Pre-Debate Poll

Proposition:
'Every Patient With CKD
Should Be Seen By A Nephrologist'

Option 1: Agree with Swap, all CKD patients need to be seen by a nephrologist

Option 2: Agree with Scott, all CKD patients do NOT need to be seen by a nephrologist

Proposition:
'Every Patient With CKD Should Be Seen By A Nephrologist'

uOttawa

The Ottawa Hospital Research Institute | L'Hôpital d'Ottawa Institut de recherche

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@hswapnil.medsky.social

Disclosures

- No financial conflicts with pharma/device companies
- Grant funding from CIHR, TOHAMO, PSI (unrelated to today's topic)

More disclosures

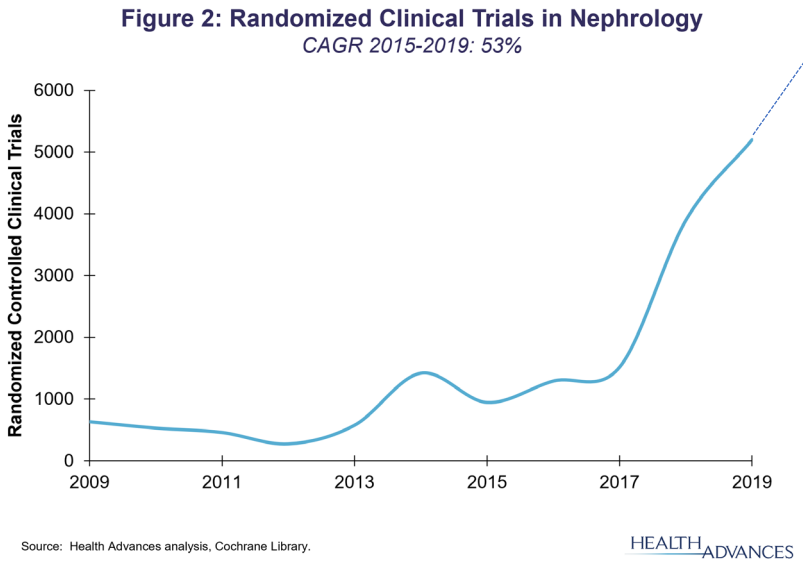
- I am still paying off my mortgage
- I have lost all previous debates at this event*

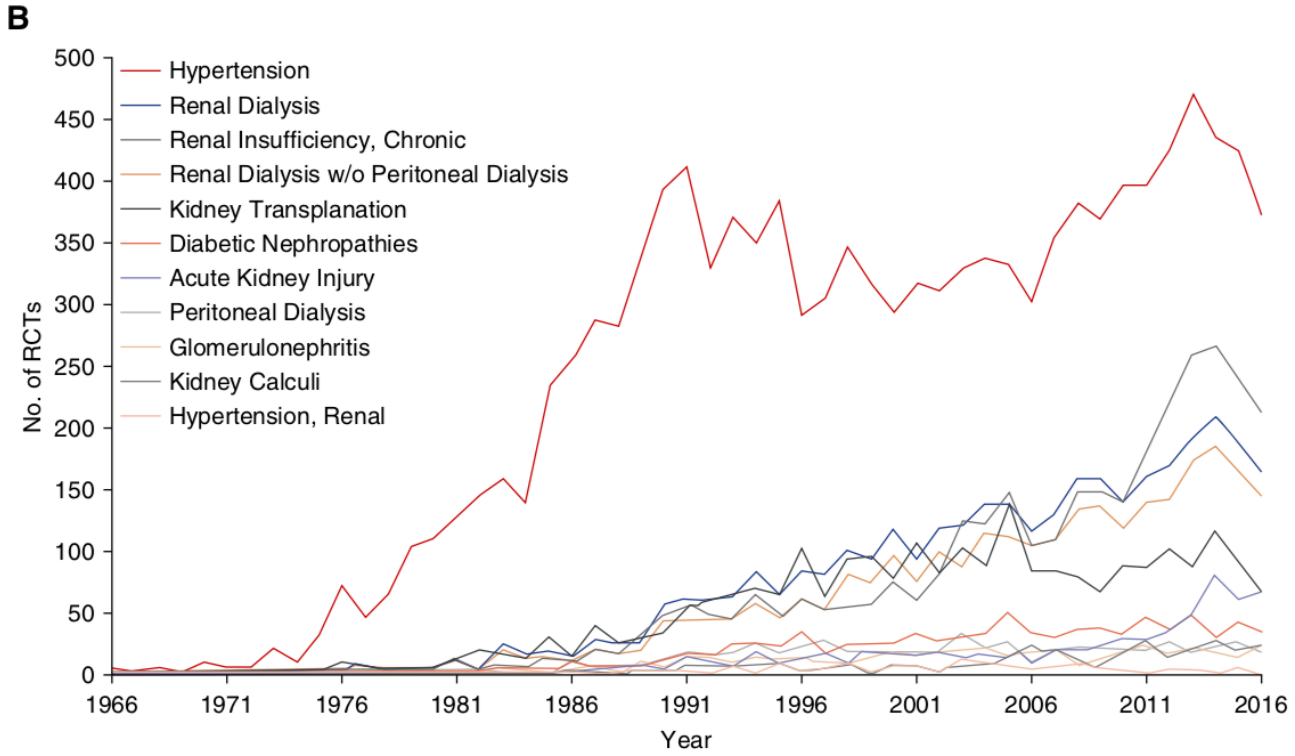
**including to Scott Brimble*

Outline

- Exploding therapeutics in kidney disease
- Diabetic kidney disease ‘pillars’ are trickier than they seem
- There’s a lot of non-diabetic CKD which requires specialized care
- CKD staging and risk stratification is getting more complicated

