

# Individualizing Care for People with Progressive Kidney Disease

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# Conflicts of Interest

- Nothing to declare

# Context and Objective

- Individualizing care in progressive chronic kidney disease (CKD) is a challenge.
- Many guidelines though high-quality evidence to support many recommendations is limited.
- Many recommendations are based on discrete biochemical cut-offs, though these laboratory results may be subject to a level of uncertainty which should temper some clinical decisions.
- Objective: This presentation will discuss individualized approaches to:
  - Screening and diagnosis of kidney disease
  - Hypertension goal
  - Glycemic control
  - Mineral bone disease counselling
  - Nutrition counselling
  - Medical management for kidney failure

# Screening and Diagnosis

# CKD Is Reduced Kidney Function and/or Kidney Damage Regardless of Etiology

- Chronic Kidney Disease

- Kidney function

- Glomerular filtration rate (GFR)  $< 60 \text{ mL/min/1.73 m}^2$  for  $\geq 3$  months with or without kidney damage

***and/or***

- Kidney damage

- $\geq 3$  months, with or without decreased GFR, manifested by either
    - Pathological abnormalities
    - Markers of kidney damage, i.e., proteinuria (albuminuria)
      - Urine albumin-to-creatinine ratio (UACR)  $> 30 \text{ mg/g}$

Reference: National Kidney Foundation. K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification and Stratification. *American Journal of Kidney Diseases*. 2002; 39: (Suppl 1) S18.

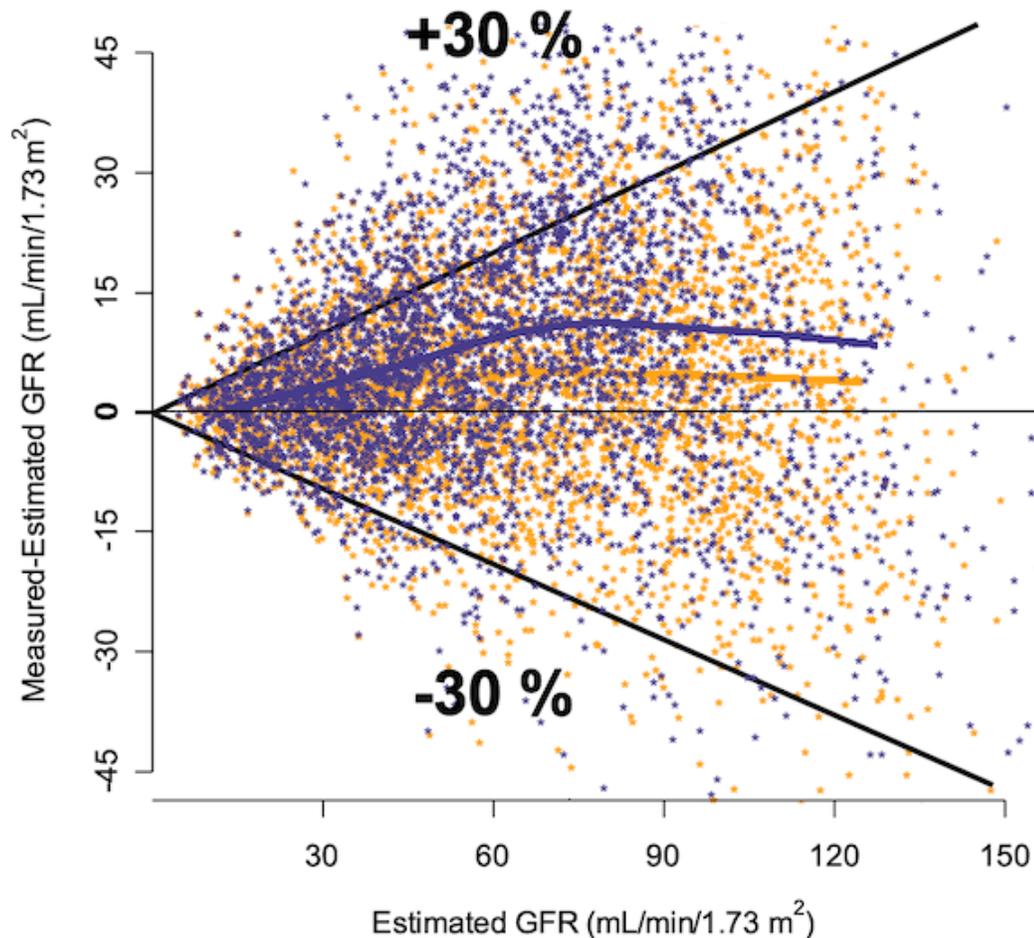
# Estimating Equations for eGFR

- The Modification of Diet in Renal Disease (MDRD) and CKD Epi study equations are most widely used for estimating GFR.
- The variables are serum creatinine, age, race, and gender.
- MDRD eGFR =  $175 \times (\text{Standardized Scr})^{-1.154} \times (\text{age})^{-0.203} \times (0.742 \text{ if female}) \times (1.212 \text{ if African American})$
- CKD-EPI eGFR =  $141 \times \min(\text{Scr} / \kappa, 1)^\alpha \times \max(\text{Scr} / \kappa, 1) - 1.209 \times 0.993 \text{ Age} \times 1.018 \text{ [if female]} \times 1.159 \text{ [if African American]}$
- The estimate is normalized to body surface area.

# eGFR Estimates the Measured GFR

- eGFR is *not* the measured GFR.
- **eGFR estimates the measured GFR**
- Estimating equations are derived from population-based studies.
- The performance measurement of the estimating equation is the **P30**
- **P30** refers to the percent of GFR estimates that are *within 30% of mGFR*
- For example, a patient with an eGFR of 59 has an **79.9%** chance of having a measured GFR **between 42 and 78**

# Comparison of the Performance of the MDRD Study and CKD-EPI equations (External Validation)



		Overall	60–89
$P_{30}$	MDRD	80.6	82.3
$P_{30}$	CKD-EPI	84.1	86.8
$P_{30}$	%	4%	5%
$1-P_{30}$	MDRD	19.4	17.7
$1-P_{30}$	CKD-EPI	15.9	13.2
$1-P_{30}$	%	18%	25%

# Measured GFR

- If using eGFR in very large or very small patients, multiply the reported eGFR by BSA in order to obtain eGFR in units of mL/min

$$x \text{ ml/min/1.73m}^2 \times y \text{ m}^2 = z \text{ ml/min}$$

- Perform confirmatory test (i.e., measured CrCl or measured GFR using exogenous filtration markers)
  - Drugs with a narrow therapeutic index
  - Individuals in whom eGFR and eCrCl provide different estimates of kidney function
  - In individuals where any estimates based on creatinine are likely to be inaccurate

# Elevated UACR Is Associated with Risk of Renal Events; Lowering UACR May Lower Risk of Progression

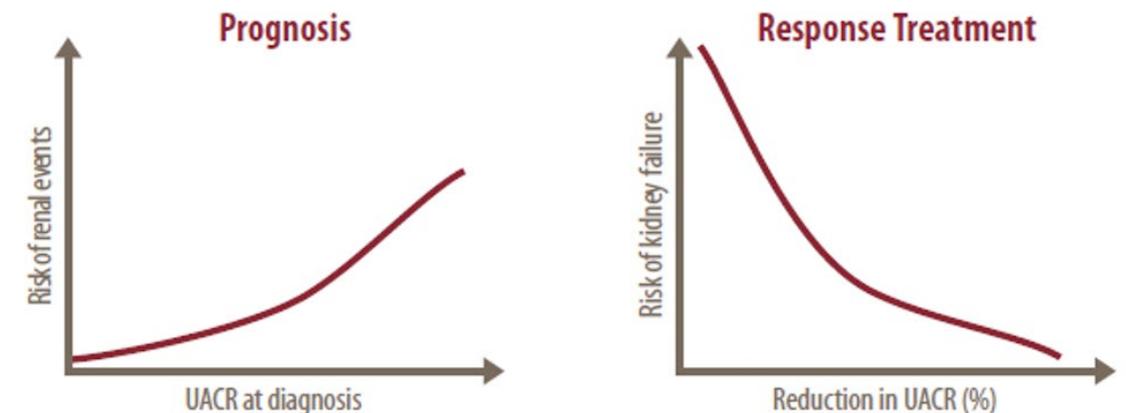
Elevated urine albumin is associated with increased risk of adverse renal events and lowering urine albumin may decrease the risk of progression. Here are the results of two important studies, represented schematically.

The figure on the left shows that the risk of adverse renal events, including loss of half of kidney function, dialysis, or death, increases with the level of urine albumin at the time of diagnosis of CKD.

The figure on the right shows the risk of an adverse renal event in relation to the response in the reduction of urine albumin following initiation of an angiotensin receptor blocker. As you move to the right, there is a greater reduction in urine albumin in response to treatment, and that is associated with a decreased risk of renal events.

So, high levels of urine albumin predict a bad outcome. Response to therapy as evidenced by decrease in urine albumin is associated with decreased risk for a bad outcome.

Chronic Renal Insufficiency Cohort Study      RENAAL



Renal events = loss of half of eGFR, dialysis, or death

Reference: NIH, February 2010; De Zeeuw et al., 2004

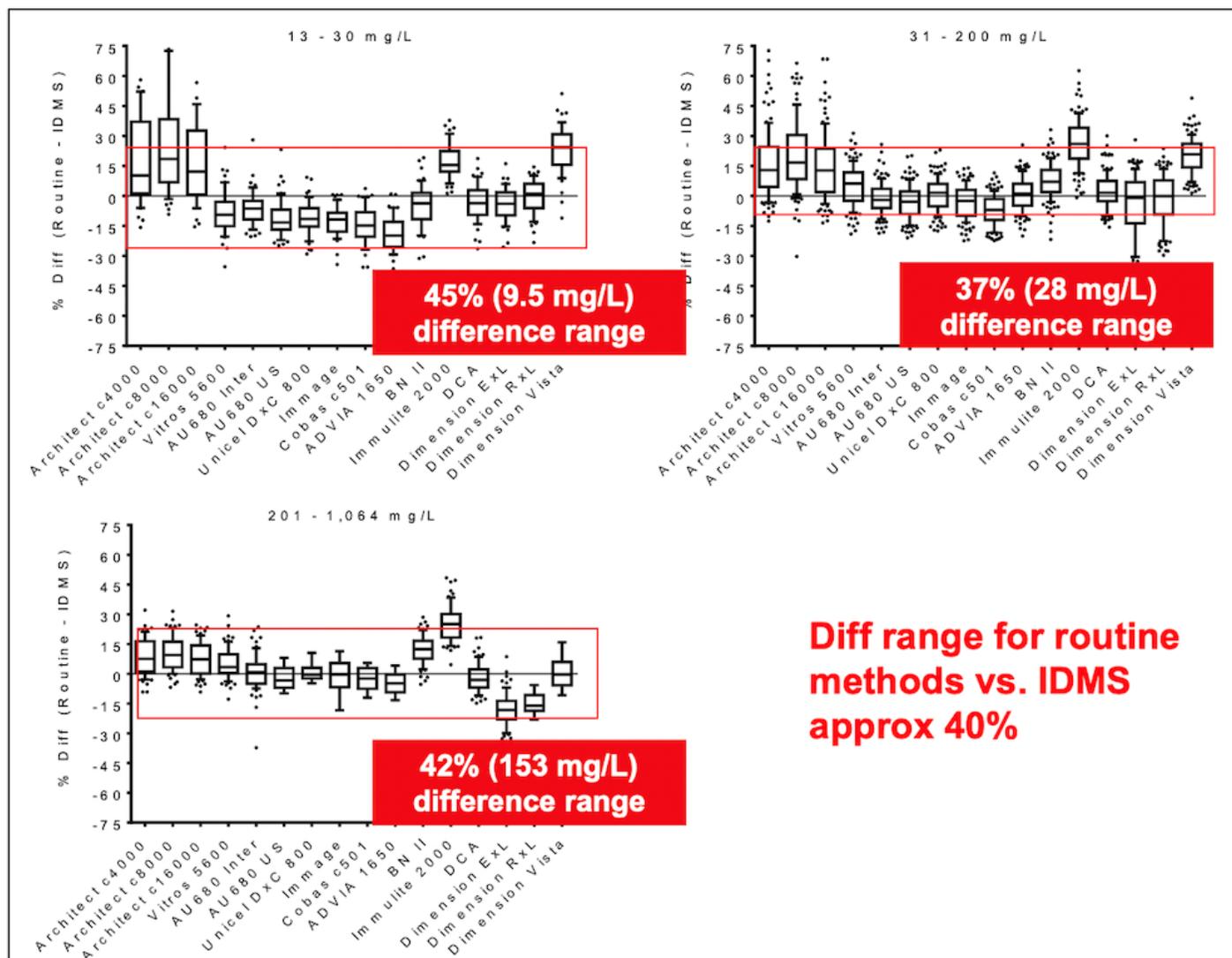
# Use Urine Albumin-to-Creatinine Ratio (UACR) for Urine Albumin Assessment

