Let us build a strong team

Patient

Primary Care Provider

Nephrologist

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Scope of the problem

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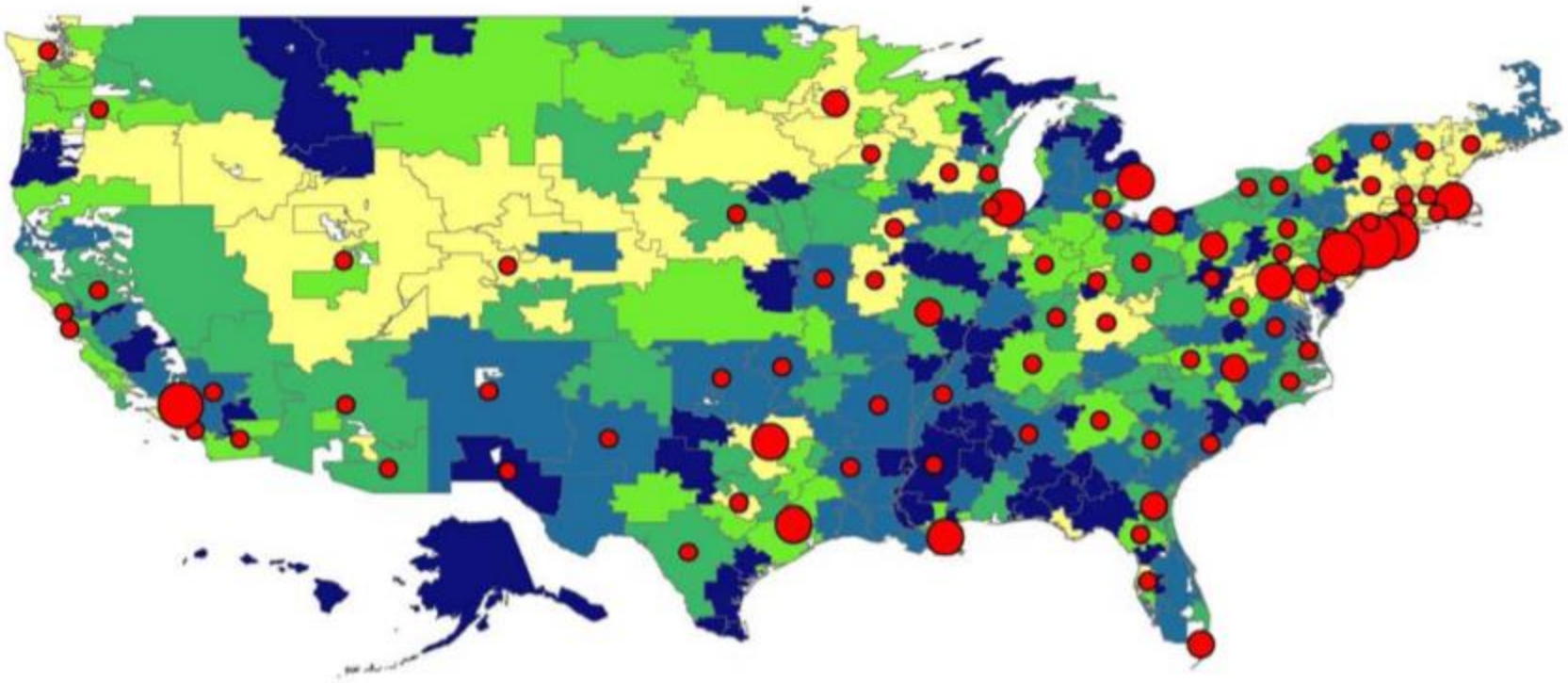
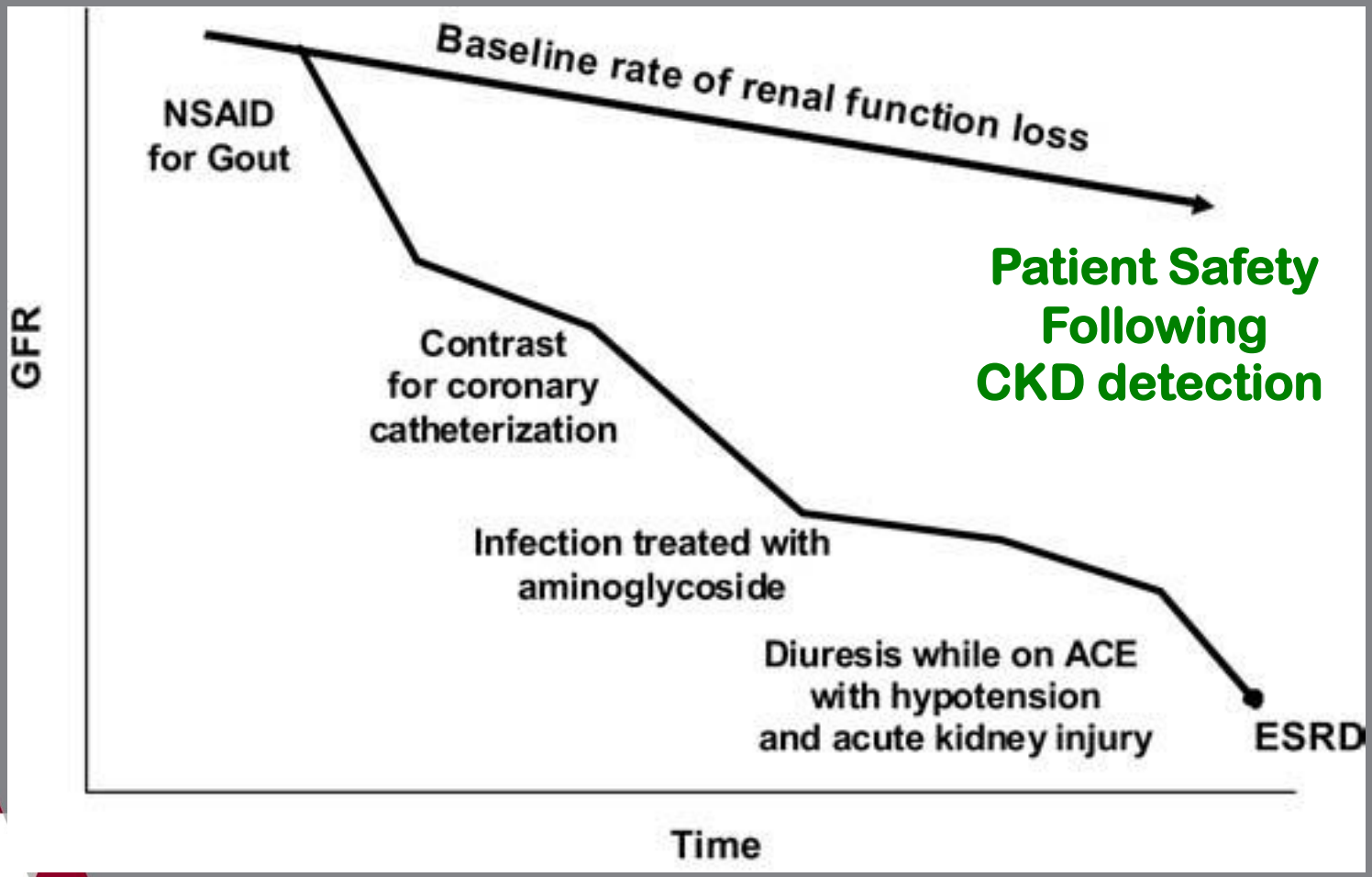
Exhibit 4. Geographical Distribution of Nephrology Fellowship Programs and ESRD Patients per Nephrologist by HRR, 2011



Who is in the best position for managing patients with chronic kidney disease?

You (primary care providers) are the first and the best line of defense in the management of patients with chronic kidney disease

Impact of primary care CKD detection with a patient safety approach



Am J Kidney Dis 2009,53:681-668

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Objectives

1. Who do I refer to nephrology?
2. Do I call my nephrology or urology friend?
3. Management of hypertension in patients with chronic kidney disease
4. Principals of diuretic dosing
5. How to overcome diuretic response

Other that CKD are there other reasons to refer a patient to a nephrologist?