Exploding Trials & Therapeutic advances





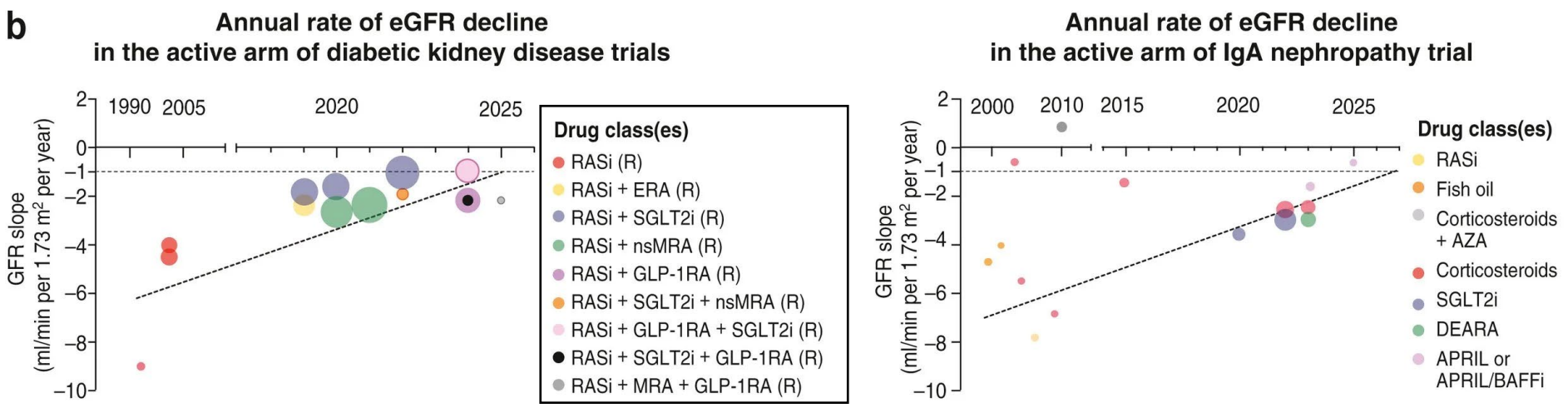
Remission of CKD?

a

	Historical paradigm: slow CKD progression	New paradigm: aim to achieve CKD remission
Goal	• Delay the inevitable loss of kidney function	• Halt decline in kidney function to normal healthy aging (<1 ml/min per 1.73 m^2 per year) OR achieve normalization of GFR and albuminuria
Therapeutic context	• Few effective therapies to prevent loss of kidney function	• Combination therapy with highly effective and safe agents (RASi, SGLT2i, ns-MRA, GLP-1RA, disease-specific therapies [e.g., B-cell–targeted therapies])
Workforce and policy focus	• Major focus on the provision of dialysis and kidney transplantation services	• Early detection, population-based screening, risk-based implementation of guideline-directed therapies

Early recognition of CKD, and those at risk of progression is now important
Especially presence of albuminuria