- UACR uses a spot urine sample.
- In adults, ratio of urine albumin to creatinine correlates closely to total albumin excretion.
- Ratio is between two measured substances (not dipstick).
- UACR of 30 mg/g is generally the most widely used cutoff for “normal.”

$$\frac{\text{Urine albumin (mg/dL)}}{\text{Urine creatinine (g/dL)}} = \text{UACR (mg/g)} \cong \text{Albumin excretion in mg/day}$$

Reference: <https://www.niddk.nih.gov/health-information/professionals/advanced-search/quick-reference-uacr-gfr>

# Difference Range for Routine Methods vs. IDMS



Clin Chem 2014, 60:3; 471-48

# Screen People at Risk, Not Everyone

- Risk factors for CKD:
  - Diabetes
  - Hypertension
  - Family history of kidney disease
  - Cardiovascular disease
  - Obesity
  - Acute kidney injury

BMJ:

# Chronic Disease Controversy: How Expanding Definitions Are Unnecessarily Labelling Many People as Diseased



BMJ 2013;347:f4298 doi: 10.1136/bmj.f4298 (Published 30 July 2013) Page 1 of 6

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**ANALYSIS**

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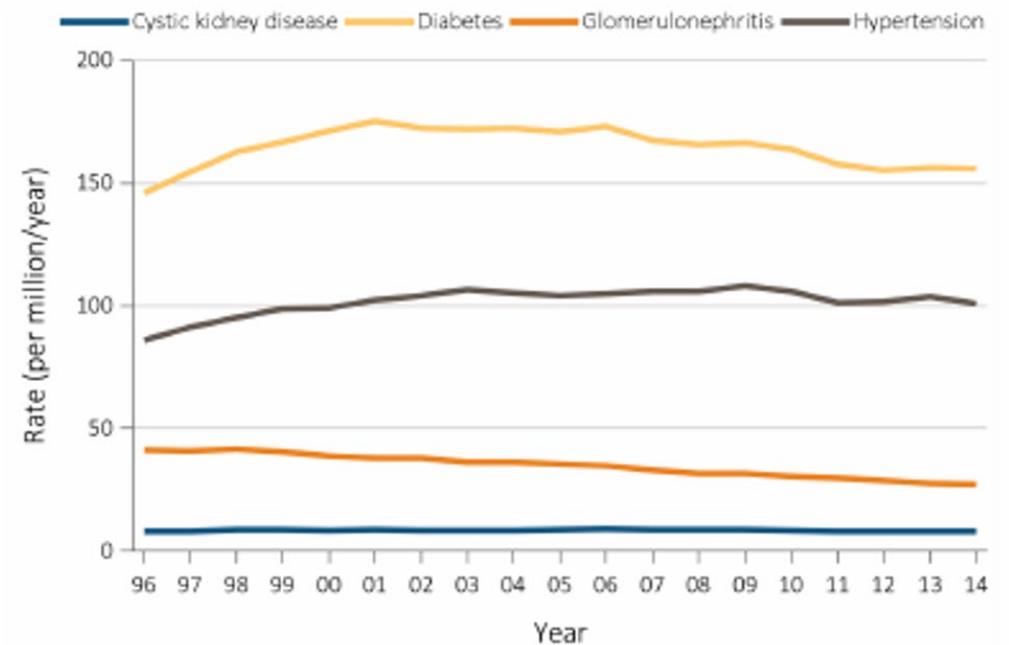
TOO MUCH MEDICINE

**Chronic kidney disease controversy: how expanding definitions are unnecessarily labelling many people as diseased**

Ray Moynihan *senior research fellow*<sup>1</sup>, Richard Glasscock *emeritus professor, department of medicine*<sup>2</sup>, Jenny Doust *professor*<sup>1</sup>

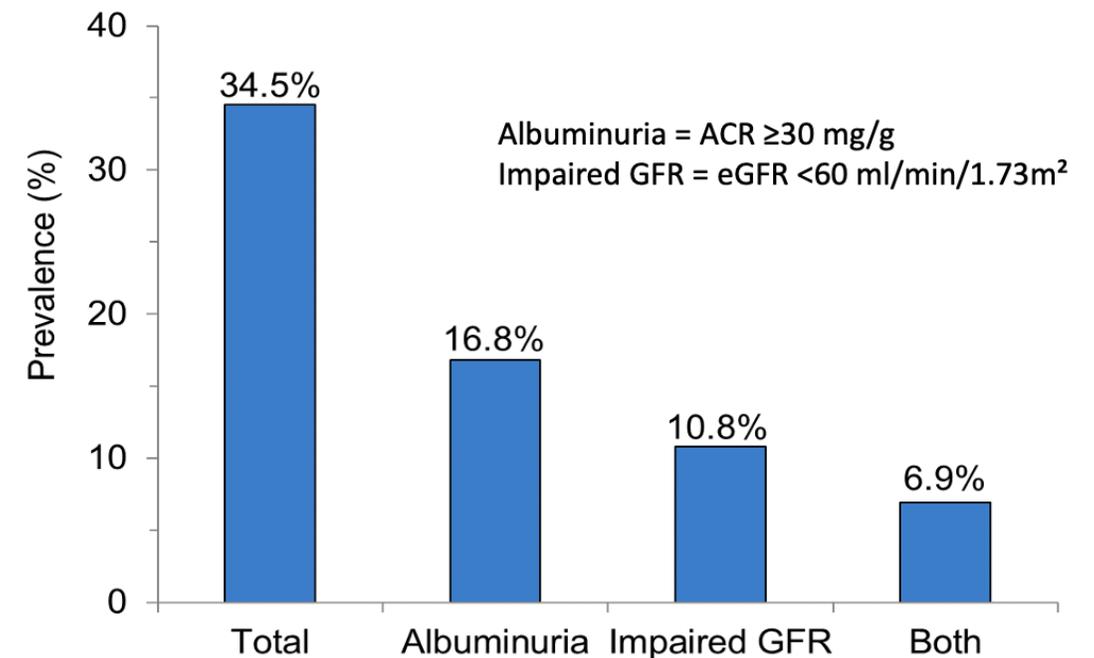
# Diabetes Is the Leading Cause of ESRD, Followed by Hypertension

- Diabetes is the leading cause of end-stage renal disease and has driven much of the increase that we've seen over the past two decades.
- This figure shows that the incidence rates of cystic kidney disease and glomerulonephritis have been relatively stable. The rates of hypertensive kidney disease have been relatively stable for the past 10 to 15 years.
- Diabetes is where there has been a dramatic increase, and most of this is type 2 diabetes.



# Prevalence of Diabetic Kidney Disease (DKD) Among Adults with Diabetes; United States, 2005–2008

- Using NHANES data, Ian de Boer and colleagues examined the prevalence of DKD, defined by presence of elevated albuminuria or reduced eGFR, among adults aged 20 years or older with diabetes.
- *JAMA* 305: 2532–2539, 2011

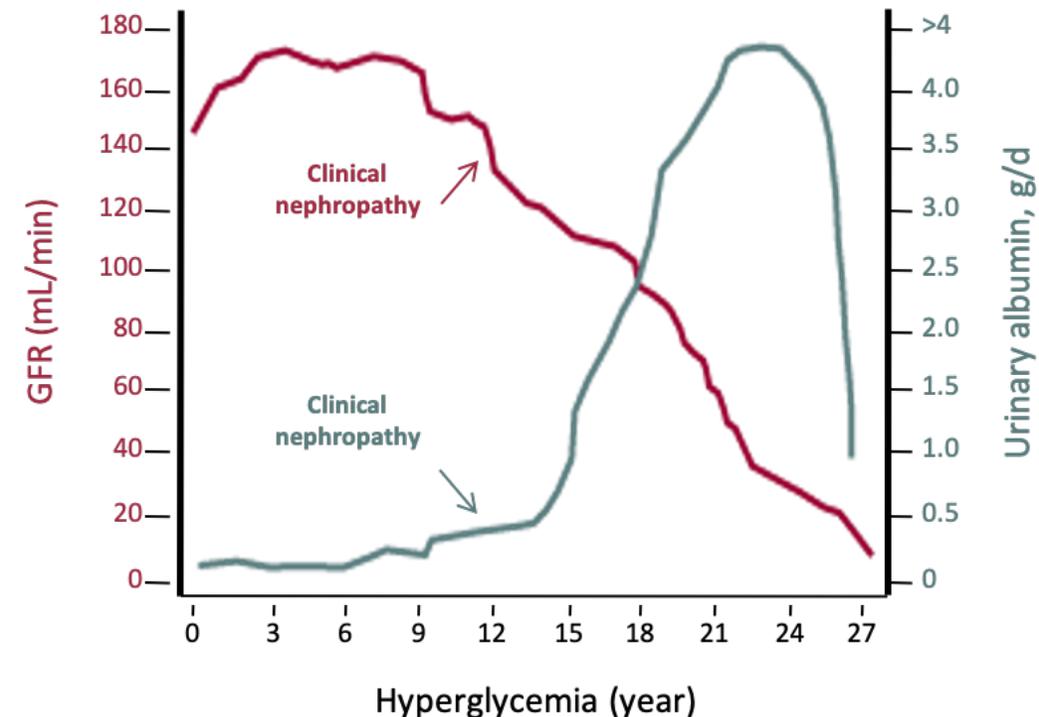


# Natural History of Diabetic Nephropathy: Hyperglycemia Causes Hyperfiltration, May Be Followed by Albuminuria

The natural history of diabetic nephropathy is diagrammed here. Along the horizontal axis is duration of hyperglycemia. The vertical axes show GFR on the left and albuminuria on the right. The red line, which tracks GFR, initially increases after the onset of hyperglycemia. Then, after a period of time, it gradually decreases.

