Outpatient Prevention and Management of Declining Renal Function

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Disclosure

Relevant Financial Relationships

None

Off-Label/Investigational Uses

None

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Learning Objectives

- To review the different methods of evaluation of kidney function and proteinuria
- To review the definition and epidemiology of chronic kidney disease
- To discuss prevention and management of kidney disease
- To review some common nephrotoxic agents to be aware of.

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Evaluating the kidney function

Estimation of kidney function:

1-Serum Creatinine

2- Serum Cystatin C

Measurement of kidney function:

Iothalamate clearance

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Evaluating the kidney function

Estimation of kidney function:

1-Serum Creatinine

2- Serum Cystatin C

MDRD equation
CKD Epi (creatinine and/or cystatin C)
Cockcroft-Gault Equation
24 h urine Creatinine clearance

Measurement of kidney function:

Iothalamate clearance (radionuclide testing)

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Evaluating the kidney function

Estimation of kidney function:

1-Serum Creatinine

Advantages	Disadvantages
Most frequently used tool Widely available and inexpensive	Affected by muscle mass May be affected by certain medications that affect its secretion (trimethoprim) Non linear relationship to GFR

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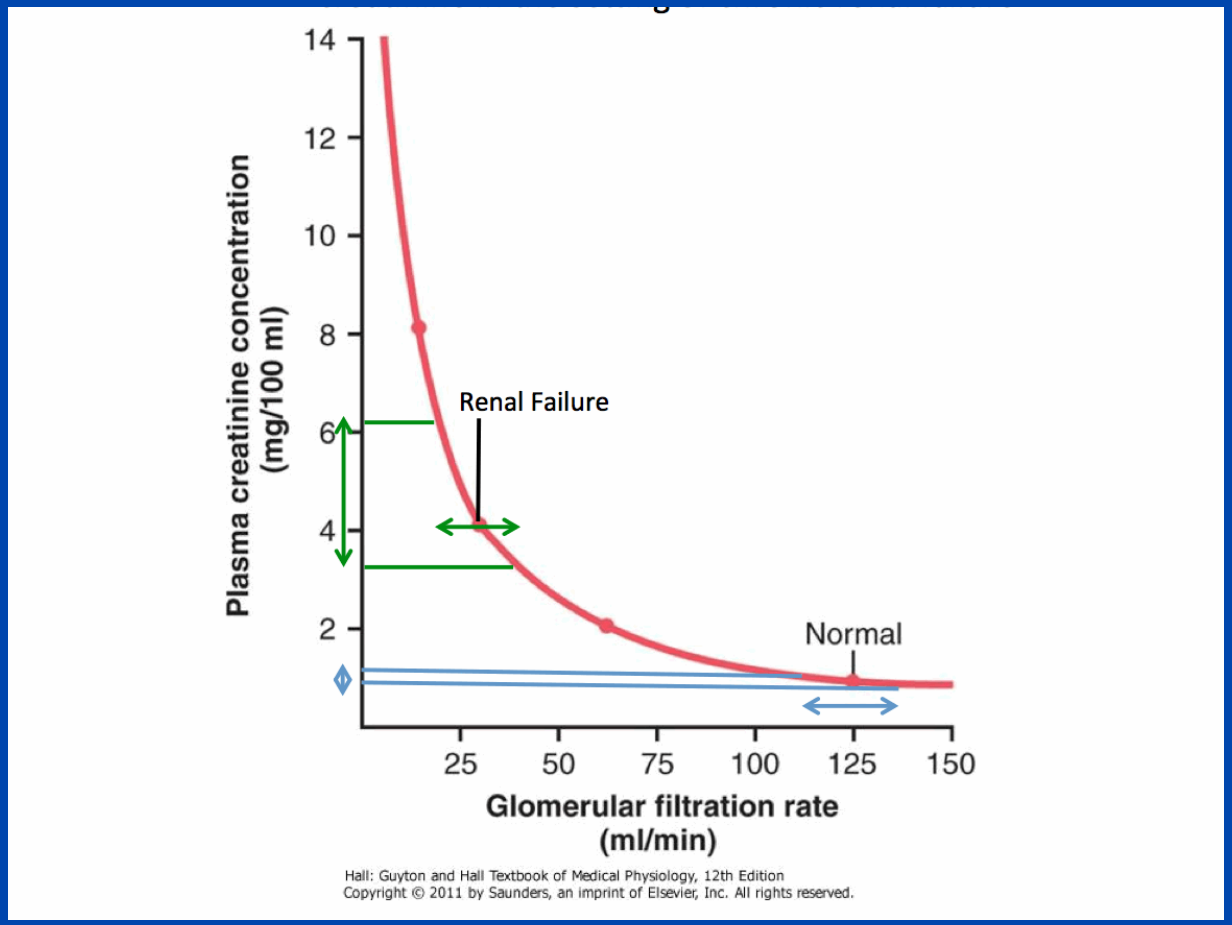
Evaluating the kidney function

- Serum creatinine



Evaluating the kidney function

Estimation of kidney function:

2- Serum Cystatin C

Advantages	Disadvantages
Produced by all nucleated cells and freely filtered by glomeruli. Not affected by muscle mass (helpful in patients with either too much muscles, or in patients who have very low muscle mass: elderly, ESLD, malnourished) May identify small changes in GFR better than creatinine	Less widely available Less widely used and as such less experience using it Levels may be affected by diabetes, thyroid disease, acute inflammation, use of steroid.

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Evaluating the kidney function

Estimation of kidney function:

1-Serum Creatinine

2- Serum Cystatin C

MDRD equation
CKD EPI (creatinine and/or cystatin C)
Cockcroft-Gault Equation
24 h urine Creatinine clearance

I would use CKD EPI estimation with Creatinine

I would use CKD EPI with both Creatinine and Cystatin C in cases with borderline eGFR to confirm CKD

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Evaluating the kidney function

Measurement of kidney function:

Iothalamate clearance:

- Has no role in primary care clinic
- Expensive and not available except in few centers
- Usually reserved for donor evaluation

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Evaluation of proteinuria

- 24 h urine protein and albumin:
  - Normal protein < 150 mg/24 h
  - Normal albumin < 30 mg/24 h
  - Macro-albuminuria > 300 mg/24 h ⟶ Glomerular injury
- Spot urine testing:
  - Urine albumin/creatinine ratio: < 30 mg/g roughly equals 30 mg/24h.
  - Urine albumin: normal < 3 mg/dl
  - Urine protein/creatinine ratio

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Definition of Chronic Kidney Disease:

Kidney Disease: Improving Global Outcomes (KDIGO) 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease

- CKD is defined as abnormalities of kidney structure or function, present for >3 months.

Criteria for CKD (either of the following present for > 3 months)

Markers of kidney damage (one or more)	Albuminuria (AER ≥30 mg/24 hours; ACR ≥30 mg/g [≥3 mg/mmol]) Urine sediment abnormalities Electrolyte and other abnormalities due to tubular disorders Abnormalities detected by histology Structural abnormalities detected by imaging History of kidney transplantation
Decreased GFR	GFR <60 ml/min/1.73 m^2 (GFR categories G3a–G5)

Abbreviations: CKD, chronic kidney disease; GFR, glomerular filtration rate.

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Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012

GFR categories (ml/min per 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			
	G2	Mildly decreased	60–89			
	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.

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Prevalence of CKD stages 1-4

Prevalence of CKD by CKD Stage and Year, 1988-1994 to 2015-2016
National Health and Nutrition Examination Survey

1988–199

CKD Is Common Among US Adults

Fast Stats

- 15% of US adults—37 million people—are estimated to have CKD.*
- Most (9 in 10) adults with CKD do not know they have it.
- 1 in 2 people with very low kidney function who are not on dialysis do not know they have CKD.

