Early Identification and Intervention of Chronic Kidney Disease Speaker's Guide

March 2021

Introduction: Statistics for Chronic Kidney Disease (CKD)

Kidney Disease Statistics for the United States: Prevalence

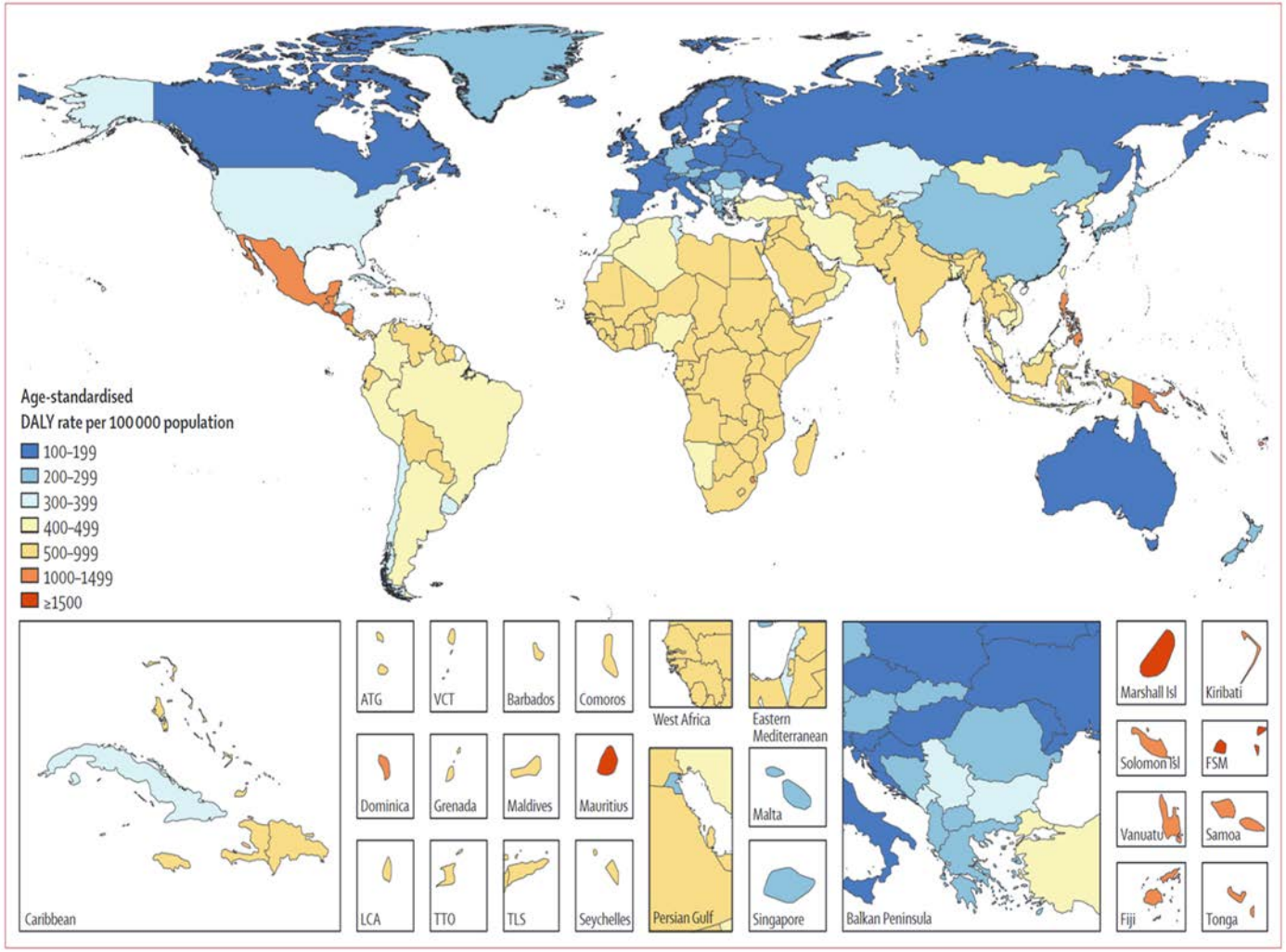


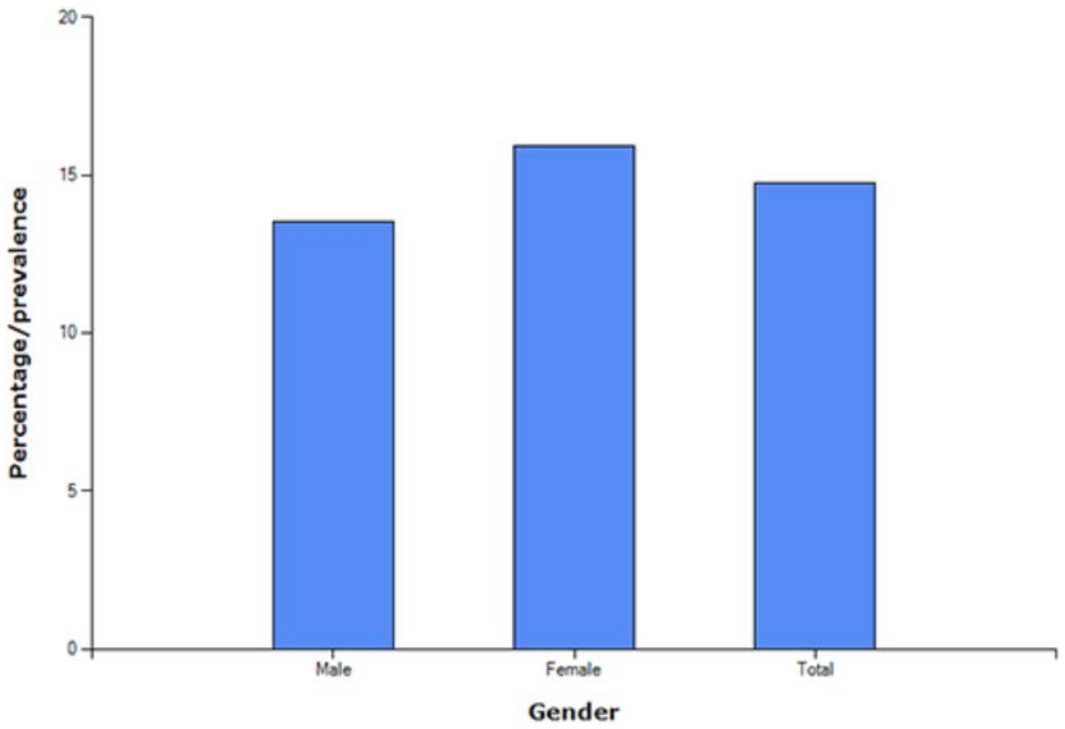
Figure 1: Age-standardised rate of DALYs for chronic kidney disease in 2017

DALY=disability-adjusted life-year. ATG=Antigua and Barbuda. FSM=Federated States of Micronesia. LCA=Saint Lucia. TLS=Timor-Leste. TTO=Trinidad and Tobago. VCT=Saint Vincent and the Grenadines.

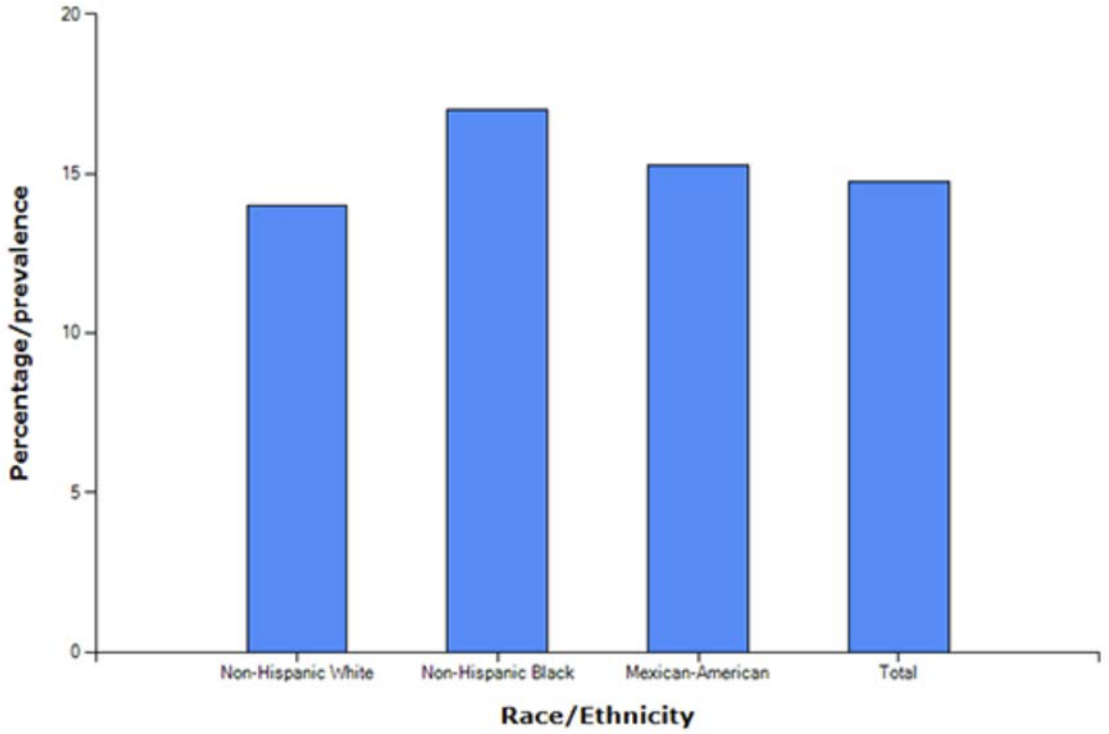
Bikbov B, Purcell CA, Levey AS, et al. Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. The Lancet 2020

Kidney Disease Statistics for the United States: Prevalence

Age-Adjusted Prevalence of CKD Stages 1-4 by Gender 1999-2012[2]



Age-Adjusted Prevalence of CKD Stages 1-4 by Race/Ethnicity 1999-2012[3]



Kidney Disease Statistics for the United States | NIDDK (nih.gov)

Kidney Disease Statistics for the United States: Costs

- Medicare spending for patients with CKD ages 65 and older exceeded $81 billion in 2018 and represented 22% of all Medicare spending in this age group.

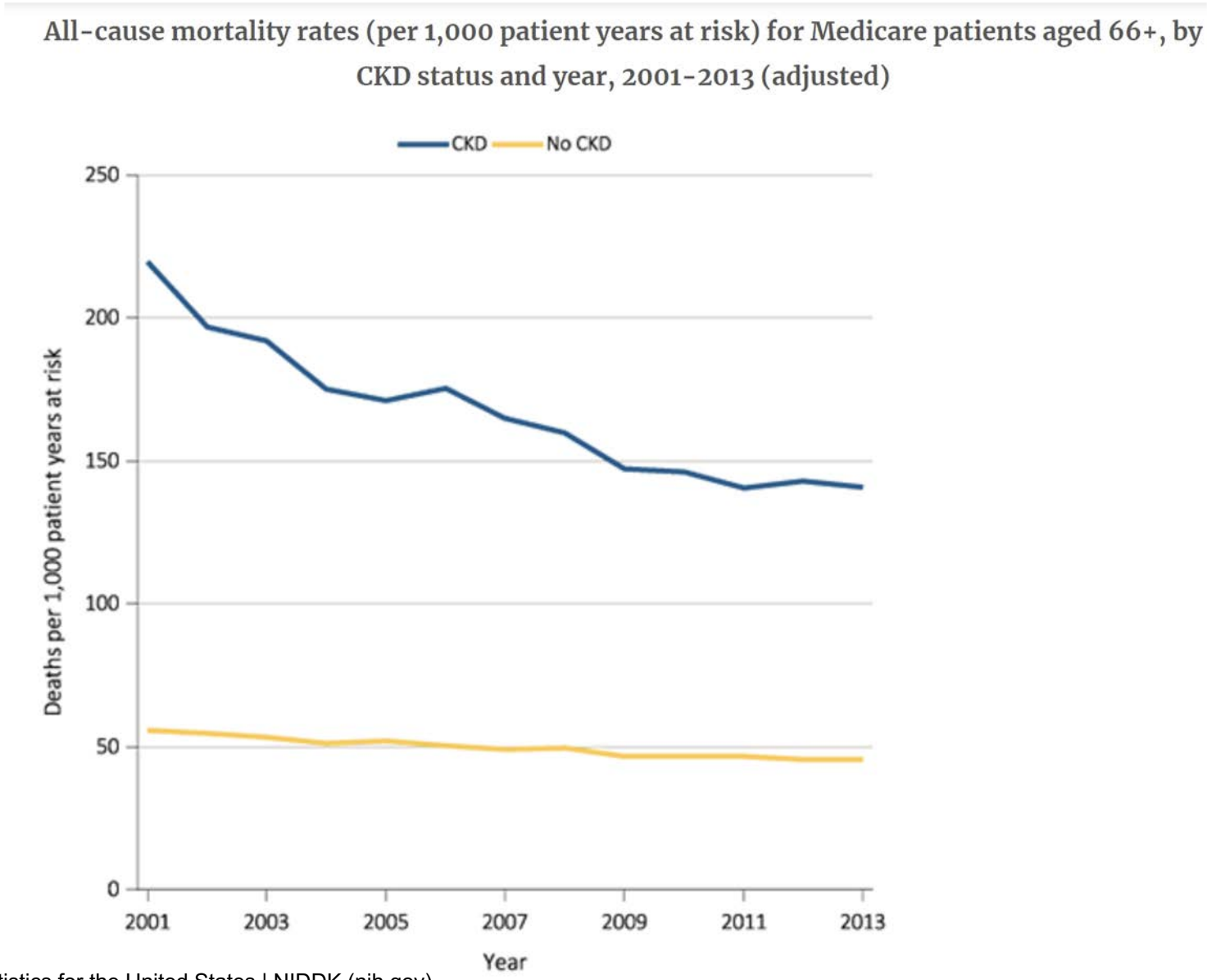
- More than 70% of Medicare spending for CKD patients age 65 and older was incurred by those who also had diabetes, congestive heart failure or both.

- Spending was more than twice as high for patients with all three chronic conditions of CKD, diabetes, congestive heart failure ($57,965) than in patients with only CKD ($25,734).

- Total Medicare-related expenditures for beneficiaries with ESRD rose to $49.2B in 2018 and accounted for 7.2% of Medicare fee-for-service expenditures.

Kidney Disease Statistics for the United States | NIDDK (nih.gov)

Kidney Disease Statistics for the United States: Mortality



Kidney Disease Statistics for the United States | NIDDK (nih.gov)

editorial

www.kidney-international.org

Burden, access, and disparities in kidney disease

Check for updates

Kidney International (2019) **95,** 242–248; https://doi.org/10.1016/j.kint.2018.11.007

KEYWORDS: acute kidney injury; end stage renal disease; global health; health equity; social determinants of health

Table 1 | World Bank country group chronic kidney disease gaps

CKD care	Low-income countries (%)	Lower-middle-income countries (%)	Upper middle-income countries (%)	High-income countries (%)
Governmental recognition of CKD as a health priority	59	50	17	29
Government funds all aspects of CKD care	13	21	40	53
Availability of CKD management and referral guidelines (international, national, or regional)	46	73	83	97
Existence of current CKD detection programs	6	24	24	32
Availability of dialysis registries	24	48	72	89
Availability of academic centers for renal clinical trial management	12	34	62	63

Crews DC, Bello AK, Saadi G, World Kidney Day Steering C. Burden, access, and disparities in kidney disease. Kidney Int Rep 2019;4:372-9.

Mean Annual Health Care Cost Per Patient with CKD (developed countries)

- Progression from CKD G1–G2 to CKD G3a-3b was associated with a 1.1–1.7 fold increase in per patient mean annual health care cost

- Mean annual total health care costs per patient:
  - CKD G1-G3b: $1,600 to $25,037
  - CKD G4–G5: $5,367 to $53,186
  - Kidney failure: $20,110 to $100,593

Elshahat S et al. *PLoS ONE* 2020; 15: e0230512

Screening for CKD: Barriers to Early Identification & Intervention

Early identification of CKD

- Screening
- Risk stratification
- Treatment

https://www.pinterest.com/pin/374361787748770734/

Professional organizations have been discordant on whether or not to screen for CKD

Annals of Internal Medicine | CLINICAL GUIDELINE

Screening for Chronic Kidney Disease: U.S. Preventive Services Task Force Recommendation Statement

Virginia A. Moyer, MD, MPH, on behalf of the U.S. Preventive Services Task Force*

Description: New U.S. Preventive Services Task Force (USPSTF) recommendation statement on screening for chronic kidney disease (CKD).

Methods: The USPSTF reviewed evidence on screening for CKD, including evidence on screening, accuracy of screening, early treatment, and harms of screening and early treatment.

Population: This recommendation applies to asymptomatic adults without diagnosed CKD. Testing for and monitoring CKD for the purpose of chronic disease management (including testing and monitoring patients with diabetes or hypertension) are not covered by this recommendation.

Recommendation: The USPSTF concludes that the evidence is insufficient to assess the balance of benefits and harms of routine screening for CKD in asymptomatic adults (I statement).

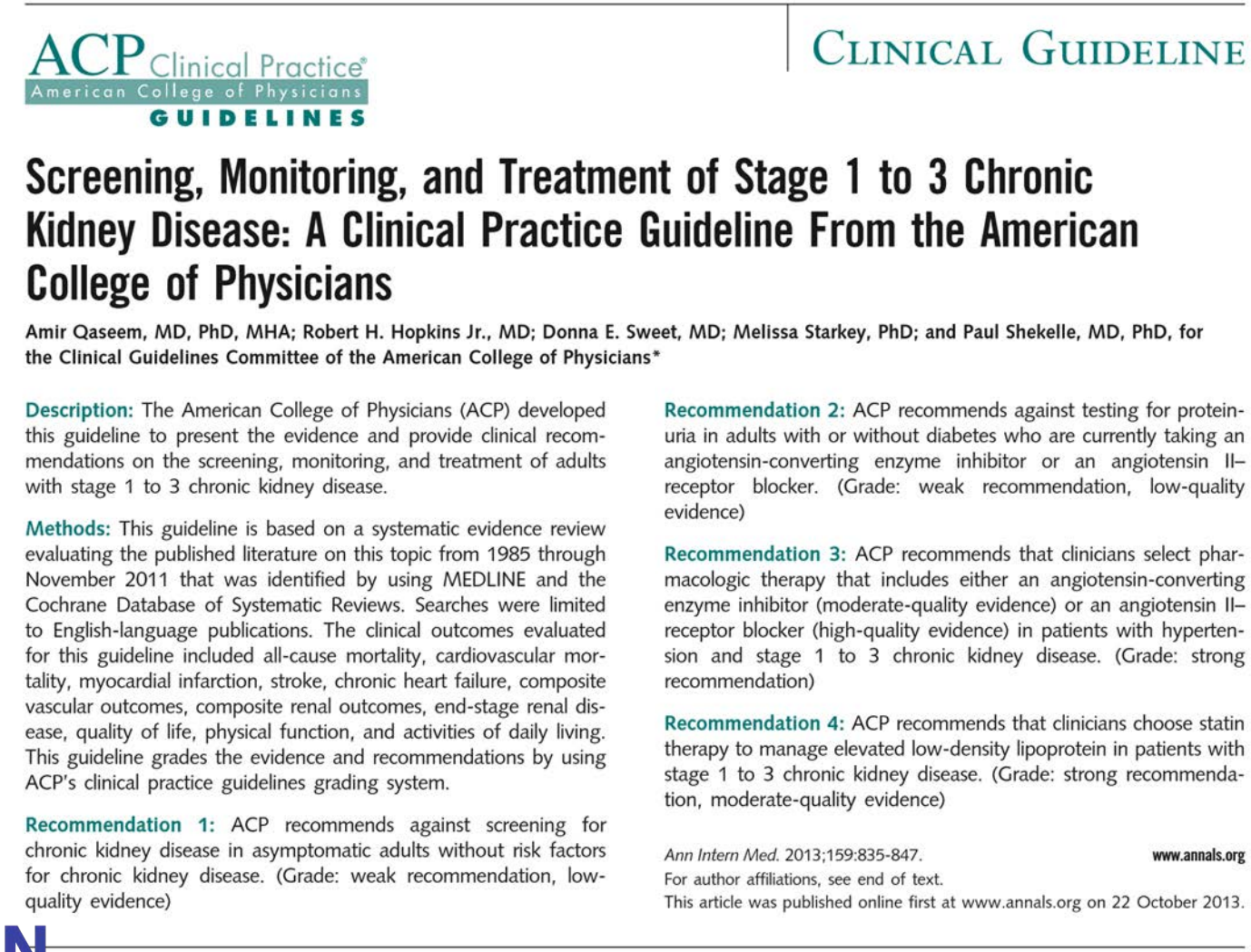
Ann Intern Med. 2012;157:567-570. **www.annals.org**

For author affiliation, see end of text.

* For a list of USPSTF members, see the **Appendix** (available at www.annals.org).

This article was published at www.annals.org on 28 August 2012.

Professional organizations have been discordant on whether or not to screen for CKD



ACP Clinical Practice® American College of Physicians GUIDELINES

CLINICAL GUIDELINE

Screening, Monitoring, and Treatment of Stage 1 to 3 Chronic Kidney Disease: A Clinical Practice Guideline From the American College of Physicians

Amir Qaseem, MD, PhD, MHA; Robert H. Hopkins Jr., MD; Donna E. Sweet, MD; Melissa Starkey, PhD; and Paul Shekelle, MD, PhD, for the Clinical Guidelines Committee of the American College of Physicians*

Description: The American College of Physicians (ACP) developed this guideline to present the evidence and provide clinical recommendations on the screening, monitoring, and treatment of adults with stage 1 to 3 chronic kidney disease.

Methods: This guideline is based on a systematic evidence review evaluating the published literature on this topic from 1985 through November 2011 that was identified by using MEDLINE and the Cochrane Database of Systematic Reviews. Searches were limited to English-language publications. The clinical outcomes evaluated for this guideline included all-cause mortality, cardiovascular mortality, myocardial infarction, stroke, chronic heart failure, composite vascular outcomes, composite renal outcomes, end-stage renal disease, quality of life, physical function, and activities of daily living. This guideline grades the evidence and recommendations by using ACP's clinical practice guidelines grading system.