Who is at a risk of worsening renal function and mortality?

eGFR: 80 ml/min
Albumin creatinine ratio: 680 mg/g

eGFR: 32 ml/min
Albumin creatinine ratio: 15 mg/g

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Risk OF PROGRESSIVE CKD

KDIGO

Progessive CKD				
	ACR <10	ACR 10-29	ACR 30-299	ACR>300
eGFR>105	Ref	Ref	0.4	3.0
eGFR 90-105	Ref	Ref	0.9	3.3
eGFR 75-90	Ref	Ref	1.9	5.0
eGFR 60-75	Ref	Ref	3.2	8.1
eGFR 45-60	3.1	4.0	9.4	57
eGFR 30-45	3.0	19	15	22
eGFR 15-30	4.0	12	21	7.7

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Risk of CARDIOVASCULAR, and ALL CAUSE MORTALITY

KDIGO

Cardiovascular mortality

	ACR <10	ACR 10-29	ACR 30-299	ACR>300
eGFR>105	0.9	1.3	2.3	2.1
eGFR 90-105	Ref	1.5	1.7	3.7
eGFR 75-90	1	1.3	1.6	3.7
eGFR 60-75	1.1	1.4	2.0	[illegible]
eGFR 45-60	1.3	2.2	2.8	4.3
eGFR 30-45	2.2	2.7	3.4	5.2
eGFR 15-30	[illegible]	7.9	4.8	8.1

All Cause Mortality

	ACR <10	ACR 10-29	ACR 30-299	ACR>300
eGFR>105	1.1	1.5	2.2	5
eGFR 90-105	Ref	1.4	1.5	[illegible]
eGFR 75-90	1	1.3	1.7	2.3
eGFR 60-75	1	1.4	1.8	2.7
eGFR 45-60	1.3	1.7	2.2	3.6
eGFR 30-45	1.9	2.3	3.3	4.9
eGFR 15-30	[illegible]	3.6	4.7	6.6

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Referral to Nephrology for proteinuria

GFR categories (ml/min/ 1.73 m²) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90		Monitor	Refer*
	G2	Mildly decreased	60–89		Monitor	Refer*
	G3a	Mildly to moderately decreased	45–59	Monitor	Monitor	Refer
	G3b	Moderately to severely decreased	30–44	Monitor	Monitor	Refer
	G4	Severely decreased	15–29	Refer*	Refer*	Refer
	G5	Kidney failure	<15	Refer	Refer	Refer

Figure 21 | Referral decision making by GFR and albuminuria. *Referring clinicians may wish to discuss with their nephrology service depending on local arrangements regarding monitoring or referring. GFR, glomerular filtration rate. Modified with permission from Macmillan Publishers Ltd: *Kidney International*. Levey AS, de Jong PE, Coresh J, *et al*.[30] The definition, classification, and prognosis of chronic kidney disease: a KDIGO controversies conference report. Kidney Int 2011; 80: 17-28; accessed http://www.nature.com/ki/journal/v80/n1/full/ki2010483a.html

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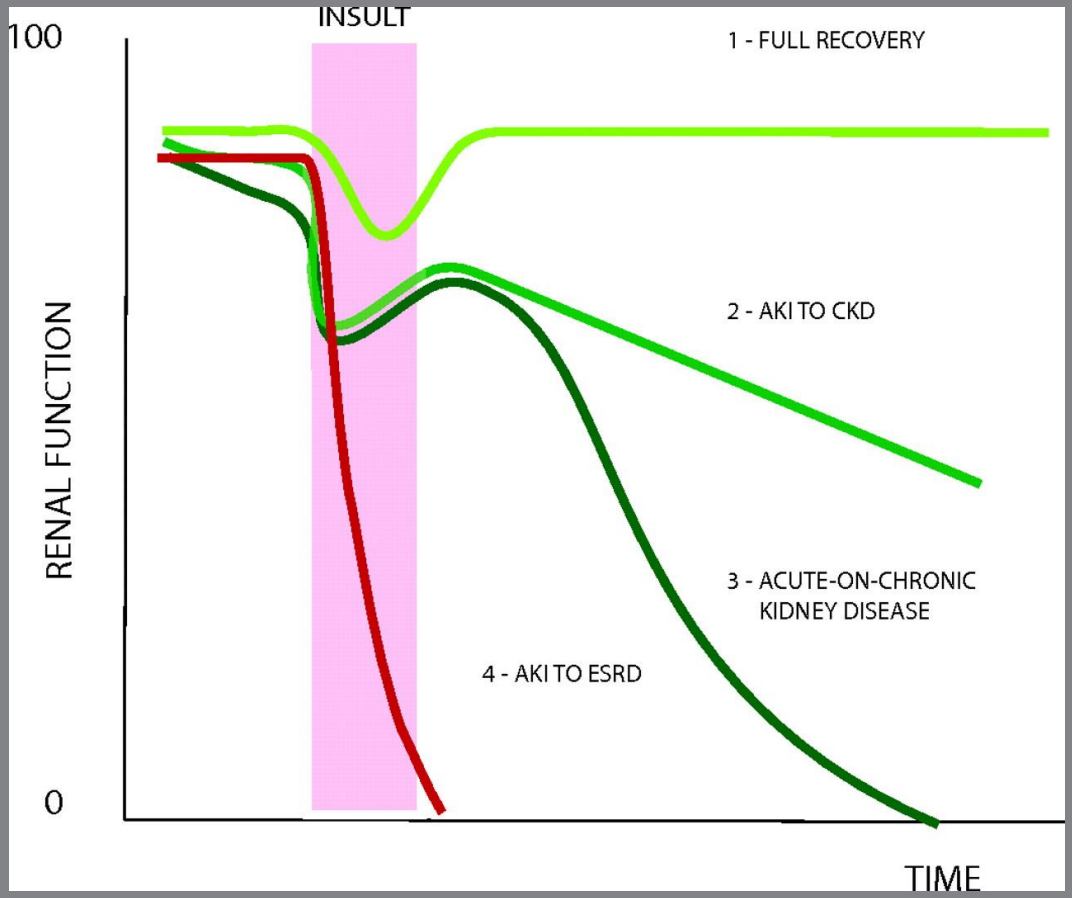
Do I need to consult a nephrologist after discharge if the patient was diagnosed with AKI while in the hospital following?

Natural history of renal function in patients who develop AKI in the hospital



AKI and Nephrology Consultation

- AKI Survivors Following Discharge within 30 days
  - 11.9% Nephrology follow up
  - 29.5% Cardiology follow up
  - 74.5% Primary care visit

- AKI Requiring Dialysis Survivors Following Discharge
  - 33% Nephrology visit within 30 days
  - 48.6% Nephrology visit within 1 year

- Acute Myocardial Infarction Survivors After Discharge
  - 76% Cardiology Consultation within 30 days