CKD Stage

Centers for Disease Control and Prevention. Chronic Kidney Disease Surveillance System—United States. website. https://nccd.cdc.gov/ckd

https://www.cdc.gov/kidneydisease/publications-resources/2019-national-facts.html

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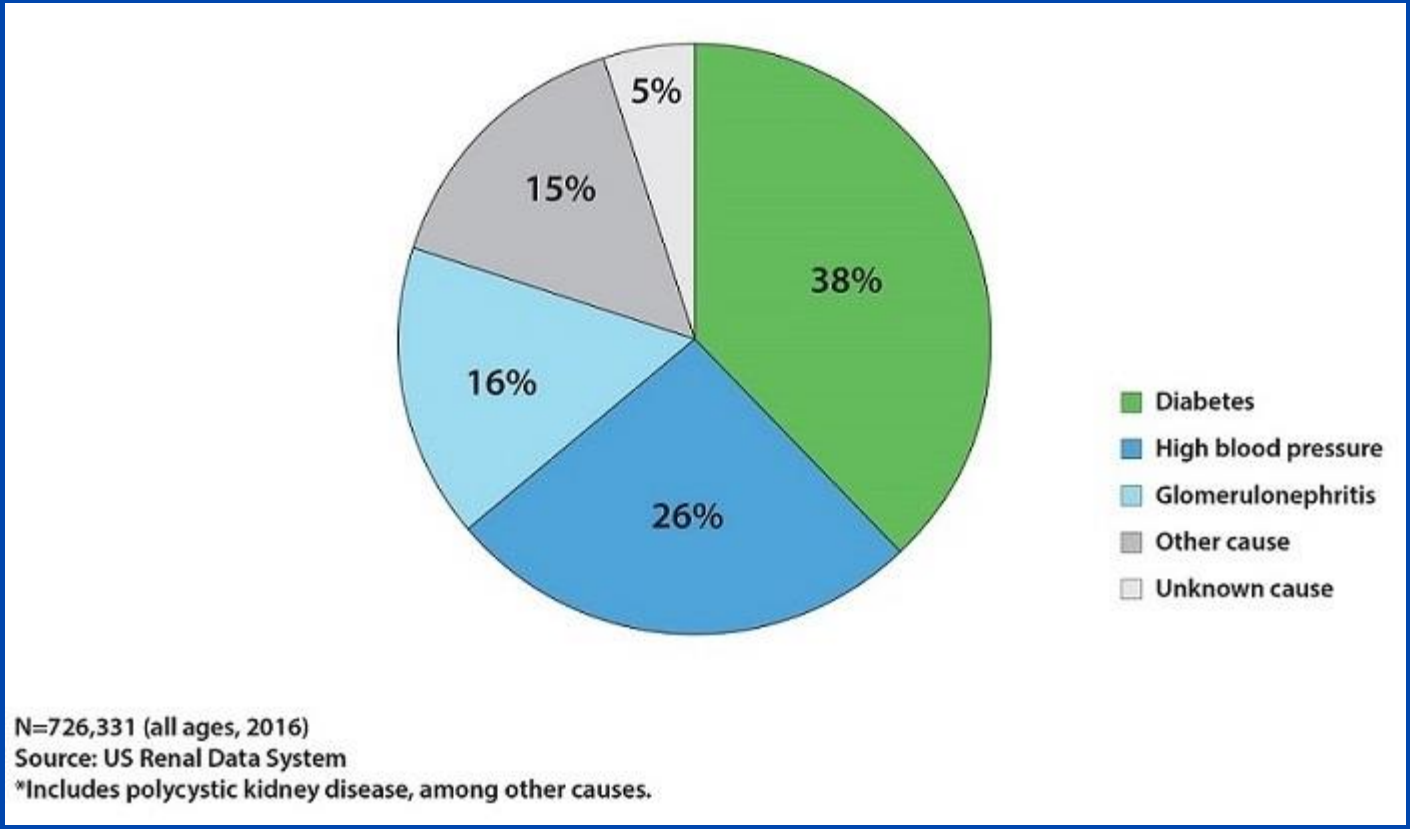
Causes of chronic kidney disease



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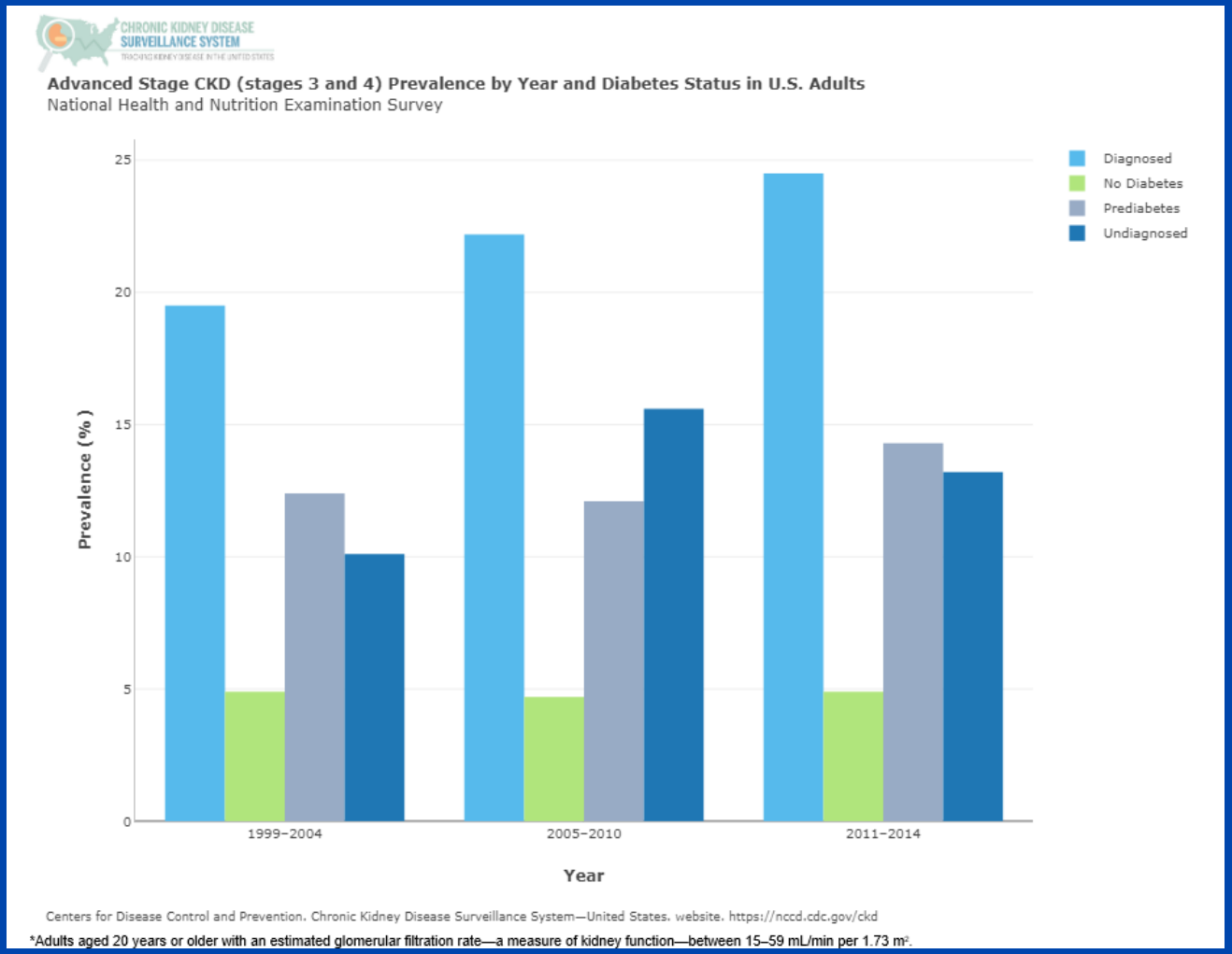
CKD risk factors: Diabetes Mellitus