Around the time that GFR passes back through the normal range, increases in urine albumin, represented by the grey line, become apparent. As a result the first clinical sign of diabetic kidney disease is usually an increase in urine albumin.

Although the estimated GFR may be normal at that point, it may actually be on a downward slope, decreased from the supernormal levels that it reached earlier. As time progresses, there's continual loss of GFR and an increase in urine albumin until the GFR declines to such a degree that urine albumin decreases.



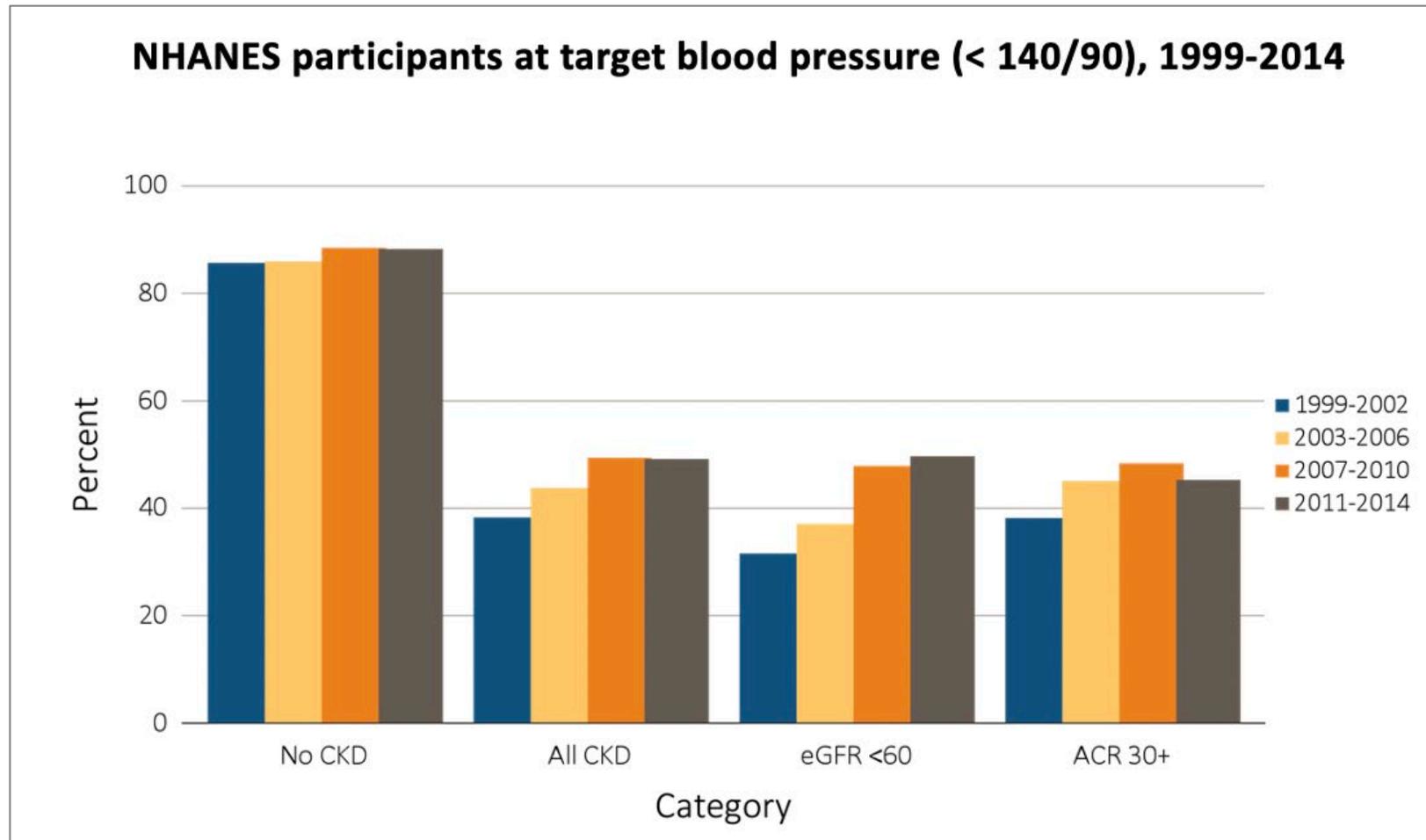
- Reference: Adapted from Friedman, 1999

# However...

- Microalbuminuria can regress
  - de Boer IH et al, *Arch Int Med* 2011
- Impaired GFR can develop without albuminuria
  - Molitch M et al, *Diabetes Care* 2010
- Disease heterogeneity often not reflected by GFR
  - Bohle et al. *American Journal of Nephrology*, 1987
- *Do not assume because a person has diabetes and kidney disease that the kidney disease is due to diabetes*

# Hypertension

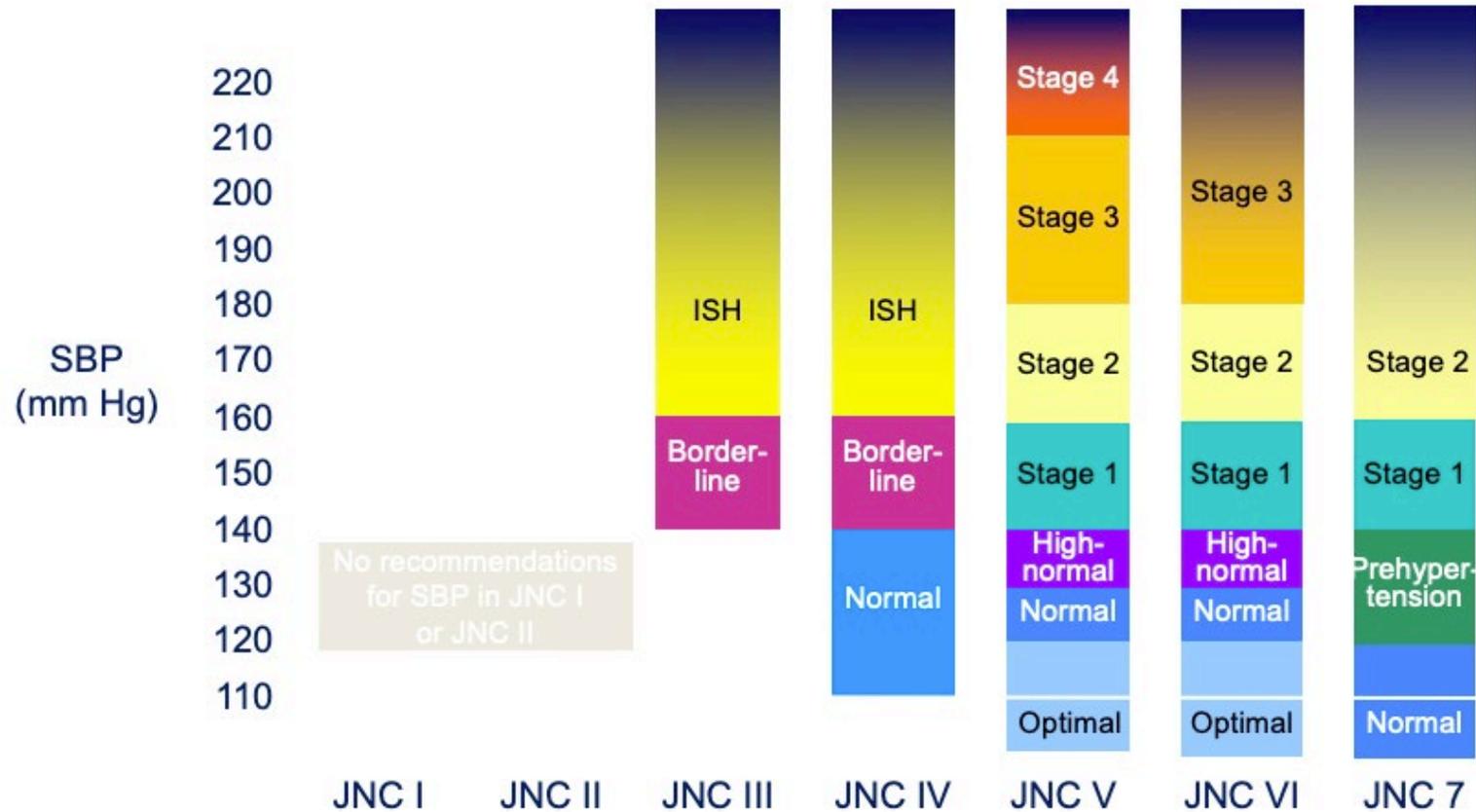
# Blood Pressure Is Poorly Controlled in People with CKD



Reference: USRDS 2017 Annual Data Report

# Hypertension: A Moving Target

## JNC Classifications: Systolic Blood Pressure



JNC I. *JAMA*. 1977; 237: 255–261.

JNC II. *Arch Intern Med*. 1980; 140: 1280–1285.

JNC III. *Arch Intern Med*. 1984;144:1045–1057.

JNC IV. *Arch Intern Med*. 1988; 148: 1023–1038.

JNC V. *Arch Intern Med*. 1993; 153: 154–183.

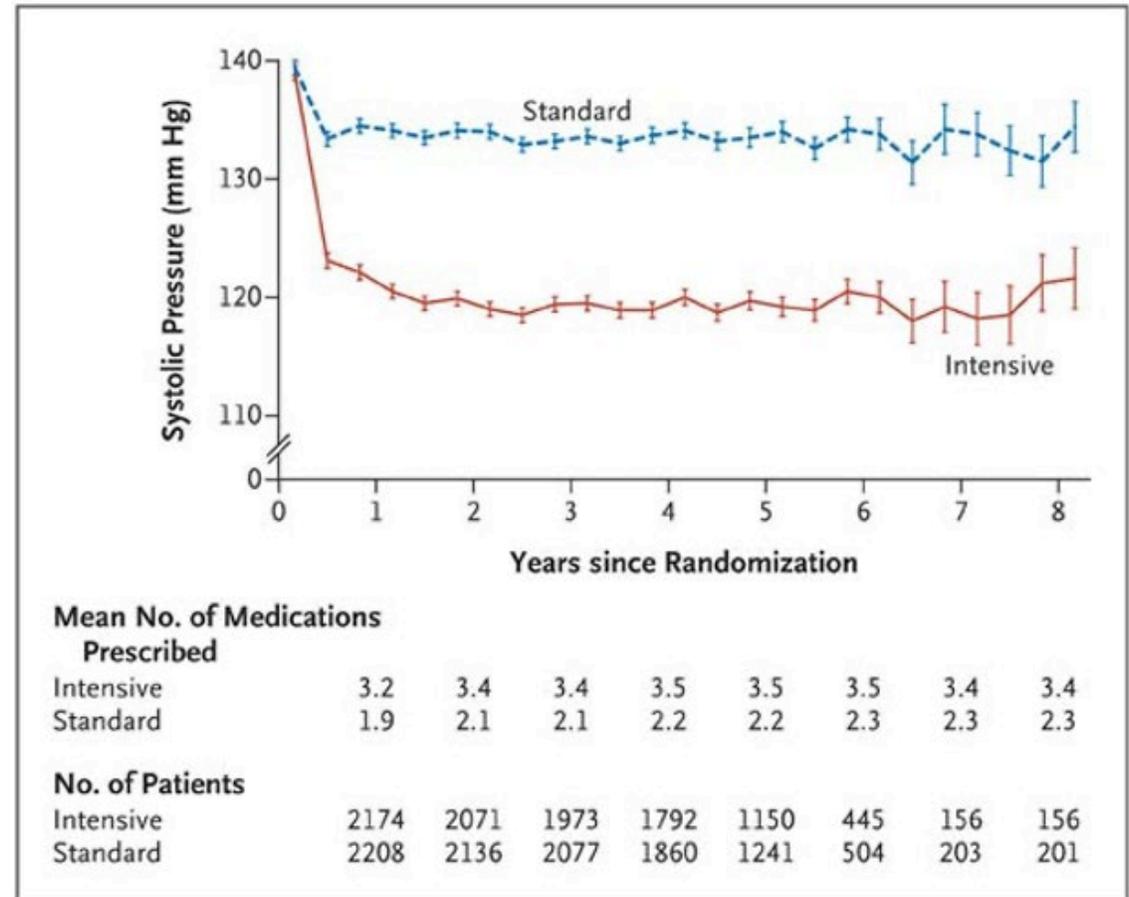
JNC VI. *Arch Intern Med*. 1997; 157: 2413–2446.