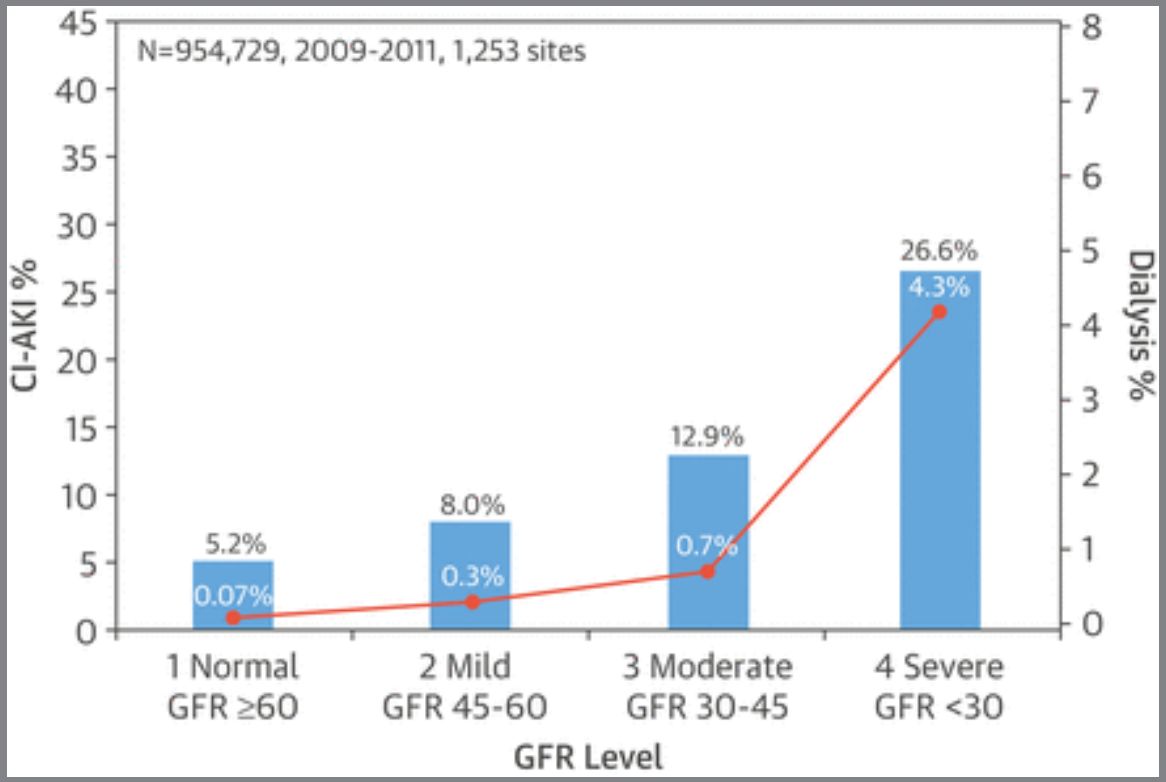
Chawla, LS; Kimmel, PL Acute kidney injury and chronic kidney disease: an integrated clinical syndrome
Kidney Int., 2012 ; 82(5) :516-24

Hypertension

- Any patient on 3 or more medications one of them a diuretic, but still with poorly controlled hypertension.
- Suspicion of hyperaldosteronism or like states; difficult to controlled hypertension, persistent hypokalemia, and or metabolic alkalosis.
- Evidence of unprovoked pulmonary edema in patients with difficult to control hypertension.

Risk stratification for contrast nephropathy

- Incidence in general population is <2%



Journal of the American College of Cardiology
Volume 68, Issue 13, September 2016

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Pre-procedural Clinical Risk Factors for Contrast Induced Nephropathy

- **Modifiable Risk Factors**
  - Contrast volume
  - Hydration status
  - Concomitant nephrotoxic agents
  - Recent contrast administrations
- **Non-modifiable Risk Factors**
  - Diabetes/Chronic kidney disease
  - Shock/hypotension
  - Advanced age (> 75 yrs)
  - Advanced congestive heart failure

Klein LW, Cathet Cardiovasc Int 2009; 74: 728-46

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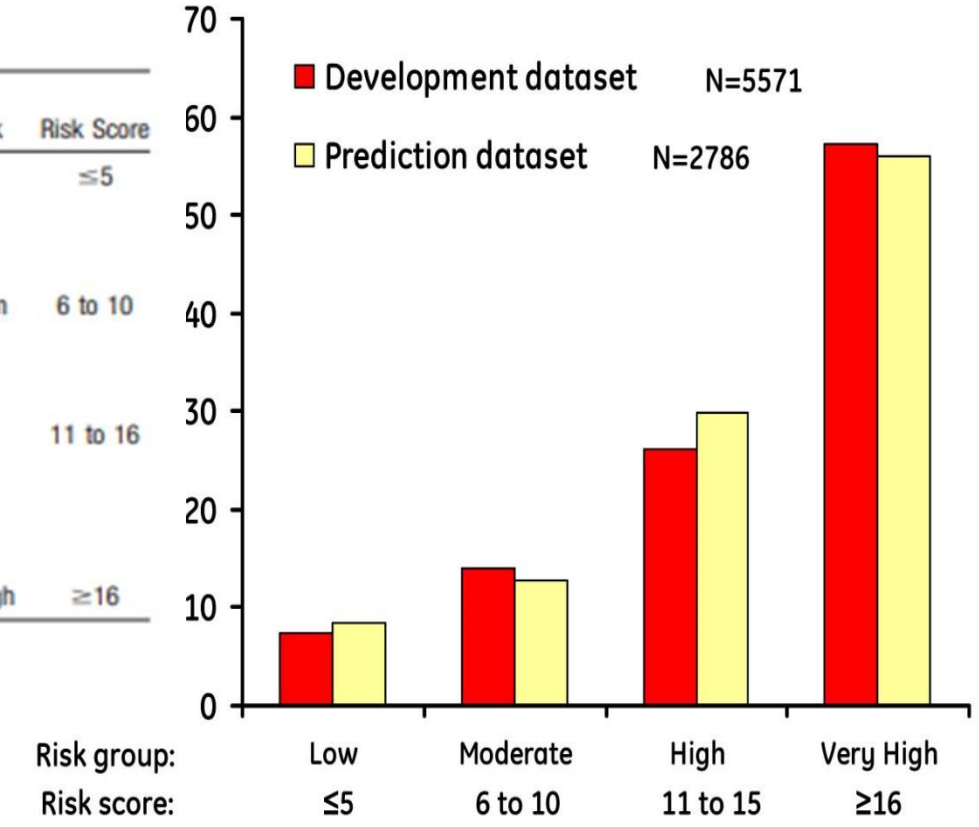
Risk scoring of AKI

A Risk Score for Prediction of CIN

Table 1. Mehran Risk Scores

Risk Factors	Integer Score		Class of Risk	Risk Score
Hypotension	5		Low	≤5
IABP	5			
CHF	5			
Age >75 y	4		Medium	6 to 10
Anemia	3	SUM		
Diabetes	3	→		
Contrast media volume	1 for each 100 cc^3		High	11 to 16
eGFR <20 mL/min/1.73 m^2	6			
eGFR 20–40 mL/min/1.73 m^2	4			
eGFR 40–60 mL/min/1.73 m^2	2		Very high	≥16



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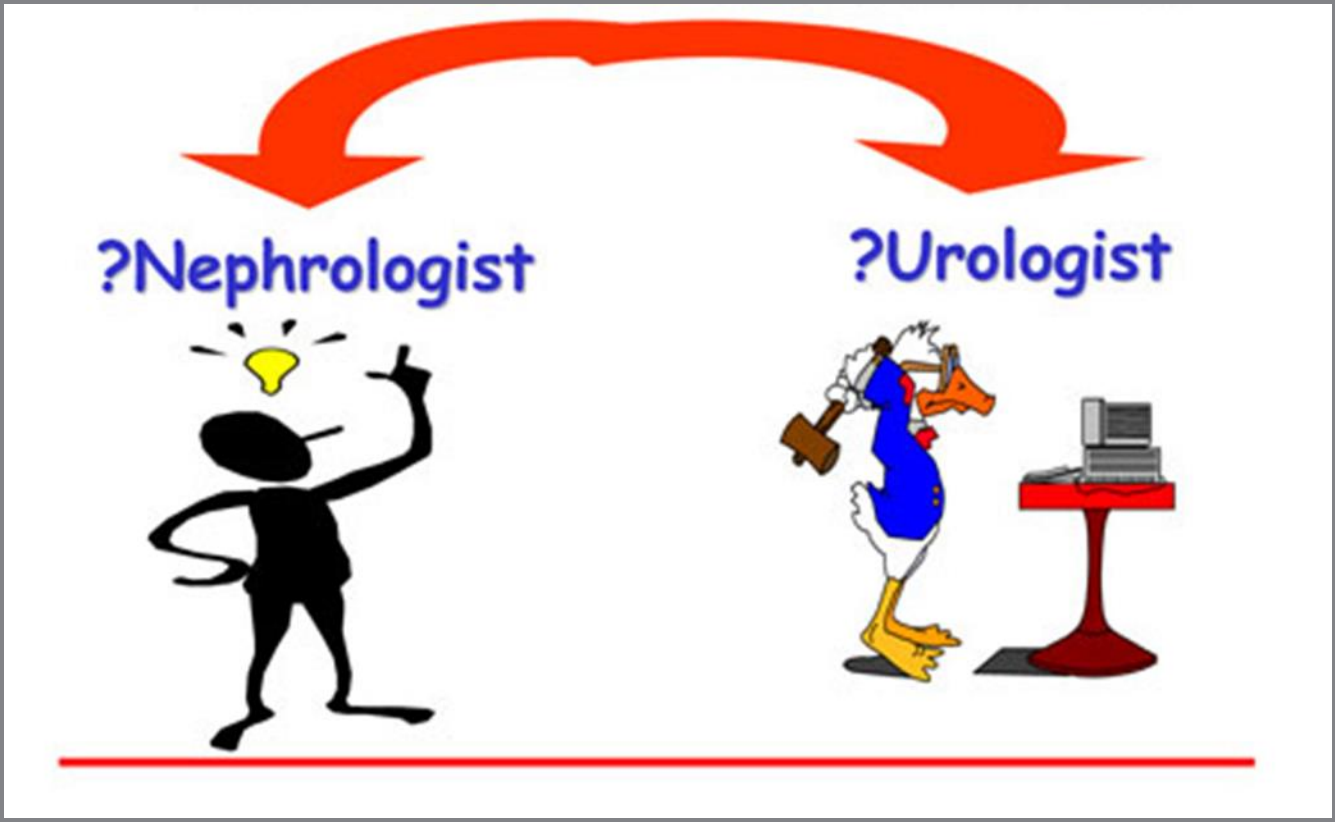
Nephrology or Urology