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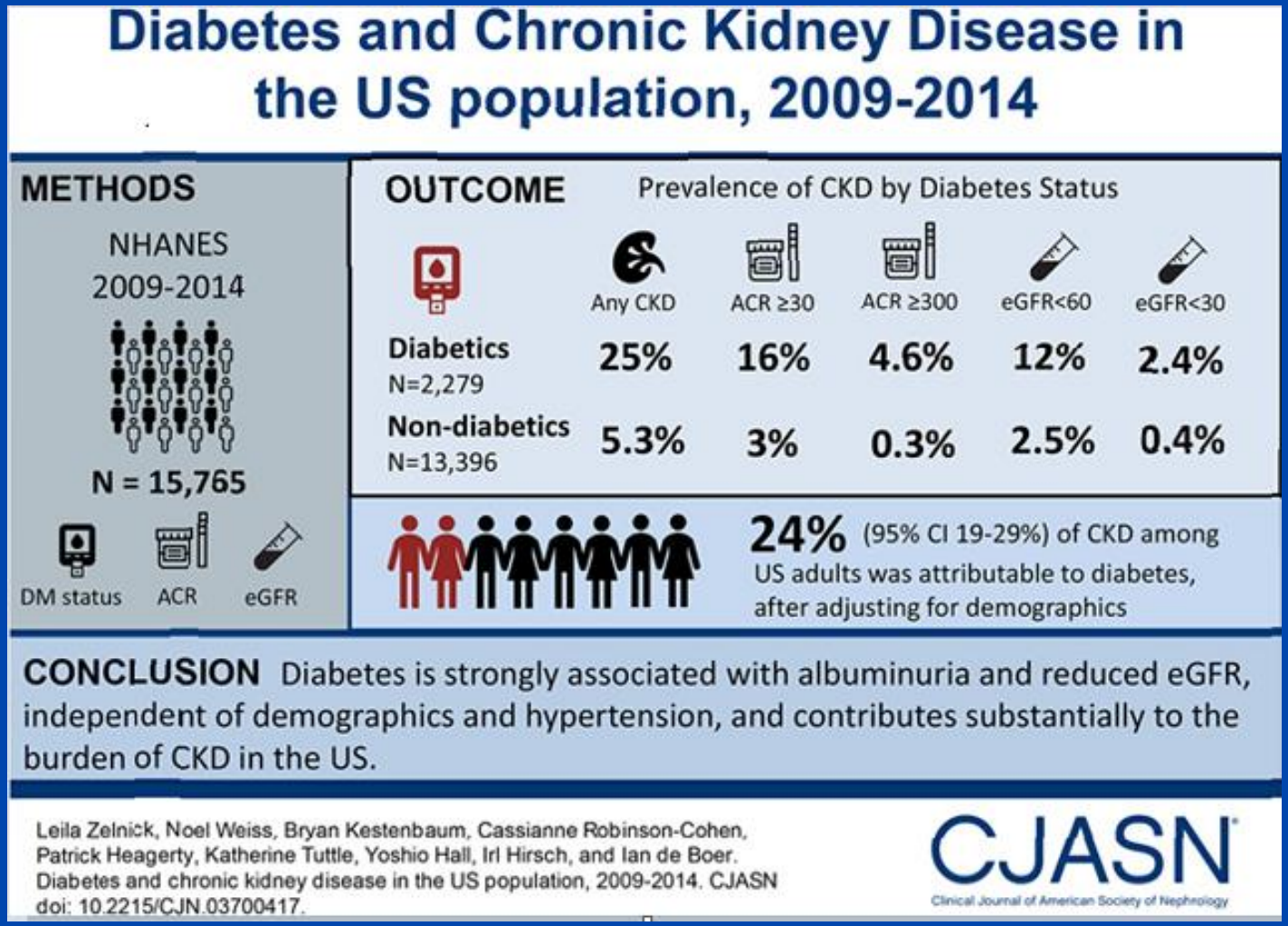

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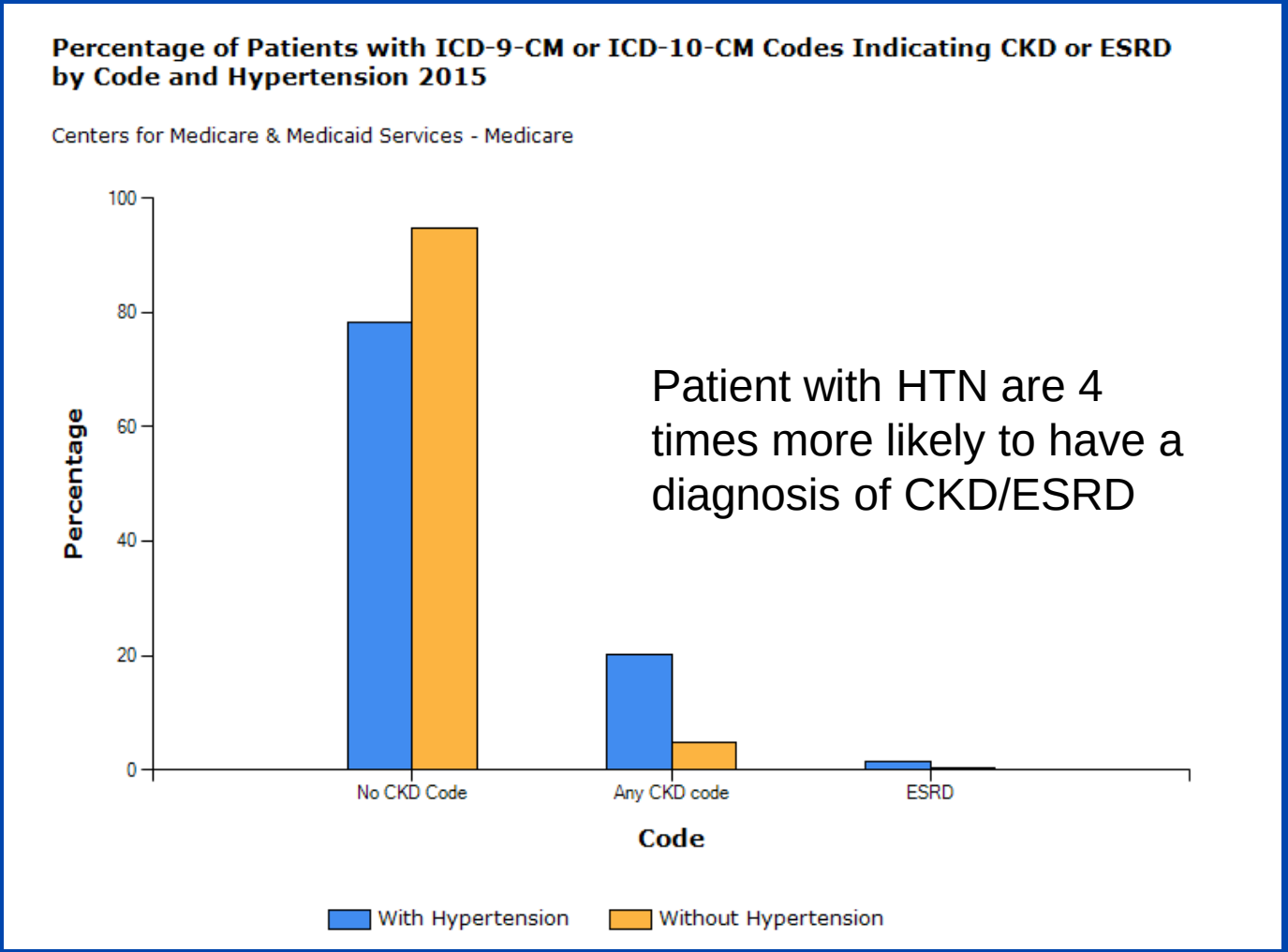
CKD risk factors: Hypertension