Chobanian AV et al. *JAMA*. 2003; 289: 2560–2572.

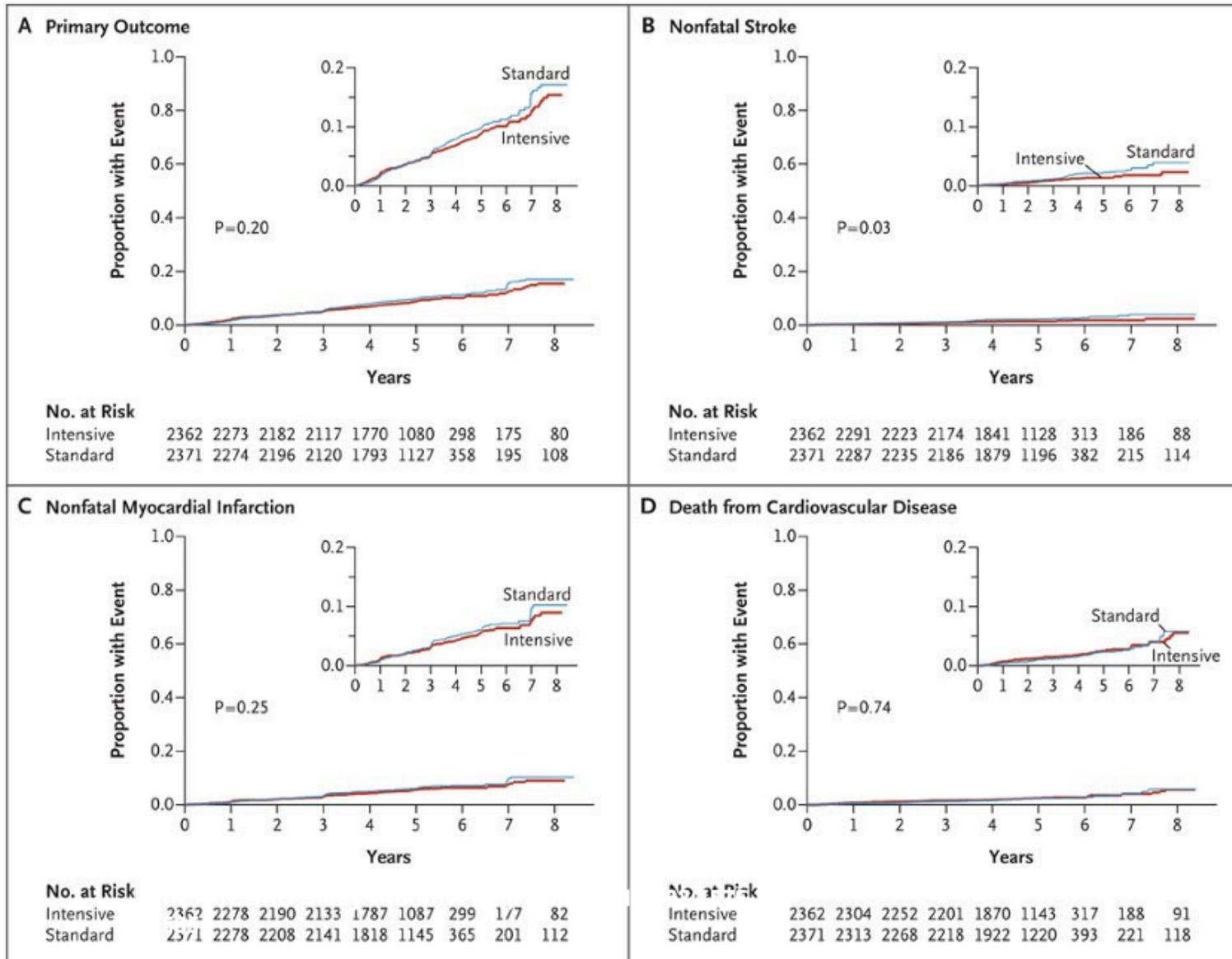
# ACCORD: Mean Systolic Blood-Pressure Levels

Figure 1. ACCORD was a randomized trial, 4,733 patients with type 2 diabetes mellitus who were at high risk for cardiovascular events received treatment aimed at a target systolic blood pressure of less than 120 mm Hg or less than 140 mm Hg. This slide shows Mean Systolic Blood-Pressure Levels at Each Study Visit. I bars indicate 95% confidence intervals.

- *NEJM* 362 (17): 1575–1585



# ACCORD: Kaplan-Meier Analyses of Selected Outcomes



At a mean follow-up of 4.7 years, the rates of the primary end point (nonfatal myocardial infarction, nonfatal stroke, or cardiovascular death) were not significantly different between the two trial groups

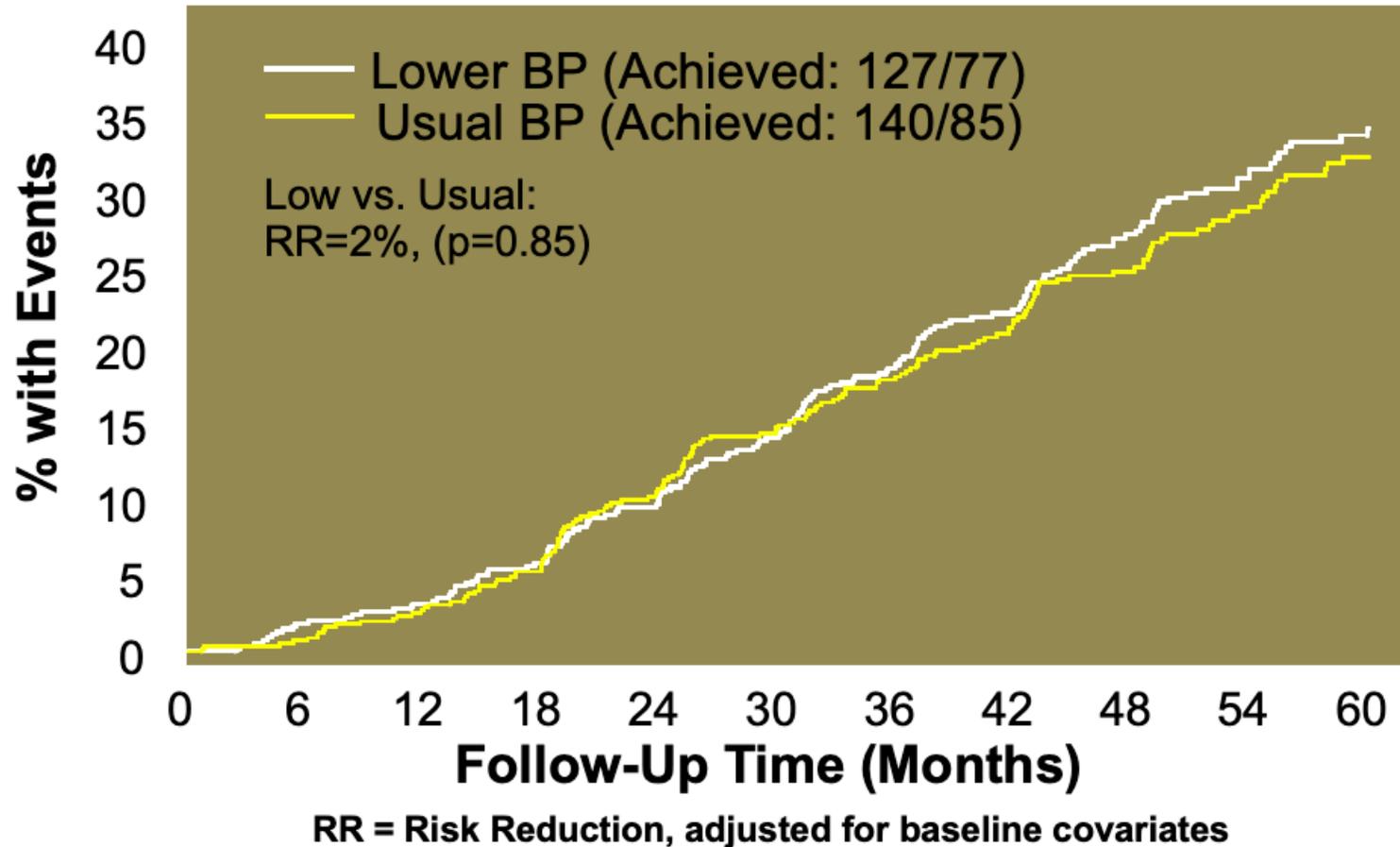
Figure 2. Kaplan-Meier Analyses of Selected Outcomes. Shown are the proportions of patients with events for the primary composite outcome (Panel A) and for the individual components of the primary outcome (Panels B, C, and D). The insets show close-up versions of the graphs in each panel.

*NEJM* 362(17): 1575–1585

# ACCORD: Conclusion

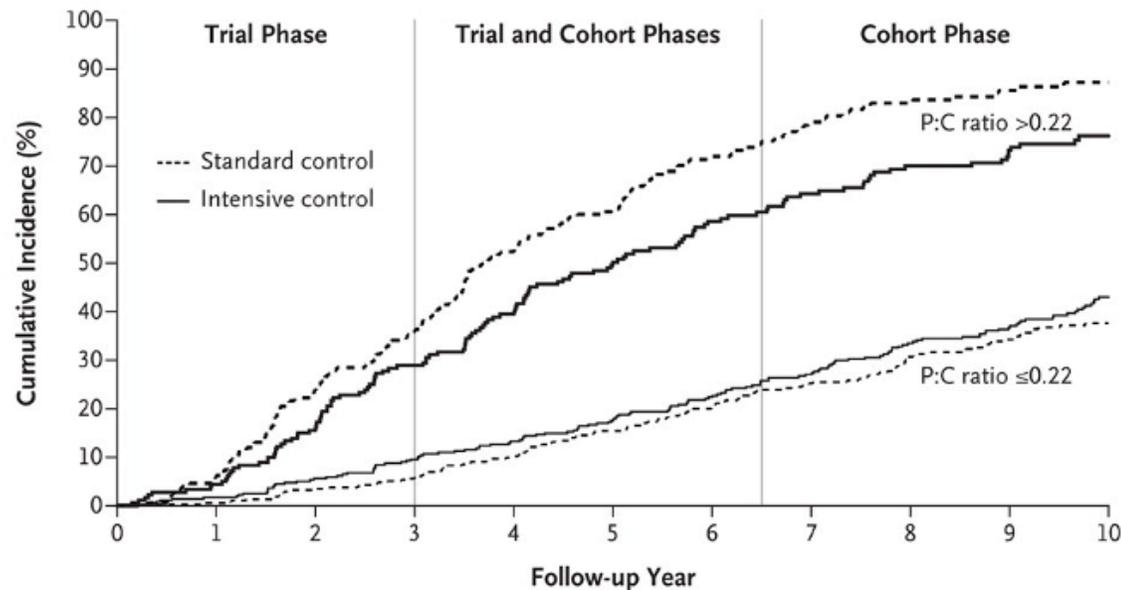
- Targeting a systolic BP of <120 versus <140 mm Hg ***did not*** reduce the rate of fatal and nonfatal major cardiovascular events in patients with type 2 diabetes at high risk for cardiovascular events
- Compared with the standard-therapy group, the intensive-therapy group had **significantly higher rates of serious adverse events** attributed to antihypertensive treatment, as well as higher rates of hypokalemia and elevations in serum creatinine level

# AASK Trial: Composite Clinical Outcome Declining GFR Event, ESRD or Death



The AASK Trial was a study of AAs with hypertension treated to two different levels of BP control on kidney outcomes. It did not include diabetics. In the whole group there was no difference.