Recommendation 1: ACP recommends against screening for chronic kidney disease in asymptomatic adults without risk factors for chronic kidney disease. (Grade: weak recommendation, low-quality evidence)

Recommendation 2: ACP recommends against testing for proteinuria in adults with or without diabetes who are currently taking an angiotensin-converting enzyme inhibitor or an angiotensin II–receptor blocker. (Grade: weak recommendation, low-quality evidence)

Recommendation 3: ACP recommends that clinicians select pharmacologic therapy that includes either an angiotensin-converting enzyme inhibitor (moderate-quality evidence) or an angiotensin II–receptor blocker (high-quality evidence) in patients with hypertension and stage 1 to 3 chronic kidney disease. (Grade: strong recommendation)

Recommendation 4: ACP recommends that clinicians choose statin therapy to manage elevated low-density lipoprotein in patients with stage 1 to 3 chronic kidney disease. (Grade: strong recommendation, moderate-quality evidence)

Ann Intern Med. 2013;159:835-847. www.annals.org
For author affiliations, see end of text.
This article was published online first at www.annals.org on 22 October 2013.

In the absence of direct evidence to support screening, we have to make tough choices using all available evidence.

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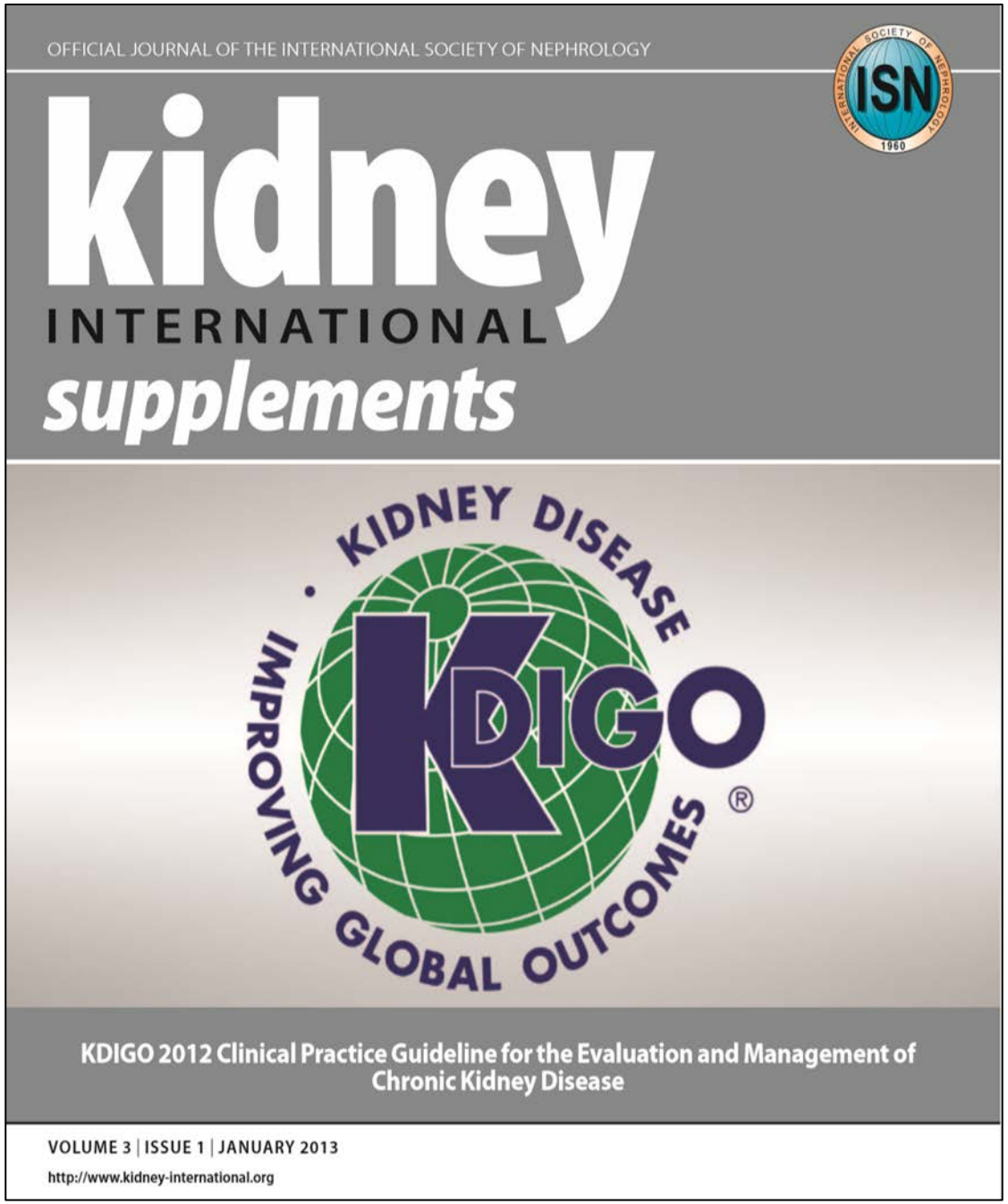
KDIGO Early Identification & Intervention in CKD Controversies Conference

KDIGO Early Identification & Intervention in CKD Controversies Conference

(Official hashtag: #KDIGOEarlyCKD)


OFFICIAL JOURNAL OF THE INTERNATIONAL SOCIETY OF NEPHROLOGY
ISN
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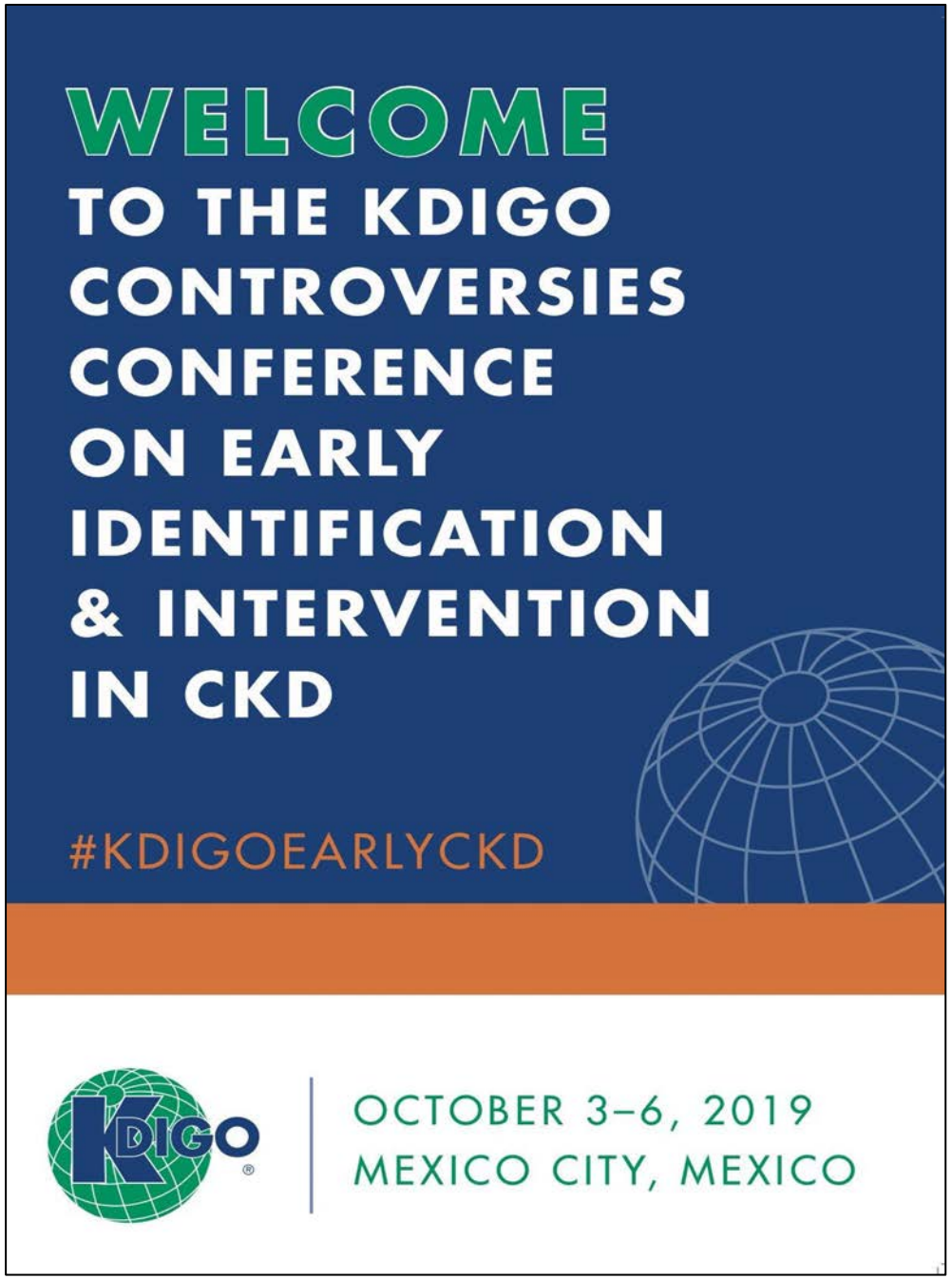
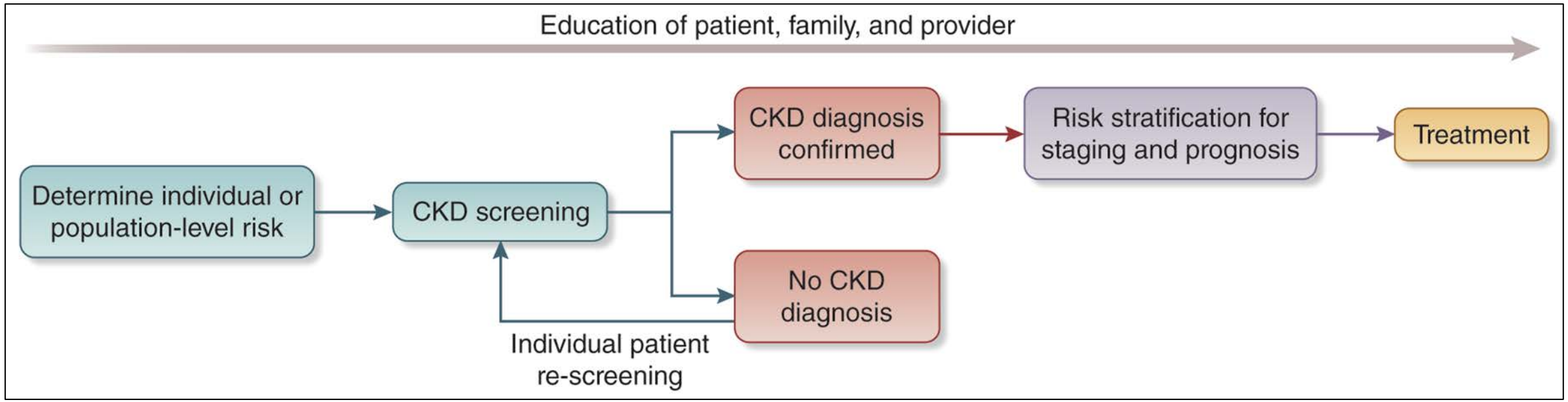
KIDNEY DISEASE
KDIGO
IMPROVING GLOBAL OUTCOMES
KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease
VOLUME 3 | ISSUE 1 | JANUARY 2013
http://www.kidney-international.org


WELCOME
TO THE KDIGO CONTROVERSIES CONFERENCE ON EARLY IDENTIFICATION & INTERVENTION IN CKD
#KDIGOEARLYCKD
KDIGO
OCTOBER 3–6, 2019
MEXICO CITY, MEXICO

Outline: Four Major Topics

1. The selection of candidate populations for CKD early detection
2. The relative diagnostic and predictive characteristics of tests for kidney disease and their potential costs
3. The evidence base for treatments that could reduce the risk of CKD progression and cardiovascular events
4. The implementation strategies for CKD early detection and treatment programs and the key factors determining resource allocation and cost-effectiveness

Conceptual framework of a CKD screening, risk stratification, and treatment program



WHO Screening Principles Apply to CKD

- Public health problem
- Early asymptomatic phase
- Detectable by affordable testing
- Treatments are effective and available
- Disease progression understood
- Screening treatment must be ongoing, not just one episode
- Affordable for overall healthcare budget

WHO

KDIGO

Additional Considerations

- Patients overwhelmingly prefer earlier CKD screening and diagnosis.
- Patient education has the potential to improve self-management and disease prognosis.
- Economic rationale must favor some program of early CKD screening/risk stratification/treatment, given the costs of kidney failure to healthcare systems and society.

Approaches considered to CKD screening, risk-stratification and treatment

- Identification of all persons with CKD
- Identification of individuals within high-risk populations to maximize testing yield
- Identification of individuals with CKD who are most likely to progress to kidney failure or experience cardiovascular or other CKD complications
- Additional topics:
  - Definitions of high-risk populations
  - Optimal frequency of rescreening

Individualized Treatment

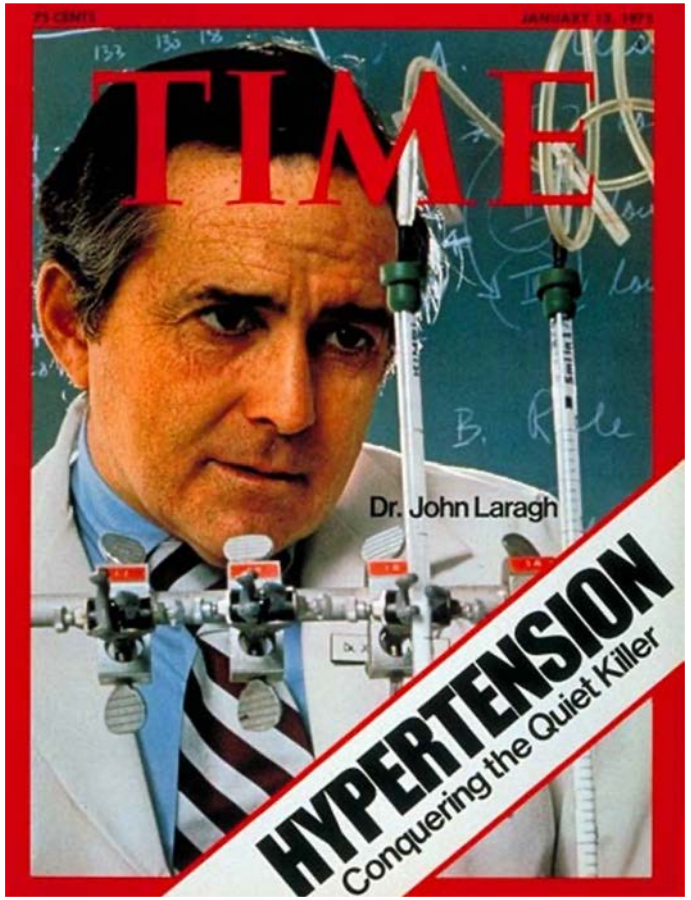
Decisions concerning the age to initiate testing, the frequency of repeat testing, and the time to forgo or end testing should all be ***individualized*** based upon:

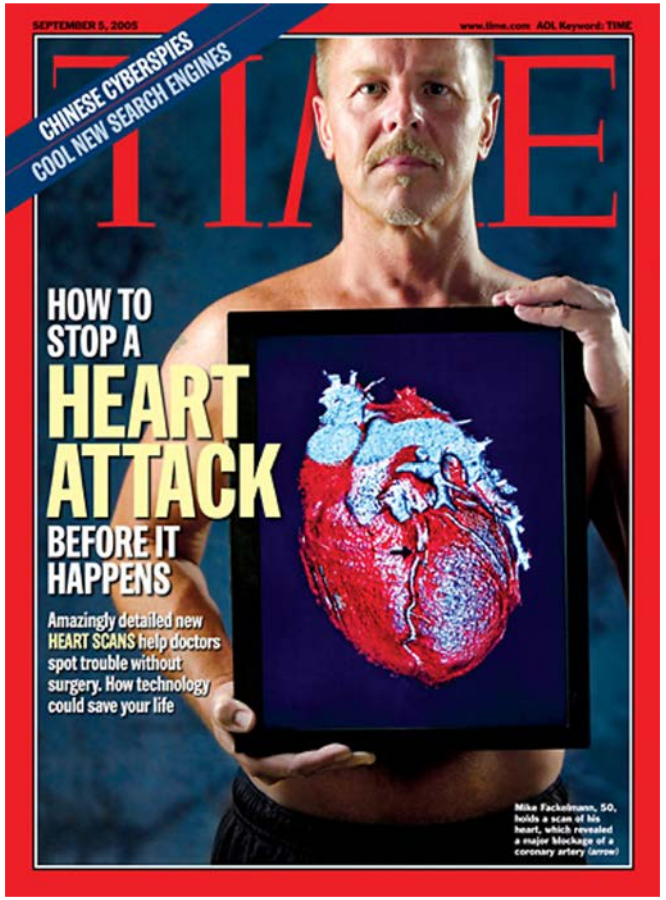
- Risk factors
- Preferences
- Life expectancy

Controversies Conference Report Conclusion 1:

Persons with hypertension, diabetes, and cardiovascular disease should be screened for CKD.

Conclusion 1: Persons with hypertension, diabetes, and cardiovascular disease should be screened for CKD.

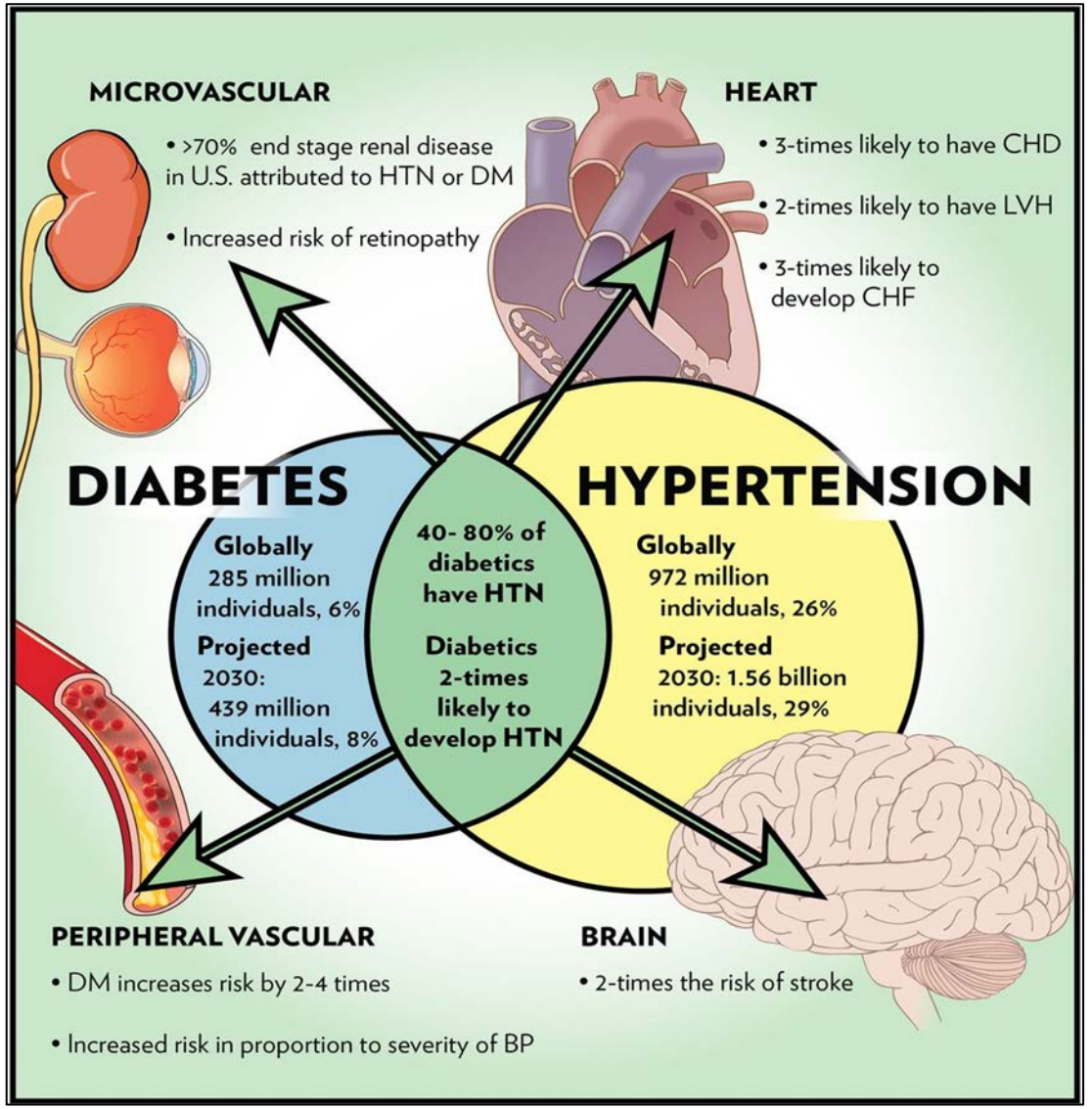




Screening Strategy

CKD screening should be implemented for groups with these well-accepted CKD risk factors:

- ❑ Hypertension,
- ❑ Diabetes, and/or
- ❑ Cardiovascular disease



https://heart.bmj.com/content/99/8/577

Controversies Conference Report Conclusion 2:

CKD screening and treatment programs should be also implemented in other high-risk individuals and populations based on comorbidities, environmental exposures, or genetic factors.

Conclusion 2: CKD screening and treatment programs should also be implemented in other high-risk individuals and populations based on comorbidities, environmental exposures, or genetic factors.