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Urology or Nephrology

- Hematuria
- Nephrolithiasis
- Recurrent UTI
- Structural lesions in the kidney

Hematuria: who do I refer to?

- **Nephrology**
  - < 50 years
  - Persistent hematuria
  - Rapid decline in renal function
  - History of autoimmune disease
  - Proteinuria
  - Gamily history of glomerular diseases
- **Urology**
  - > 50 years
  - History of kidney stones
  - Exposure to benzenes
  - History of smoking
  - Blood clots

Hematuria: what workup do I order?

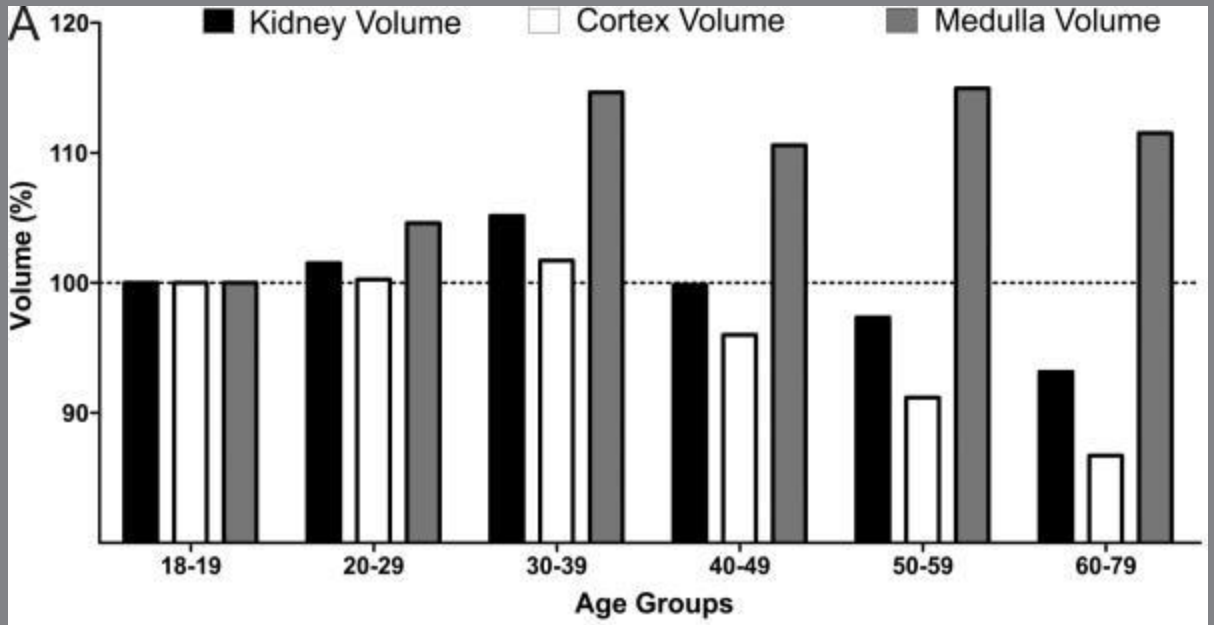
- Renal ultrasound
- Urine protein creatinine ratio
- CBC
- Urinalysis and microscopy
- Pregnancy

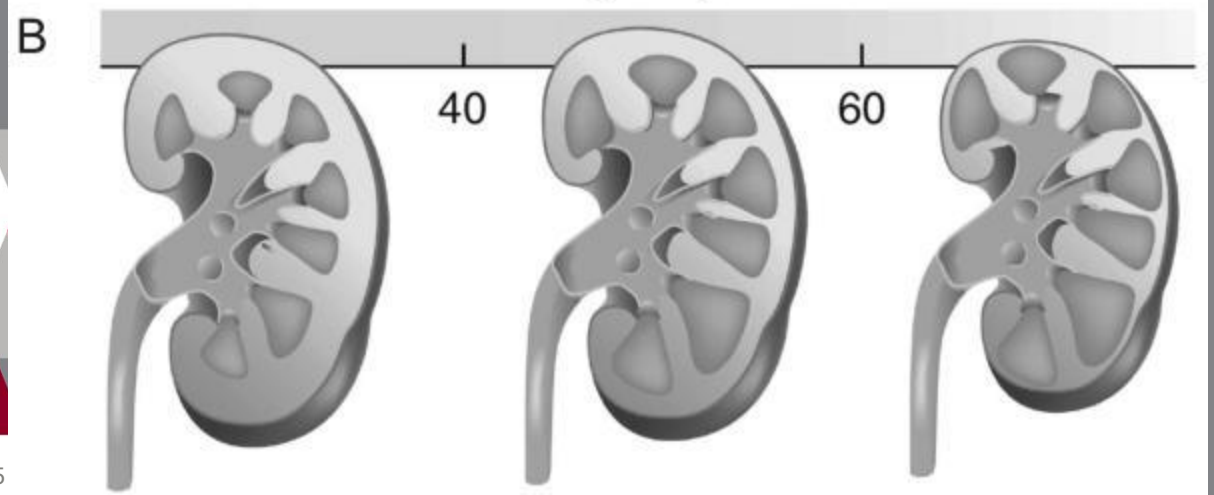
Kidney stones: who do I refer to?

- **Nephrology**
  - **Evaluation and prevention**
  - Recurrent kidney stones
- **Urology**
  - **Treatment**
  - Management of acute episode of kidney stone