b



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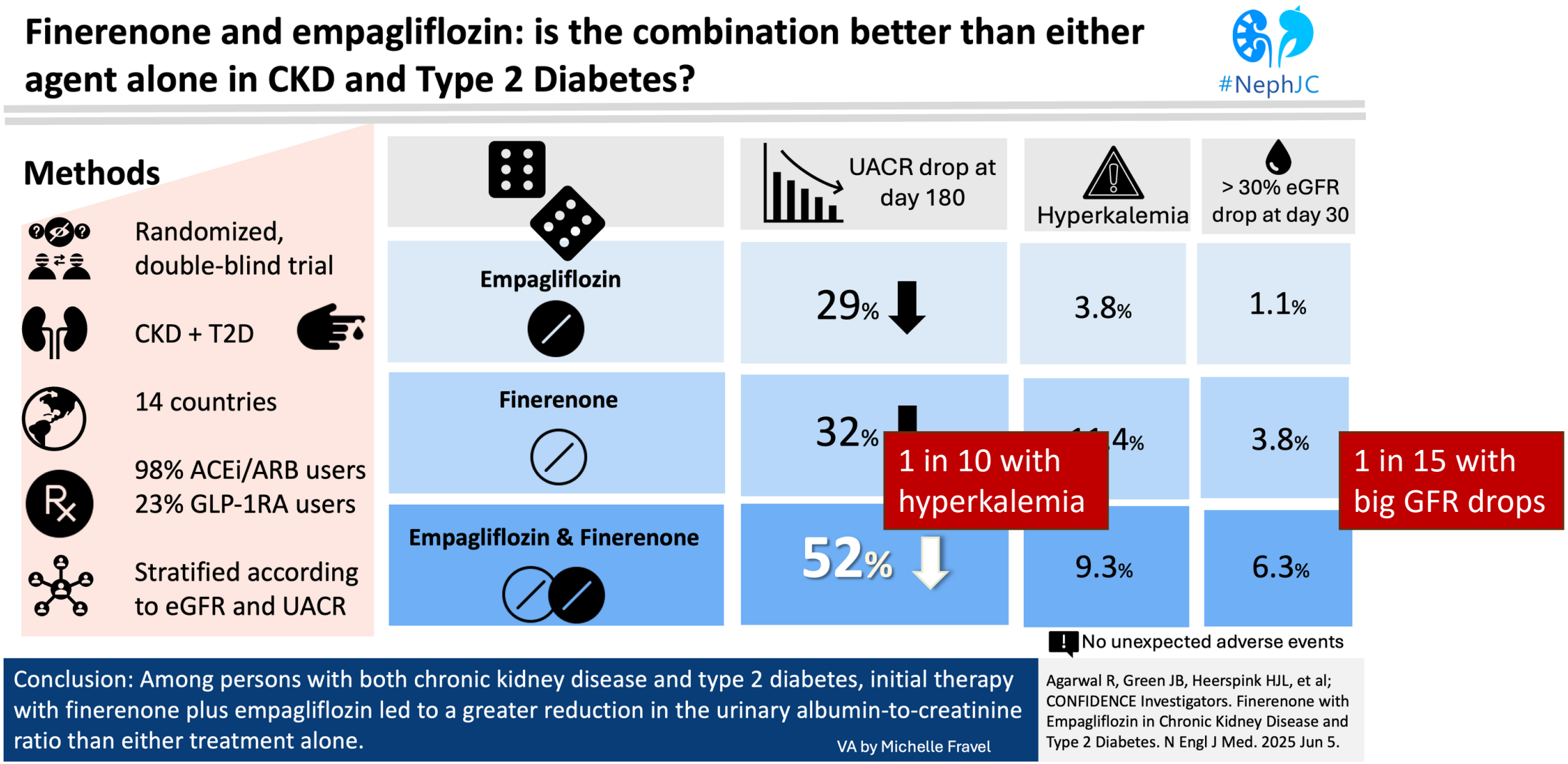
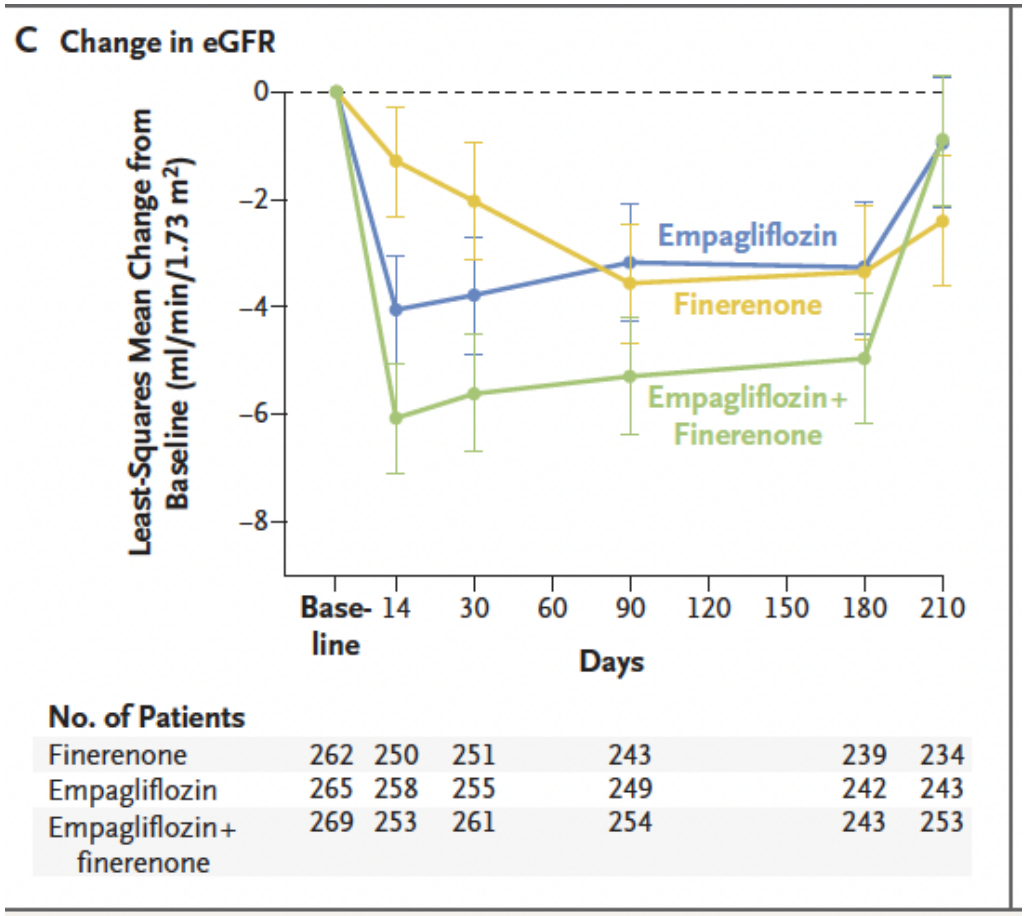
The Four Pillars Of DKD Management?

The Parthenon today

CONFIDENCE trial: Doing a flozin + finerenone together?



GFR drops in CONFIDENCE trial



No. of Patients						
Finerenone	262	250	251	243	239	234
Empagliflozin	265	258	255	249	242	243
Empagliflozin+ finerenone	269	253	261	254	243	253

Using Finerenone in Ontario

Reason For Use Code	Clinical Criteria
700	For use as an adjunct to standard-of-care (SOC) therapy in adult patients diagnosed with BOTH chronic kidney disease (CKD) and type 2 diabetes (T2D) to reduce the risk of end-stage kidney disease and a sustained decrease in estimated glomerular filtration rate (eGFR), and cardiovascular death, nonfatal myocardial infarction, and hospitalization for heart failure in patients who meet the following criteria: 1. 18 years of age or older; AND 2. Diagnosed with CKD with an eGFR level greater than or equal to 25mL/min/1.73 square metres AND an albuminuria level greater than or equal to 30mg/g (or 3mg/mmol); AND 3. Patient is also diagnosed with T2D; AND 4. Finerenone is prescribed in addition to standard-of-care (SOC)* therapy for patients diagnosed with CKD with comorbid T2D; AND * SOC therapy is defined as maximally tolerated doses of angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) therapy in combination with a sodium-glucose cotransporter-2 (SGLT2) inhibitor unless SGLT2 inhibitors are contraindicated or not tolerated. 5. Patient does not have a diagnosis of chronic heart failure (CHF) with reduced ejection fraction and persistent symptoms meeting New York Heart Association Class II to IV; AND 6. Patient is not using finerenone in combination with another mineralocorticoid receptor antagonist (MRA); AND 7. Finerenone is prescribed in consultation with a nephrologist or other clinician with experience in the diagnosis and management of patients with CKD and T2D.