Older age

Race/ ethnicity

SLE

HIV

Family History

Genetic Risk Factors

Low Socioeconomic Status

Environmental Exposures

Prior AKI

Preeclampsia

Nephrotoxins

Obesity

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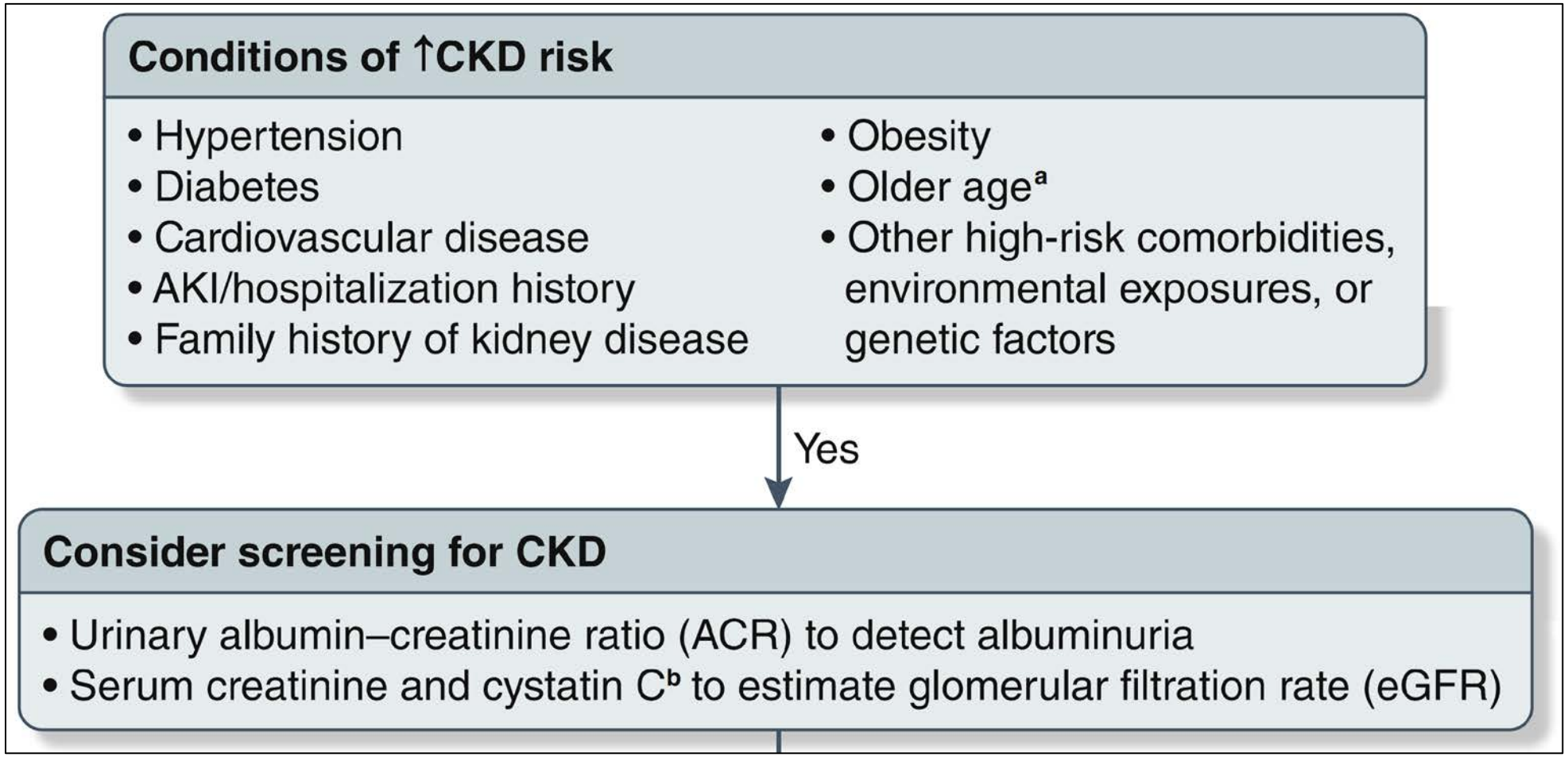
Conclusion 2: CKD screening and treatment programs should also be implemented in other high-risk individuals and populations based on comorbidities, environmental exposures, or genetic factors.

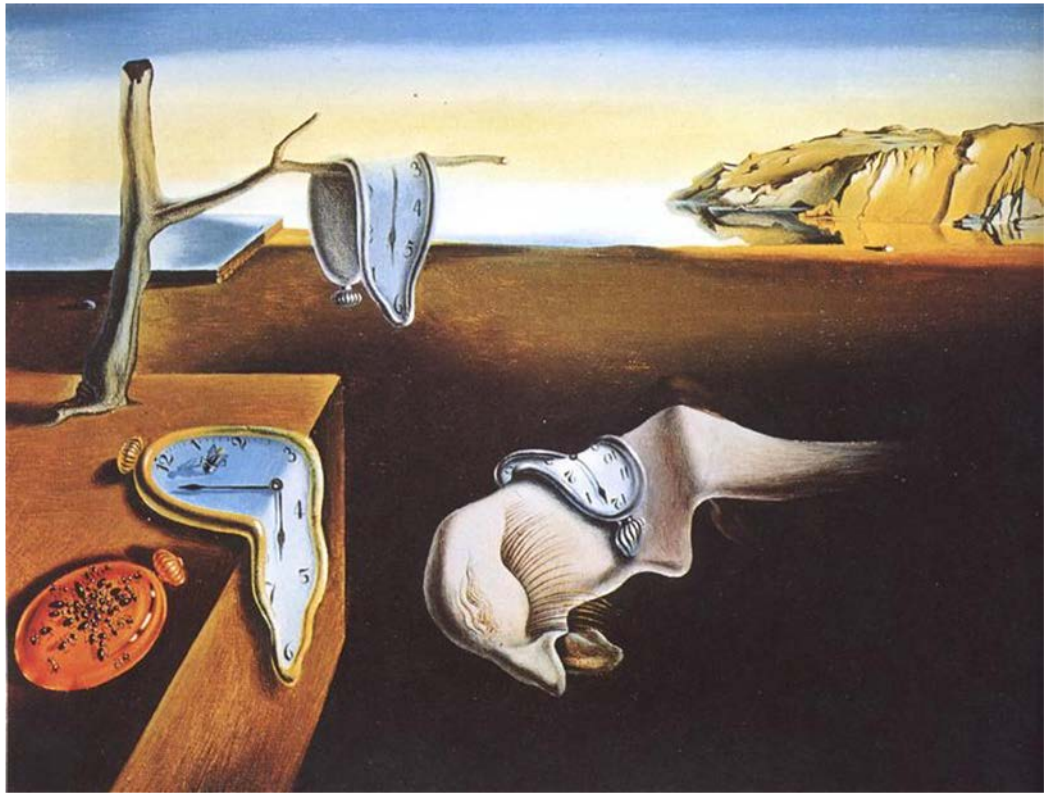


Controversies Conference Report Conclusion 3:

The initiation, frequency, and cessation of CKD screening should be individualized based on kidney and cardiovascular risk profiles and individual preferences.

Conclusion 3: The initiation, frequency, and cessation of CKD screening should be individualized based on kidney and cardiovascular risk profiles and individual preferences.

The **timing of initiation of CKD screening** should be based on comorbidities and individualized risk assessment, rather than at a specific chronologic age.



https://www.wikiart.org/en/salvador-dali/the-persistence-of-memory-1931

- The **frequency of testing** is a critical aspect of CKD screening programs and has substantial impact on costs.
- Must be individualized and could range from 1 to 10 years.
- **Risk equations that estimate future CKD probabilities** could be used to guide the timing of the subsequent testing.

Research

JAMA | Original Investigation

Development of Risk Prediction Equations for Incident Chronic Kidney Disease

Robert G. Nelson, MD, PhD; Morgan E. Grams, MD, PhD; Shoshana H. Ballew, PhD; Yingying Sang, MS; Fereidoun Azizi, MD; Steven J. Chadban, MD, PhD; Layal Chaker, MD, PhD; Stephan C. Dunning, MBA; Caroline Fox, MD; Yoshihisa Hirakawa, MD; Kunitoshi Iseki, MD, PhD; Joachim Ix, MD, MAS; Tazeen H. Jafar, MD, MPH; Anna Köttgen, MD, MPH; David M. J. Naimark, MD, MSc; Takayoshi Ohkubo, MD, PhD; Gordon J. Prescott, BSc, MSc, PhD, CStat; Casey M. Rebholz, PhD; Charumathi Sabanayagam, PhD; Toshimi Sairenchi, PhD; Ben Schöttker, PhD; Yugo Shibagaki, MD; Marcello Tonelli, MD, SM; Luxia Zhang, MD; Ron T. Gansevoort, MD, PhD; Kunihiro Matsushita, MD, PhD; Mark Woodward, PhD; Josef Coresh, MD, PhD; Varda Shalev, MD; for the CKD Prognosis Consortium

IMPORTANCE Early identification of individuals at elevated risk of developing chronic kidney disease (CKD) could improve clinical care through enhanced surveillance and better management of underlying health conditions.

OBJECTIVE To develop assessment tools to identify individuals at increased risk of CKD, defined by reduced estimated glomerular filtration rate (eGFR).

DESIGN, SETTING, AND PARTICIPANTS Individual-level data analysis of 34 multinational cohorts from the CKD Prognosis Consortium including 5 222 711 individuals from 28 countries. Data were collected from April 1970 through January 2017. A 2-stage analysis was performed, with each study first analyzed individually and summarized overall using a weighted average. Because clinical variables were often differentially available by diabetes status, models were developed separately for participants with diabetes and without diabetes. Discrimination and calibration were also tested in 9 external cohorts (n = 2 253 540).

Overdiagnosis vs the greater relative burden of CKD on the elderly

Prevalence of Chronic Kidney Disease in the United States

Josef Coresh, MD, PhD
Elizabeth Selvin, PhD, MPH
Lesley A. Stevens, MD, MS
Jane Manzi, PhD
John W. Kusek, PhD
Paul Eggers, PhD
Frederick Van Lente, PhD
Andrew S. Levey, MD

Context The prevalence and incidence of kidney failure treated by dialysis and transplantation in the United States have increased from 1988 to 2004. Whether there have been changes in the prevalence of earlier stages of chronic kidney disease (CKD) during this period is uncertain.

Objective To update the estimated prevalence of CKD in the United States.

Design, Setting, and Participants Cross-sectional analysis of the most recent National Health and Nutrition Examination Surveys (NHANES 1988-1994 and NHANES 1999-2004), a nationally representative sample of noninstitutionalized adults aged 20 years or older in 1988-1994 (n=15 488) and 1999-2004 (n=13 233).

Main Outcome Measures Chronic kidney disease prevalence was determined based on persistent albuminuria and decreased estimated glomerular filtration rate (GFR). Persistence of microalbuminuria (>30 mg/g) was estimated from repeat visit data in NHANES 1988-1994. The GFR was estimated using the abbreviated Modification of Diet in Renal Disease Study equation reexpressed to standard serum creatinine.

Results The prevalence of both albuminuria and decreased GFR increased from 1988-1994 to 1999-2004. The prevalence of CKD stages 1 to 4 increased from 10.0% (95% confidence interval [CI], 9.2%-10.9%) in 1988-1994 to 13.1% (95% CI, 12.0%-

CHRONIC KIDNEY DISEASE (CKD) is now recognized as a common condition that elevates the risk of cardiovascular disease as well as kidney failure and other complications.[1-3] The num-

Age and Association of Kidney Measures With Mortality and End-stage Renal Disease

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Corri Black, MBChB, MSc, FFPH
Areef Ishani, MD, MS
Nanne Kleefstra, MD, PhD
David Naimark, MD, MSc, FRCP(C)
Paul Roderick, MD, FRCP
Marcello Tonelli, MD, SM
Jack F. M. Wetzels, MD, PhD
Brad C. Astor, PhD, MPH
Ron T. Gansevoort, MD, PhD
Adeera Levin, MD
Chi-Pang Wen, MD, MPH, DrPH
Josef Coresh, MD, PhD
for the Chronic Kidney Disease Prognosis Consortium

Context Chronic kidney disease (CKD) is prevalent in older individuals, but the risk implications of low estimated glomerular filtration rate (eGFR) and high albuminuria across the full age range are controversial.

Objective To evaluate possible effect modification (interaction) by age of the association of eGFR and albuminuria with clinical risk, examining both relative and absolute risks.

Design, Setting, and Participants Individual-level meta-analysis including 2 051 244 participants from 33 general population or high-risk (of vascular disease) cohorts and 13 CKD cohorts from Asia, Australasia, Europe, and North/South America, conducted in 1972-2011 with a mean follow-up time of 5.8 years (range, 0-31 years).

Main Outcome Measures Hazard ratios (HRs) of mortality and end-stage renal disease (ESRD) according to eGFR and albuminuria were meta-analyzed across age categories after adjusting for sex, race, cardiovascular disease, diabetes, systolic blood pressure, cholesterol, body mass index, and smoking. Absolute risks were estimated using HRs and average incidence rates.

Results Mortality (112 325 deaths) and ESRD (8411 events) risks were higher at lower eGFR and higher albuminuria in every age category. In general and high-risk cohorts, relative mortality risk for reduced eGFR decreased with increasing age; eg, adjusted HRs at an eGFR of 45 mL/min/1.73 m^2 vs 80 mL/min/1.73 m^2 were 3.50 (95% CI, 2.55-4.81), 2.21 (95% CI, 2.02-2.41), 1.59 (95% CI, 1.42-1.77), and 1.35 (95% CI, 1.23-1.48) in age categories 18-54, 55-64, 65-74, and ≥75 years, respectively ($P<.05$ for age interaction). Absolute risk differences for the same comparisons were higher at older age (9.0 [95% CI, 6.0-12.8], 12.2 [95% CI, 10.3-14.3], 13.3 [95% CI, 9.0-18.6], and 27.2 [95% CI, 13.5-45.5] excess deaths per 1000 person-years, respectively). For increased

Measures of chronic kidney disease and risk of incident peripheral artery disease: a collaborative meta-analysis of individual participant data

*Kunihiro Matsushita, Shoshana H Ballew, Josef Coresh, Hisatomi Arima, Johan Ärnlöv, Massimo Cirillo, Natalie Ebert, Jade S Hiramoto, Heejin Kimm, Michael G Shlipak, Frank L J Visseren, Ron T Gansevoort, Csaba P Kovesdy, Varda Shalev, Mark Woodward, Florian Kronenberg, for the Chronic Kidney Disease Prognosis Consortium**

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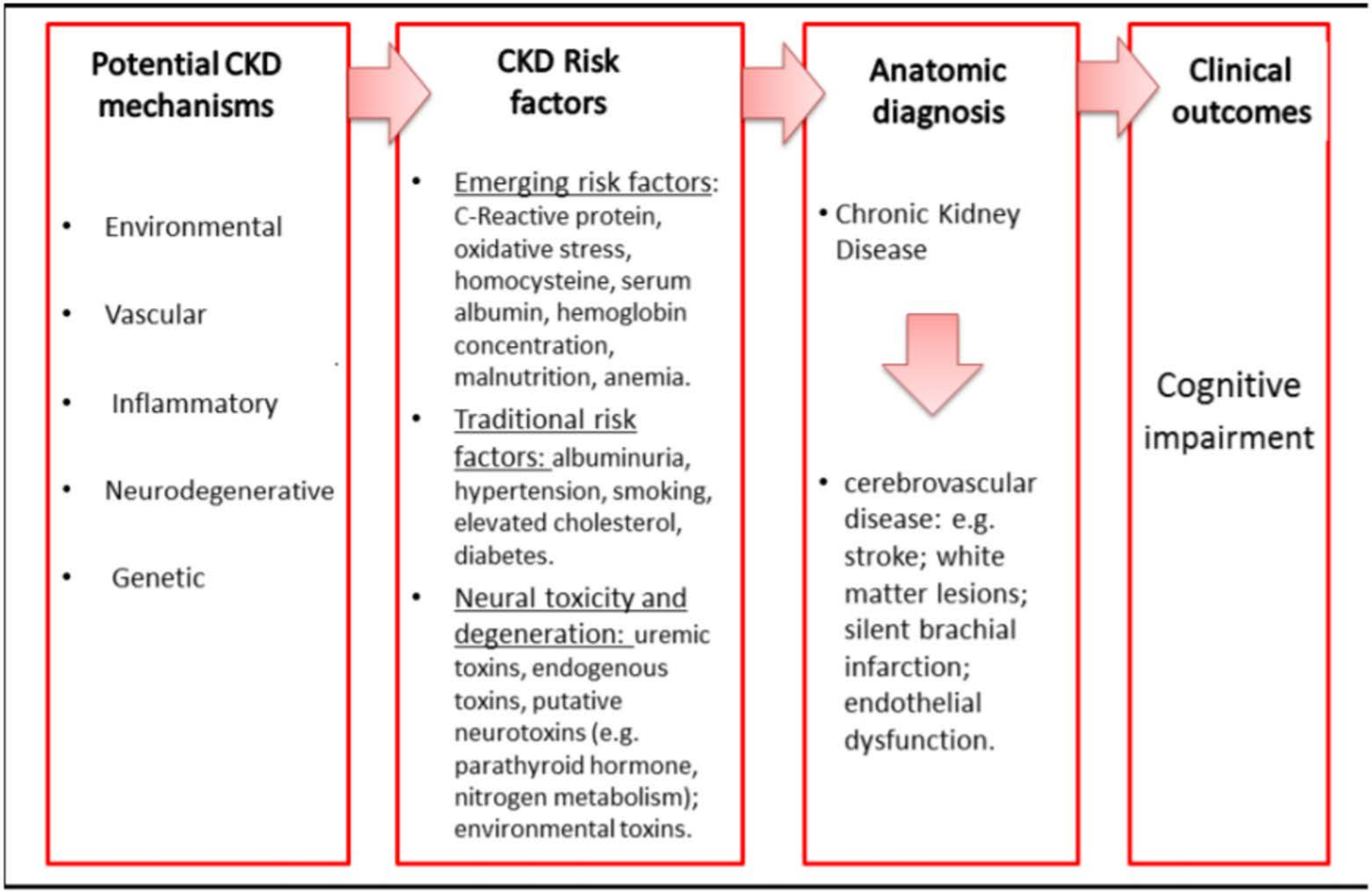
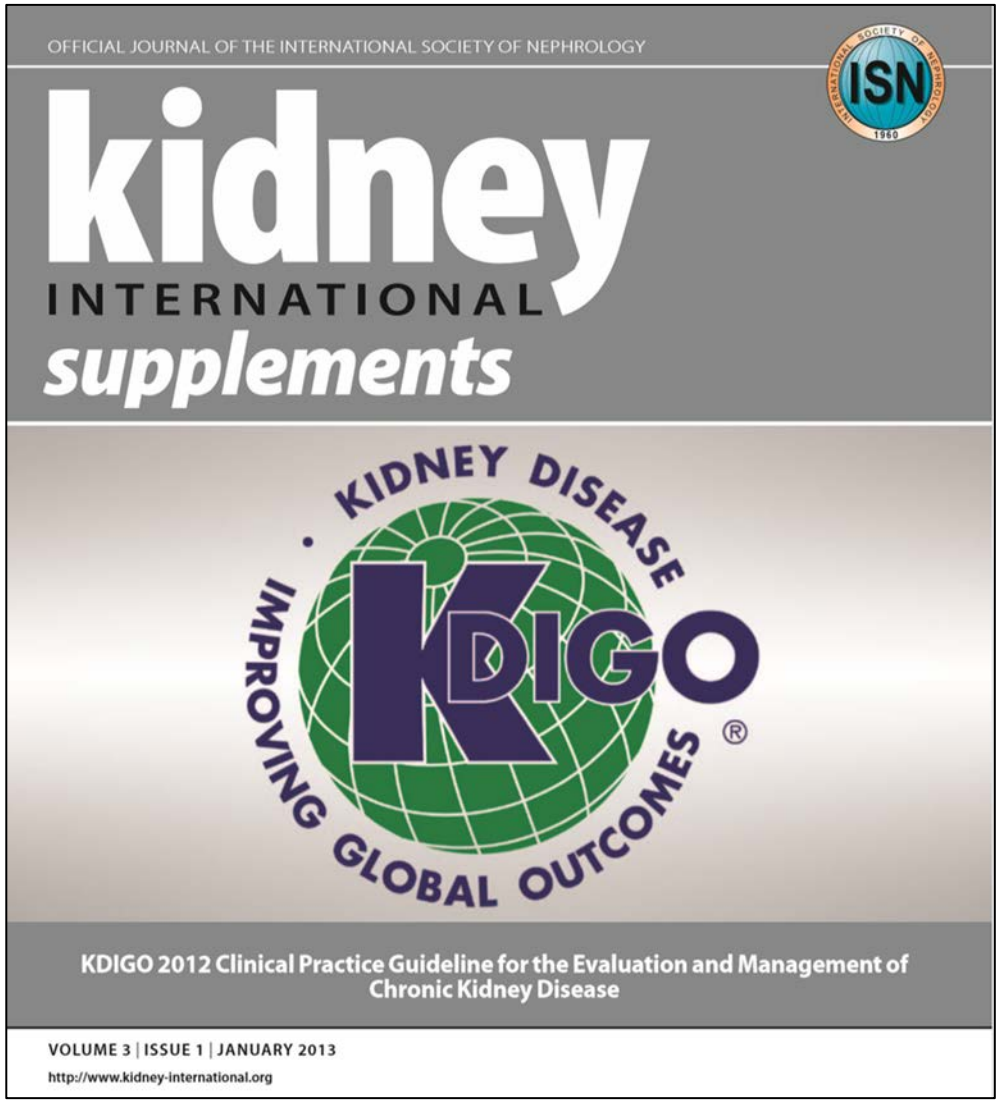

Potential CKD mechanisms
• Environmental
• Vascular
• Inflammatory
• Neurodegenerative
• Genetic
CKD Risk factors
• Emerging risk factors: C-Reactive protein, oxidative stress, homocysteine, serum albumin, hemoglobin concentration, malnutrition, anemia.
• Traditional risk factors: albuminuria, hypertension, smoking, elevated cholesterol, diabetes.
• Neural toxicity and degeneration: uremic toxins, endogenous toxins, putative neurotoxins (e.g. parathyroid hormone, nitrogen metabolism); environmental toxins.
Anatomic diagnosis
• Chronic Kidney Disease
• cerebrovascular disease: e.g. stroke; white matter lesions; silent brachial infarction; endothelial dysfunction.
Clinical outcomes
Cognitive impairment

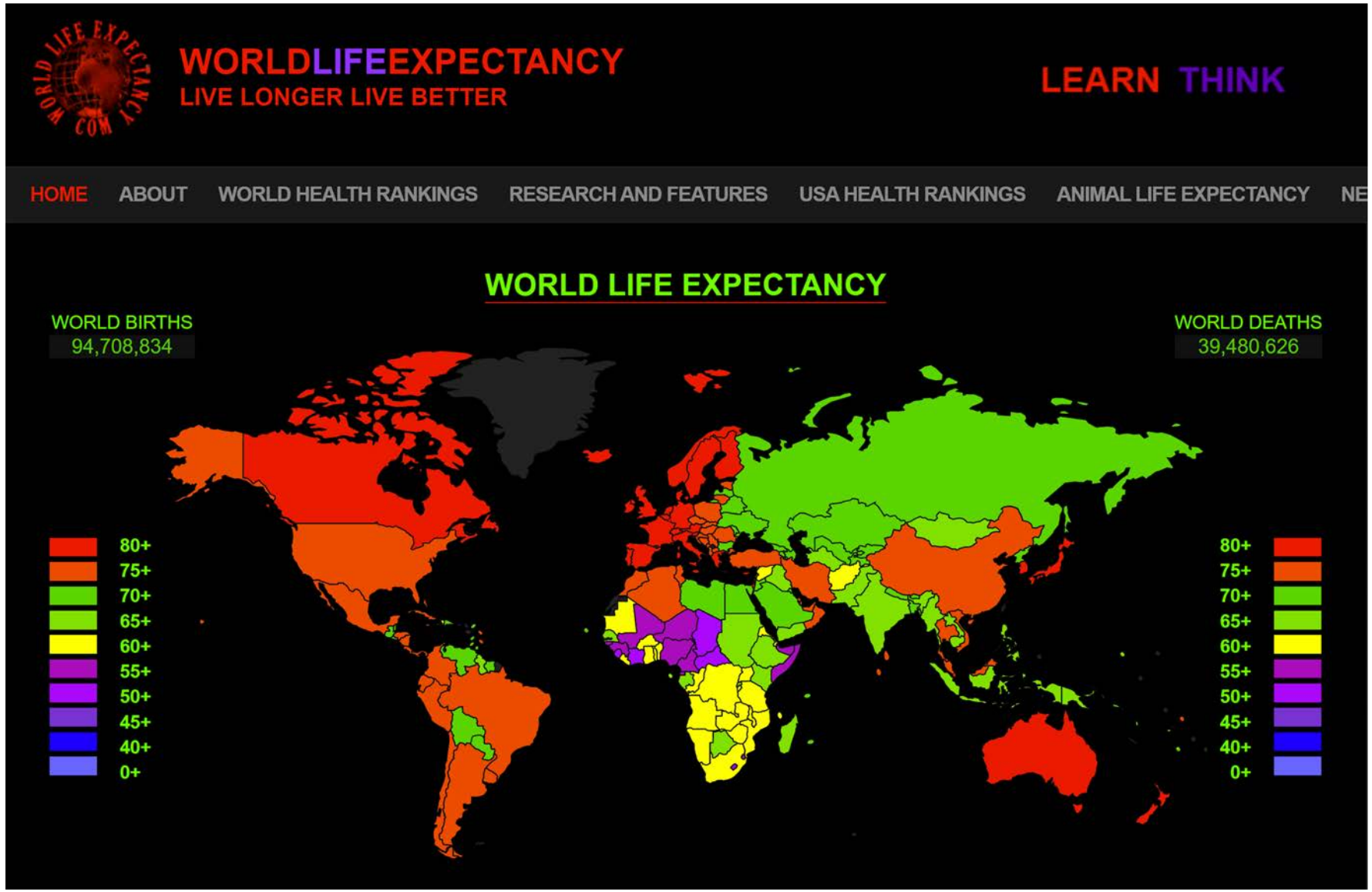
Potential harms associated with CKD overdiagnosis in older adults can be mitigated using available diagnostic and risk tools.