Abnormal radiology findings

Understanding age related changes in the kidney





Adv Chronic Kidney Dis. 2016 Jan; 23(1): 19–28

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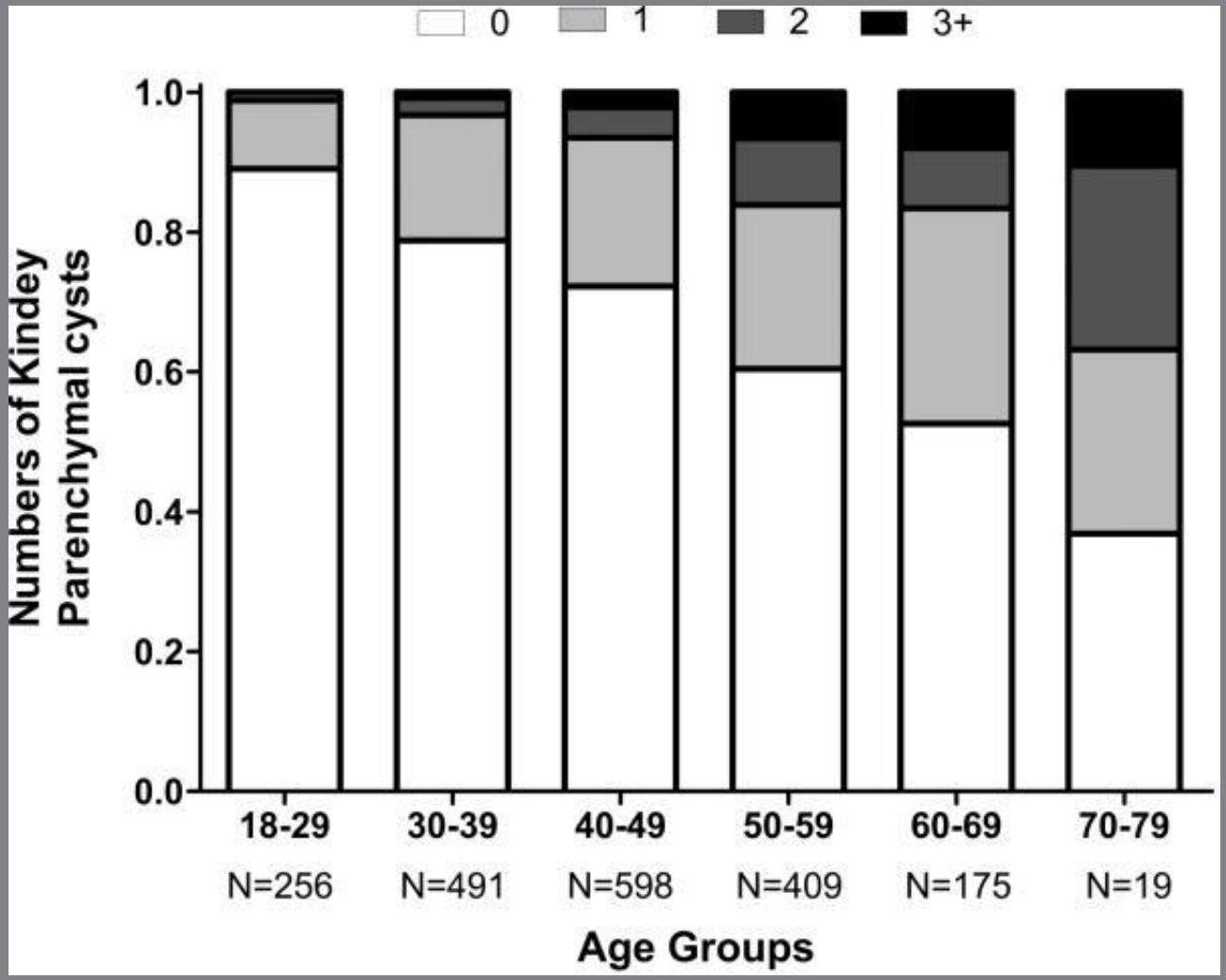
What do I do if I find a renal cyst?



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Cysts : who do I refer to?

- **Nephrology**

- Multiple renal cysts in both kidneys
- Cysts with decline in kidney function

- **Urology**

- Complex cysts
- Mass in the kidney
- Cyst with blood
- Painful cysts.

Guidelines for managing Hypertension

- 2003: The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure
- 2012: The National Kidney Foundation
- 2012: Kidney Disease Improving Global Outcome
- 2013: American Society of Hypertension and International Society of Hypertension
- 2013: JNC 8
- 2017: The American College of Cardiology/American Heart Association

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Population	JNC 8	ACC/AHA	NKF	KDIGO
Age > 60 years	<150/90	<130/80	NA	
Age < 60 years	<140/90	<130/80	NA	
Diabetics	<140/90	<130/80	NA	
With CKD	<140/90	<130/80	<130/80	<140/90
With CVD	<140/90	<130/80	NA	
Urine Albumin > 300 mg/24 hrs				<130/80

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Sprint Trial

SPRINT: Population

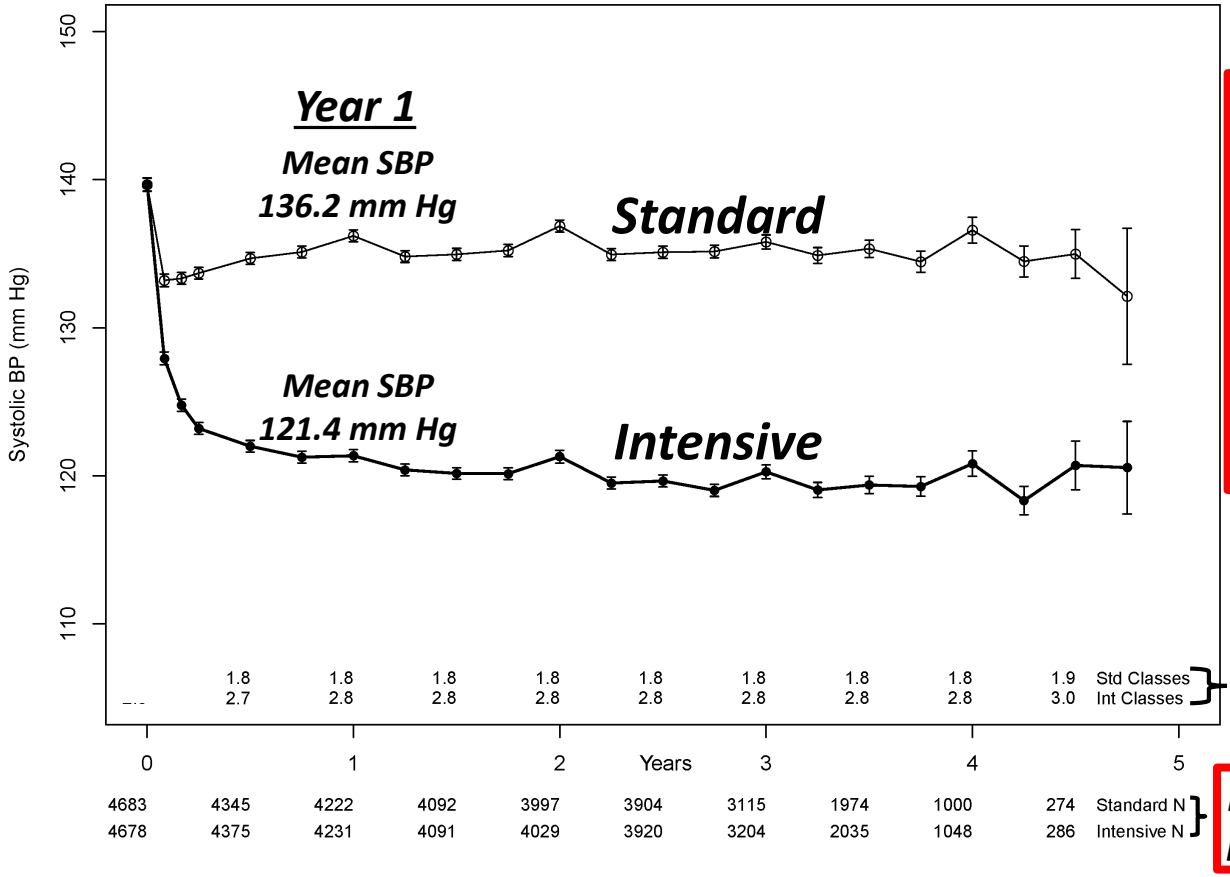
- Aged 50 years and older
- • Systolic blood pressure ≥ 130 mm Hg and at least one other cardiovascular risk factor:
- – Presence of clinical or subclinical cardiovascular disease other than stroke
- – Estimated glomerular filtration rate between 20-59 mL/min/1.73 m2
- – A Framingham 10-year cardiovascular risk score ≥ 15%
- – Age ≥ 75 years

SPRINT: Interventions

- In the intensive BP (< 120 mm Hg) arm, additional pills were “required” if SBP ≥ 120 mm Hg.

- In the standard BP (< 140 mm Hg) arm, doses were to be down-titrated if SBP < 130 mm Hg at 1 visit, or < 135 mm Hg at 2 consecutive visits!