Diabetic Kidney Disease management is complicated

- Polypharmacy
- Access may require specialist involvement
- May have huge GFR drips with simultaneous medication starts
- May have (slower but) huge GFR dips with sequential medication starts
- Electrolyte problems
- Other adverse events

Non-Diabetic causes of CKD: IgA Nephropathy

a

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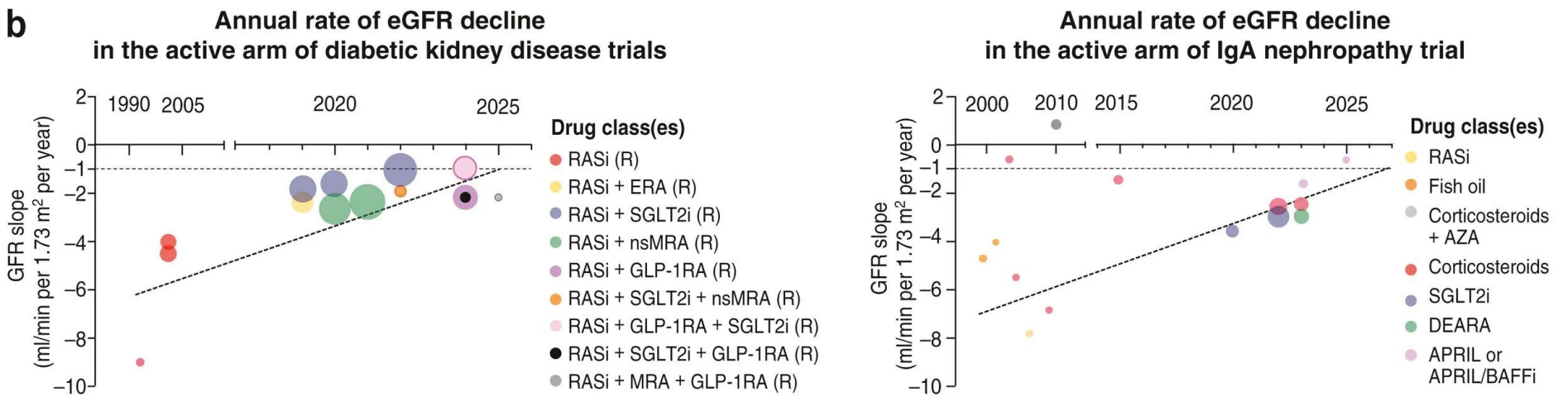
Targeted release budesonide
DEARA
APRIL inhibitors
APRIL/BAFF inhibitors
Complement inhibitors*

b



We have a specialized glomerulonephritis clinic at TOH

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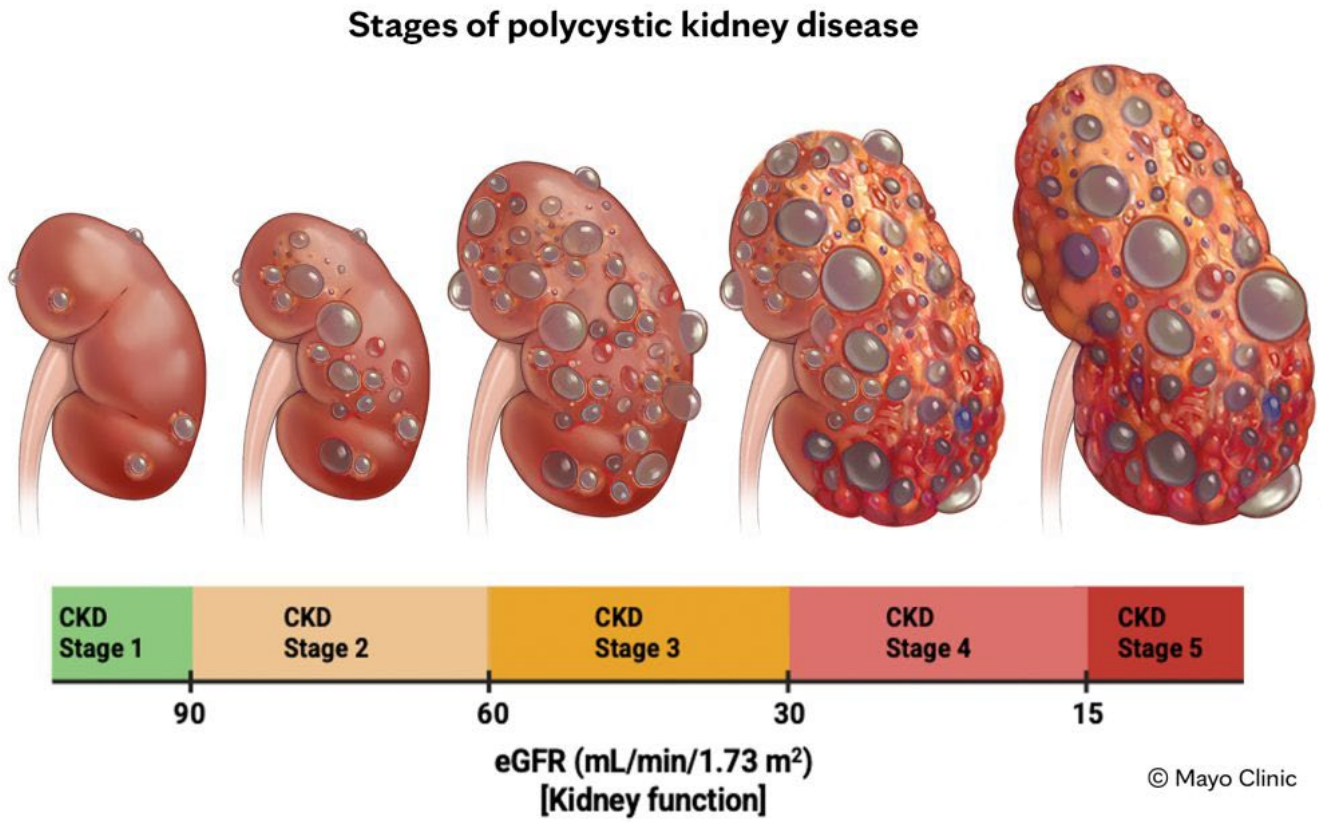
Non-diabetic causes of CKD: PKD



- We have a therapy: tolvaptan (requires monitoring, adverse effects)*
- Often after calculating risk of progression
- Genetic testing
- Other systemic complications

**We have a cystic kidney disease clinic at TOH*

Non-diabetic CKD care is also complicated

- Good news: we do have therapeutic options for many disease
- Bad news: access is not easy, use is not easy, managing adverse effects is not easy

- Even within a nephrology set up we have disease-specific specialized clinics

What even is CKD?