Patient with HTN are 4 times more likely to have a diagnosis of CKD/ESRD

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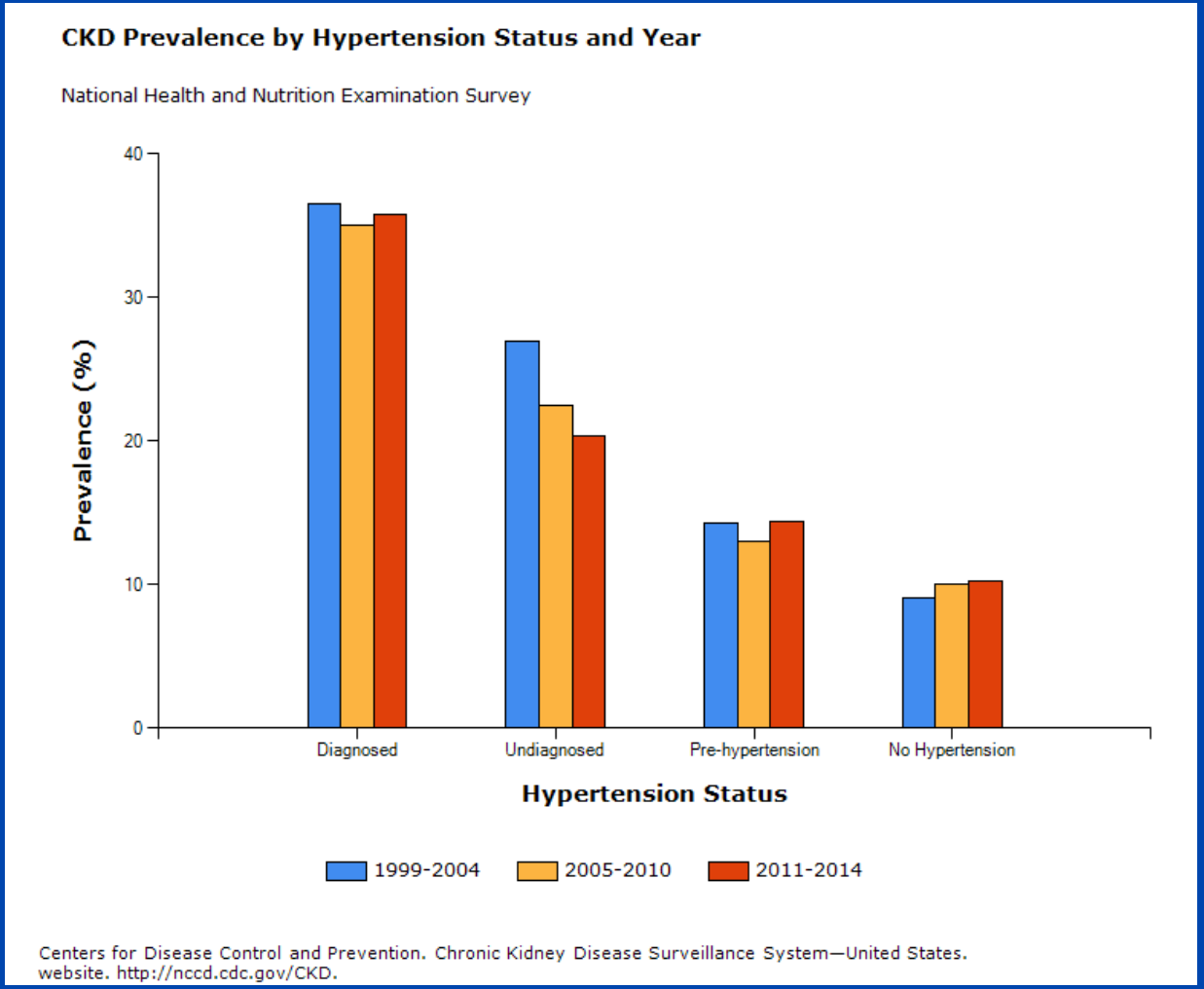
CKD risk factors: Hypertension



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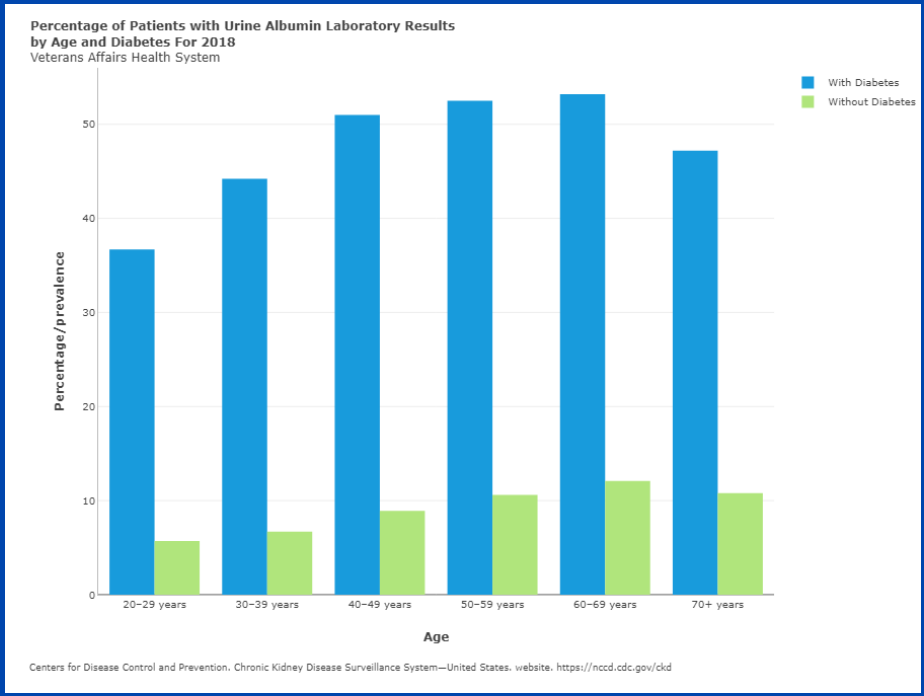
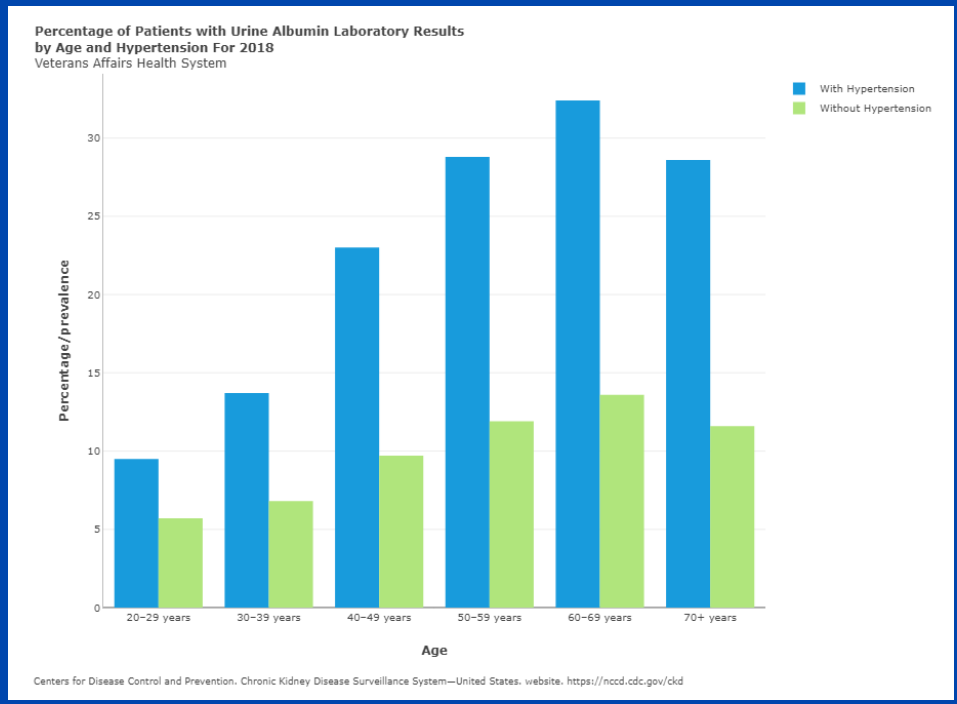
Frequency of monitoring albuminuria is low





