAPY 2024

- RAAS agents-$20/month
- Nonsteroidal MRA-$650/month
- SGLT2 inhibitors-$390/month
- GLP-1 agonist-$950/month
- Total-$2010/month



SUMMARY

- We are all actively treating CKD everyday
- BP, BG control remain key
- SGLT-2 inhibitors are now in the "must have" group
- My goal as a nephrologist is to help the patient's kidneys last one day longer than the rest of the patient
- How do we afford all these recommendations?
- "You are what your kidneys choose to keep."
- Dr.poole@nephassociates.com,
- Twitter-@cvpoole14, Yourin Trouble