- ~~Renal Insufficiency/Impairment~~
- ~~Chronic Renal Failure~~
- Chronic Kidney Disease

‘CKD staging’

- ~ 2000

Table 10. Stages of Chronic Kidney Disease

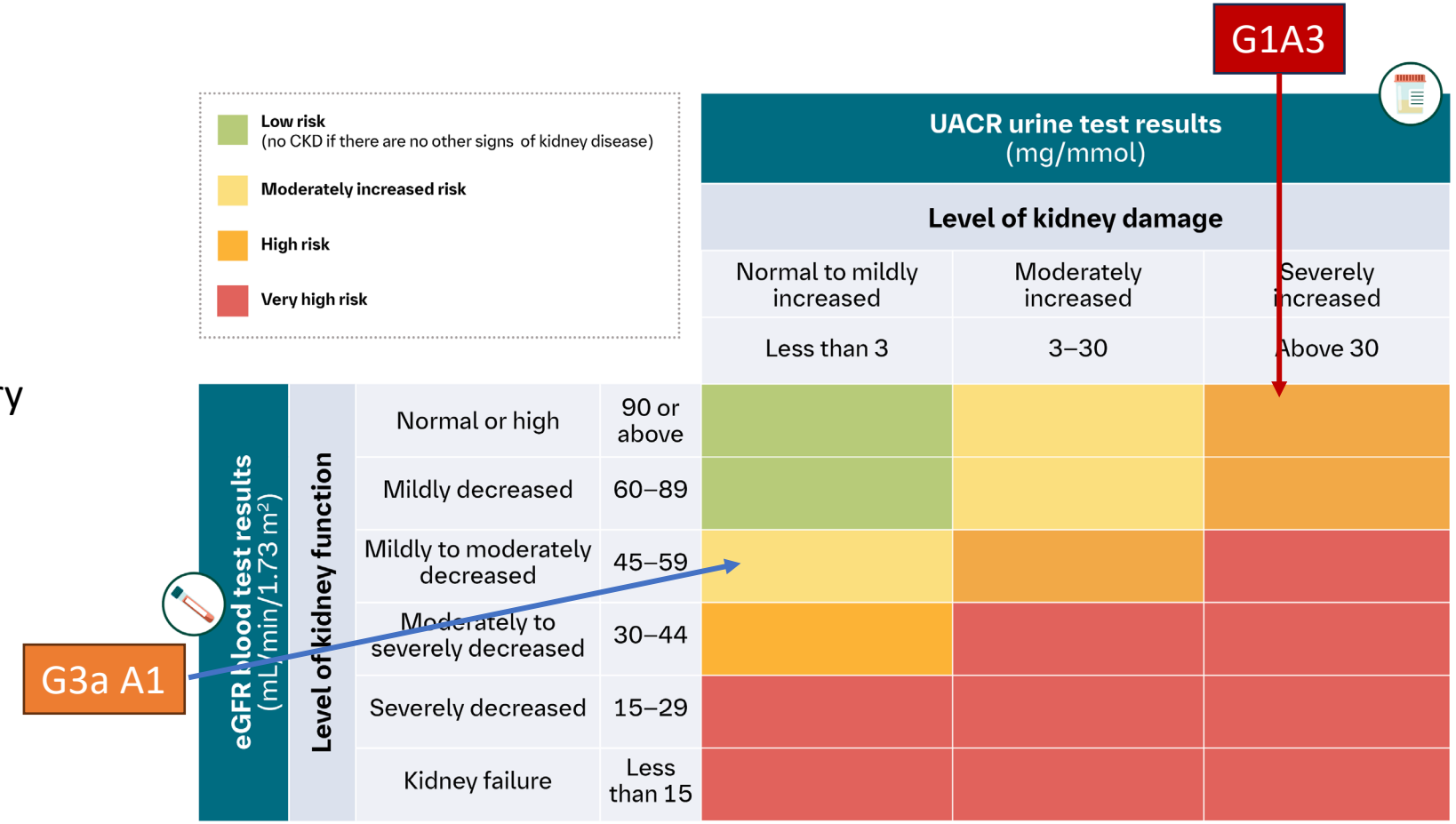
Stage	Description	GFR (mL/min/1.73 m^2)
1	Kidney damage with normal or ↑ GFR	≥90
2	Kidney damage with mild ↓ GFR	60–89
3	Moderate ↓ GFR	30–59
4	Severe ↓ GFR	15–29
5	Kidney failure	<15 (or dialysis)

Chronic kidney disease is defined as either kidney damage or GFR <60 mL/min/1.73 m^2 for ≥3 months. Kidney damage is defined as pathologic abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies.

CKD staging re-done from NKF K/DOQI to KDIGO

Staging has a G and an A category

G1 A3 is ‘worse’ than G3a A1



How do you even calculate kidney function?

- Elevated creatinine
- Creatinine clearance (Cockroft-Gault formula)

$$\text{CrCl (mL/min)} = \frac{(140 - \text{age}) \times \text{body weight}^{*}\ (\text{kg})}{\text{plasma creatinine (micromol/L)} \times 0.8} \quad (\times 0.85 \text{ if female})$$

*Use the lower CrCl result from the patient's ideal body weight or actual body weight.

- Ideal body weight (males) = 50 kg + 0.9 kg for each cm over 150 cm in height.
- Ideal body weight (females) = 45 kg + 0.9 kg for each cm over 150 cm in height.