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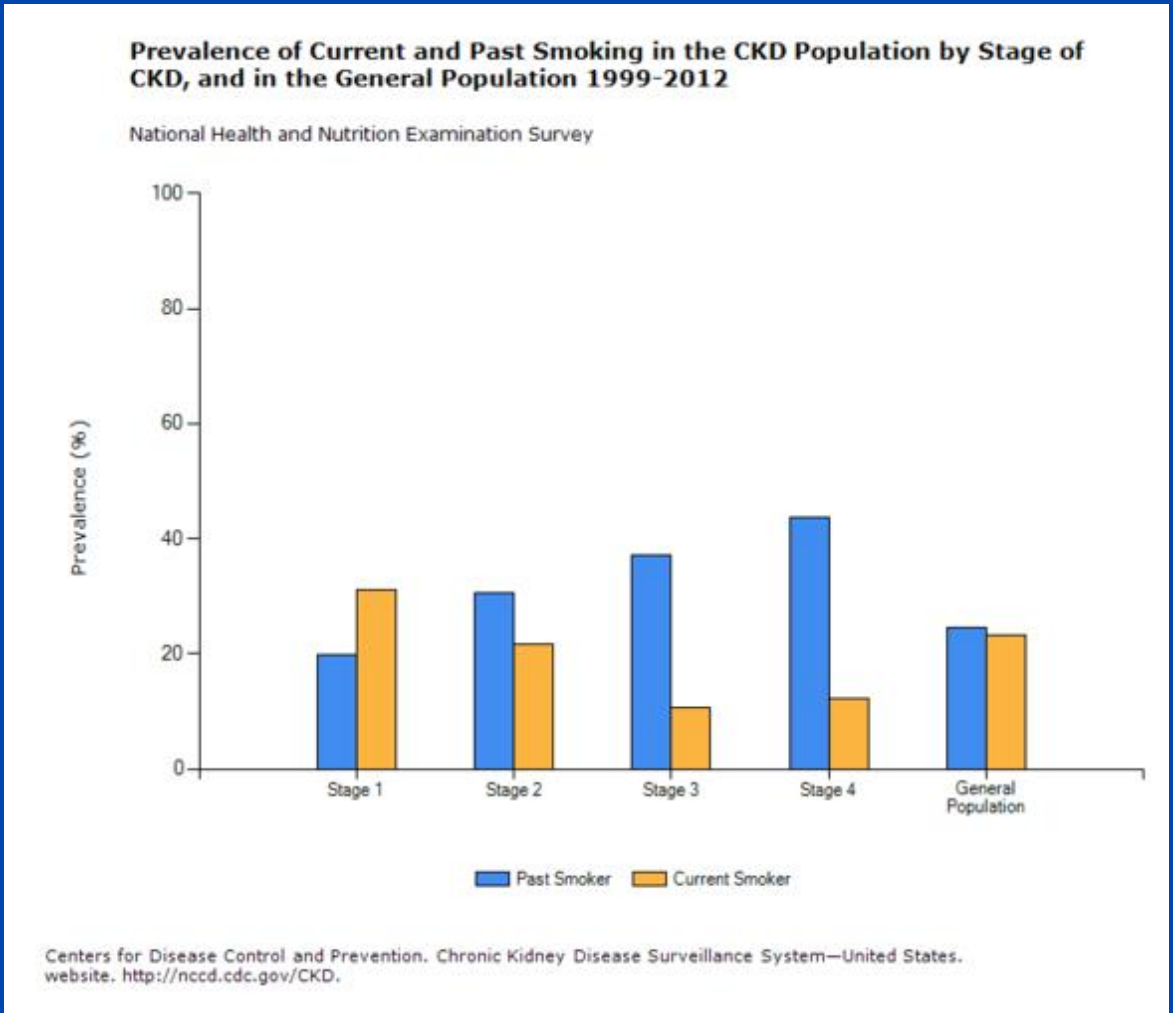
CKD risk factors: Smoking



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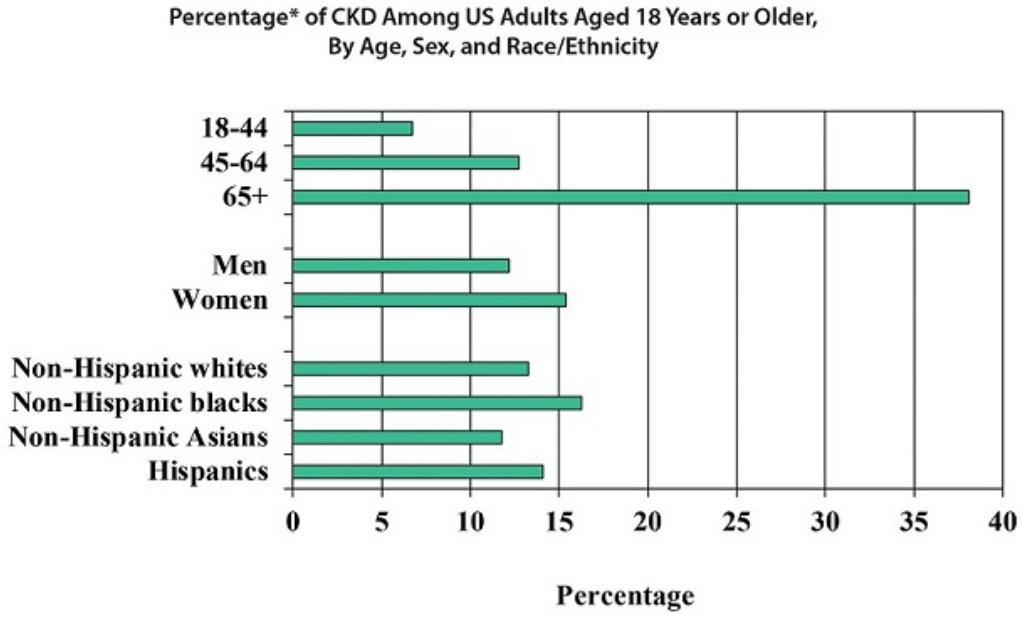
CKD Risk factors: Age/Gender/Ethnicity

- CKD is more common in people aged 65 years or older (38%) than in people aged 45–64 years (13%) or 18–44 years (7%).
- CKD is more common in women (15%) than men (12%).
- CKD is more common in non-Hispanic blacks (16%) than in non-Hispanic whites (13%) or non-Hispanic Asians (12%).
- About 14% of Hispanics have CKD.



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Evaluation of Kidney Dysfunction

- Repeat the serum Creatinine.
- If question about validity, consider serum Cystatin C.
- If low GFR (< 60 ml/min) is confirmed:

- Review of personal and family history (including and physical exam (BP, BMI).
- Review of medication list.
- Obtain urine analysis.
- Obtain imaging of the kidneys (ultrasound).

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Prevention of Kidney Function Decline

1- Recognizing reversible causes:

2- Managing irreversible risk factors and preventing further kidney function damage:

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Prevention of Kidney Function Decline

1- Recognizing reversible causes:

Pre-renal, Post-renal, intrinsic causes of kidney function decline.

2- Managing irreversible risk factors and preventing further kidney function damage:

HTN, DM, heart disease, liver disease.

Avoidance of nephrotoxic agents.

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Referral to Nephrology: indication

- AKI or abrupt sustained fall in GFR.
- GFR < 30 ml/min/1.73 m2 (GFR categories G4-G5).
- Consistent finding of significant albuminuria (ACR >300 mg/g or 24 h urine albumin >300 mg) or proteinuria (PCR >500 mg/g).
- Progression of CKD (rapid progression is defined as a sustained decline in eGFR of more than 5 ml/min/1.73 m2/yr).
- Urinary red cell casts, RBC >20 per high power field sustained and not readily explained.
- CKD and hypertension refractory to treatment with 4 or more antihypertensive agents.
- Recurrent or extensive nephrolithiasis.
- Hereditary kidney disease.

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KDIGO 2012 CKD guidelines

Prevention of Kidney Function Decline

1- Recognizing reversible causes:

Pre-renal, Post-renal, intrinsic causes of kidney function decline.