# AASK Trial and Cohort: Composite Primary Outcome, According to Baseline Proteinuria Status



## P:C Ratio >0.22

Standard control	176	165	134	113	81	66	45	32	26	22	13
Intensive control	181	172	151	128	109	87	67	56	47	40	25

## P:C Ratio ≤0.22

Standard control	376	373	362	353	332	302	267	234	214	196	128
Intensive control	357	350	335	321	306	282	254	228	206	189	128

Figure 2. However, among patients with baseline proteinuria, which was defined as a urinary protein-to-creatinine ratio (P:C) of more than 0.22, those who received intensive blood-pressure control had a significantly lower cumulative incidence of the composite primary outcome (a doubling of the serum creatinine level, end-stage renal disease, or death) than those who received standard blood-pressure control (hazard ratio in the intensive-control group, 0.73; 95% confidence interval [CI], 0.58 to 0.93;  $P=0.01$ ). However, the between-group difference was not significant among patients with a P:C of 0.22 or less (hazard ratio, 1.18; 95% CI, 0.93 to 1.50;  $P=0.16$ ).

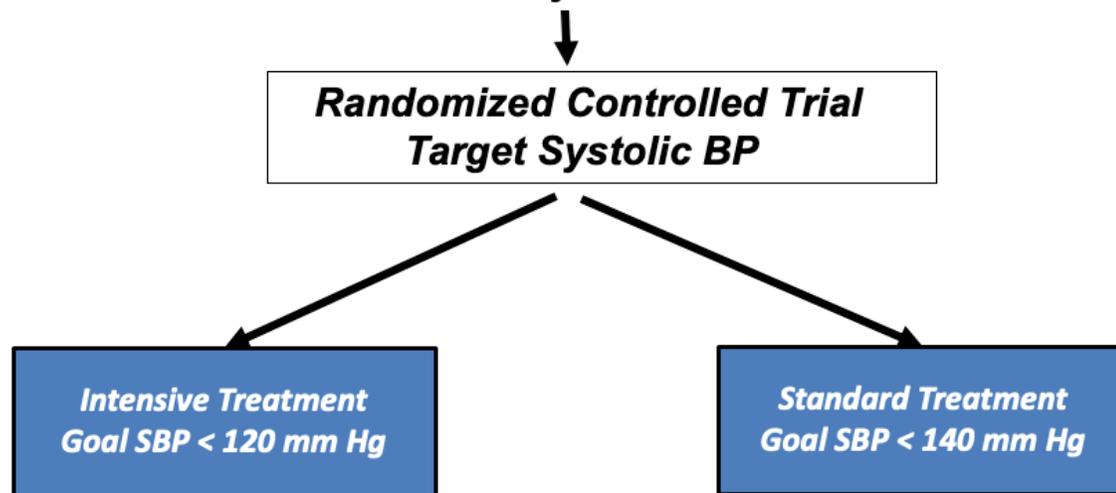
Appel LJ et al. *N Engl. J Med* 2010; 363: 918–929

# JNC 8 Blood Pressure Goals

- For age 60+ years without diabetes or kidney disease, strong evidence to support Goal BP <150/90 based on Grade A level evidence
- For all others, we recommend Goal BP <140/90 based on expert opinion
- Randomized controlled trials target <130/80 vs <140/90: MDRD, AASK, REIN-2: all negative in decreasing CV or renal events

# SPRINT Research Question

***Examine effect of more intensive high blood pressure treatment than is currently recommended***

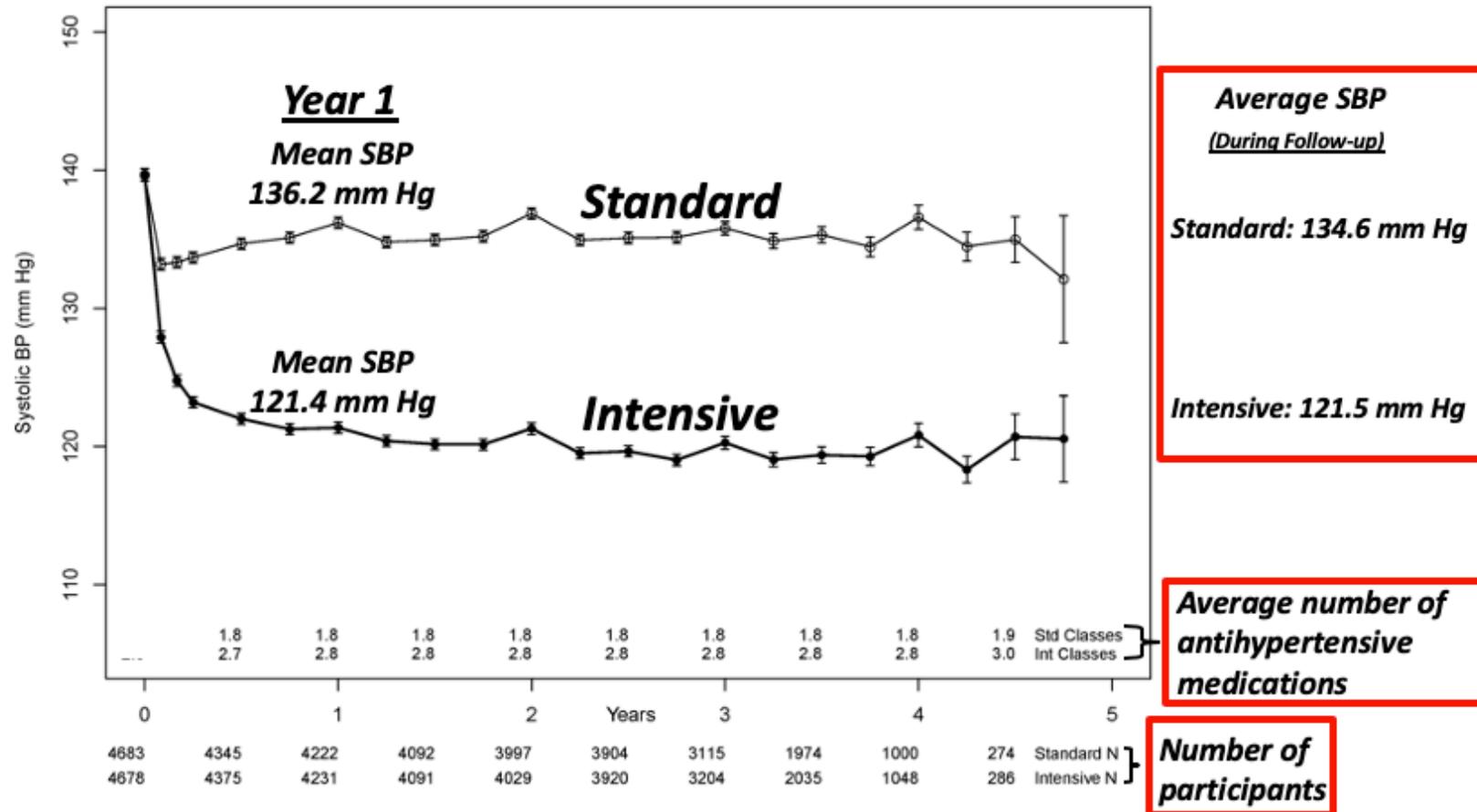


The only major evidence which has been published since JNC 8 is the SPRINT trial. SPRINT (Systolic Blood Pressure Intervention Trial) was a randomized, controlled trial that compared aggressive treatment to a target systolic blood pressure (BP) less than 120 mm Hg with a target less than 140 mm Hg in patients at increased cardiovascular risk. It was stopped early, and its results were promoted widely months before publication (1). Participants were mostly men (64%) with a mean age of 68 years and comorbidities that increased their cardiovascular risk, but patients with diabetes were excluded.

# Systolic BP During Follow-up

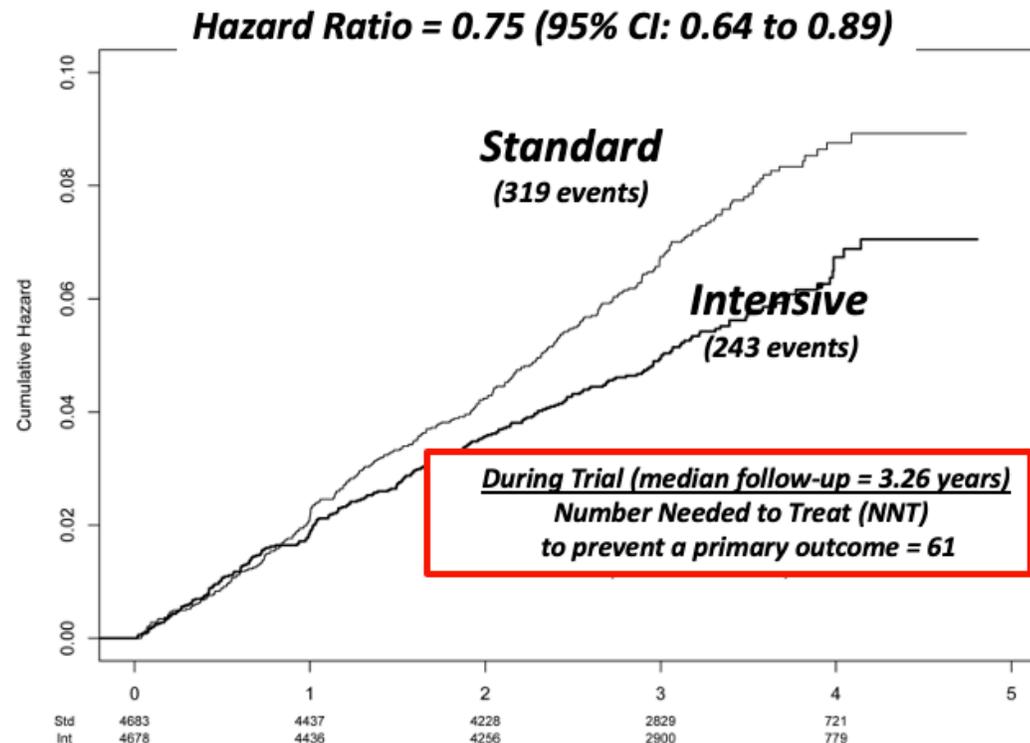
## NEJM, 2015

Figure 1: Mean Systolic BP (95% CI)



# SPRINT Primary Outcome: Cumulative Hazard

With the lower treatment target, the trial found a 25% relative risk reduction in the primary composite outcome. Although a 25% reduction sounds impressive, it corresponds to a decrease in event rates from 6.8% to 5.2% over 3.2 years, or an absolute risk reduction of 1.6%. For 1,000 persons treated over 3.2 years to a systolic BP goal less than 120 mm Hg compared with less than 140 mm Hg, an average of 16 persons will benefit, 22 persons will be seriously harmed, and 962 will not experience benefits or harms. 98.4% of persons receiving more intensive treatment will not benefit. Serious adverse drug events occurred more frequently in the aggressively treated group, with an increase from 2.5% to 4.7% (1). These harms, which were classified by investigators as possibly or definitely related to the intervention, included significant increases in hypotension, syncope, electrolyte abnormalities, and acute kidney injury, bradycardia and injurious falls.