How do you even calculate kidney function? From creatinine to GFR

MDRD GFR

$$\mathrm{GFR(mL/min/1.73m^2)} = 170 \times [\mathrm{P_{CR}}]^{-0.999} \times [\mathrm{Age}]^{-0.176} \times [\mathrm{SUN}]^{-0.170} \times [\mathrm{Alb}]^{+0.318} \times 0.762 \text{ if patient is female} \times 1.180 \text{ if patient is black}$$

TABLE 3

Formulas for Estimating GFR in Adults*

Abbreviated MDRD study equation[12]†

GFR (mL per minute per 1.73 m^2) = 186 × $(S_{Cr})^{-1.154}$ × $(age)^{-0.203}$ × (0.742, if female) × (1.210, if black)

How do you even calculate kidney function? Changing GFR formulae

CKD EPI GFR

The CKD-EPI creatinine equation is:

$$GFR = 141 \times \min(Scr/\kappa, 1)^{\alpha} \times \max(Scr/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018[\text{if female}] \times 1.159[\text{if black}]$$

$\kappa = 0.7$ if female
$\kappa = 0.9$ if male

$\alpha = -0.329$ if female
$\alpha = -0.411$ if male

min = The minimum of Scr/κ or 1
max = The maximum of Scr/κ or 1

Scr = serum creatinine (mg/dL)

CKD EPI GFR 2021 (without race)

CKD-EPI Equation for Estimating GFR on the Natural Scale Expressed for Specified Sex, Standardized Serum Creatinine and Standardized Serum Cystatin C (From New Eng J Med 2021)

Sex	Serum Creatinine (mg/dL)	Equation
Female	≤0.7	$GFR = 142 \times (Scr/0.7)^{-0.241} \times 0.9938^{Age} \times 1.012$
Female	>0.7	$GFR = 142 \times (Scr/0.7)^{-1.200} \times 0.9938^{Age} \times 1.012$
Male	≤0.9	$GFR = 142 \times (Scr/0.9)^{-0.302} \times 0.9938^{Age}$
Male	>0.9	$GFR = 142 \times (Scr/0.9)^{-1.200} \times 0.9938^{Age}$

Estimating kidney function summary

Estimating Kidney Function

#NephJC

	Cockcroft-Gault 1973	MDRD 1999	CKD-EPI 2009	CKD-EPI 2021
Study Design	Two measurements of 24h creatinine excretion per kg, n=236	Cross sectional study, n=1628, estimation of GFR using serum Cr	Cross sectional validation analysis, n=3896, estimation of GFR using Cr	Cross sectional validation analysis, n=4050, estimation of GFR using Cr
Population	18-92 yrs All white men	Non-diabetic CKD population 18-70 yrs,~80% White	31.5% Black, median age 47, mGFR 67.6	14.3% black, 10 years older, 9 points higher mGFR than 2009 dataset
Equations	$CrCl = (140 - age) \times weight/72 \times S_{Cr}$	$eGFR = 186.3 \times (S_{Cr})^{-1.154} \times (Age)^{-0.203}$	$eGFR = 141 \times \min(S_{Cr}/\kappa, 1)^{\alpha} \times \max(S_{Cr}/\kappa, 1)^{-1.209} \times 0.9929^{Age}$	$eGFR = 142 \times \min(S_{Cr}/\kappa, 1)^{\alpha} \times \max(S_{Cr}/\kappa, 1)^{-1.200} \times 0.9938^{Age}$
Race/Sex	Multiply by 0.85 if female No race variable	Multiply by 0.742 if female Multiply by 1.21 if Black	Multiply by 1.018 if female Multiply by 1.159 if Black	Multiply by 1.012 if female No race variable
Limitations	Uses weight, needs adjustment for BSA and BMI >30	Underestimates measured GFR at higher level	Limited no. of elderly, racial and ethnic minorities	Limited no. of Black patients with low GFR; using both CysC and Cr was more accurate

*Note: κ is 0.7 for females and 0.9 for males; α in 2009 is -0.329 for females and -0.411 for males, α in 2021 is -0.241 for females and -0.302 for males

@michaelturk6 @nefron1310

But GFR/CKD staging =/= risk of kidney failure!

Low risk
(no CKD if there are no other signs of kidney disease)

Moderately increased risk

High risk

Very high risk

eGFR blood test results (mL/min/1.73 m²)	Level of kidney function		UACR urine test results (mg/mmol)		
			Level of kidney damage		
			Normal to mildly increased	Moderately increased	Severely increased
			Less than 3	3–30	Above 30
	Normal or high	90 or above			
	Mildly decreased	60–89			
	Mildly to moderately decreased	45–59			
	Moderately to severely decreased	30–44			
	Severely decreased	15–29			
	Kidney failure	Less than 15			

THE PROJECTED RISK OF KIDNEY FAILURE

Kidney failure risk equation

www.kidneyfailurerisk.com

KFRE is useful: Crystal Ball edition

- 65-year old woman
- GFR 45
- ACR 5

What is their risk of kidney failure at 2 years? At 5 years?

KFRE
2 year 0.5%
5 year 1.2%

- 45-year old man
- GFR 45
- ACR 400

What is their risk of kidney failure at 2 years? At 5 years?