2- Managing irreversible risk factors and preventing further kidney function damage:

HTN, DM, smoking, obesity.

Avoidance of nephrotoxic agents.

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Prevention of Kidney Function Decline: KDIGO 2012 Guidelines for HTN

- In both diabetic and non-diabetic adults with CKD and urine albumin excretion <30 mg/24 hours (or equivalent*) whose office BP is consistently >140mm Hg systolic or >90mm Hg diastolic be treated with BP-lowering drugs to maintain a BP that is consistently <140mm Hg systolic and <90mm Hg diastolic. (1B)

- In both diabetic and non-diabetic adults with CKD and with urine albumin excretion of >30 mg/24 hours (or equivalent*) whose office BP is consistently >130mm Hg systolic or >80mm Hg diastolic be treated with BP-lowering drugs to maintain a BP that is consistently <130mm Hg systolic and <80mm Hg diastolic. (2D)

Prevention of Kidney Function Decline: KDIGO 2012 Guidelines for HTN

- ARB or ACE-I be used in diabetic adults with CKD and urine albumin excretion 30–300 mg/24 hours (or equivalent*). (2D)

- ARB or ACE-I be used in both diabetic and non-diabetic adults with CKD and urine albumin excretion >300 mg/24 hours (or equivalent*). (1B)

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Prevention of Kidney Function Decline: KDIGO 2012 Guidelines for DM

- We recommend a target hemoglobin A1c (HbA1c) of <7.0% to prevent or delay progression of the microvascular complications of diabetes, including diabetic kidney disease. (1A).
- We recommend not treating to an HbA1c target of <7.0% in patients at risk of hypoglycemia. (1B).
- We suggest that target HbA1c be extended above 7.0% in individuals with comorbidities or limited life expectancy and risk of hypoglycemia. (2C)
- In people with CKD and diabetes, glycemic control should be part of a multifactorial intervention strategy addressing blood pressure control and cardiovascular risk, promoting the use of angiotensin-converting enzyme inhibition or angiotensin receptor blockade, statins, and antiplatelet therapy where clinically indicated. (Not Graded).

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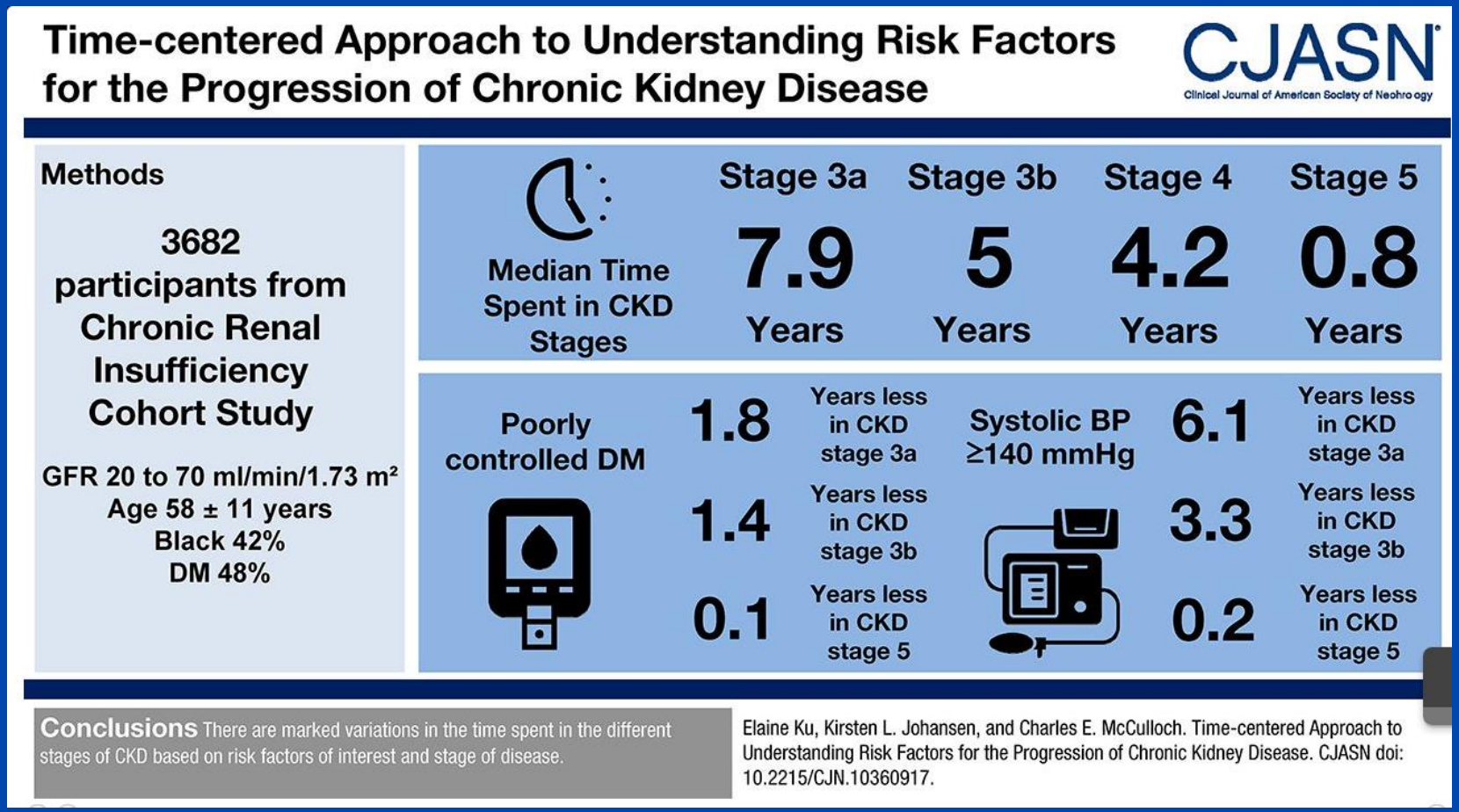
Better control of risk factor help decrease progression of CKD



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Prevention of Kidney Function Decline: Dietary interventions

Protein intake:

Lowering protein intake to 0.8 g/kg/day in adults with diabetes (2C) or without diabetes (2B) and GFR <30 ml/min/ 1.73 m^2 (GFR categories G4-G5).

Avoiding high protein intake (>1.3 g/kg/day) in adults with CKD at risk of progression.

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Prevention of Kidney Function Decline: Dietary interventions

Salt intake:

Lowering salt intake to <90mmol (<2 g) per day of sodium (corresponding to 5 g of sodium chloride). (1C).

Potassium, Phosphorus management:

Individuals with CKD receive expert dietary advice and information in the context of an education program, tailored to severity of CKD and the need to intervene on salt, phosphate, potassium, and protein intake where indicated. (1B).

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Prevention of Kidney Function Decline: Lifestyle interventions

- Smoking cessation.
- Weight loss to target BMI 20 to 25.
- Undertake physical activity compatible with cardiovascular health and tolerance (aiming for at least 30 minutes 5 times per week).

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Prevention of Kidney Function Decline: Nephrotoxic agents

Non steroidal anti-inflammatory agents

- Metanalysis: A total of 14 studies from 13 publications met our inclusion criteria. There were eight cohort and three cross-sectional studies, two quality improvement intervention studies and one prospective survey, representing a total of 49 209 CKD patients.

- Cross-sectional point prevalence of NSAID use in CKD patients ranged from 8 to 21%. Annual prevalence rates ranged from 3 to 33%.

- Conclusions: Evidence suggests that NSAID prescriptions/use in primary care among patients with CKD is variable and relatively high.

Clin Kidney J. 2019 May 20;13(1):63-71.