1.4.3.5: We suggest measuring cystatin C in adults with $eGFR_{creat}$ 45-59 ml/min/1.73m^2 who do not have markers of kidney damage if confirmation of CKD is required. (*2C*)

- If $eGFR_{cys}/eGFR_{creat\text{-}cys}$ is also <60 ml/min/1.73 m^2, the diagnosis of CKD is confirmed.
- If $eGFR_{cys}/eGFR_{creat\text{-}cys}$ is ≥ 60 ml/min/1.73 m^2, the diagnosis of CKD is not confirmed.

Older adults should not be excluded from CKD screening programs



Controversies Conference Report Conclusion 4:

CKD screening and risk stratification must consist of a dual assessment of estimated glomerular filtration rate (eGFR) and albuminuria (UACR).

Conclusion 4: CKD screening and risk stratification must consist of a dual assessment of estimated glomerular filtration rate (eGFR) and albuminuria (UACR).

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.

Measurements for Early CKD

The ***ideal initial screening and diagnosis approach*** would consist of the **triple marker panel**:

- Serum creatinine
- Serum cystatin C, and
- Urine albumin-to-creatinine ratio (UACR)

ORIGINAL RESEARCH

Use of Clinical Decision Support to Improve Primary Care Identification and Management of Chronic Kidney Disease (CKD)

Cara B. Litvin, MD, MS, J. Madison Hyer, MS, and Steven M. Ornstein, MD

Primary care physicians' familiarity, beliefs, and perceived barriers to practice guidelines in non-diabetic CKD: a survey study

Khaled Abdel-Kader[1*], Raquel C Greer[2,3], L Ebony Boulware[4] and Mark L Unruh[5]

Incident chronic kidney disease: trends in management and outcomes

Robert M. Perkins[1], Alex R. Chang[1], Kenneth E. Wood[2], Josef Coresh[3], Kunihiro Matsushita[4] and Morgan Grams[3]

[1]Bayer HealthCare, Whippany, NJ, USA, [2]Geisinger Medical Center, Danville, PA, USA, [3]Welch Center for Prevention, Epidemiology and Clinical Research, Johns Hopkins University, Baltimore, MD, USA and [4]Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

Low rates of albuminuria testing in CKD

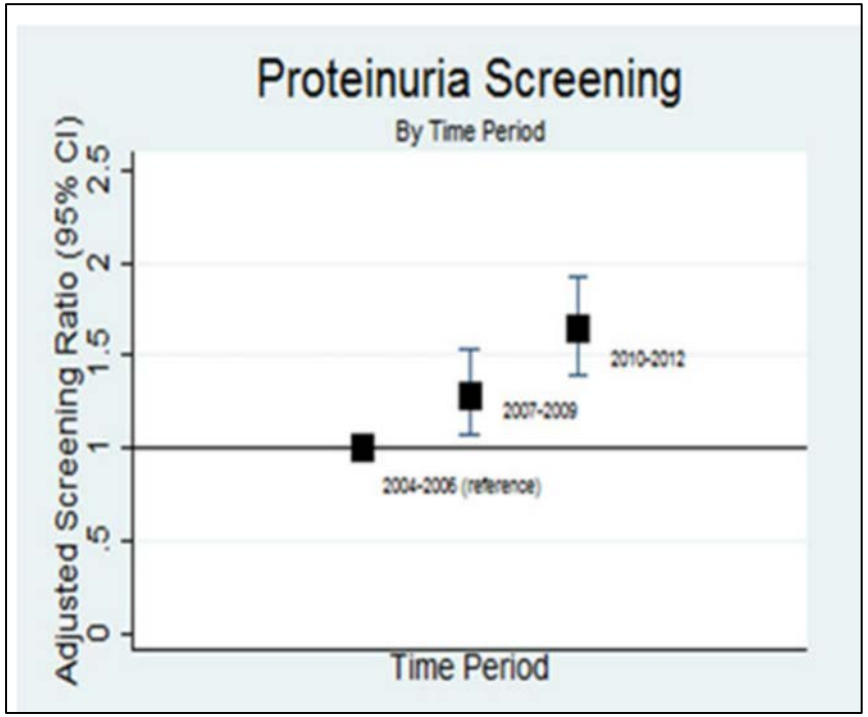
In a US study of more than one million patients with eGFR < 60 ml/min/1.73 m^2, only 19% of the participants had the necessary ACR testing to calculate the 4-variable KFRE.

Further examples:

Cleveland Clinic: 36% of patients with CKD had no proteinuria assessed

UK Cohort: 17% reported ACR testing within the first year of registration of CKD

Naranjo FS., et al. *Kidney360* in press



Perkins et al. *CKJ* 2016; 9: 432-437

In this population of incident CKD Stage G3 patients, quantification rates of urinary protein excretion doubled over the study period, but remained low in absolute terms; less than half of the incident CKD population in 2010–12 underwent urinary protein quantification.

How attuned are PCPs to isolated albuminuria abnormalities?

Abdel-Kader *et al. BMC Nephrology* 2014, **15**:64
http://www.biomedcentral.com/1471-2369/15/64

BMC Nephrology

RESEARCH ARTICLE Open Access

Primary care physicians' familiarity, beliefs, and perceived barriers to practice guidelines in non-diabetic CKD: a survey study

Khaled Abdel-Kader[1*], Raquel C Greer[2,3], L Ebony Boulware[4] and Mark L Unruh[5]

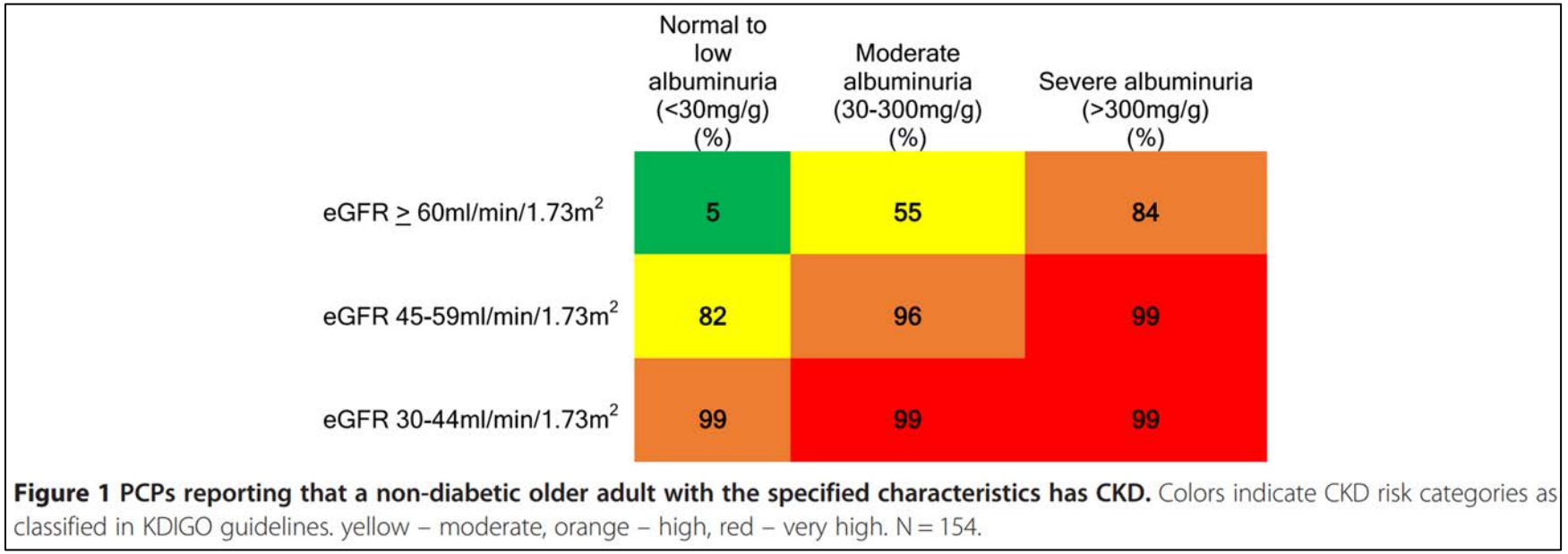


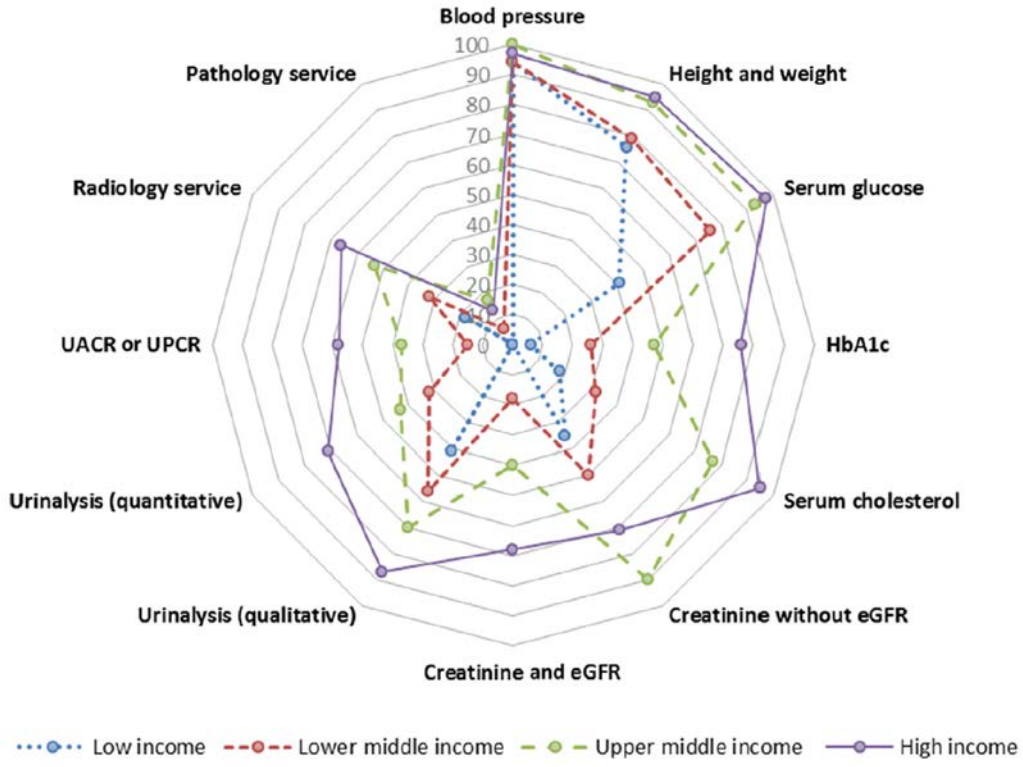
Figure 1 PCPs reporting that a non-diabetic older adult with the specified characteristics has CKD. Colors indicate CKD risk categories as classified in KDIGO guidelines. yellow – moderate, orange – high, red – very high. N = 154.

Poor Adherence to CKD Screening Guidelines in Patients with CKD Risk Factors (e.g., diabetes, hypertension)

Htay H et al. *KI Suppl* .8: 64-73, 2018

- Albuminuria testing in persons with diabetes
  - 41.8% of Medicare
  - 49% of Optum Clinformatics™
- Albuminuria testing – HTN alone
  - 6.6% of Medicare
  - 7.1% of Optum Clinformatics™

2018 USRDS Annual Data Report. NIDDK, 2018

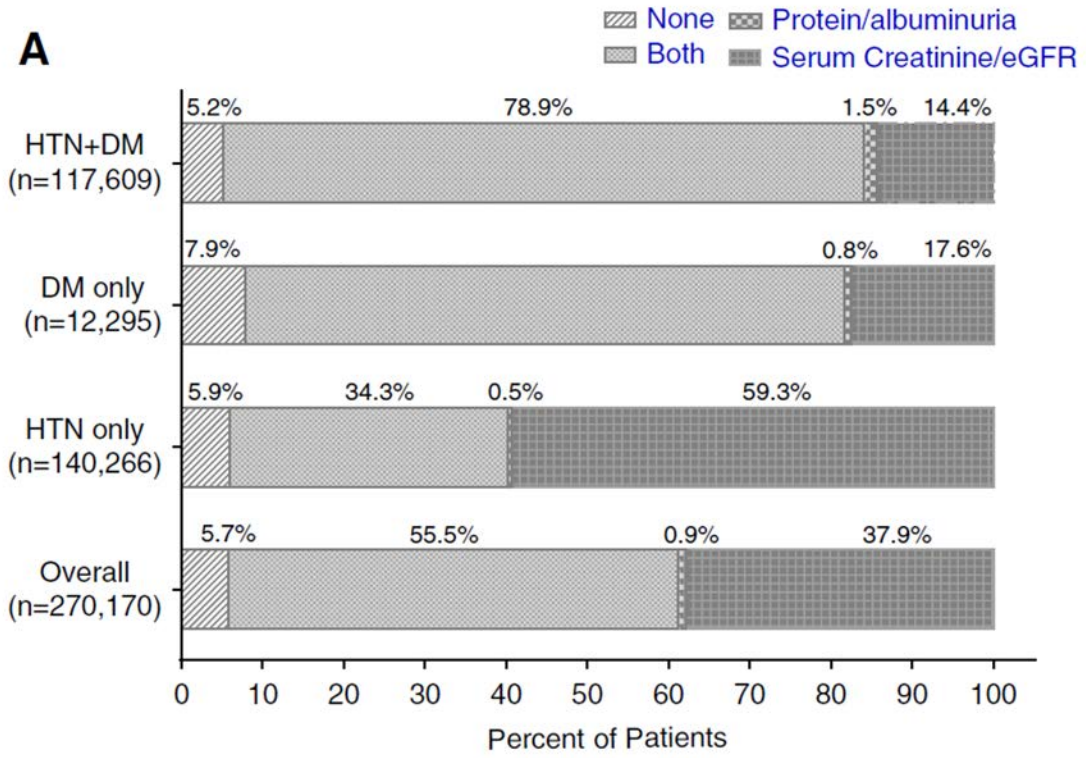


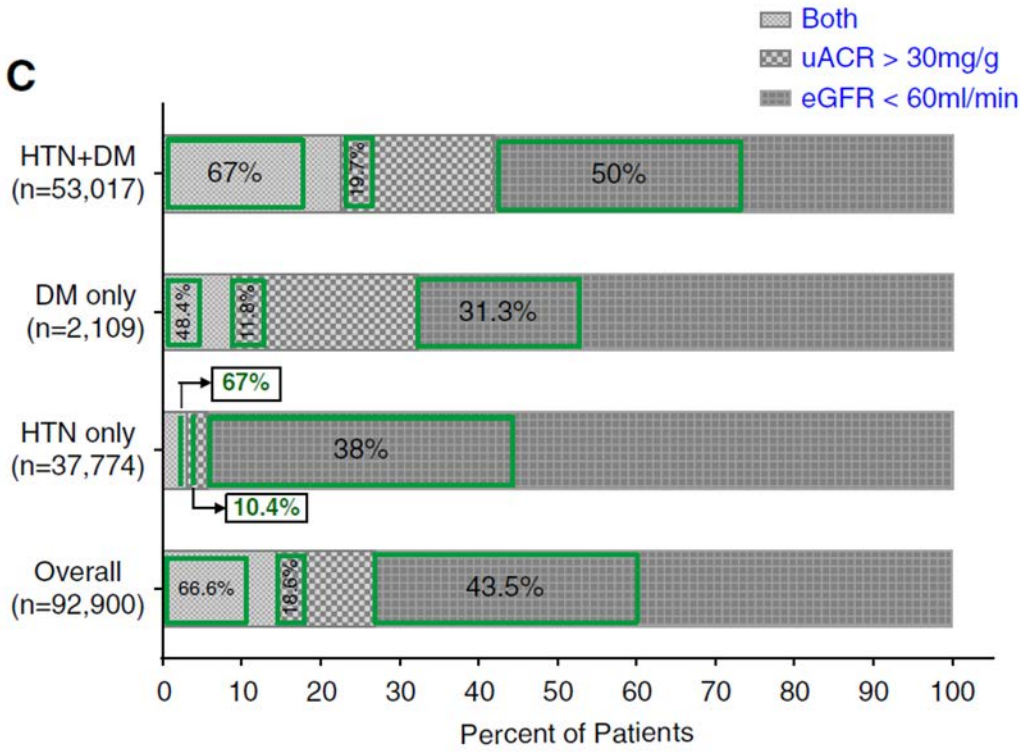
Capacities of primary health care services for CKD (by income groups): Qualitative urinalysis using test strips for albumin or protein or both was available in 41% of low-income countries, 58% of high-income countries in primary care. Only one-third of low-income countries were able to measure serum creatinine in primary care, and none was able to access eGFR.

Poor Adherence to CKD Screening Guidelines in Patients with CKD Risk Factors (e.g., diabetes, hypertension)

Screening and Recognition of CKD in VA Health Care System Primary Care Clinics

Bansal S. et al. *Kidney360*. 2020; 1:904-915





Percentage of patients with diabetes (DM), hypertension (HTN), or both who had screening tests in the chart

Within each criterion of CKD, green box represents the percentage of patients who were recognized to have CKD

Annals of Internal Medicine ORIGINAL RESEARCH

Conversion of Urine Protein–Creatinine Ratio or Urine Dipstick Protein to Urine Albumin–Creatinine Ratio for Use in Chronic Kidney Disease Screening and Prognosis

An Individual Participant–Based Meta-analysis

Keiichi Sumida, MD, MPH, PhD*; Girish N. Nadkarni, MD, MPH*; Morgan E. Grams, MD, PhD; Yingying Sang, MSc; Shoshana H. Ballew, PhD; Josef Coresh, MD, PhD; Kunihiro Matsushita, MD, PhD; Aditya Surapaneni, PhD; Nigel Brunskill, MD, PhD; Steve J. Chadban, MD, PhD; Alex R. Chang, MD, MS; Massimo Cirillo, MD; Kenn B. Daratha, PhD; Ron T. Gansevoort, MD, PhD; Amit X. Garg, MD, PhD; Licia Iacoviello, MD, PhD; Takamasa Kayama, MD, PhD; Tsuneo Konta, MD, PhD; Csaba P. Kovesdy, MD; James Lash, MD; Brian J. Lee, MD; Rupert W. Major, MD, PhD; Marie Metzger, PhD; Katsuyuki Miura, MD, PhD; David M.J. Naimark, MD, MSc; Robert G. Nelson, MD, PhD; Simon Sawhney, MD, PhD; Nikita Stempniewicz, MSc; Mila Tang, MSc; Raymond R. Townsend, MD; Jamie P. Traynor, MD; José M. Valdivielso, PhD; Jack Wetzels, MD, PhD; Kevan R. Polkinghorne, MBChB, PhD†; and Hiddo J.L. Heerspink, PhD†; for the Chronic Kidney Disease Prognosis Consortium‡

Background: Although measuring albuminuria is the preferred method for defining and staging chronic kidney disease (CKD), total urine protein or dipstick protein is often measured instead.

Objective: To develop equations for converting urine protein–creatinine ratio (PCR) and dipstick protein to urine albumin–creatinine ratio (ACR) and to test their diagnostic accuracy in CKD screening and staging.

Design: Individual participant–based meta-analysis.

Setting: 12 research and 21 clinical cohorts.

Participants: 919 383 adults with same-day measures of ACR and PCR or dipstick protein.