KFRE
2 year 7%
5 year 20%

- 78-year old man
- GFR 25
- ACR 2

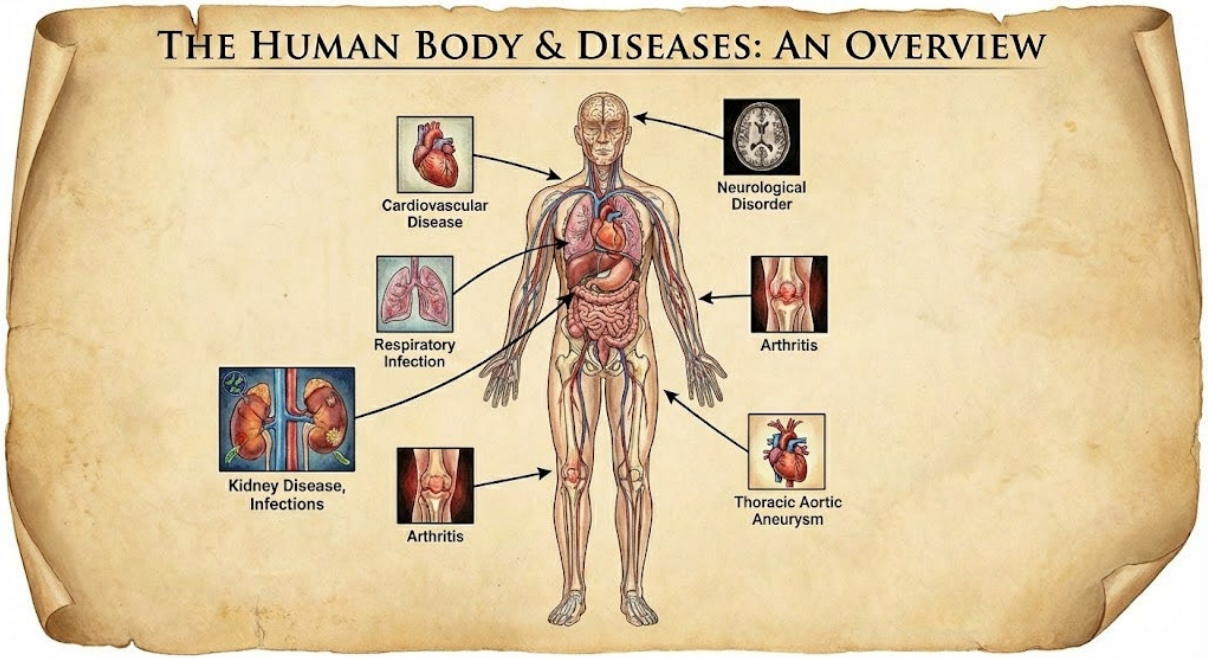
What is their risk of kidney failure at 2 years? At 5 years?

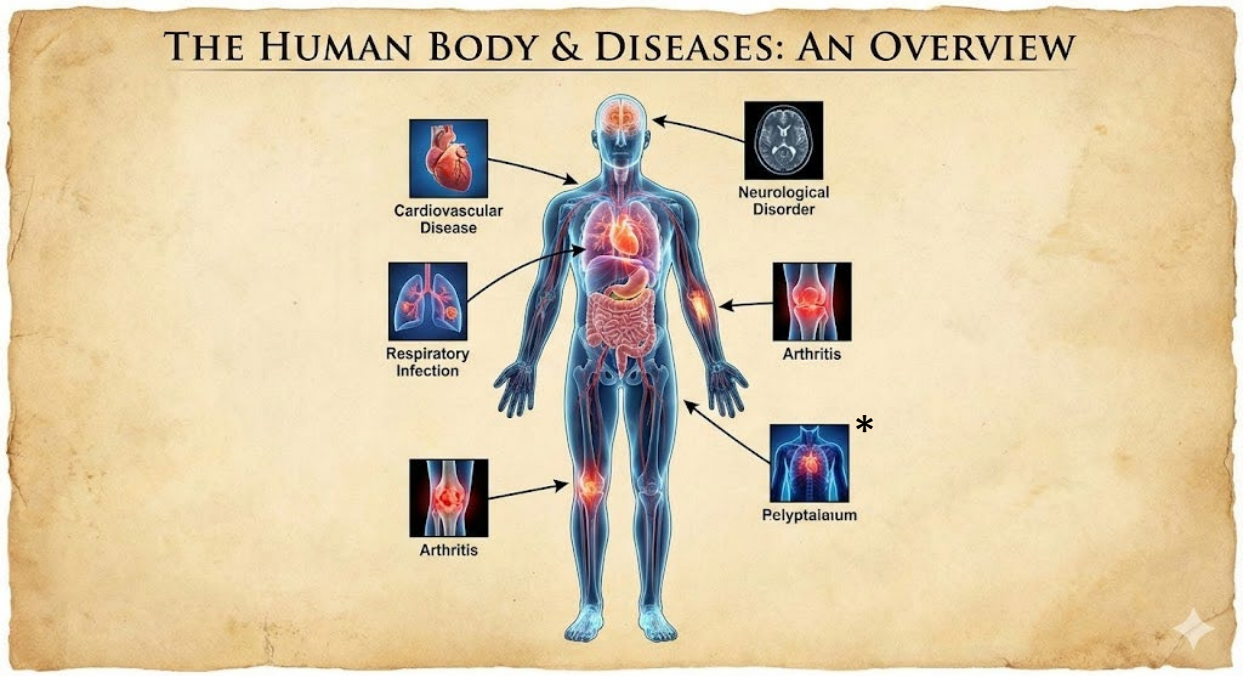
KFRE
2 year 2.5%
5 year 7.8%

Should KFRE be used to decide referral to nephrology?

- KFRE was meant to show risk of dialysis in 2 and 5 years – not to decide nephrology referral!
- KFRE is an estimate at a population level, individual patient trajectories might be different
- KFRE is agnostic of diagnosis – but mostly vascular disease, diabetes
- Diagnosis of CKD will be important for specific management (eg glomerulonephritis, PKD)

As a primary care provider, it’s not just about kidneys





** AI/LLM hallucinated condition*

But there’s more

- Vaccinations
- Screening for cancer
- Guidelines from different societies
- Seasonal flu
- EMR clicking
- ..
- ….
- ……