Systolic BP During Follow-up



Average SBP
(During Follow-up)

Standard: 134.6 mm Hg

Intensive: 121.5 mm Hg

Average number of antihypertensive medications

Number of participants

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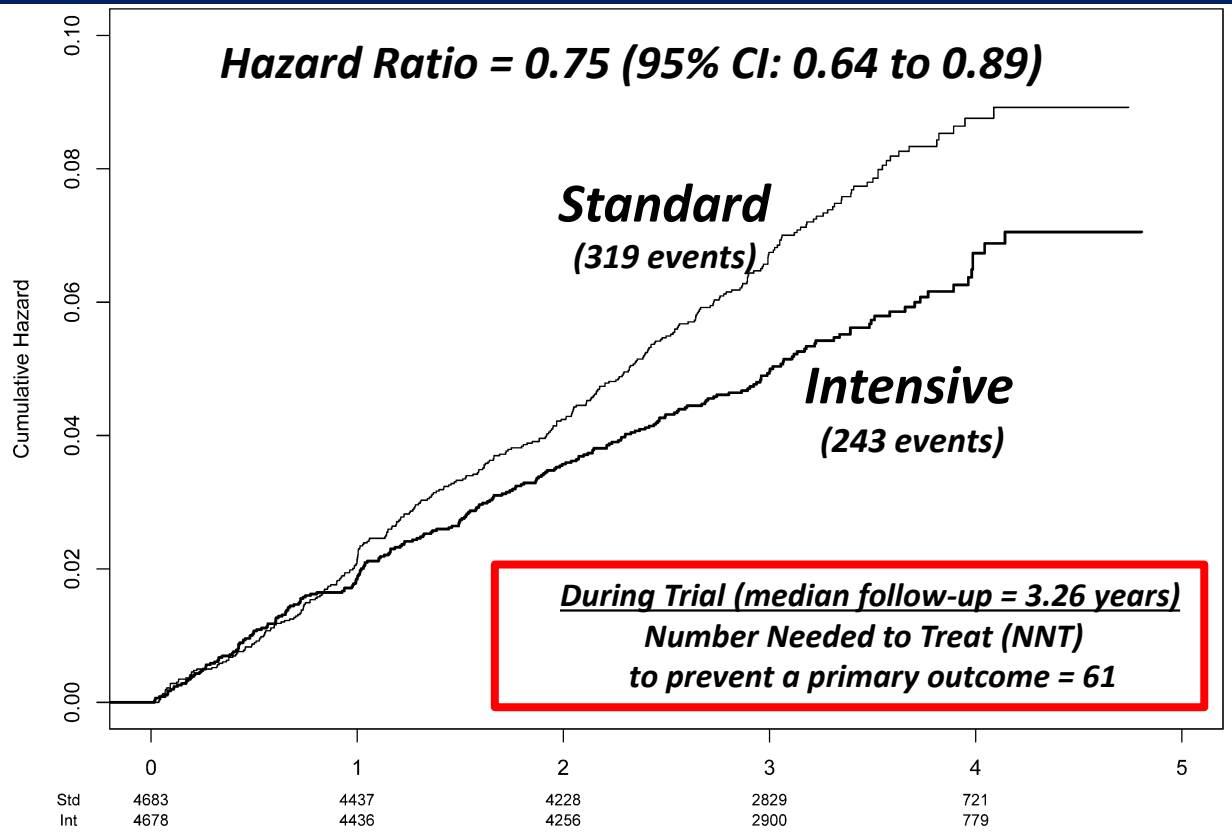
SPRINT Primary Outcome
Cumulative Hazard



SPRINT Systolic Blood Pressure Intervention Trial

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SPRINT Primary Outcome and its Components

Event Rates and Hazard Ratios

	Intensive		Standard			
	No. of Events	Rate, %/year	No. of Events	Rate, %/year	HR (95% CI)	P value
Primary Outcome	243	1.65	319	2.19	0.75 (0.64, 0.89)	<0.001
All MI	97	0.65	116	0.78	0.83 (0.64, 1.09)	0.19
Non-MI ACS	40	0.27	40	0.27	1.00 (0.64, 1.55)	0.99
All Stroke	62	0.41	70	0.47	0.89 (0.63, 1.25)	0.50
All HF	62	0.41	100	0.67	0.62 (0.45, 0.84)	0.002
CVD Death	37	0.25	65	0.43	0.57 (0.38, 0.85)	0.005

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Population	JNC 8	ACC/AHA	NKF	KDIGO
Age > 60 years	Initial Thiazide diuretic or ACE I or ARB or CCB	Initial Thiazide diuretics	NA	
Age < 60 years			NA	
Diabetics		ACE I or ARB	NA	ACE I or ARB
With CKD	ACE I or ARB	ACE I or ARB	Thiazide	ACE I or ARB
With CVD			NA	
Urine Albumin > 30 mg/24 hrs				ACE I or ARB

Diuretic Handling “Art and science”

Case

- 55 yr old male with history of HTN, CHF, DM and CKD stage 3 (GFR 45 ml/min). BP 156/82 mm Hg, 1+ lower ext edema. He is currently on lisinopril 40 mg

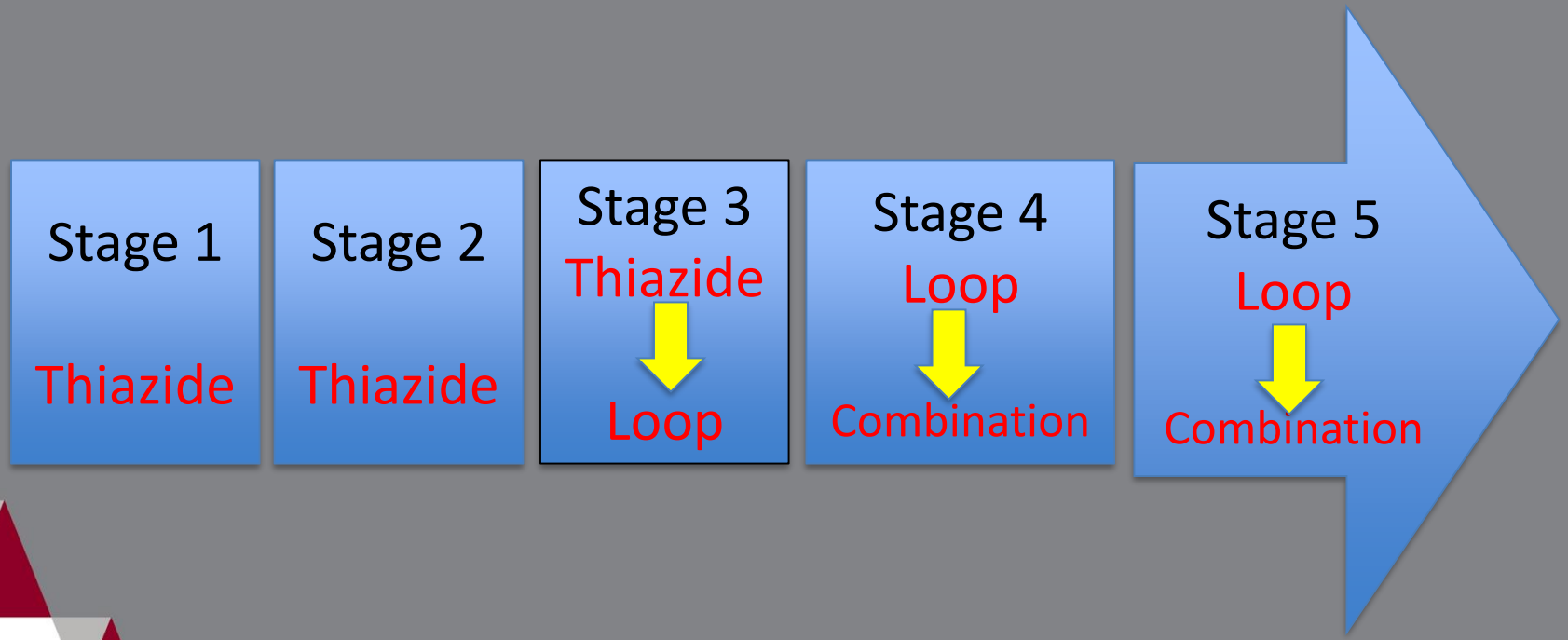
- How do you manage his HTN and edema?