Measurements: Equations to convert urine PCR and dipstick or greater, trace to +, and ++ for screening for ACR values greater than 30 mg/g and classification into stages A2 and A3, respectively, had moderate sensitivity (62%, 36%, and 78%) and high specificity (88%, 88%, and 98%). For individual risk prediction, the estimated 2-year 4-variable kidney failure risk equation using predicted ACR from PCR had discrimination similar to that of using observed ACR.

Limitation: Diverse methods of ACR and PCR quantification were used; measurements were not always performed in the same urine sample.

Conclusion: Urine ACR is the preferred measure of albuminuria; however, if ACR is not available, predicted ACR from PCR or urine dipstick protein may help in CKD screening, staging, and prognosis.

For CKD screening, staging and prognosis: is urine dipstick protein good enough?

#NephJC

Study Design & Cohort

Individual participant–based meta-analysis

12 research cohorts

21 clinical cohorts

919 383 adults

Equations derived:

From Urine PCR & dipstick protein values

To predict A/C ratios

To detect Presence of CKD (ACR ≥ 30mg/g)

And to classify Stage A2 or A3 (moderately or severely increased albuminuria)

Conclusion: Urine ACR is the preferred measure of albuminuria; however, if ACR is not available, predicted ACR from PCR or urine dipstick protein may help in CKD screening, staging, and prognosis.

Results

Source of predictive ACR	Predicted state or classification	Sensitivity	Specificity
PCR	CKD	91%	87%
	A2	75%	89%
	A3	87%	98%
Dipstick			
Trace	CKD	62%	88%
+	A2	36%	88%
++	A3	78%	98%

PCR = ACR to predict 2-4 year risk

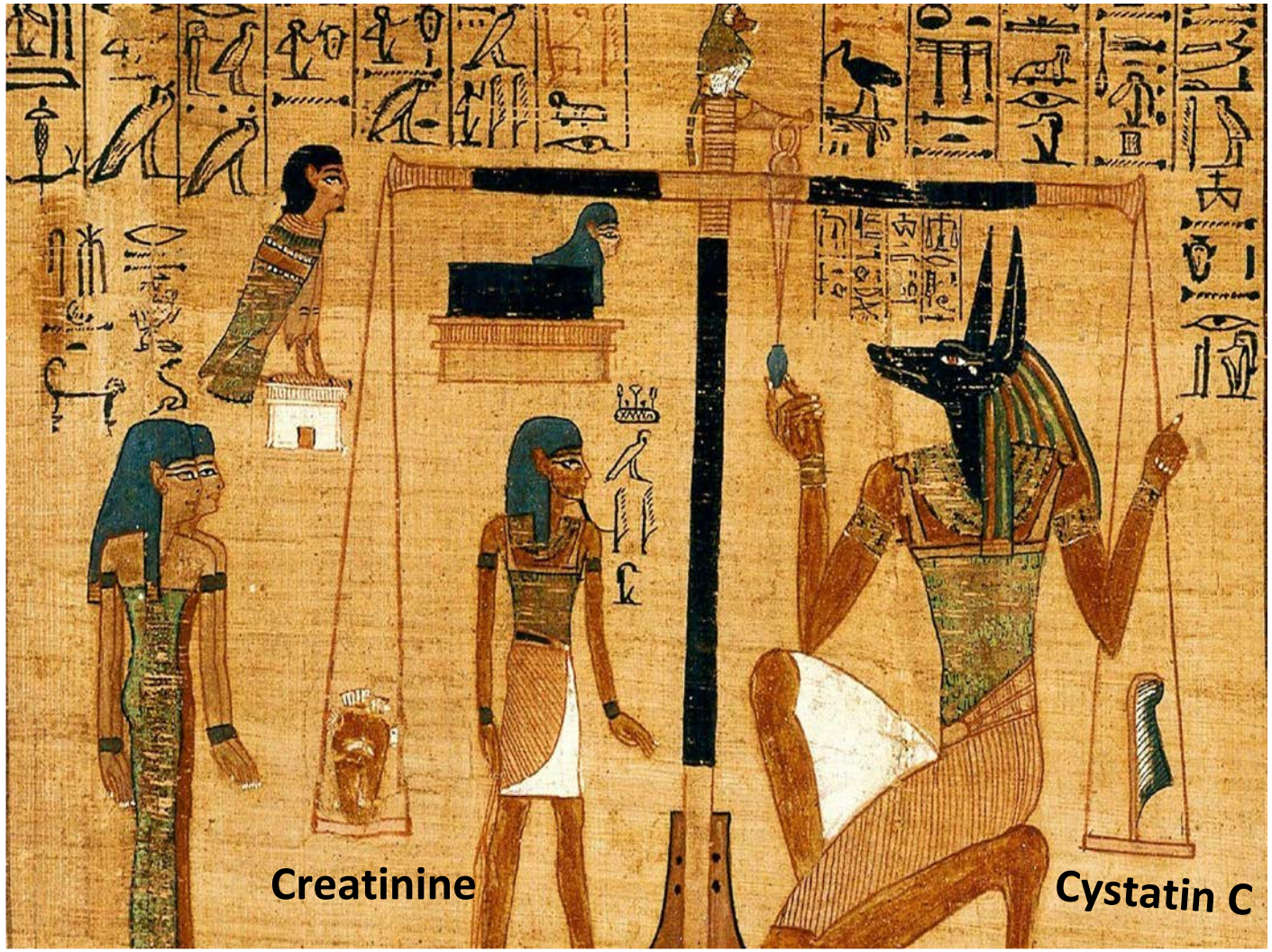
Sumida, K , Nadkami, G, Grams, M et al. ***Conversion of Urine Protein–Creatinine Ratio or Urine Dipstick Protein to Urine Albumin–Creatinine Ratio for Use in Chronic Kidney Disease Screening and Prognosis An Individual Participant–Based Meta-analysis.*** doi: 10.7326/M20-0529

VA by @AnnaGaddy

Controversies Conference Report Conclusion 5:

Accurate GFR estimation includes both creatinine and cystatin C measurement for initial diagnosis and staging.

Conclusion 5: Accurate GFR estimation includes both creatinine and cystatin C measurement for initial diagnosis and staging.

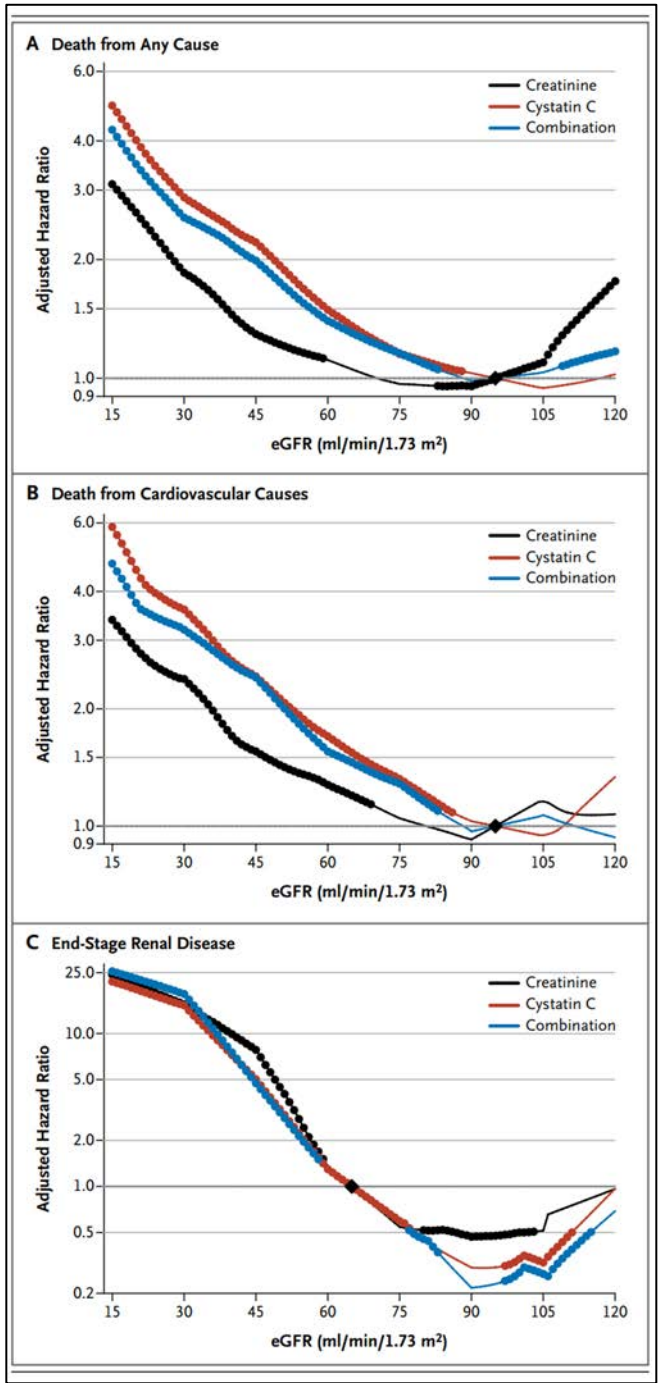


The NEW ENGLAND JOURNAL of MEDICINE

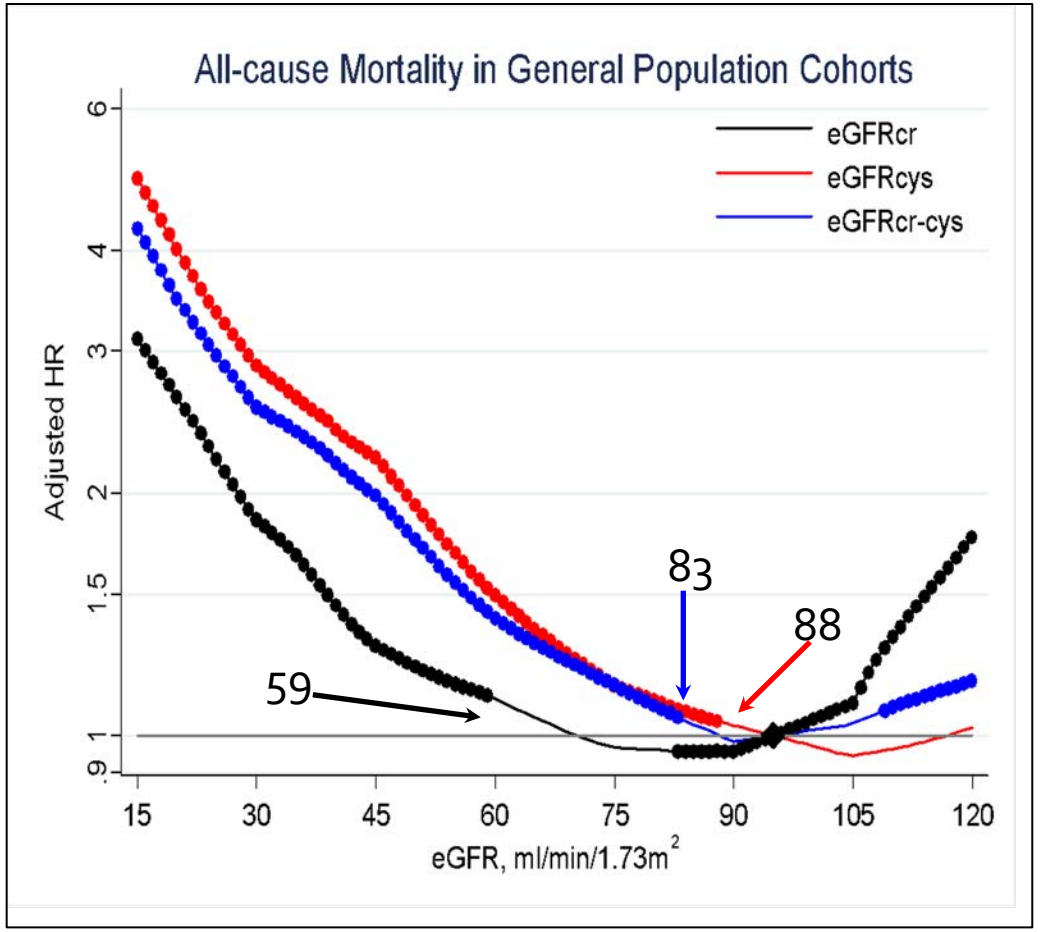
ORIGINAL ARTICLE

Cystatin C versus Creatinine in Determining Risk Based on Kidney Function

Michael G. Shlipak, M.D., M.P.H., Kunihiro Matsushita, M.D., Ph.D., Johan Ärnlöv, M.D., Ph.D., Lesley A. Inker, M.D., Ronit Katz, D.Phil., Kevan R. Polkinghorne, F.R.A.C.P., M.Clin.Epi., Ph.D., Dietrich Rothenbacher, M.D., M.P.H., Mark J. Sarnak, M.D., Brad C. Astor, Ph.D., M.P.H., Josef Coresh, M.D., Ph.D., Andrew S. Levey, M.D., and Ron T. Gansevoort, M.D., Ph.D., for the CKD Prognosis Consortium*



Comparisons of eGFR Using Creatinine, Cystatin C, or both with All-Cause Mortality



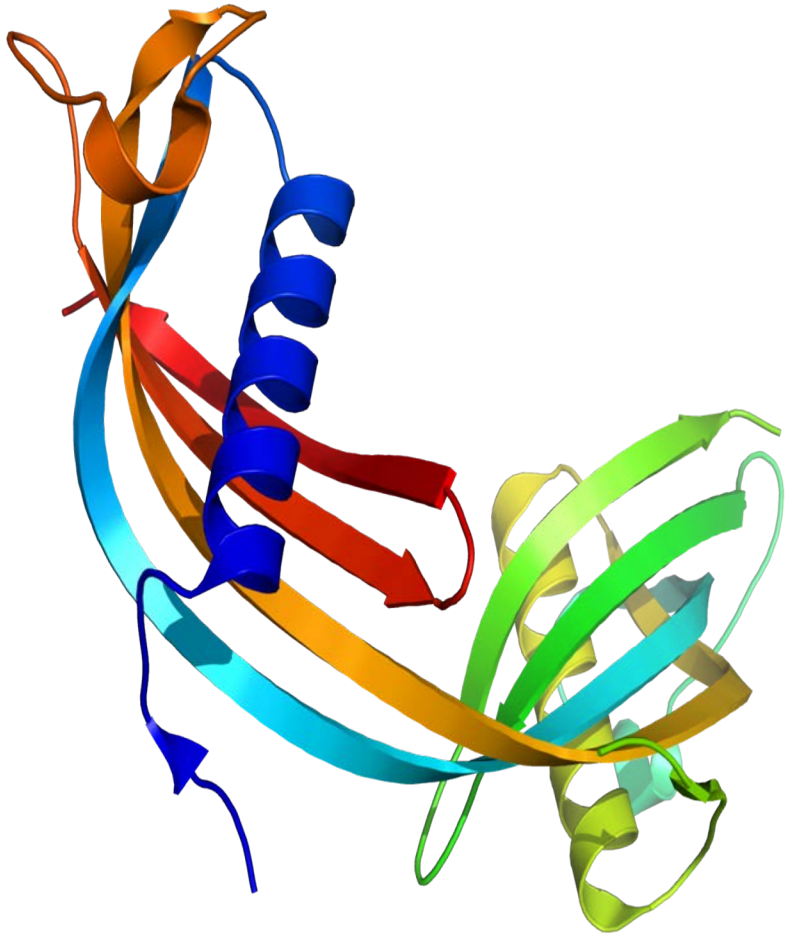
N= 90,750
12,351 deaths

The use of cystatin C alone or in combination with creatinine strengthens the association between the eGFR and the risks of death and end-stage renal disease across diverse populations

Shlipak MG. et al. *N Engl J Med*, 2013.

Cystatin C

Cystatin C has the additional advantage of offering GFR estimates that **do not require the incorporation of a race coefficient**, as is required for creatinine.

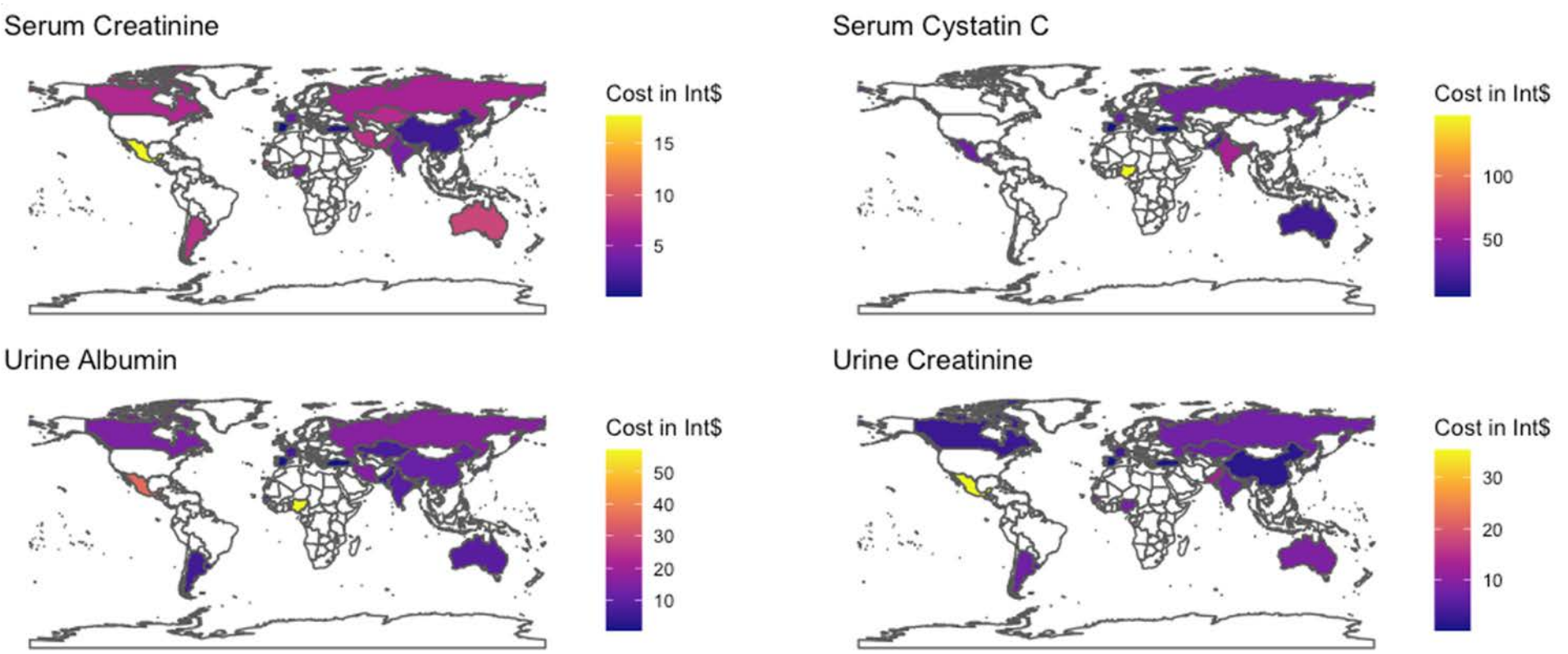


http://www.nephjc.com/news/cystatinc

Controversies Conference Report
Conclusion 6:

The combination of Creatinine, Cystatin C, and UACR for CKD screening is affordable in high income settings.

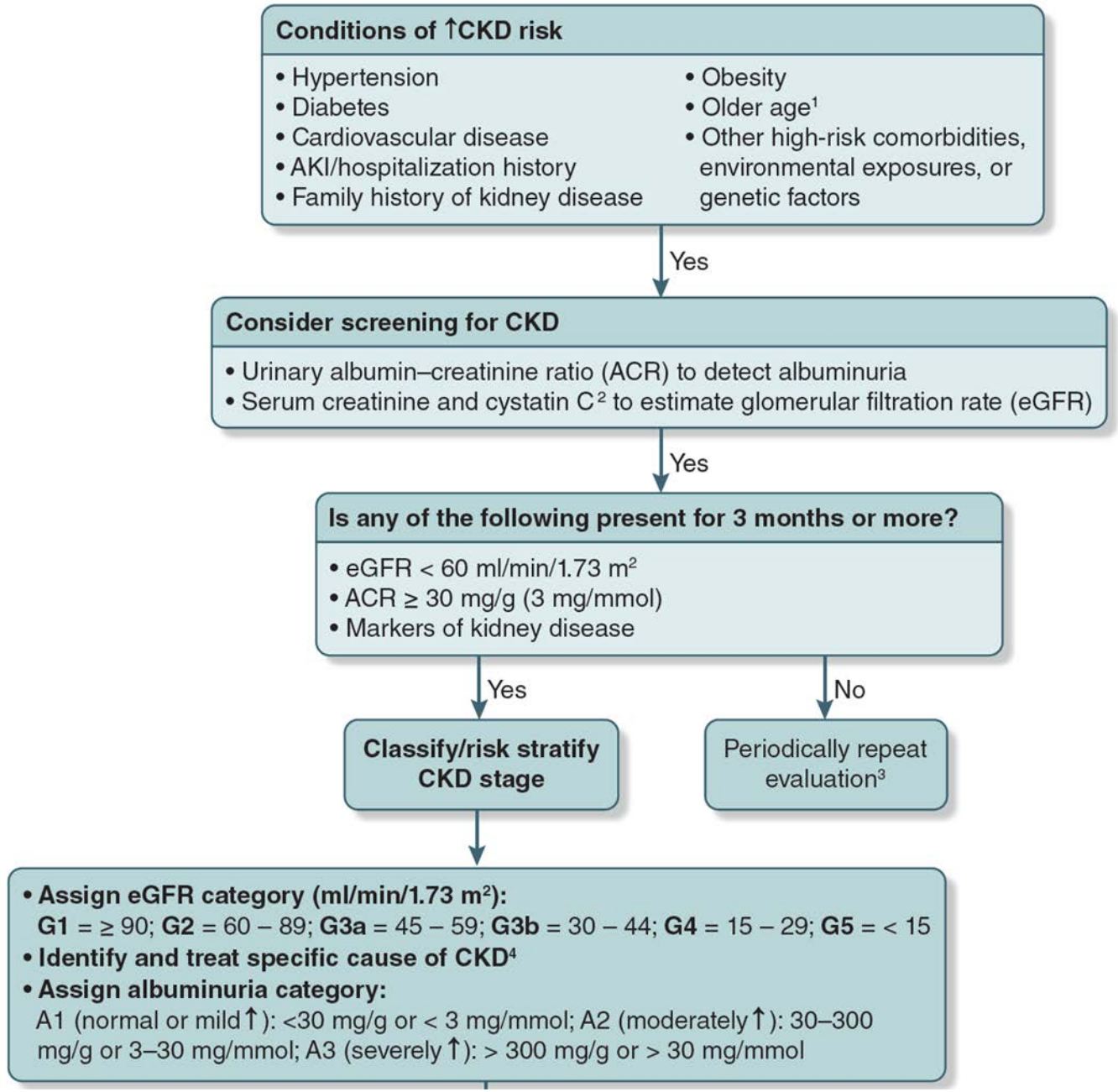
Conclusion 6: The combination of Creatinine, Cystatin C, and UACR for CKD screening is affordable in high income settings.