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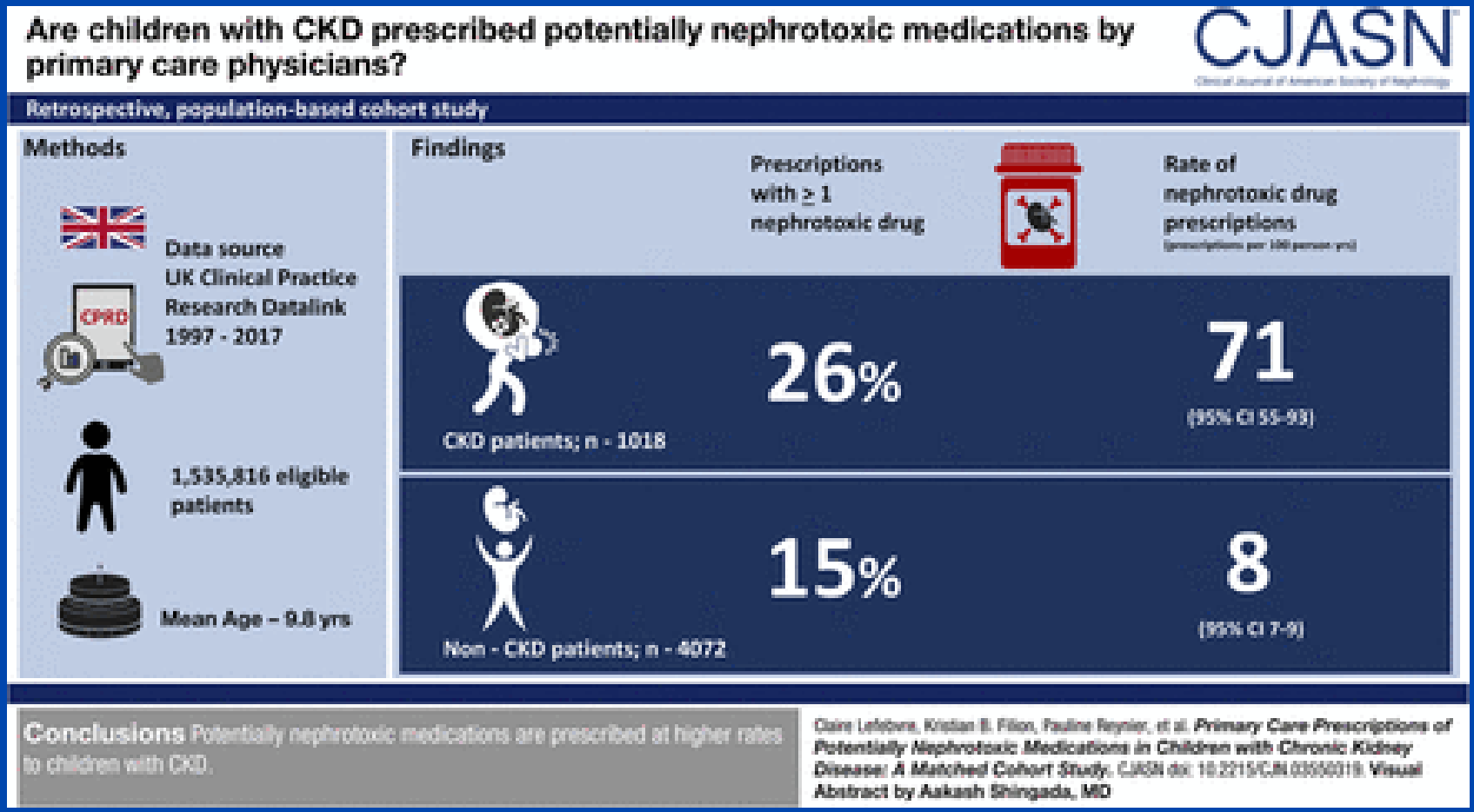
Prevention of Kidney Function Decline: Nephrotoxic agents



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Prevention of Kidney Function Decline: Nephrotoxic agents

- Herbal supplements:

Table 1. Review of nephrotoxic dietary supplements[a]

Common Name	Familiar Indications	Nephrotoxic Manifestations
Cat's claw	Anti-inflammatory GI disorder	Acute allergic interstitial nephritis (43)
Chaparral	Antibiotic Anti-inflammatory Antioxidant	Renal cystic disease and low-grade cystic renal cell carcinoma (34)
Chromium	Glucose control Lipid lowering Weight loss	ATN (15,17) Interstitial nephritis (16)
Cranberry	Antibiotic Urinary acidifier and deodorizer	Nephrolithiasis secondary to oxaluria (58)
Creatine	Enhancement of muscle performance during brief, high-intensity exercise	Acute focal interstitial nephritis and focal tubular injury (18) Nonspecific renal dysfunction (19) AKI secondary to rhabdomyolysis (61–63)
Ephedra	Allergic rhinitis Asthma Hypotension Sexual arousal Weight loss	Nephrolithiasis secondary to ephedrine, norephedrine, and pseudoephedrine stone formation (55,56)
Germanium	Anti-inflammatory Immunostimulant	Tubular degeneration with minor glomerular abnormalities (23–32)
Hydrazine	Anorexia and cachexia Chemotherapeutic	Autolysis of the kidneys in the setting of hepatorenal syndrome (40)
Licorice	Antibiotic Anti-inflammatory GI disorders	Renal tubular injury secondary to prolonged hypokalemia (64–66) AKI secondary to hypokalemic rhabdomyolysis in the setting of pseudoaldosteronism (65)
L-Lysine	Antiviral Wound healing	Fanconi syndrome and tubulointerstitial nephritis (33)
Pennyroyal	Abortifacient Menstrual stimulant	Edematous hemorrhagic kidneys with ATN and proximal tubular degeneration in the setting of hepatorenal syndrome (69,71)
Thunder god vine	Immunosuppressant	Unknown supplement effects in conjunction with prolonged shock (42)
Vitamin C	Enhance iron absorption Prevention of cancer and heart disease Wound healing	Nephrolithiasis secondary to oxaluria (45–53)
Willow bark	Analgesic Anti-inflammatory	Necrotic papillae consistent with analgesic nephropathy (41)
Wormwood oil	Anemia Antipyretic Appetite stimulant Asthma GI disorders	AKI secondary to rhabdomyolysis in the setting of supplement-induced tonic-clonic seizures (60)
Yellow oleander	Anti-inflammatory	Renal tubular necrosis with vacuolated areas in the glomerular spaces in the setting of hepatorenal syndrome (73)
Yohimbe	Erectile dysfunction Sexual arousal	SLE with resultant renal dysfunction (37)

[a]AKI, acute kidney injury; ATN, acute tubular necrosis; GI, gastrointestinal; SLE, systemic lupus erythematosus.

A Review of Dietary Supplement–Induced Renal Dysfunction. Gabardi et al. CJASN 2007.

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Prevention of Kidney Function Decline: Nephrotoxic agents

- Herbal supplements:

Table 3. Dietary supplements (common names) with known or potential diuretic properties (39,67)

Aloe vera	Creatine	L-Arginine
Antineoplaston	Dandelion	Lovage
Artichoke	Elder flower	Meadowsweet
Asparagus	Ephedra	Mistletoe
Astragalus	Gingko	Oleander
Birch	Glucosamine	Shepherd's purse
Bladderwrack	Goldenrod	Sorrel
Bupleurum	Gotu kola	Uva ursi
Burdock	Green tea	White horehound
Copper	Horsetail	Yarrow flowers
Corn silk	Juniper berry	
Couch grass	Kava	