# AHA ACC: Summary

Clinical Conditions	BP Threshold mm Hg	BP Goal mm Hg
<b>General</b>		
Clinical CVD or 10-year ASCVD risk $\geq 10\%$	$\geq 130/80$	$< 130/80$
No clinical CVD and 10-year ASCVD risk $< 10\%$	$\geq 140/90$	$< 130/80$
Older persons ( $\geq 65$ years of age; noninstitutionalized, ambulatory, community-living adults)	$\geq 130$ (SBP)	$< 130$ (SBP)
<b>Specific Comorbidities</b>		
Diabetes mellitus	$\geq 130/80$	$< 130/80$
Chronic kidney disease	$\geq 130/80$	$< 130/80$
Chronic kidney disease after renal transplantation	$\geq 130/80$	$< 130/80$
Heart failure	$\geq 130/80$	$< 130/80$
Stable ischemic heart disease	$\geq 130/80$	$< 130/80$
Secondary stroke prevention	$\geq 130/80$	$< 130/80$
Secondary stroke prevention (lacunar)	$\geq 130/80$	$< 130/80$
Peripheral arterial disease	$\geq 130/80$	$< 130/80$

# Uncertainty Persists

**Annals of Internal Medicine**

IDEAS AND OPINIONS

## Let's Not SPRINT to Judgment About New Blood Pressure Goals

Eduardo Ortiz, MD, MPH, and Paul A. James, MD

**S**PRINT (Systolic Blood Pressure Intervention Trial), a randomized, controlled trial that compared aggressive treatment to a target systolic blood pressure (BP) less than 120 mm Hg with a target less than 140 mm Hg in patients at increased cardiovascular risk, was stopped early and its results were promoted widely months before publication (1). Participants were mostly men (64%) with a mean age of 68 years and comorbidities that increased their cardiovascular risk, but patients with diabetes were excluded. With the lower treatment target, the trial found a 25% relative risk reduction in the primary composite outcome. Although a 25% re-

cluded significant increases in hypotension, syncope, electrolyte abnormalities, and acute kidney injury or acute renal failure. Emergency department visits also occurred more frequently for each of these events, as well as for bradycardia and injurious falls (4). These adverse drug events underscore a concern about potential overtreatment in both groups, given that previous evidence from randomized trials has not demonstrated a benefit in important health outcomes of drug treatment to a BP goal less than 140/90 mm Hg compared with less than 150/90 mm Hg, especially in those without underlying cardiovascular disease (5).

# ADA Hypertension Control Recommendations

## Treatment Goals

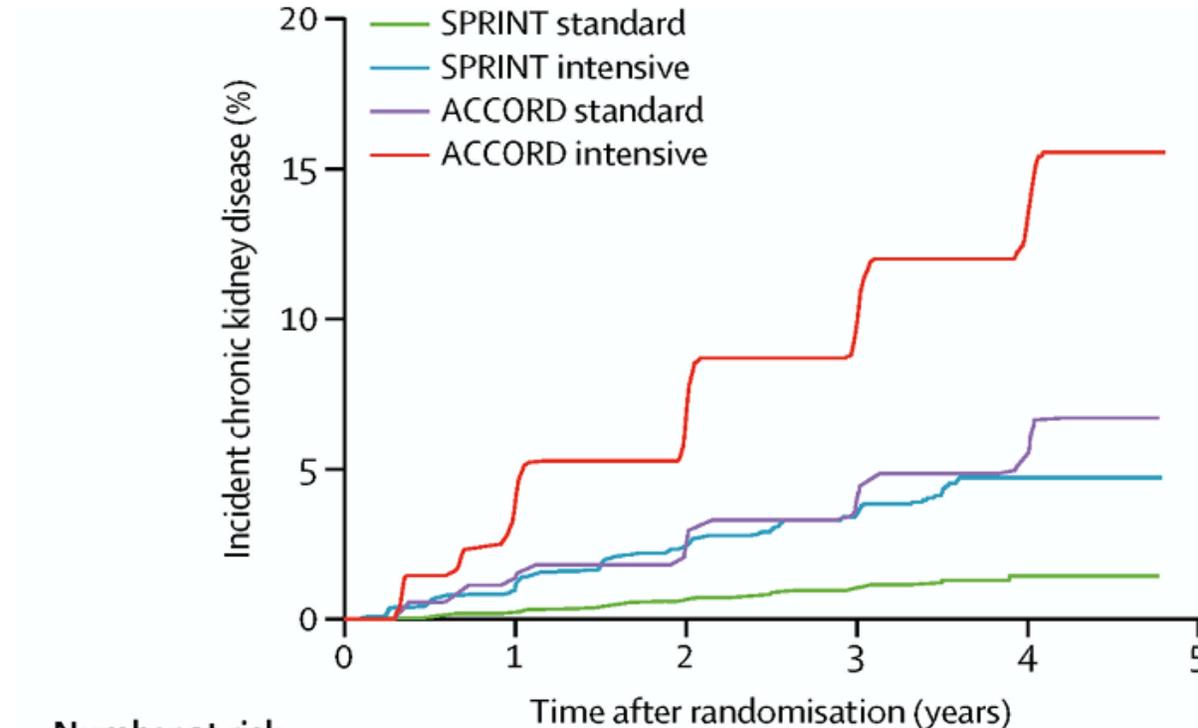
- Most people with diabetes and hypertension should be treated to a systolic BP goal of <140 mmHg and a diastolic BP goal of <90 mmHg. **A (strong)**
- Lower systolic and diastolic BP targets, such as 130/80 mmHg, may be appropriate for individuals at high risk of CVD, if they can be achieved without undue treatment burden. **C (weak)**
- **2020 guidelines essentially unchanged**

Cardiovascular Disease and Risk Management:

Standards of Medical Care in Diabetes, 2018. Diabetes Care 2018; 41 (Suppl. 1): S86-S104

# Cumulative Incidence of CKD in SPRINT and ACCORD

Lancet, July 2018



	Number at risk					
	0	1	2	3	4	5
SPRINT standard	3295	3224	3117	2133	525	..
SPRINT intensive	3304	3186	3061	2089	500	..
ACCORD standard	2157	2041	1961	1874	1580	..
ACCORD intensive	2148	1981	1872	1723	1388	..

# CKD vs. CVD

The risk of incident chronic kidney disease is higher in people with type 2 diabetes than in those without this disease with intensive systolic blood pressure lowering. Chronic kidney disease is known to be a risk factor for future cardiovascular events.

However, it is unclear whether incident chronic kidney disease due to intensive lowering of systolic blood pressure increases the risk of future cardiovascular events. Further studies are warranted to **ascertain whether the higher risk of incident chronic kidney disease with intensive lowering of systolic blood pressure is outweighed by the expected reductions in cardiovascular disease and all-cause mortality in type 2 diabetes in the long term.**

# Individualized Blood Pressure (BP) Goal and Medication in CKD

- Target <140/90 mmHg was endorsed by JNC 8 in 2014.
- Target < 130/80 mmHg was recommended by the American College of Cardiology and American Heart Association in 2017.
- SPRINT trial showed intensive lowering (SBP <120 mmHg) reduced fatal and nonfatal CVD events.
- Excluded people with diabetes or >1g/day proteinuria, among others
- Uncontrolled hypertension (systolic blood pressure >160) is a major challenge.
- A guideline is not a substitute for clinical judgment

James et al. *JAMA* 2014; 311(5):507–520;

Wright et al. *NEJM* 2015; 373:2103-2106;

The SPRINT Research Group. *NEJM* 2015; 373:2103-2116

Whelton et al. *J AM Coll Cardiology*. 2017 DOI:10.1016/j.jack.2017.11.006

# Hyperglycemia

# Use Caution in Interpreting A1C

- Hemoglobin (Hgb) in the red blood cells (RBCs) is glycated when glucose in the serum cross links to certain amino acids on the beta chain of HgbA.
- The glycosylation is essentially irreversible and proportional to glucose concentration.
- The higher the glucose level, the higher the A1C.
- **In CKD, the A1C may not be as accurate due to shortened lifespan of the red blood cells.**

Hahr AJ, Molitch ME. 2015

# Treating Hyperglycemia in Patients with Chronic Kidney Disease

- Evidence that intensive glycemic control reduces the kidney complications of diabetes is based almost exclusively on prevention of micro- and macro-albuminuria.
- The benefits of intensive glycemic control must be balanced against the potential harm of this intervention.
- Hypoglycemia may be a sign that kidney disease has progressed.

# A1C Goal Is Individualized in CKD

- Intensive control to near normal glucose levels early in the course of DM may delay the onset of CKD.
- Less stringent goal may be appropriate for frequent severe hypoglycemia, limited life expectancy and DM complications.
- Goals:
  - A1C <7% for most non-pregnant adults
  - A1C <6.5% may be desirable for new onset DM, type 2 DM treated with lifestyle or metformin.
  - A1c <8% may be appropriate for advanced CKD

ADA Standards of Medical Care, 2019

# The Role of Newer Hypoglycemic Agents

- **Kidney**

- Both SGLT2i and GLP-1 RA reduce albuminuria
- SGLT2i slow decline in eGFR
- SGLT2i may reduce Risk of acute kidney injury (AKI)