- JNC 8 recommends Thiazide diuretics as the initial choice of drug for patients with diabetes and chronic kidney disease .
- HCTZ :
  - Hypertension: 12.5 to 25 mg once daily.
  - Edema: 25 to 100 mg in 1 or 2 divided doses.
- Chlorthalidone:
  - Hypertension: 25 to 50 mg once daily.
  - Edema: 50 to 100 mg once daily.

Case

- You start HCTZ 25 mg once daily. You see him after 3 weeks. His BP is 132/74 mm Hg, edema has improved. You follow this patient yearly for the next 3 yrs.
- The patient comes back to seen 2 yrs after his last visit. He is complaining of worsening lower ext edema for the last few months. He is on HCTZ 50 mg once daily. On exam his BP is 140/82 mm Hg, has 2 +pitting edema. Cr is 3.2 mg/dl, GFR 20 ml/min.

Selecting diuretics in patients with CKD



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Salt restriction

- Salt restriction should be continued, and is a critical step in patients on diuretic therapy.

- Salt restriction: 1.5 to 2 gram sodium restriction is the most important step in managing edema.

How to determine compliance?

- Check 24 urine for sodium excretion.

  Important considerations during 24 urine test.
  - Make sure it is an accurate 24 hr urine collection.
  - Total 24 urine creatinine
    - Males: 20-25 mg/kg
    - Females: 15-20 mg/kg.
  - Wait for 5-7 days after starting diuretics or after changing the dose of diuretic.

Interpreting results.

- Total sodium in 24 hour urine collection
  - Greater than 100 meq: The patient is consuming more than 2 grams of sodium per day.
  - Less than 100 meq: Patient is compliant with sodium intake.

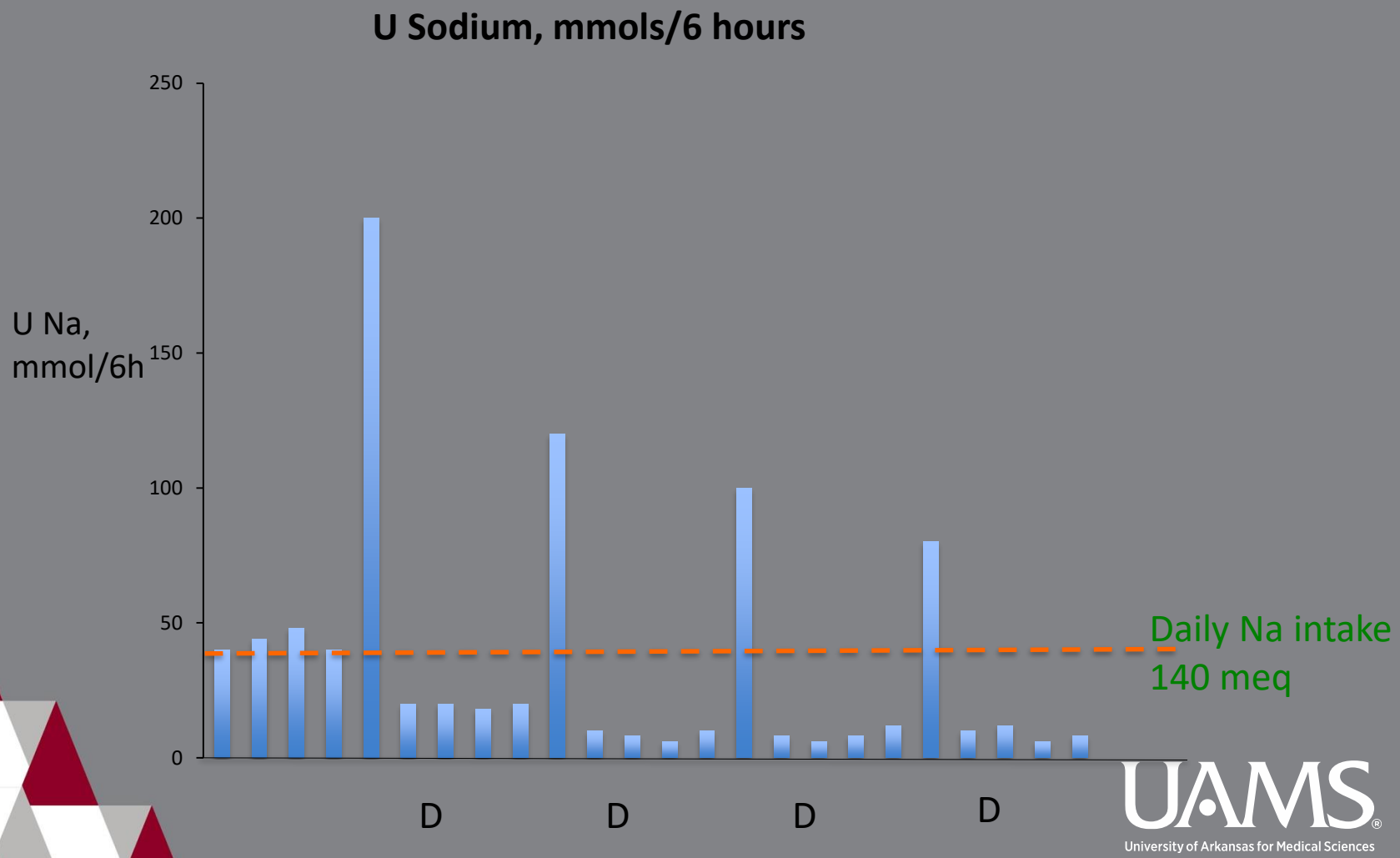
Case

- You stop HCTZ and start the patient on lasix 40 mg once daily. He calls you back in 3 days and tells that the swelling is starting to improve. You see him in clinic after a month and the patient tells you that his LE swelling has been worsening for the last 2 weeks.

Frequency of dosing

- Half life of diuretics is relative short.
- Diuretic concentration is below the therapeutic range for a significant period of the day.
- During this period there is increased Na reabsorption.

Effect of once daily diuretic dosing



Diuretics

	Onset of action	Peak effect	Duration	Half life	Oral Bioavailability %
Furosemide	30 to 60 min	1-2 hr	6 hr	0.5 to 2 hr	20-90
Torsemide	1 hr	1-2 hr	~10 hr	3-4 hr	80-100
Bumetanide	30 to 60 min	1-2 hr	6 hr	0.5 to 2 hr	80-100
Metolazone	1 hr	6-8 hr	24 hr		70
HCTZ	2 hr	4-6 hr	8-12 hr	3 hr	75

How to manage post diuretic Na retention?

- Strict salt restriction
- Increase frequency of diuretic dosing to every 8 hrs to 12 hrs.
- Switch to longer acting loop diuretic like torsemide.

- Acute decompensated heart failure: Consider continuous lasix infusion in patient admitted to the hospital with acute decompensated heart failure.