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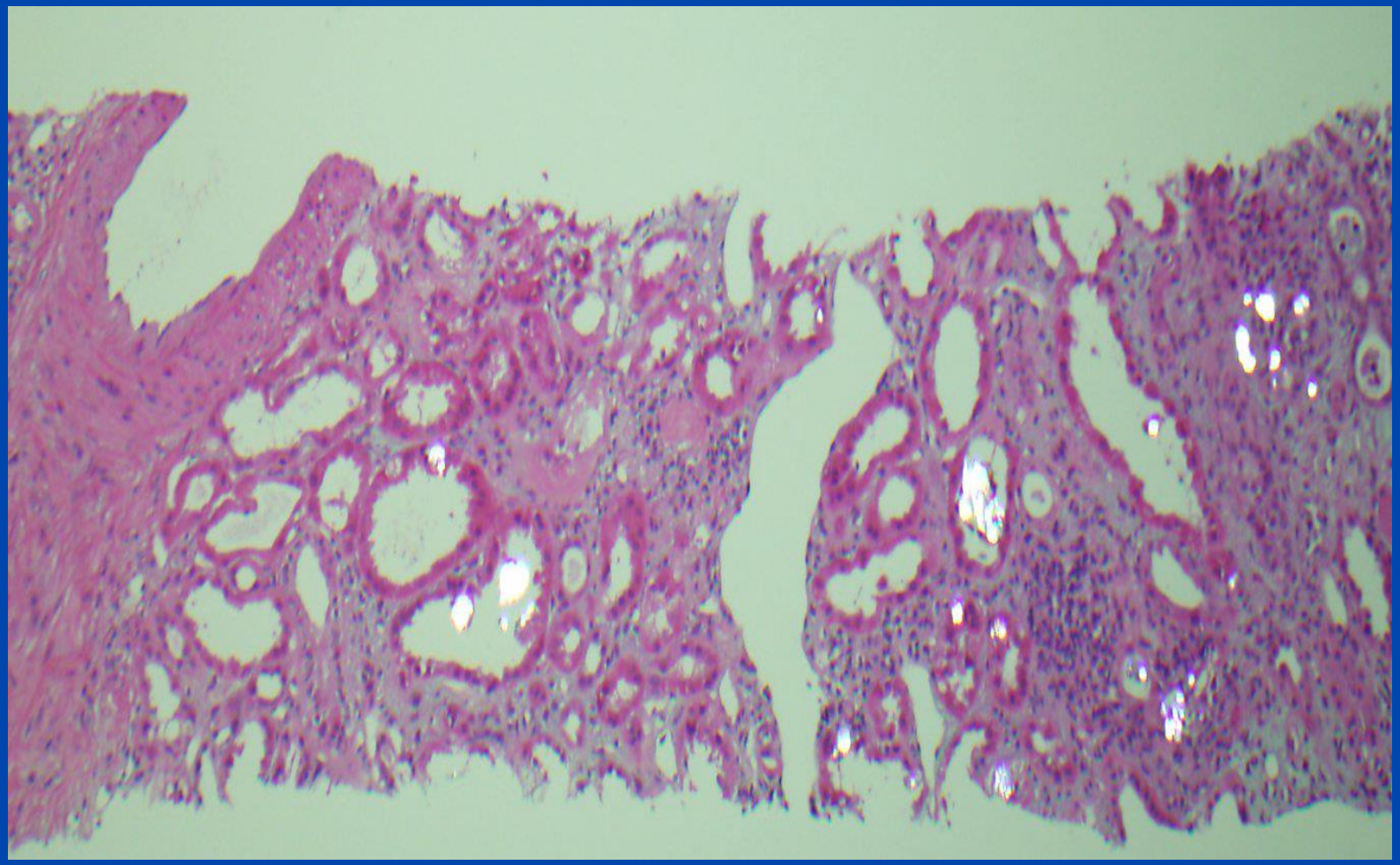
Prevention of kidney disease
Oxalate Nephropathy

- Suspect oxalate nephropathy in patients with following conditions:

- Mal-absorptive procedure for weight loss (RYGB).
- Other conditions requiring bowel resections with chronic diarrhea.
- Fad diet with sudden decline in kidney function.
- High doses of vitamin C (including in homeopathic clinic).

Kidney Biopsy
Oxalate Nephropathy



H&E stain – Numerous Intratubular Calcium Oxalates with Acute Tubular Injury

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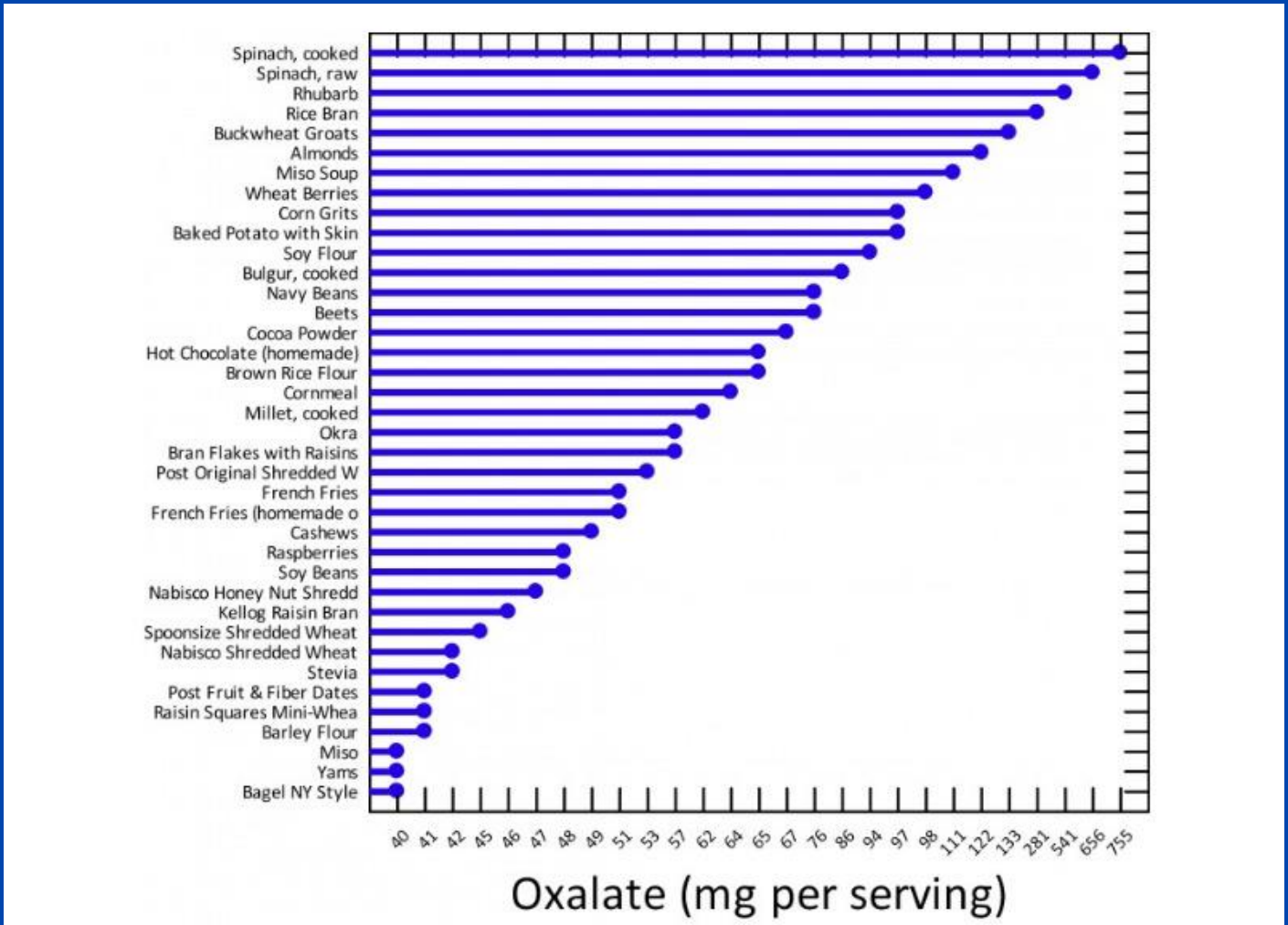
Prevention of kidney disease
Diet/Oxalate



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KDIGO 2012 CKD guidelines

Referral to Transplantation: indication

- Patients with estimated GFR < 20 ml/min should be referred for kidney transplant evaluation.

- Preemptive kidney transplantation is preferable to dialysis, and confers mortality advantages especially among patients with DM.

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Summary

- About 15% of US population has chronic kidney disease (CKD).
- Most of the cases of CKD are not advanced and as such managed by primary care providers.
- Control of risk factors is key: HTN, DM, obesity, smoking.
- Review of medication list, including over the counter medication is key.
- Review and adjustment of diet is key.

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Thank you

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