Information Overload

We are nephrologists – not dialysis-ologists

Just-in-time referrals leads to …suboptimal starts

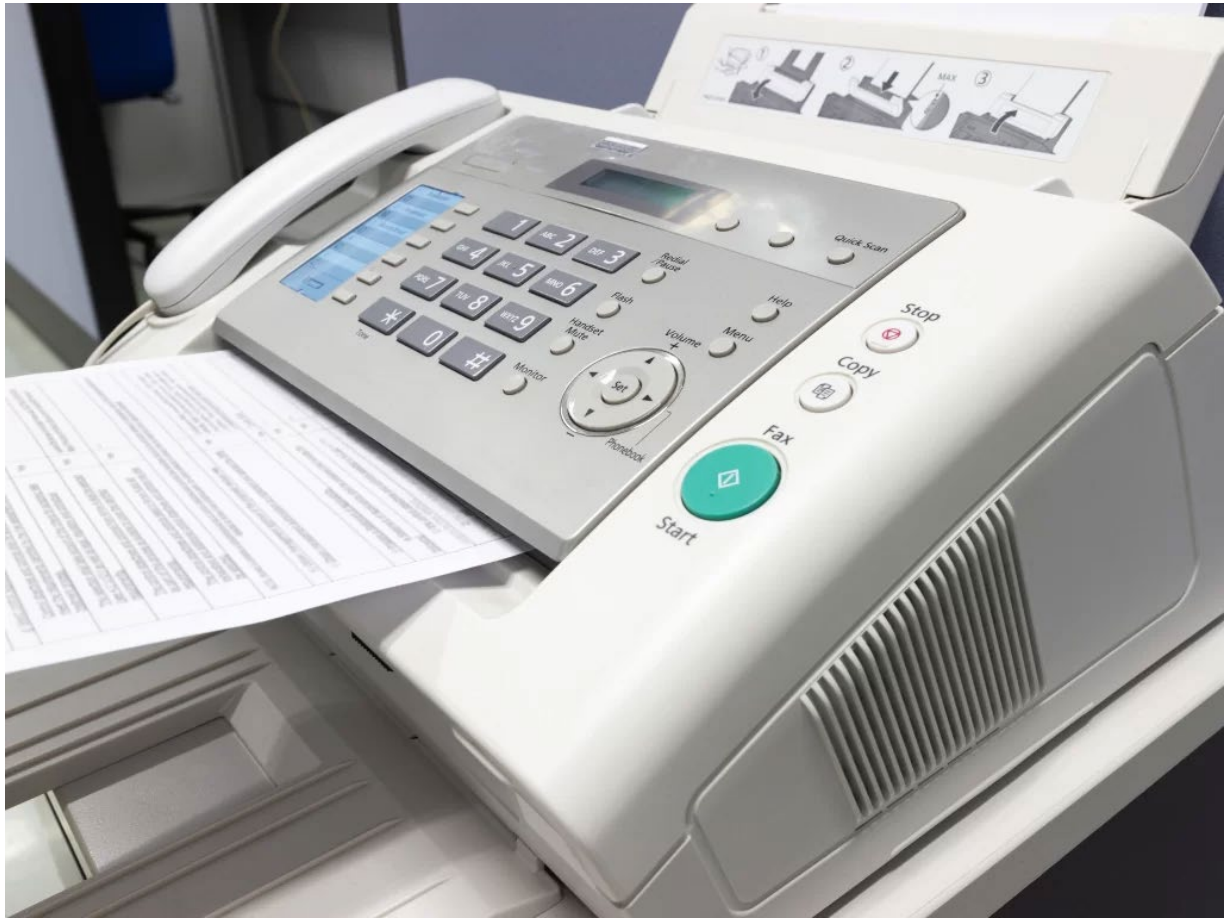
Risk Factors for Suboptimal Dialysis Initiation
A Prospective Cohort Study

Amber O. Molnar,[1,2,3] K. Scott Brimble,[1] Sarah E. Bota,[3,4] Yuguang Kang,[3,4] J.P. Harmon,[5] Pierre A. Brown,[6] Samuel A. Silver,[7] and Ayub Akbari[6]

As kidneys fail, not just about dialysis
- There is preemptive transplant
- Not all patients may want to have dialysis

Even for dialysis, there are options apart from being hooked up to the dialysis machine 3 x week
- Patients can do home dialysis
- They can do dialysis with an AV Fistula (rather than a catheter)

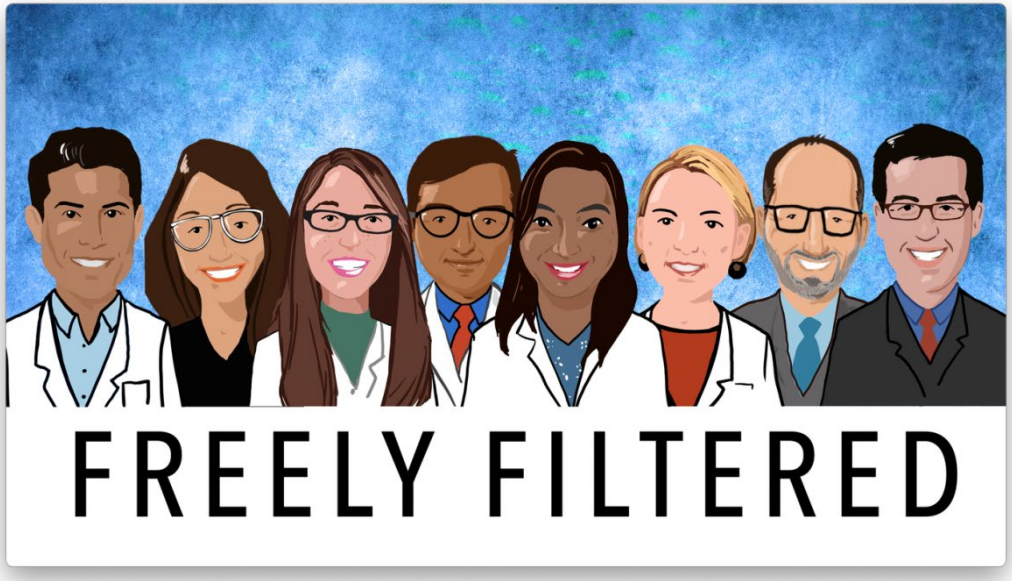
Send us your referrals!



- CKD
- Hematuria, Proteinuria
- Hypertension
- Kidney stones
- Electrolytes

Thank You!

- @hswapnil.medsky.social
- shiremath@toh.ca



My opponent

Formidable debater

#ScottDisagrees

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Rebuttals