N Engl J Med 2011; 364:797-805

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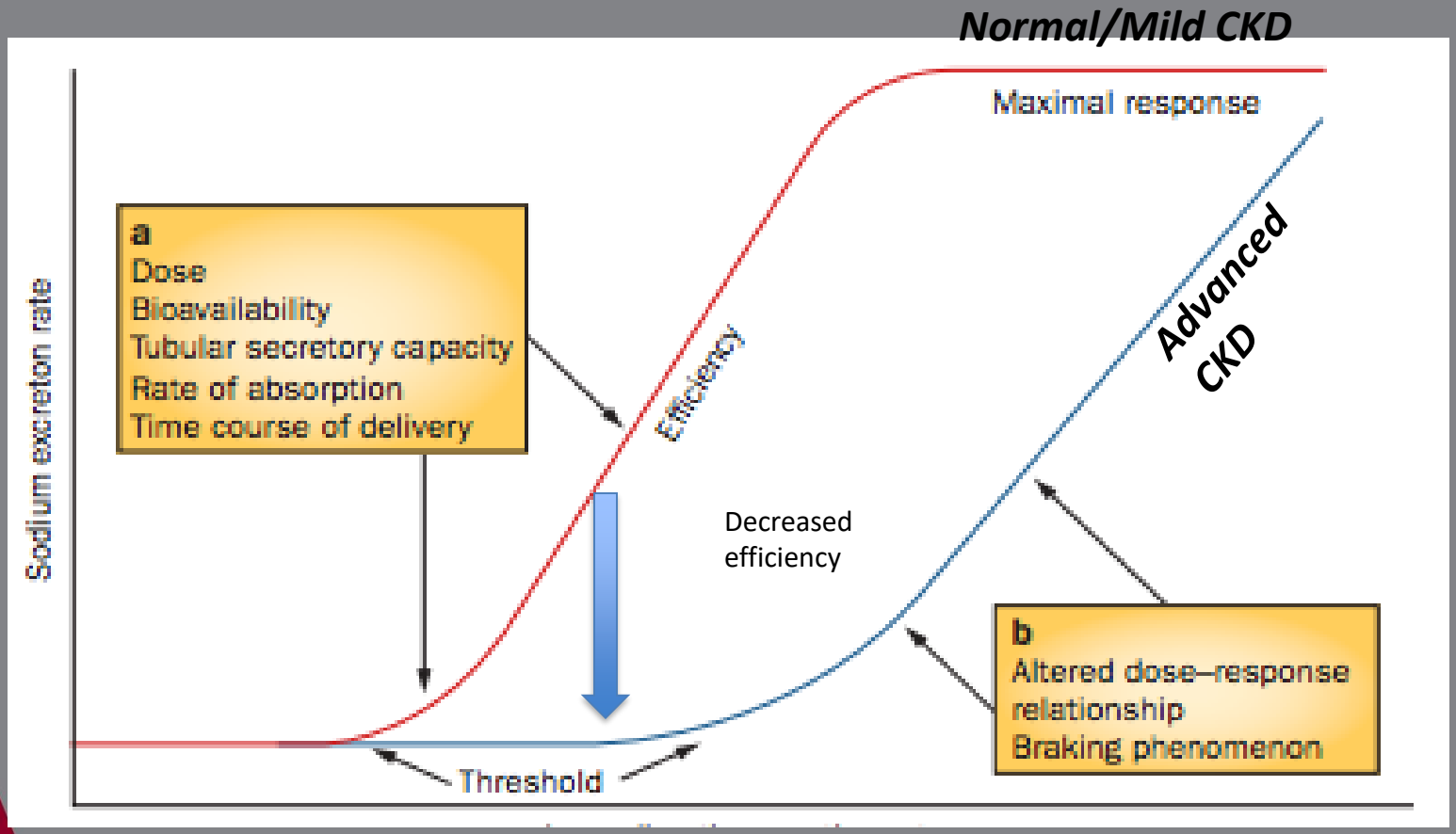
Case

- You increase frequency of lasix to 40 mg twice daily. Patient call you in 4 days and tells you that that his swelling is not improving, you increase lasix to 3 times a day. When you see the patient in clinic in 3 weeks you notice that the swelling has not improved.

Diuretic dosing in CKD

- In patients with CKD there is significant increase in total body volume increasing the volume of distribution (V_d), causing decreased serum concentration of the drug.
- Decreased secretion of the diuretic into the proximal tubule causing decreased drug availability at the site of action.

Diuretic Dose Responsive Curve



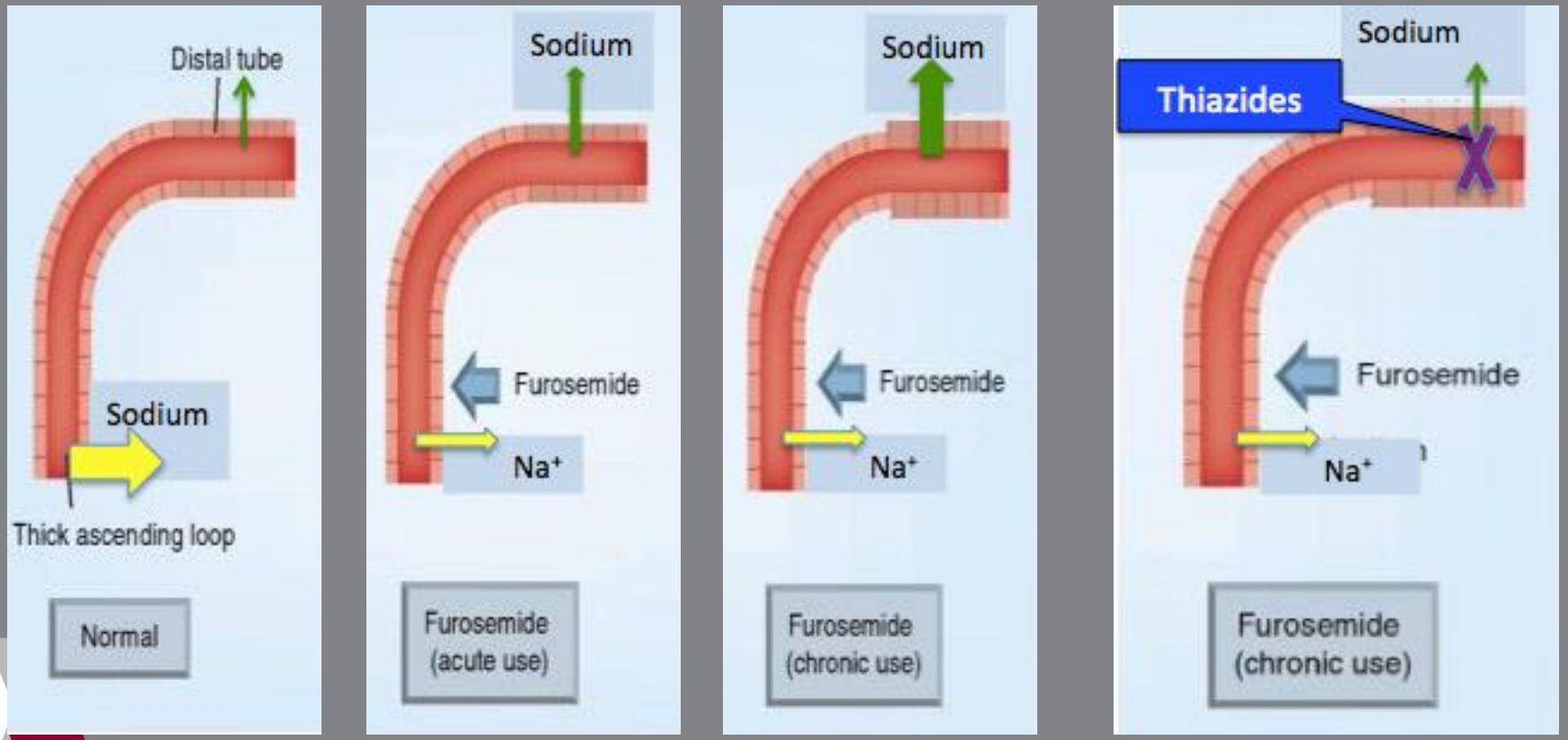
Managing diuretic dosing in CKD

- The diuretic dose that was effective in patient with mild CKD may not be effective in advanced CKD.
- Increasing the frequency of diuretics below the threshold dose is of little or no benefit.
- Double the dose of diuretic till diuresis is achieved or till ceiling dose reached.
- Switch to loop diuretics with high bioavailability: Torasemide and Bumetanide.

Daily ceiling doses for commonly used loop diuretics

	Furosemide/day		Bumetanide/day		Torsemide/day	
	IV (mg)	PO (mg)	IV (mg)	PO (mg)	IV (mg)	PO (mg)
GFR 60 to 30ml/min	80	80-160	2-4	2-4	20-60	20-60
GFR <30ml/min	160	240	8-10	8-10	50-100	50-100
CHF with normal GFR	80-120	160-240	2-3	2-3	20-50	20-50

Braking Phenomenon



Combination therapy

- Combination therapy with loop diuretic and thiazide like drug are synergistic in patients with CHF and advanced CKD.
- Metolazone 2.5 to 10 mg once daily enhances diuresis in furosemide resistance patients.
- Combination therapy should be started under close observation to avoid hypokalemia.

Conclusion

- Please refer any patient you think could benefit from a nephrology consult
- Or call us with any questions.
- Phone: 732-829-6182

QUESTIONS?