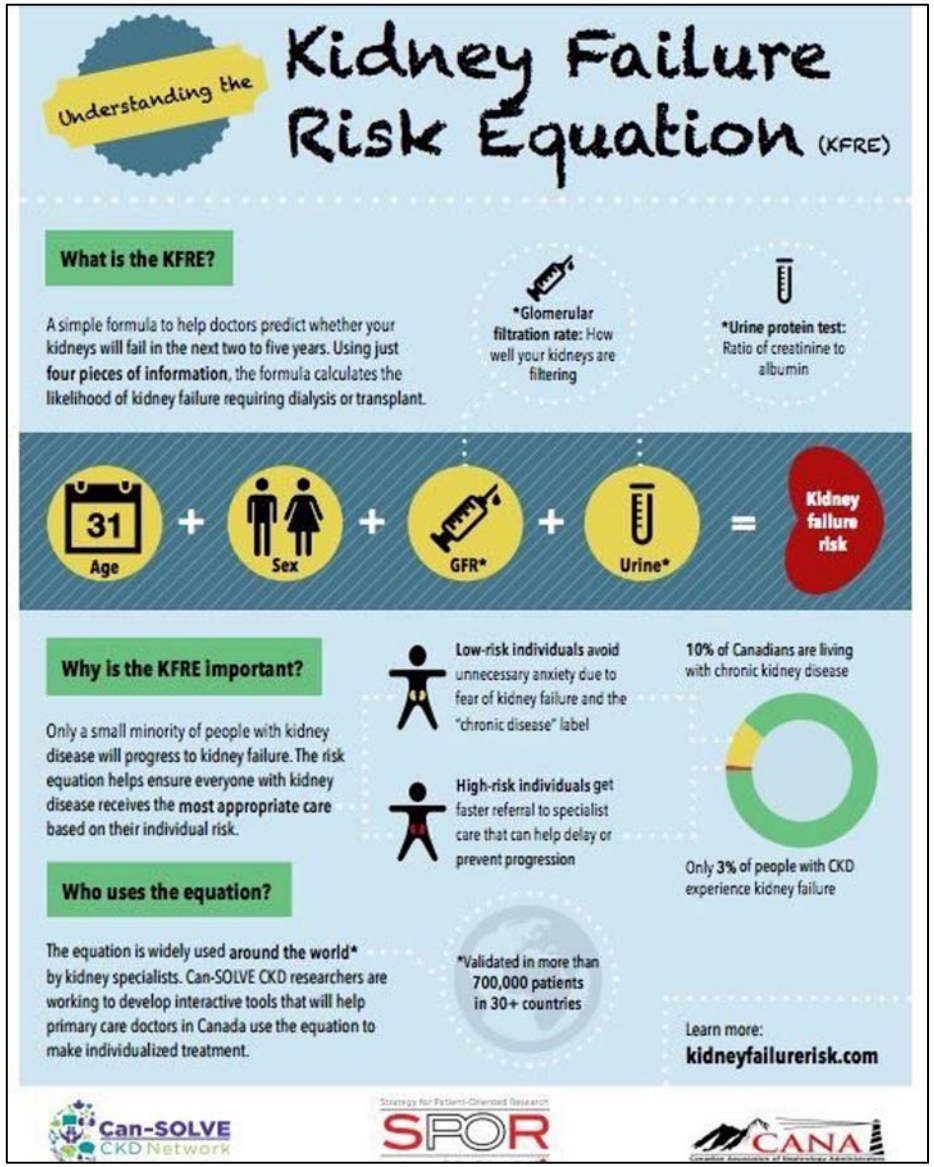


Tummalapalli SL, et al. *Am J Nephrol*. 2020; 51:959-965

SCREEN

RISK STRATIFY





Original Investigation

Multinational Assessment of Accuracy of Equations for Predicting Risk of Kidney Failure
A Meta-analysis

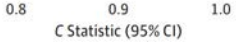
Navdeep Tangri, MD, PhD, FRCPC; Morgan E. Grams, MD, PhD; Andrew S. Levey, MD; Josef Coresh, MD, PhD; Lawrence J. Appel, MD; Brad C. Astor, PhD, MPH; Gabriel Chodick, PhD; Allan J. Collins, MD; Ognjenka Djurdjev, MSc; C. Raina Elley, MBCHB, PhD; Marie Evans, MD, PhD; Amit X. Garg, MD, PhD; Stein I. Hallan, MD, PhD; Lesley A. Inker, MD, MS; Sadayoshi Ito, MD, PhD; Sun Ha Jee, PhD; Csaba P. Kovesdy, MD; Florian Kronenberg, MD; Hiddo J. L. Heerspink, PharmD, PhD; Angharad Marks, MBBCh, MRCP, MSc, PhD; Girish N. Nadkarni, MD, MPH; Sankar D. Navaneethan, MD, MPH; Robert G. Nelson, MD, PhD; Stephanie Titze, MD, MSc; Mark J. Sarnak, MD, MS; Benedicte Stengel, MD, PhD; Mark Woodward, PhD; Kunitoshi Iseki, MD, PhD; for the CKD Prognosis Consortium

Figure 3. Discrimination Statistics (C Statistics) for Original 4-Variable and 8-Variable Equations at 2 and 5 Years by Subgroup

A 4-Variable equation

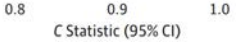
2-Year predicted probability of kidney failure

Cohort	No. of Patients	C Statistic (95% CI)
Diabetes		
Yes	140947	0.897 (0.869-0.924)
No	126536	0.918 (0.898-0.937)
Black		
Yes	13125	0.910 (0.892-0.928)
No	236463	0.896 (0.879-0.914)
Age, y		
≥65	196626	0.903 (0.879-0.926)
<65	70847	0.898 (0.874-0.922)



5-Year predicted probability of kidney failure

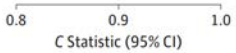
Cohort	No. of Patients	C Statistic (95% CI)
Diabetes		
Yes	105343	0.881 (0.863-0.900)
No	118543	0.893 (0.873-0.914)
Black		
Yes	8997	0.884 (0.856-0.912)
No	199073	0.878 (0.857-0.899)
Age, y		
≥65	162600	0.885 (0.857-0.913)
<65	61276	0.874 (0.851-0.897)



B 8-Variable equation

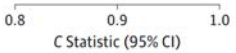
2-Year predicted probability of kidney failure

Cohort	No. of Patients	C Statistic (95% CI)
Diabetes		
Yes	17770	0.890 (0.874-0.906)
No	22223	0.902 (0.889-0.915)
Black		
Yes	3311	0.892 (0.874-0.909)
No	31420	0.898 (0.886-0.911)
Age, y		
≥65	24336	0.905 (0.882-0.927)
<65	15678	0.891 (0.876-0.905)

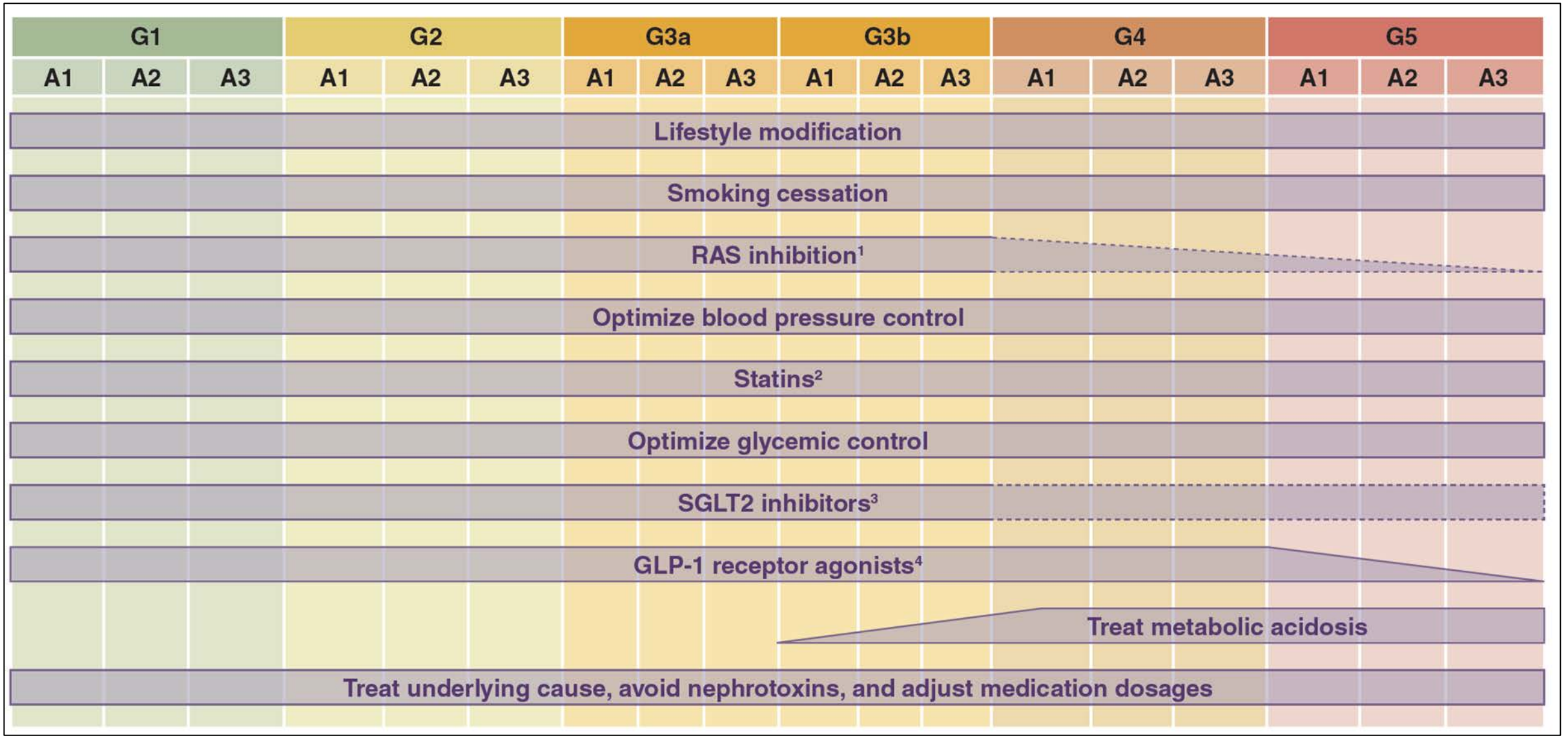


5-Year predicted probability of kidney failure

Cohort	No. of Patients	C Statistic (95% CI)
Diabetes		
Yes	16040	0.862 (0.848-0.875)
No	22223	0.867 (0.847-0.887)
Black		
Yes	2991	0.851 (0.827-0.876)
No	30307	0.867 (0.850-0.884)
Age, y		
≥65	23527	0.874 (0.858-0.889)
<65	14513	0.853 (0.834-0.871)



Interventions for CKD



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KDIGO KIDNEY DISEASE · IMPROVING GLOBAL OUTCOMES

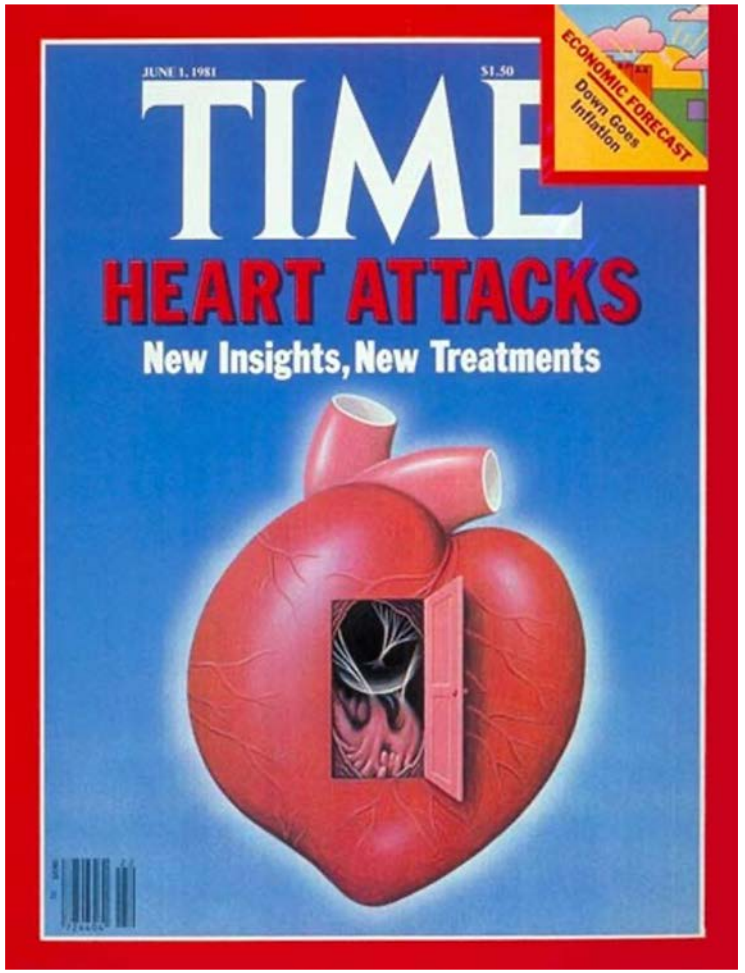
Controversies Conference Report Conclusion 7:

A key rationale for CKD screening is the availability of many effective interventions to delay CKD progression and reduce cardiovascular risk.

ISN INTERNATIONAL SOCIETY OF NEPHROLOGY

KDIGO KIDNEY DISEASE · IMPROVING GLOBAL OUTCOMES

Conclusion 7: A key rationale for CKD screening is the availability of many effective interventions to delay CKD progression and reduce cardiovascular risk.



Lifestyle Improvements May Help Reduce Progression at All Stages of CKD

Modifiable lifestyle factors for primary prevention of chronic kidney disease: a systematic review and meta-analysis

METHODS

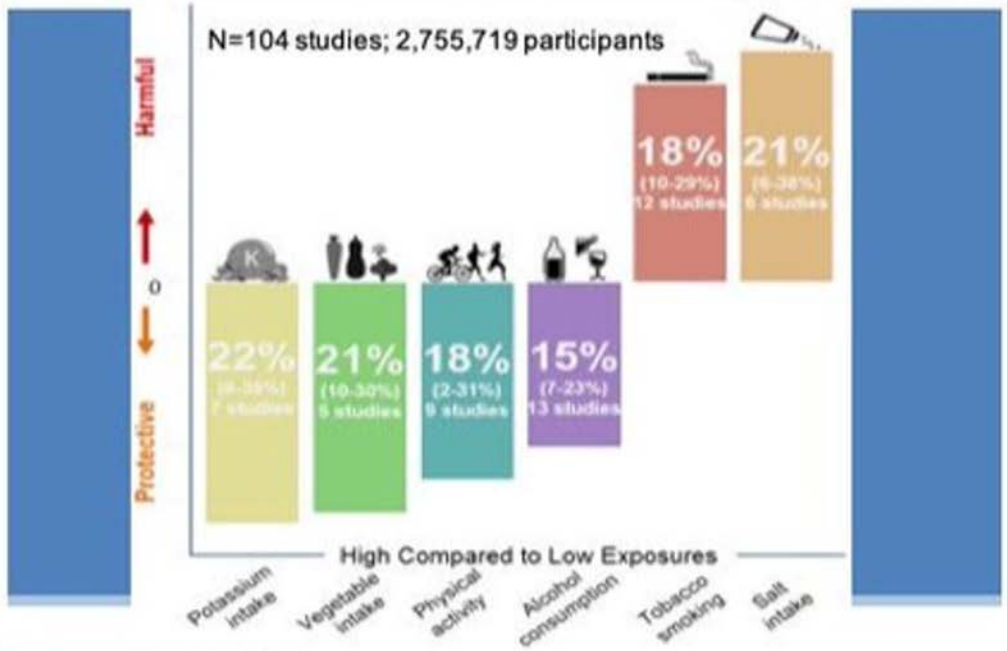
Systematic review of electronic databases, MEDLINE, EMBASE and CINAHL

Cohort studies reporting on lifestyle (diet, physical activity, alcohol and smoking) on kidney outcomes:

- Incident CKD (GFR <60mL/min²
- Kidney replacement therapy
- GFR decline
- Albuminuria

Screening, data extraction and risk of bias performed by at least 2 review authors

RESULTS: Incident Chronic Kidney Disease



CONCLUSION

Modifiable lifestyle hazards can predict the incidence of CKD in the community and may inform both public health recommendations and clinical practice.

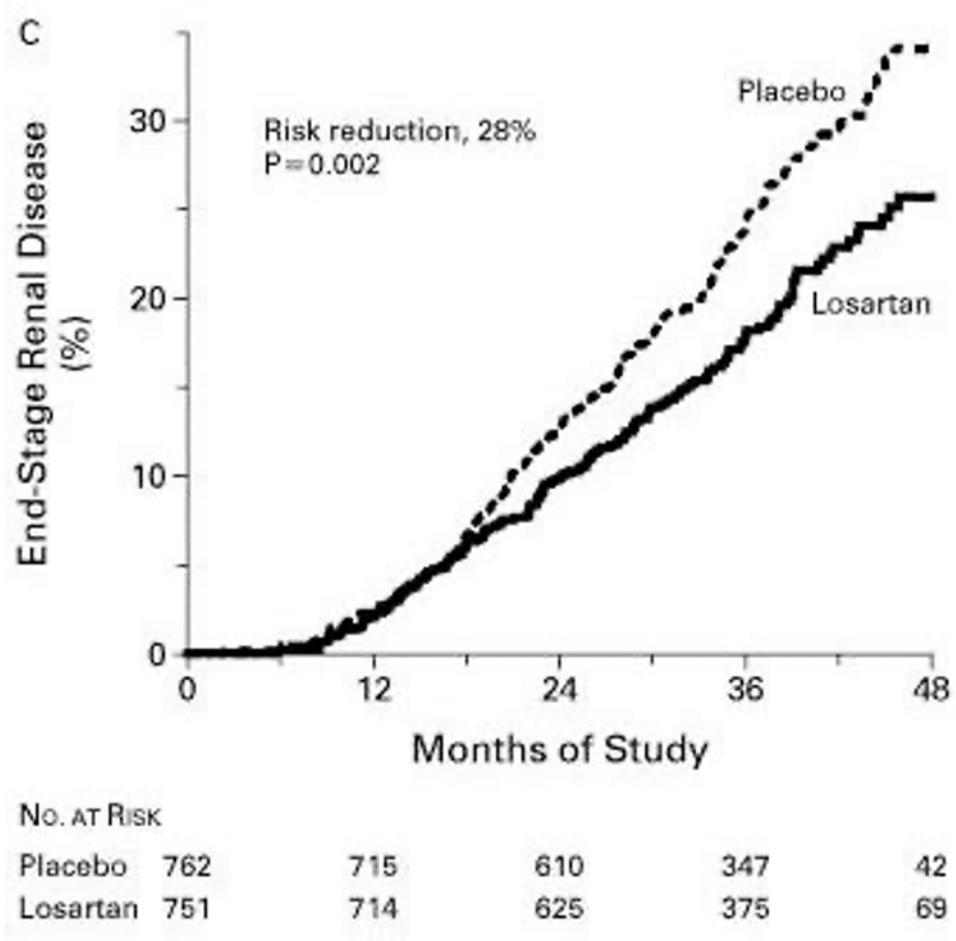
DOI: https://doi.org/10.1681/ASN.2020030384

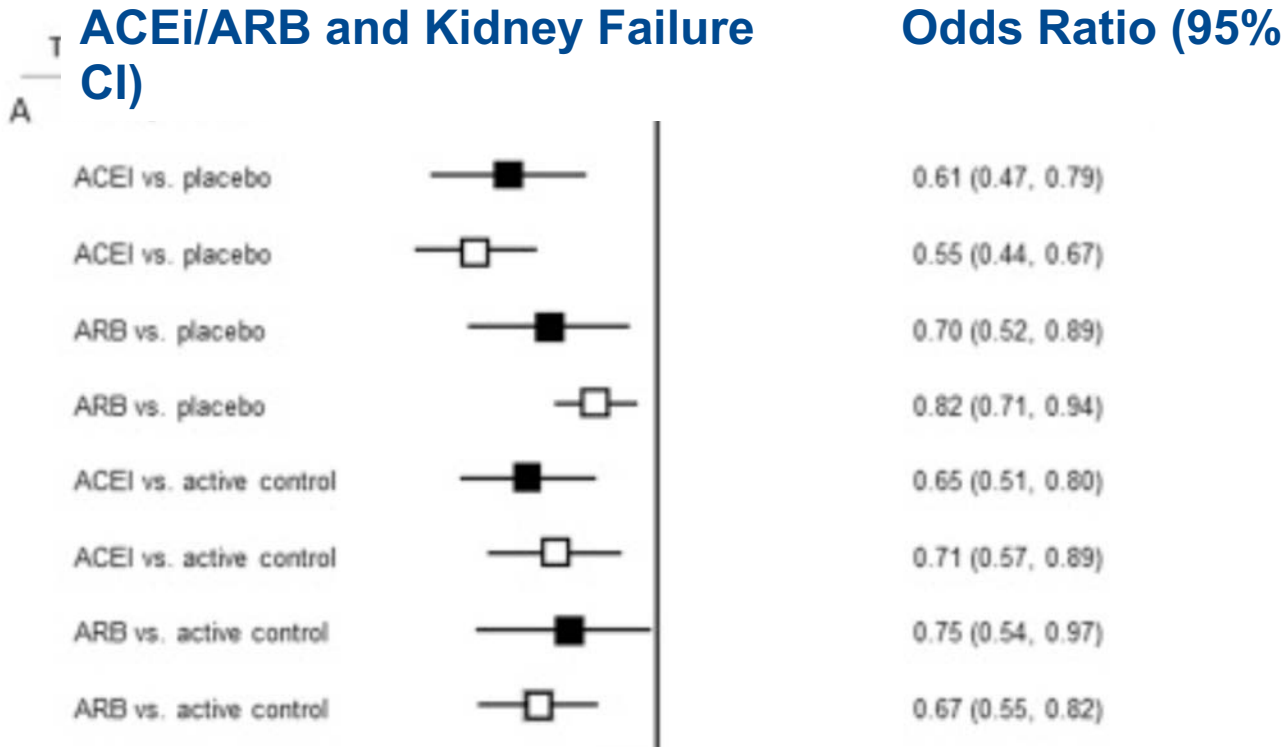
JASN
JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY

ISN INTERNATIONAL SOCIETY OF NEPHROLOGY

KDIGO KIDNEY DISEASE IMPROVING GLOBAL OUTCOMES

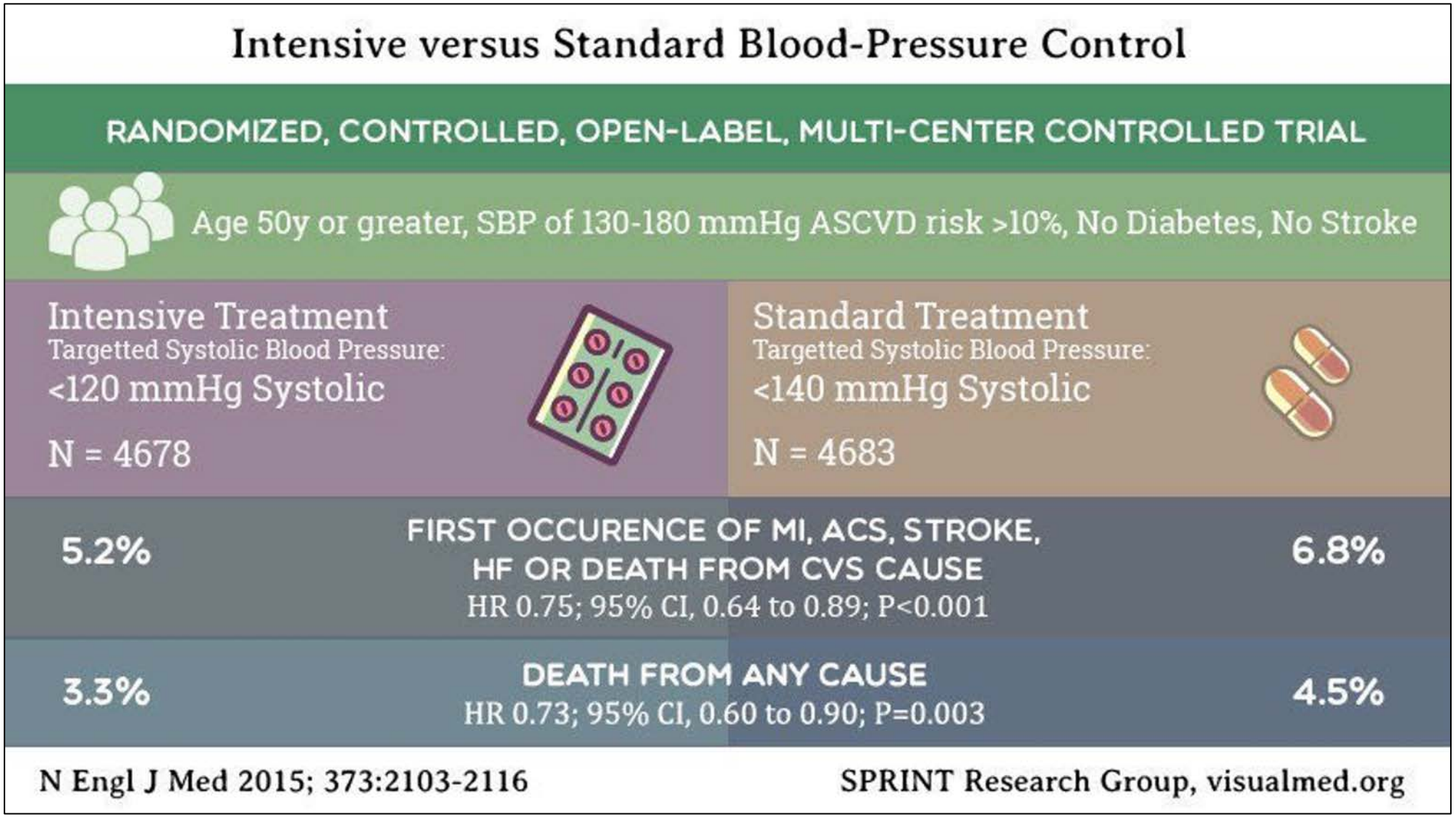
ACEi/ARB Reduce the Risk of CKD Progression and Kidney Failure



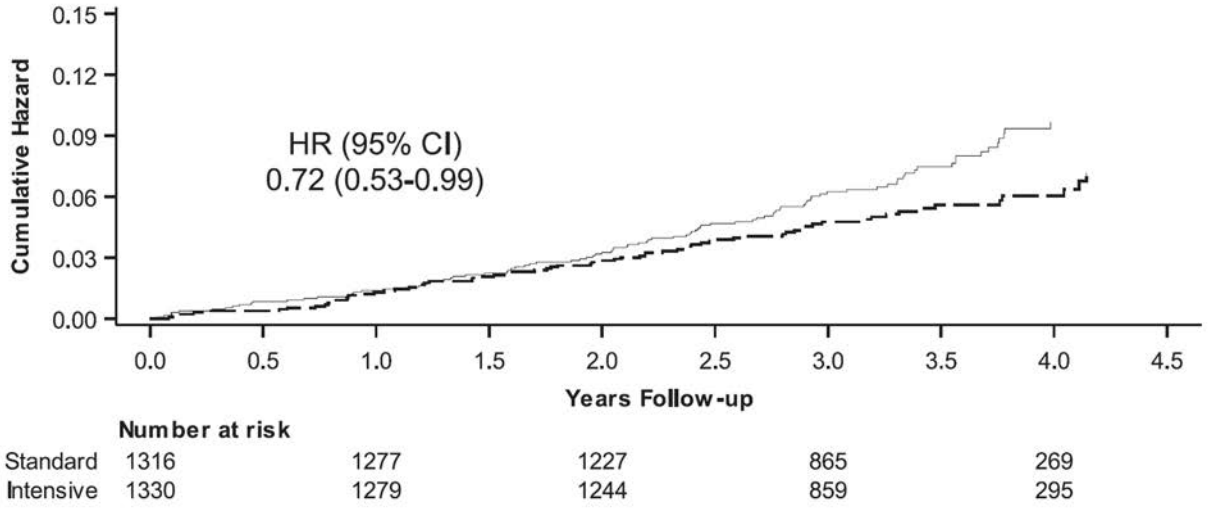


Brenner BM et al. *N Engl J Med*. 2001; Xie X et al. *AJKD*. 2016.

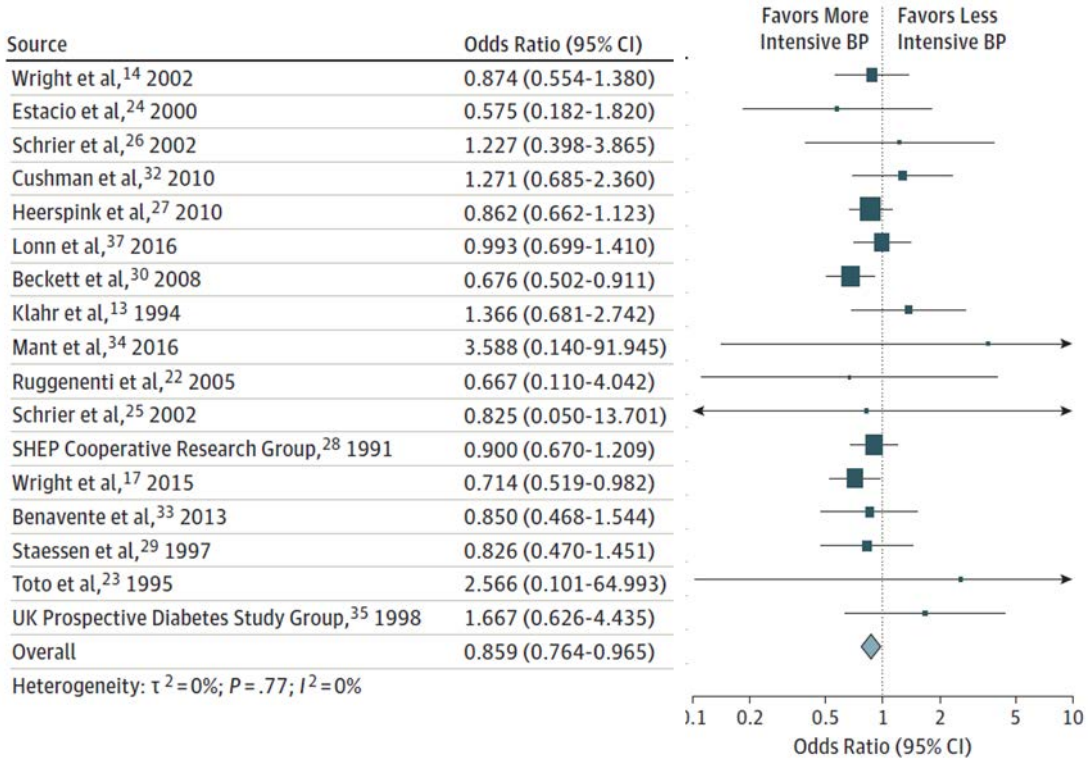
Benefits of Intensive BP Lowering in CKD



Mortality Benefits of Intensive BP Lowering in CKD



Cheung AK et al. *JASN*. 28: 2812–2823, 2017

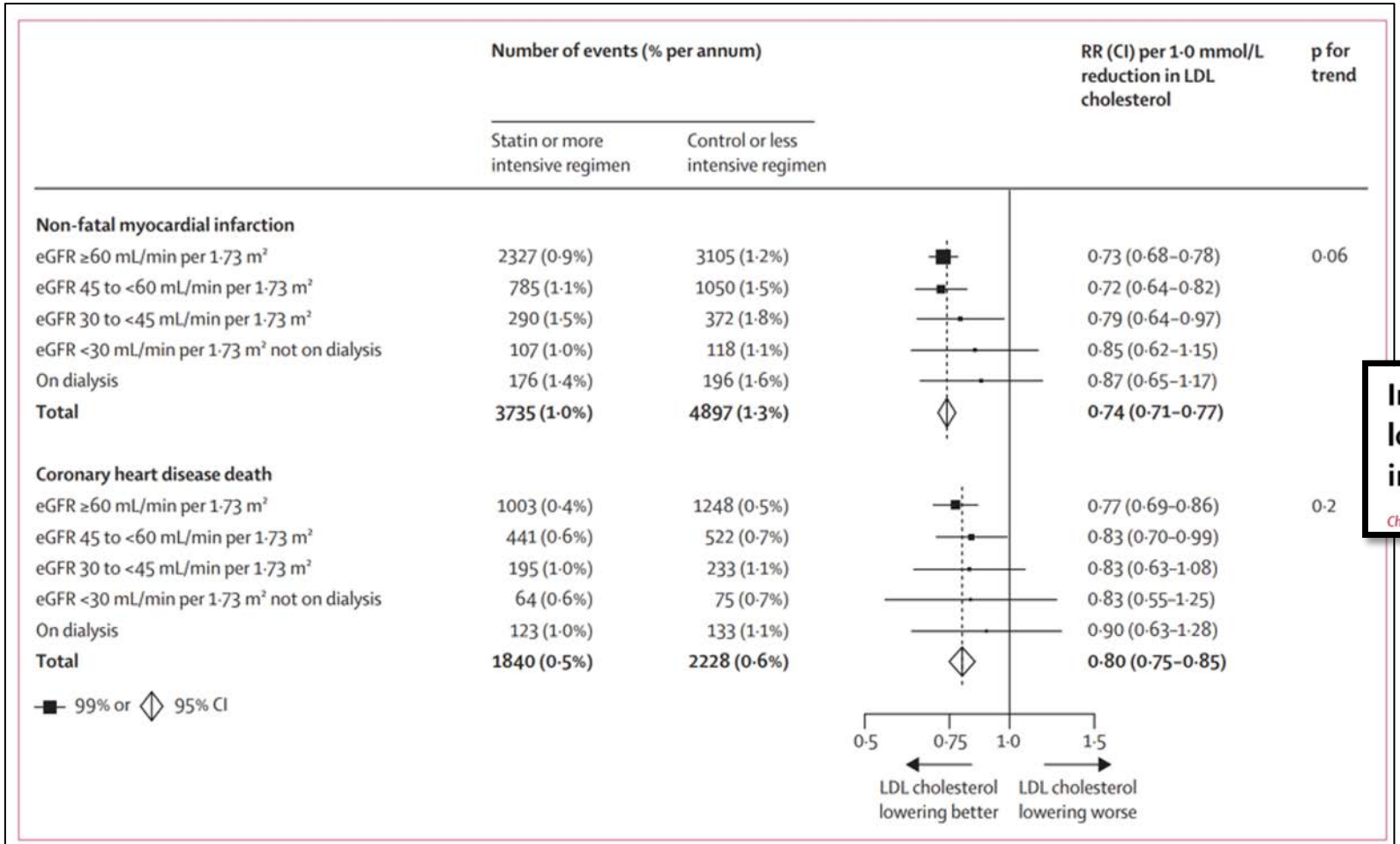


Malhotra R., et al. *JAMA Intern Med*. 177: 1498-1505, 2017

SPRINT

Malhotra et al. systematic review and meta-analysis

Statins Lower CVD Risk in Persons with CKD G3 or G4



	Number of events (% per annum)		RR (CI) per 1·0 mmol/L reduction in LDL cholesterol	p for trend
	Statin or more intensive regimen	Control or less intensive regimen		
Non-fatal myocardial infarction				
eGFR ≥60 mL/min per 1·73 m²	2327 (0·9%)	3105 (1·2%)	0·73 (0·68–0·78)	0·06
eGFR 45 to <60 mL/min per 1·73 m²	785 (1·1%)	1050 (1·5%)	0·72 (0·64–0·82)	
eGFR 30 to <45 mL/min per 1·73 m²	290 (1·5%)	372 (1·8%)	0·79 (0·64–0·97)	
eGFR <30 mL/min per 1·73 m² not on dialysis	107 (1·0%)	118 (1·1%)	0·85 (0·62–1·15)	
On dialysis	176 (1·4%)	196 (1·6%)	0·87 (0·65–1·17)	
Total	**3735 (1·0%)**	**4897 (1·3%)**	**0·74 (0·71–0·77)**	
Coronary heart disease death				
eGFR ≥60 mL/min per 1·73 m²	1003 (0·4%)	1248 (0·5%)	0·77 (0·69–0·86)	0·2
eGFR 45 to <60 mL/min per 1·73 m²	441 (0·6%)	522 (0·7%)	0·83 (0·70–0·99)	
eGFR 30 to <45 mL/min per 1·73 m²	195 (1·0%)	233 (1·1%)	0·83 (0·63–1·08)	
eGFR <30 mL/min per 1·73 m² not on dialysis	64 (0·6%)	75 (0·7%)	0·83 (0·55–1·25)	
On dialysis	123 (1·0%)	133 (1·1%)	0·90 (0·63–1·28)	
Total	**1840 (0·5%)**	**2228 (0·6%)**	**0·80 (0·75–0·85)**	

Figure 2: **Effects on major coronary events per mmol/L reduction in LDL cholesterol, by baseline renal function**
Data for participants with missing creatinine values at baseline are included in totals. Black squares and horizontal lines represent 99% CIs. White diamonds represent 95% CIs. Vertical dotted line represents overall RR for each outcome. eGFR=estimated glomerular filtration rate. RR=rate ratio.

Impact of renal function on the effects of LDL cholesterol lowering with statin-based regimens: a meta-analysis of individual participant data from 28 randomised trials

*Cholesterol Treatment Trialists' (CTT) Collaboration**

Glucose Control Lowers Risk of CKD Progression in Type 2 Diabetes

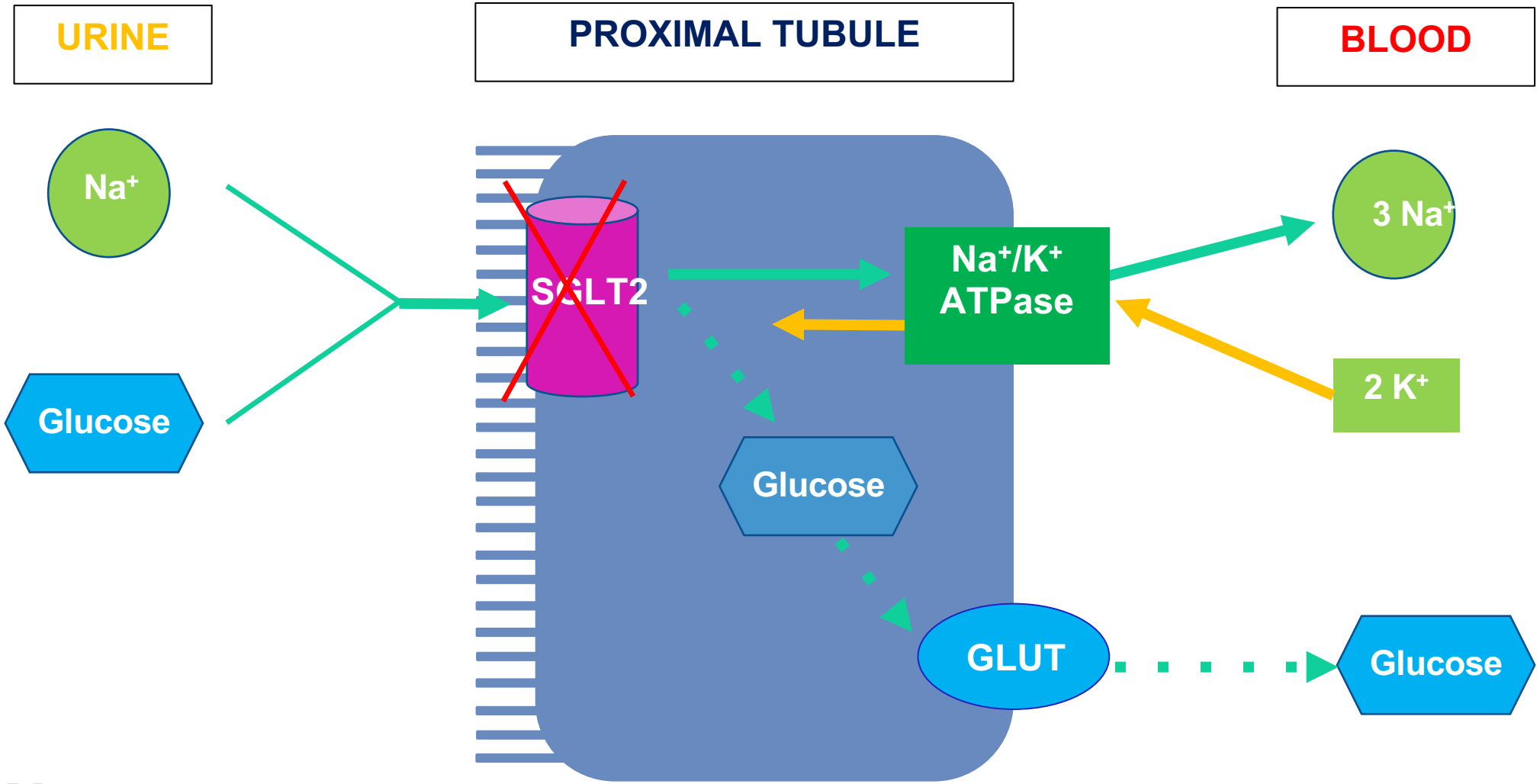
Effects of intensive glucose control on microvascular outcomes in patients with type 2 diabetes: a meta-analysis of individual participant data from randomised controlled trials

the, Collaborators on Trials of Lowering Glucose (CONTROL) group

Supplementary Table 3. Effects of more versus less intensive glucose control on the primary outcomes by years of follow up

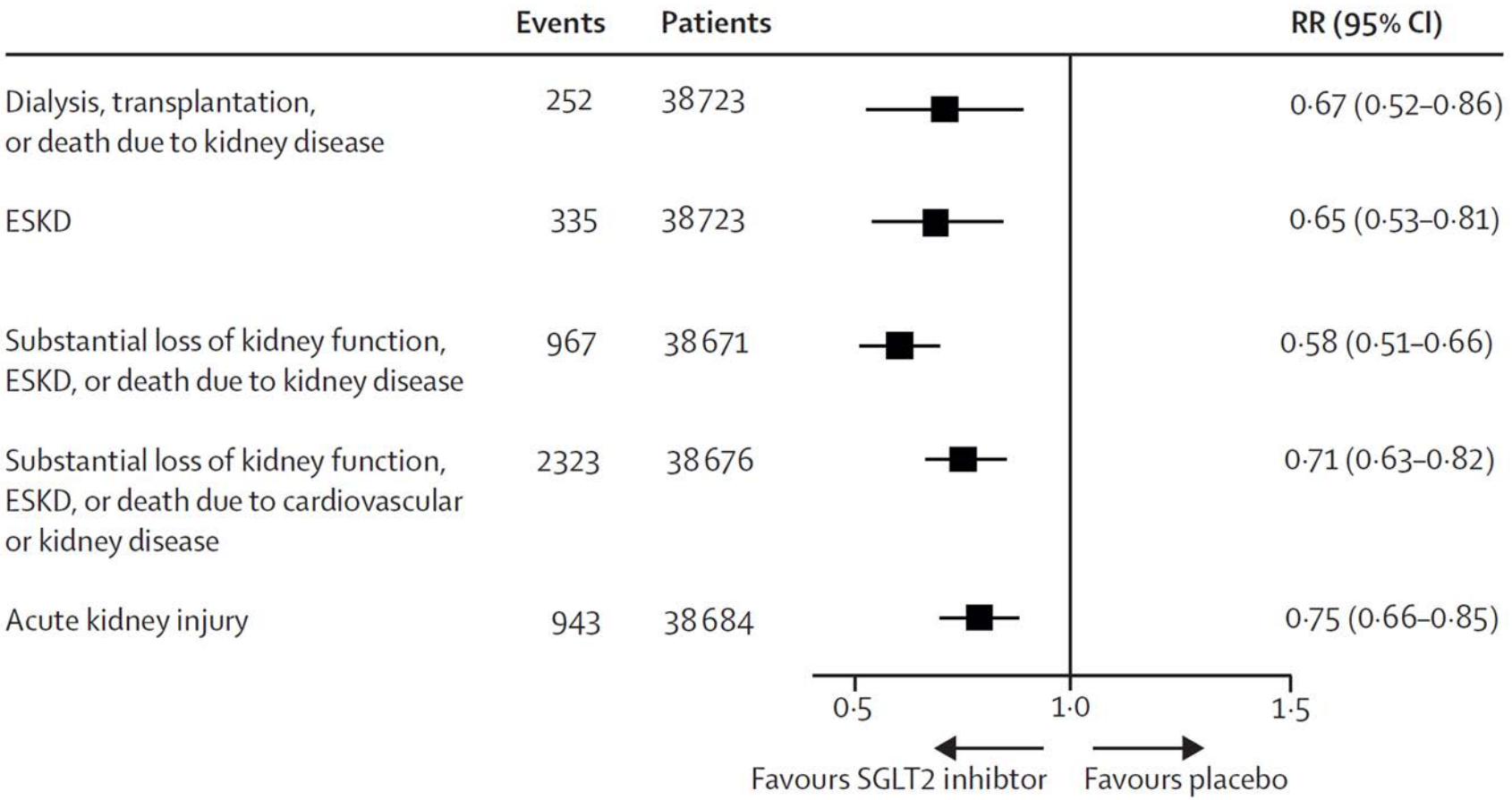
	Event number		Pooled HR (95%CI)	p value
	More intensive	Less intensive		
Primary kidney outcome				
0-1 years	120	112	1.04 (0.60 to 1.79)	0.896
0-2 years	264	279	0.84 (0.68 to 1.04)	0.102
0-3 years	408	456	0.79 (0.69 to 0.91)	0.001
0-4 years	584	655	0.80 (0.72 to 0.90)	<0.001
0-5 years	761	865	0.80 (0.72 to 0.88)	<0.001

SGLT2 Inhibitors: the New Cardiorenal Miracle Drugs



Ferrannini, E. *Cell Metab*. 2017;26:27-38.