- **Vascular**

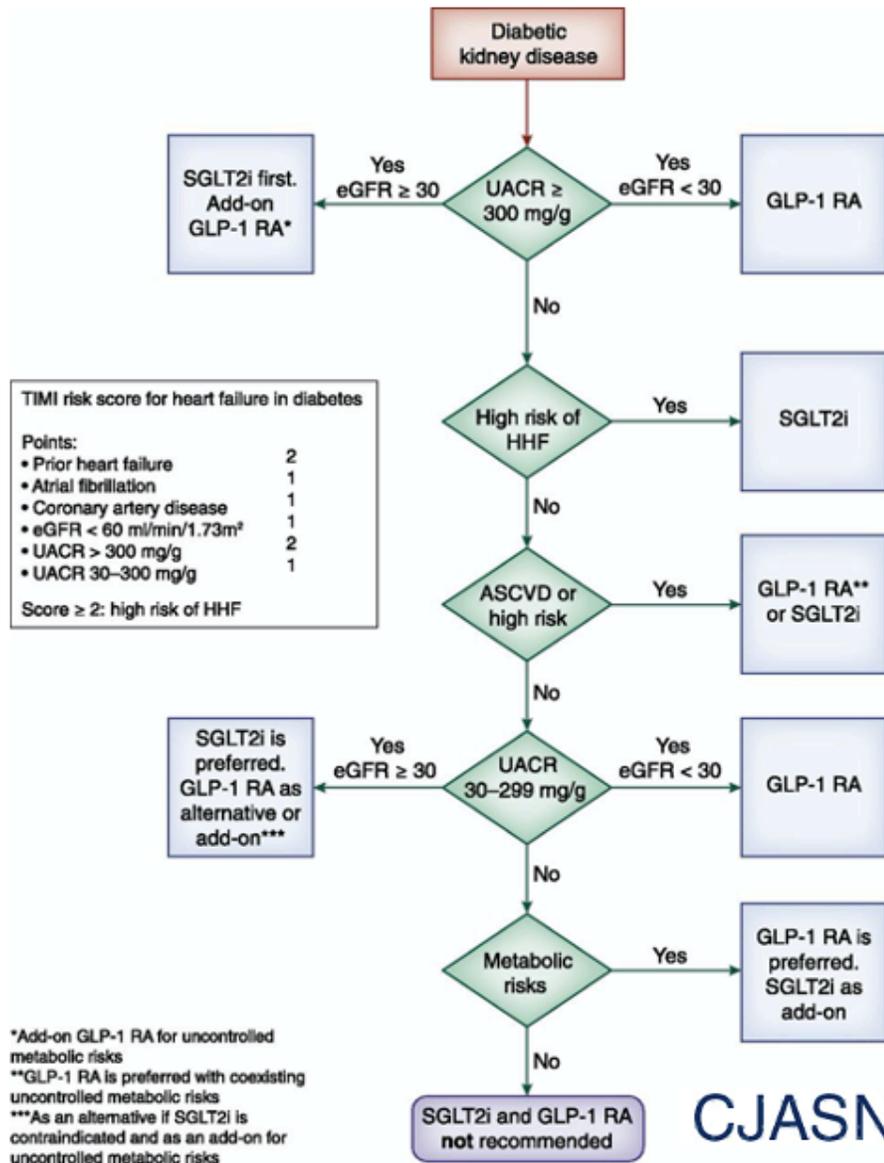
- SGLT2i reduce risk of heart failure more than GLP-1 RA
- Both SGLT2i and GLP-1 RA reduce risk of CV events (CAD, CVD, PVD)

- **Metabolic**

- GLP-1 RA reduces metabolic risks (uncontrolled DM, obesity) more than SGLT2i

Jiahua Li et al. CJASN doi:10.2215/CJN.02690320

# Decision Algorithm for Prescribing SGLT2i and GLP-1 RA Optimizes Heart and Kidney Protection in Patients with Diabetic Kidney Disease.



This algorithm prioritizes the prescription of SGLT2i and GLP-1 RA for maximal heart and kidney protection on the basis of risk stratum.

ACEi/ARB, angiotensin-converting enzyme inhibitor/angiotensin II receptor blocker; ASCVD, atherosclerotic cardiovascular disease; GLP-1 RA, glucagon-like peptide 1 receptor agonist; HHF, hospitalization of heart failure; SGLT2i, sodium-glucose-cotransporter 2 inhibitor; TIMI, Thrombolysis in Myocardial Infarction; UACR, urinary albumin-to-creatinine ratio.

Jiahua Li et al. *CJASN* doi:10.2215/CJN.02690320

# Recommendations for SGLT2i Versus GLP-1 RA on the Basis of Kidney Failure Risk Stratification.

eGFR	UACR <30 mg/g	UACR 30–299 mg/g	UACR ≥300 mg/g
>60 ml/min per 1.73 m <sup>2</sup>	SGLT2i or GLP-1 RA <sup>a</sup>	SGLT2i is preferred. GLP-1 RA as an alternative if SGLT2i is contraindicated or not tolerated, and as an add-on for uncontrolled metabolic risk <sup>b</sup>	SGLT2i should be initiated. GLP-1 RA as an add-on for uncontrolled metabolic risk <sup>c</sup>
30–60 ml/min per 1.73 m <sup>2</sup>	SGLT2i is preferred. GLP-1 RA as an alternative if SGLT2i is contraindicated or not tolerated, and as an add-on for uncontrolled metabolic risk <sup>b</sup>		SGLT2i should be initiated. GLP-1 RA as an add-on for uncontrolled metabolic risk <sup>c</sup>
15–29 ml/min per 1.73 m <sup>2</sup>	GLP-1 RA (dulaglutide) is preferred. Initiation of SGLT2i is currently contraindicated <sup>d</sup>		

SGLT2i, sodium glucose co-transporter 2 inhibitor; GLP-1 RA, glucagon-like peptide 1 receptor agonist; UACR, urinary albumin-to-creatinine ratio.

<sup>a</sup>In patients with low kidney failure risk, SGLT2i and GLP1-RA are similar in preventing worsening albuminuria. Consider SGLT2i if patients have a high risk for heart failure hospitalization. Consider GLP-1 RA if patients have uncontrolled metabolic risks.

<sup>b</sup>In patients with moderate kidney failure risk and adequate eGFR >30 ml/min per 1.73 m<sup>2</sup>, SGLT2i is preferred. Consider adding GLP-1 RA for uncontrolled metabolic risks.

<sup>c</sup>In patients with high kidney failure risk and adequate eGFR >30 ml/min per 1.73 m<sup>2</sup>, SGLT2i is preferred. Consider adding GLP-1 RA for uncontrolled metabolic risks.

<sup>d</sup>In patients with high kidney failure risk but eGFR is <30 ml/min per 1.73 m<sup>2</sup>, GLP-1 RA (dulaglutide) is recommended for safer glycemic control and potential kidney protection. Currently, the data to support the use of SGLT2i for kidney failure prevention in eGFR <30 ml/min per 1.73 m<sup>2</sup> is lacking.

# Nutrition

# National Kidney Disease Education Program (NKDEP): Steps to Eating Right for Kidney Health

Eating Right for

## Kidney Health

Tips for People with Chronic Kidney Disease (CKD)

**W**hat you eat and drink can help slow down chronic kidney disease. Some foods are better for your kidneys than others. Cooking and preparing your food from scratch can help you eat healthier.

These tips will help you eat right as you manage your CKD. The First Steps to Eating Right (pages 1 and 2) are important for all people with CKD. The Next Steps to Eating Right (page 3) may become important as your kidneys slow down.

Work with your dietitian to choose the right foods for you.

### THE FIRST STEPS TO EATING RIGHT

**STEP 1**  
**Choose and prepare foods with less salt and sodium.**  
*Why?* To help control your blood pressure. Your diet should contain less than 2,300 milligrams of sodium each day.



**STEP 2**  
**Eat the right amount and the right types of protein.**  
*Why?* To help protect your kidneys.



**STEP 3**  
**Choose foods that are healthy for your heart.**  
*Why?* To help keep fat from building up in your blood vessels, heart, and kidneys.



# More Steps to Eating Right for Kidney Health

## Eating Right for Kidney Health

### THE FIRST STEPS TO EATING RIGHT

#### STEP 1 Choose and prepare foods with less salt and sodium.

- Buy fresh food more often. Sodium (a part of salt) is added to many packaged foods.
- Use spices, herbs, and sodium-free seasonings in place of salt.
- Check the Nutrition Facts label on food packages for sodium. A Daily Value of 20% or more means the food is high in sodium.
- Try lower-sodium versions of frozen dinners and other convenience foods.
- Rinse canned vegetables, beans, meats, and fish with water before eating.

#### Look for Food Labels that Say

- Sodium free • Salt free • Very low sodium • Low sodium • Reduced or less sodium
- Light in sodium • No salt added • Unsalted • Lightly salted

#### STEP 2 Eat the right amount and right types of protein.

- Eat small portions of protein foods.
- Protein is found in foods from plants and animals. Talk to your dietitian about how to choose the right combination for you.

#### Animal-protein Foods

- Chicken • Fish • Meat • Eggs • Dairy

#### Plant-protein Foods

- Beans • Nuts • Grains

#### STEP 3 Choose foods that are healthy for your heart.

- Grill, broil, bake, roast, or stir-fry foods, instead of deep frying.
- Cook with nonstick cooking spray or a small amount of olive oil instead of butter.
- Trim fat from meat and remove skin from poultry before eating.

#### Heart-healthy Foods

- Lean cuts of meat, like loin or round • Poultry without the skin • Fish • Beans
- Vegetables • Fruits • Low-fat milk, yogurt, cheese

## Eating Right for Kidney Health

### THE NEXT STEPS TO EATING RIGHT

As your kidneys slow down, you *may* need to eat foods that are lower in phosphorus and potassium. Your health care provider will use lab tests to watch your levels.

#### STEP 4 Choose foods with less phosphorus.

*Why?* To help protect your bones and blood vessels.

- Many packaged foods have added phosphorus. Look for phosphorus—or for words with “PHOS”—on ingredient labels.
- Deli meats and some fresh meat and poultry can have added phosphorus. Ask the butcher to help you pick fresh meats without added phosphorus.

#### Foods Lower in Phosphorus

- Fresh fruits and vegetables
- Rice milk (not enriched)
- Light-colored sodas/pop

#### Foods Higher in Phosphorus

- Breads, pasta, rice
- Corn and rice cereals
- Meat, poultry, fish
- Dairy foods
- Bran cereals and oatmeal
- Beans, lentils, nuts
- Colas

#### STEP 5 Choose foods that have the right amount of potassium.

*Why?* To help your nerves and muscles work the right way.

- Salt substitutes can be very high in potassium. Read the ingredient label. Check with your provider about using salt substitutes.
- Drain canned fruits and vegetables before eating.

#### Foods Lower in Potassium

- Apples, peaches
- White bread and pasta
- Rice milk (not enriched)
- Cooked rice and wheat cereals, grits

#### Foods Higher in Potassium

- Carrots, green beans
- White rice
- Rice milk (not enriched)
- Oranges, bananas
- Brown and wild rice
- Dairy foods
- Potatoes, tomatoes
- Bran cereals
- Whole wheat bread and pasta
- Beans and nuts

# Restrict Dietary Potassium When Indicated

- Not everyone with CKD is at risk for hyperkalemia.
- The eGFR is not predictive of need to restrict potassium.
- Monitor levels and make changes as needed.

# Mineral Bone Disease

# Dysregulation of Phosphate May Lead to CVD

- Phosphate retention may initiate secondary hyperparathyroidism, and bone and cardiovascular disease in CKD.
- Hyperphosphatemia may be associated with vascular calcification.
- In CKD, calcium and phosphorus may be deposited into the medial layer of the blood vessels; this may lead to stiffening of the blood vessels.
- In CVD, calcification of the intimal layer is associated with atherosclerotic plaque.

# Study Background: Building an Evidence-based Phosphate (P) Target

- End Stage Renal Disease (ESRD)
  - Affects ~500,000 patients in the U.S. alone
  - Hospitalization: Average ~2 per patients per year
  - Mortality: 15–20% per year
  - Driven primarily by high risk of cardiovascular disease (CVD)
  - Established CVD treatments do not work well in ESRD
- Hyperphosphatemia
  - Very common complication in ESRD
  - Lab studies suggest that high P might cause CVD—arterial calcification & cardiac hypertrophy
  - In patients, high P is associated with CVD and death
- Our current opinion-based approach tells us to lower P to <5.5 mg/dl using P binders and a low P diet.
- **But ... there is no proof in patients that lowering high phosphate helps!**

# We May (or May Not) Be Managing HyperP Correctly

- We have no randomized trials to inform the best way to treat hyperP
  - No trials tested how low or close to normal we should try to push P levels.
  - We know from trials that P binders can lower serum P levels - that we can "treat the numbers."
  - But no trials have tested if treating the numbers improves outcomes and what matters most to patients, such as hospitalizations, death, and quality of life.
- Without randomized trials, we don't know:
  - The ideal serum phosphate target: should it be 4, 5, 6, or 7 mg/dl?
  - If the way we currently manage P levels helps improve only "the numbers" or does it help improve outcomes and what matters most to patients.
  - If our current opinion-based approach might actually make things worse ...

# Despite Our Best Intentions to Help Patients, Might We Be Doing Things Wrong?



By trying to achieve unnecessarily low P targets, we might be increasing risks by:

- Giving too much calcium, lanthanum or iron in P binders.
- Worsening GI side effects and nutritional status by increased use of P binders.
- Worsening quality of life by adding large doses of P binders to an already high pill usage.
- Subconsciously worsening other aspects of care by labeling individual patients as “non-compliant.”

We may be introducing these potential harmful risks because we have no evidence from trials

We need to learn from the past:

- Correcting anemia in ESRD was thought to be beneficial.
- When the trials were finally done, we learned that treating anemia was not helpful!
- Use of aluminum-based P binders was thought to be effective and safe until we learned about their toxicity.

# Goals of Hilo: To determine How to Best Manage Hyperphosphatemia in Patients Receiving Hemodialysis



**Primary:** Hilo will test which of two P management strategies will confer lower rates of all-cause mortality and hospitalization in patients with ESRD undergoing hemodialysis:

- Lo: Usual target P of <5.5 mg/di; or
- Hi: Less strict target P of 6–7 mg/di

**Secondary:** Hilo will test which P management strategy will enhance markers of diet and nutrition and improve quality of life.

# Preparation for Renal Replacement... or Not

# Most People Are Not Prepared for Kidney Failure

- People who are not prepared and need treatment do not have much choice. They may start hemodialysis using a temporary vascular access (catheter).
- In 2016, more than 80% of people started hemodialysis with a temporary vascular access.
- Discuss treatment choices early with progressive kidney disease.
- “Early” depends on the eGFR and the rate of decline.

# Supportive Care Without Dialysis or Transplant May Be the Choice for an Individual Who:

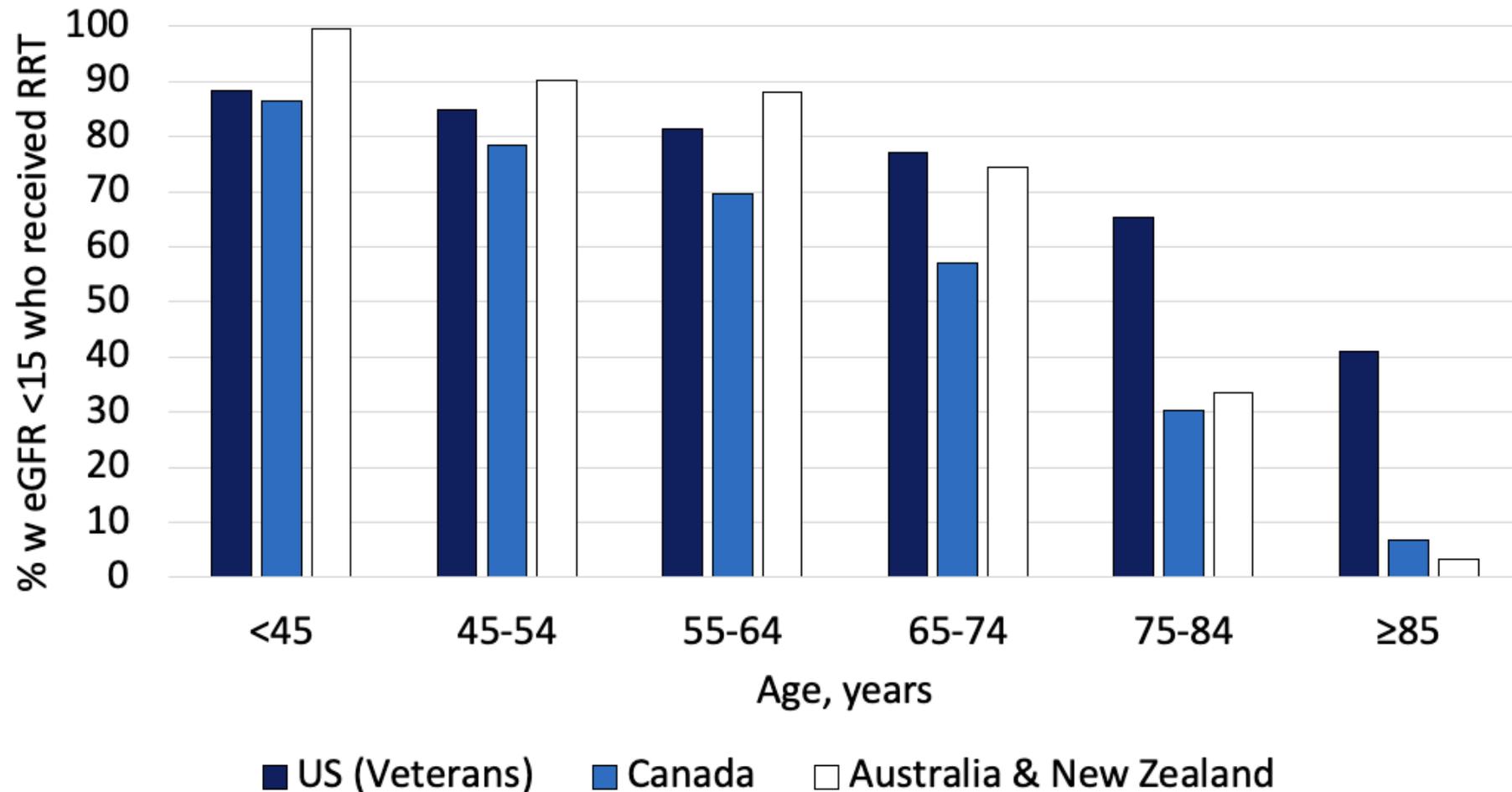
- Feels treatment will not improve their health.
- Feels they have done what they wanted to do in life.
- Has family and friends who are in support of this decision.

# Dialysis or Medical Management (MM)

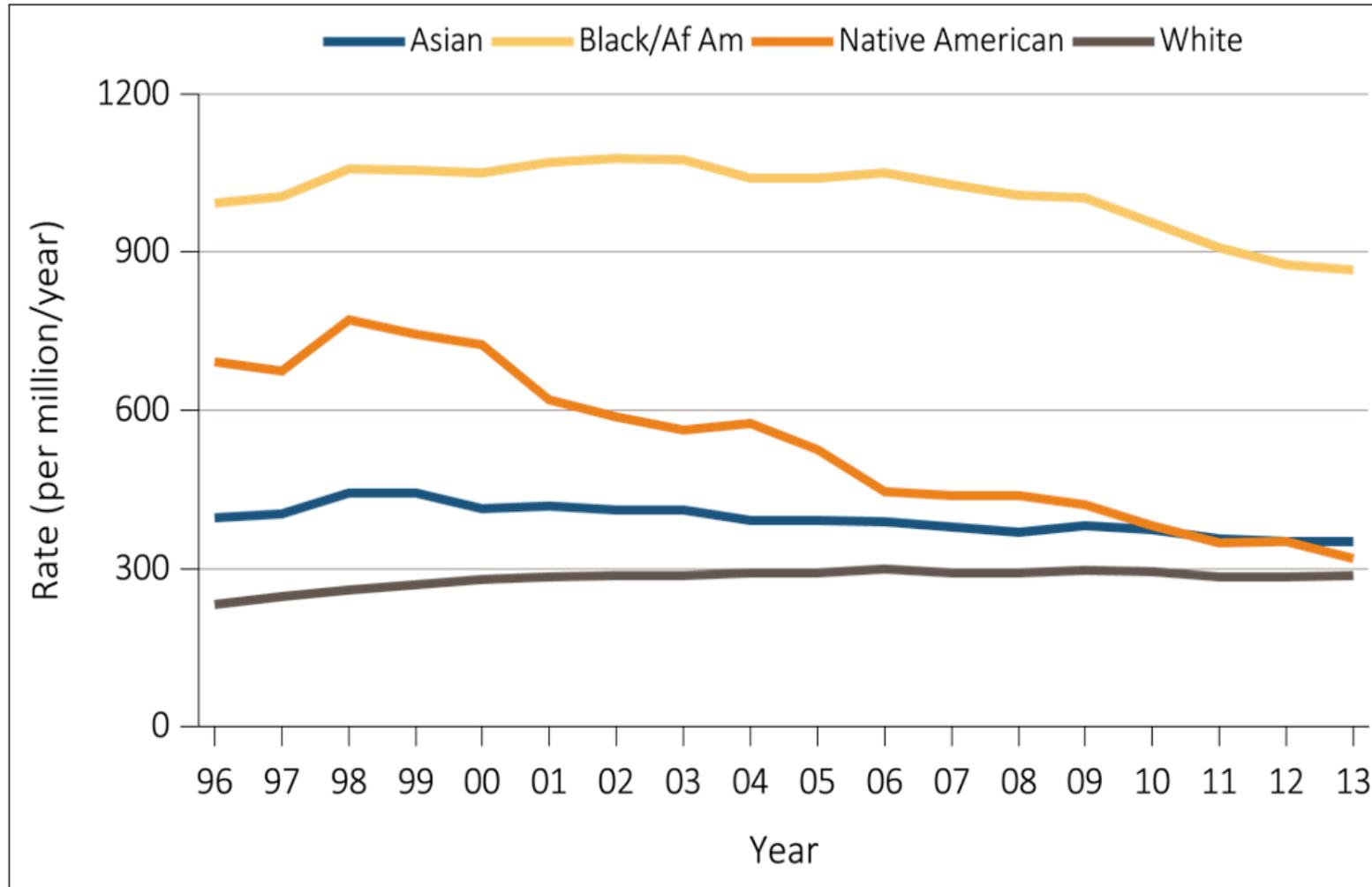
- Dialysis is a powerful default, and patients face an uphill battle to receive MM.
- Survival and quality of life may be similar between patients opting for MM vs. dialysis among certain patient groups.
- MM is a patient-centered, multidisciplinary and whole-person approach to advanced kidney disease.
- More work is needed to understand care practices and outcomes of MM in the U.S.

# RRT Rates in U.S. and Other Developed Countries

Wong, CJASN 2016



# Trends in Adjusted\* ESRD Incidence Rate (Per Million/Year), by Race, in the U.S. Population, 1996–2013, MMWR, Jan 10, 2017



# Population Health: The System Is the Intervention

- Chronic kidney disease is best addressed through population management
- Improvement in care results from changes implemented by in the community and in the clinic by all health professionals (Chronic Care Model)
- Implemented through diabetes care delivery system; not specialty clinic based
- Surveillance and prevention are part of multisystem chronic disease control
- Emphasis on ensuring that patient received care from competent and interested individual, not referral

# NKDEP Resources



# Questions and Comments

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All materials available (maybe) at:

<http://nkdep.nih.gov/>