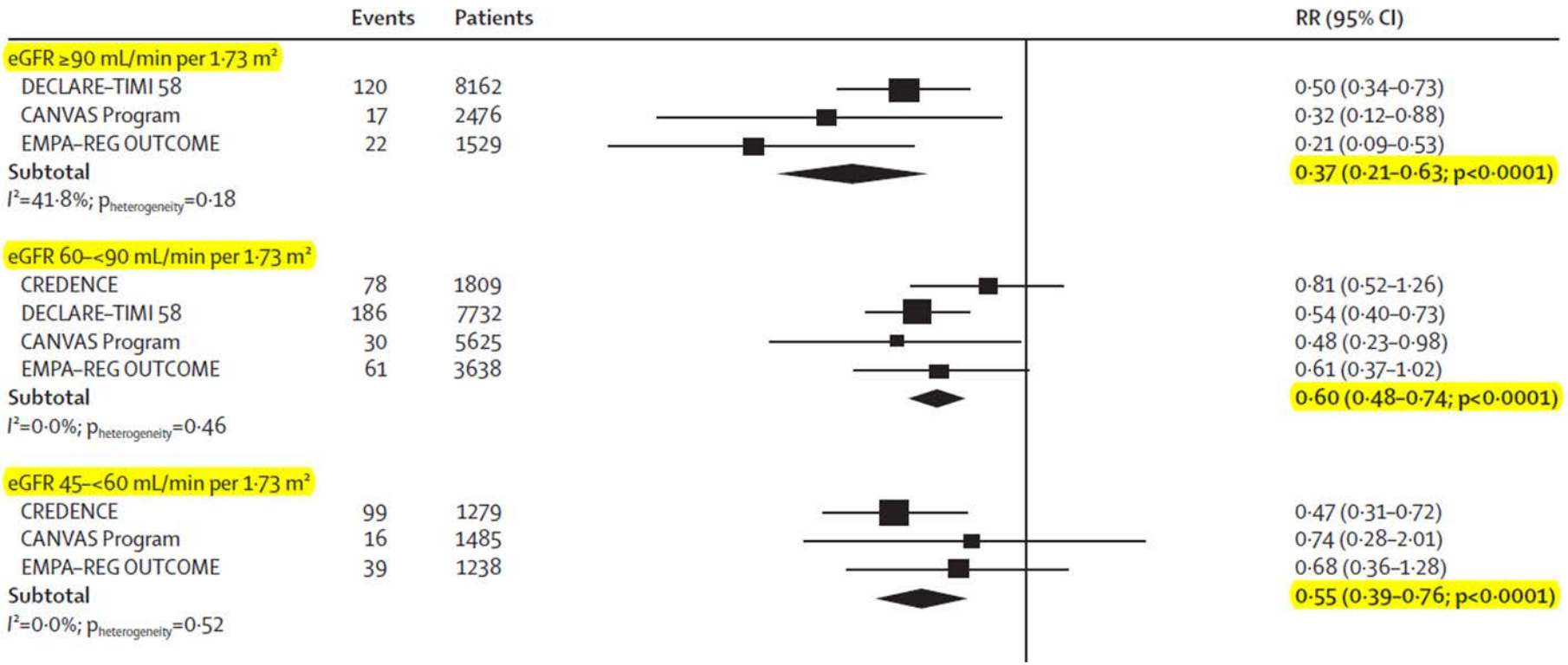
Effects of SGLT2 Inhibitors on Major Kidney Outcomes*



*based on CANVAS, DECLARE-TIMI 58, EMPA-REG, and CREDENCE

Neuen BL et al. *Lancet Diabetes Endocrinol*. 7: 845-854, 2019

Effects of SGLT2 Inhibitors on Early CKD*



*based on CANVAS, DECLARE-TIMI 58, EMPA-REG, and CREDENCE

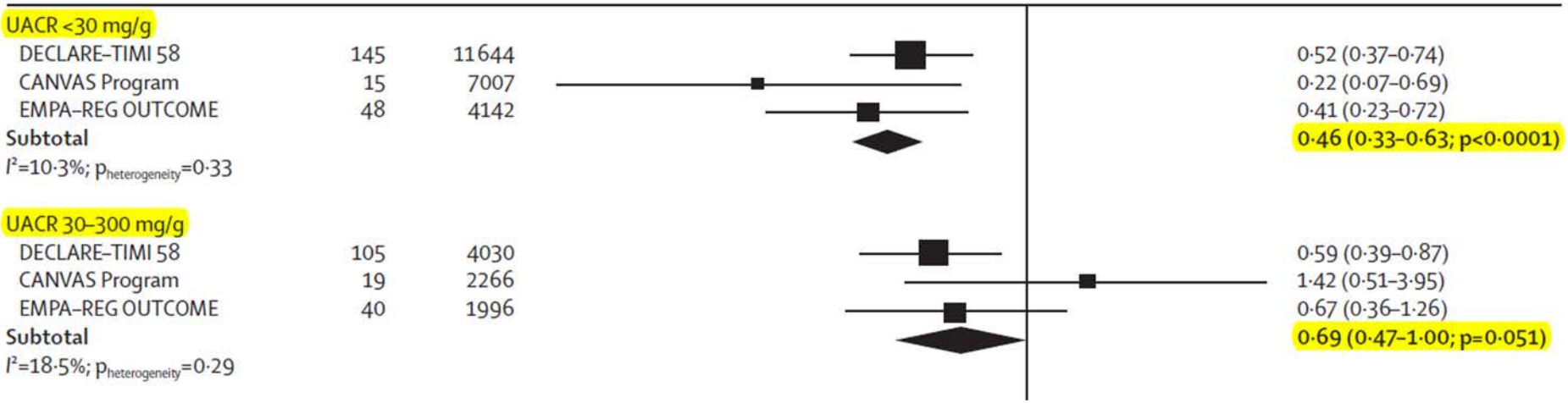
Effect of SGLT2 inhibitors on substantial loss of kidney function, kidney failure, or death due to kidney disease as stratified by **baseline GFR**

Neuen BL et al. *Lancet Diabetes Endocrinol*. 7: 845-854, 2019

Effects of SGLT2 Inhibitors on Early CKD*

A1

A2



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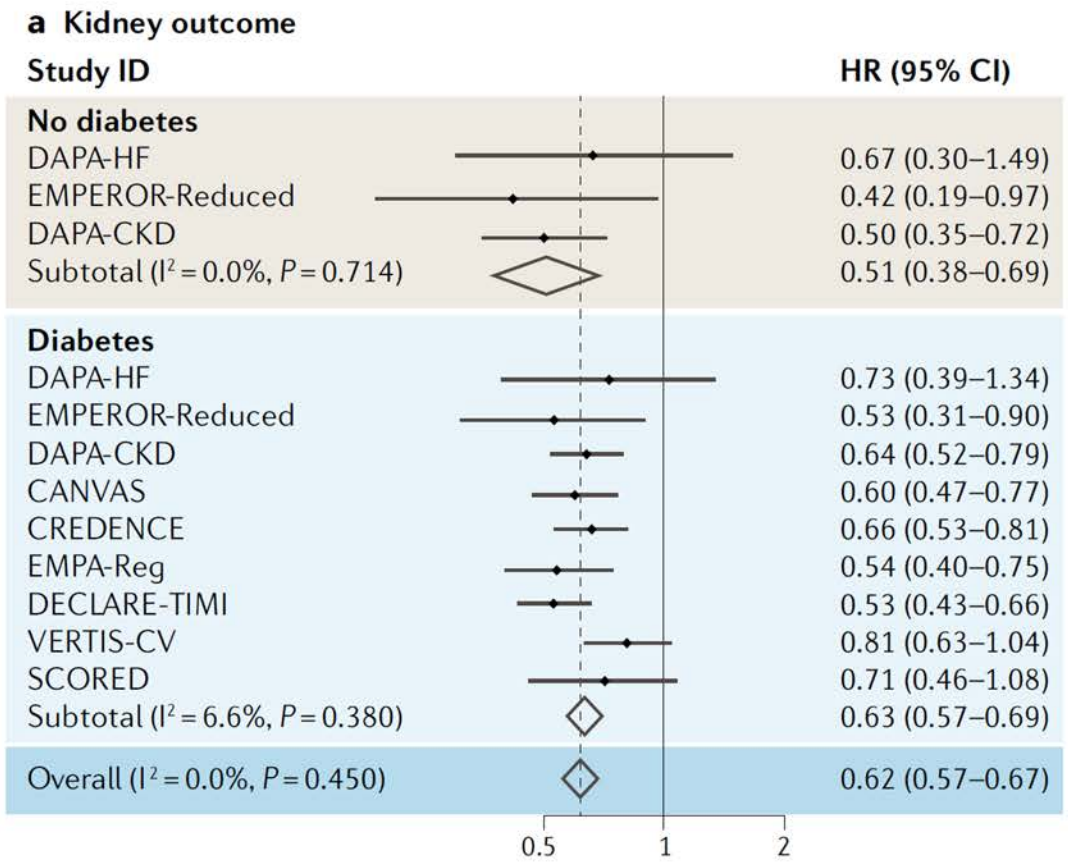
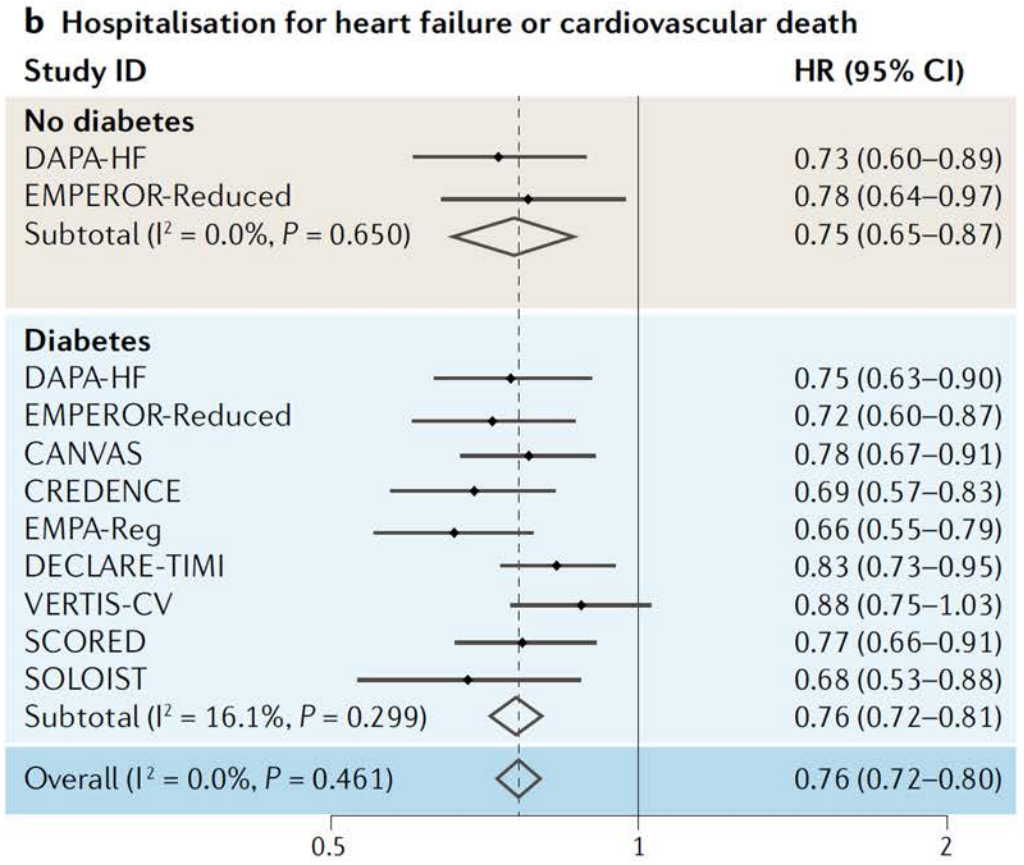
Effect of SGLT2 inhibitors on substantial loss of kidney function, kidney failure, or death due to kidney disease as stratified by **baseline albuminuria**

Neuen BL et al. *Lancet Diabetes Endocrinol*. 7: 845-854, 2019

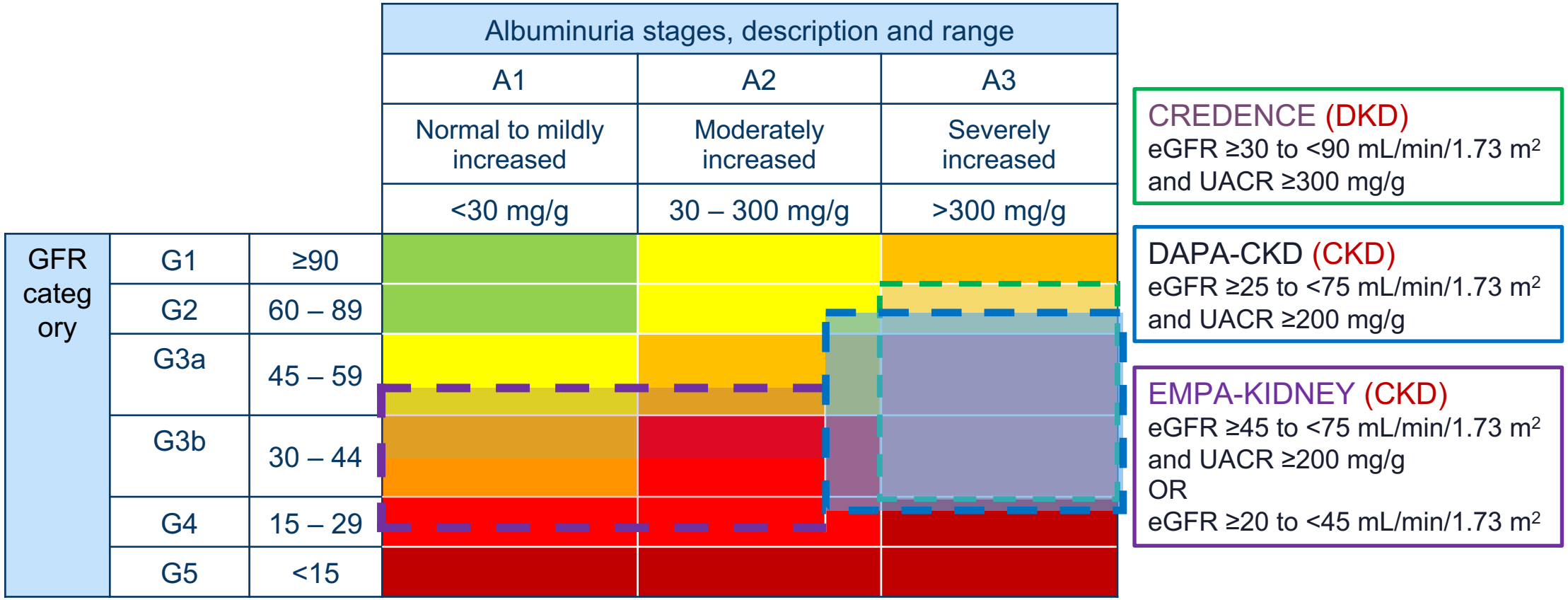
SGLT2 Inhibitors: Evidence Summary of Cardiovascular and Kidney Benefits





Kang A & Jardine M. *Nat Rev Nephrol*. 17: 83-84, 2021

SGLT2 Inhibitors: Primary Kidney Outcome Trials



The cardiovascular outcome trials are indicated in the circles and positioned based on their mean eGFR and median UACR

CREDENCE: Perkovic et al. *N Engl J Med* 2019, 380: 2295-2306
DAPA-CKD: Heerspink et al. *N Engl J Med*. 2020; 383: 1436-1446
EMPA-KIDNEY: Ongoing; Herrington WG, et al. *Clin Kidney J*. 2018; 11:749-761.

Courtesy of Dr. Peter Rossing

CREDENCE: Canagliflozin and renal outcomes in type 2 diabetes and nephropathy

The George Institute for Global Health

Study design and participants

4401 patients with T2DM & UACR >300 mg/g

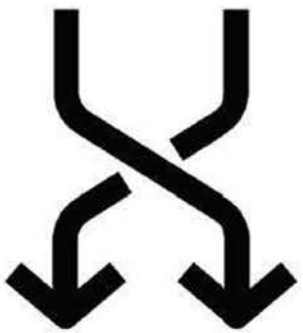
62 years

eGFR 57

UACR 927 mg/g

Intervention

Stable on maximum dose tolerated ACEi or ARB for 4 weeks

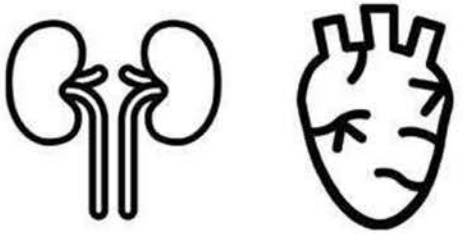


Canagliflozin **Placebo**

Outcomes

Primary outcome

(Doubling of serum creatinine, ESKD, death due to cardiovascular or kidney disease)



HR 0.70
(95% CI 0.59-0.82)

NNT 21

End-stage kidney disease

HR 0.68
(95% CI 0.54-0.86)

NNT 42

No increased risk of:

Amputations

HR 1.10
(95% CI 0.79-1.56)

Fractures

HR 0.98
(95% CI 0.70-1.37)

Conclusion

In patients with type 2 diabetes and kidney disease, canagliflozin reduces the risk of kidney failure and cardiovascular events

Does Dapagliflozin compared to placebo reduce the risk of kidney failure and CV events in CKD patients with and without T2DM?

DAPA-CKD

21 Countries
286 Centers

≥ 18 yo

eGFR ≥ 25 to ≤ 75ml/min

UACR ≥ 200 to ≤ 5000mg/g

Max tolerated dose of ACEi/ARB

With and without T2DM

Mean Age 62y, 67% ♂
eGFR 43ml/min
UACR 949mg/g
ACEi/ARB 97%
With T2DM 67.5%

MEAN FOLLOW-UP: 2.4 YEARS

N=4304

10 mg

DAPAGLIFLOZIN
+STANDARD CARE
N=2152

P

PLACEBO
+STANDARD CARE
N=2152

Sustained ≥ 50% decline in GFR, ESKD, Renal or CV Death	Sustained ≥ 50% decline in GFR, ESKD, Renal Death	CV Death or hHF	All-cause Mortality
9.2%	6.6%	4.6%	4.7%
HR 0.61 (95% CI 0.51-0.72) p<0.001 NNT=19	HR 0.56 (0.45-0.68) p<0.001	HR 0.71 (0.55-0.92) p=0.009	HR 0.69 (0.53-0.88) p=0.004
14.5%	11.3%	6.4%	6.8%

Benefit of Dapagliflozin on primary end-point was consistent in patients with and without T2DM
% of patients who discontinued the drug or who experienced SAE was similar in both groups
DKA, 2 in placebo group vs none in Dapagliflozin group
No DKA or severe hypoglycemia in patients without T2DM

CONCLUSION: Dapagliflozin compared to placebo significantly reduced the risk of kidney failure, CV death or hospitalization for HF and all-cause mortality in patients with CKD with and without T2DM. Dapagliflozin was well-tolerated, in keeping with its established safety profile.

DAPA-CKD
Heerspink et al (2020). Dapagliflozin in Patients with Chronic Kidney Disease. *New England Journal of Medicine.* September 24,2020
DOI: 10.1056/NEJMoa2024816
Visual Abstract by: Ana Naidas, MD

KDIGO KIDNEY DISEASE · IMPROVING GLOBAL OUTCOMES

CREDENCE: DM + eGFR of 30 to <90 ml/min/1.73 m² and albuminuria (UACR >300 to 5000)

Perkovic V *et al. N Engl J Med* 2019;380:2995

Primary composite outcome

ESKD, doubling of serum creatinine, death from kidney causes or CV death

↓30% RRR
p=0.00001

Secondary outcomes

CV death or HHF

↓31% RRR
p<0.001

3P-MACE†

↓20% RRR
p=0.01

HHF

↓39% RRR
p<0.001

DAPA-CKD: noDM & DM + eGFR of 25 to <75 ml/min/1.73 m² and albuminuria (UACR >200 to 5000)

Primary composite outcome

Decline in eGFR ≥50%; ESKD*; renal or CV death

↓39% RRR
p=0.000000028

*Defined as eGFR <15 ml/min/1.73 m², need for chronic dialysis and/or renal transplantation

Secondary outcomes

≥50% sustained decline in eGFR or reaching ESRD or renal death

↓44% RRR
P=0.000000018

CV death or HHF

↓29% RRR
p=0.008

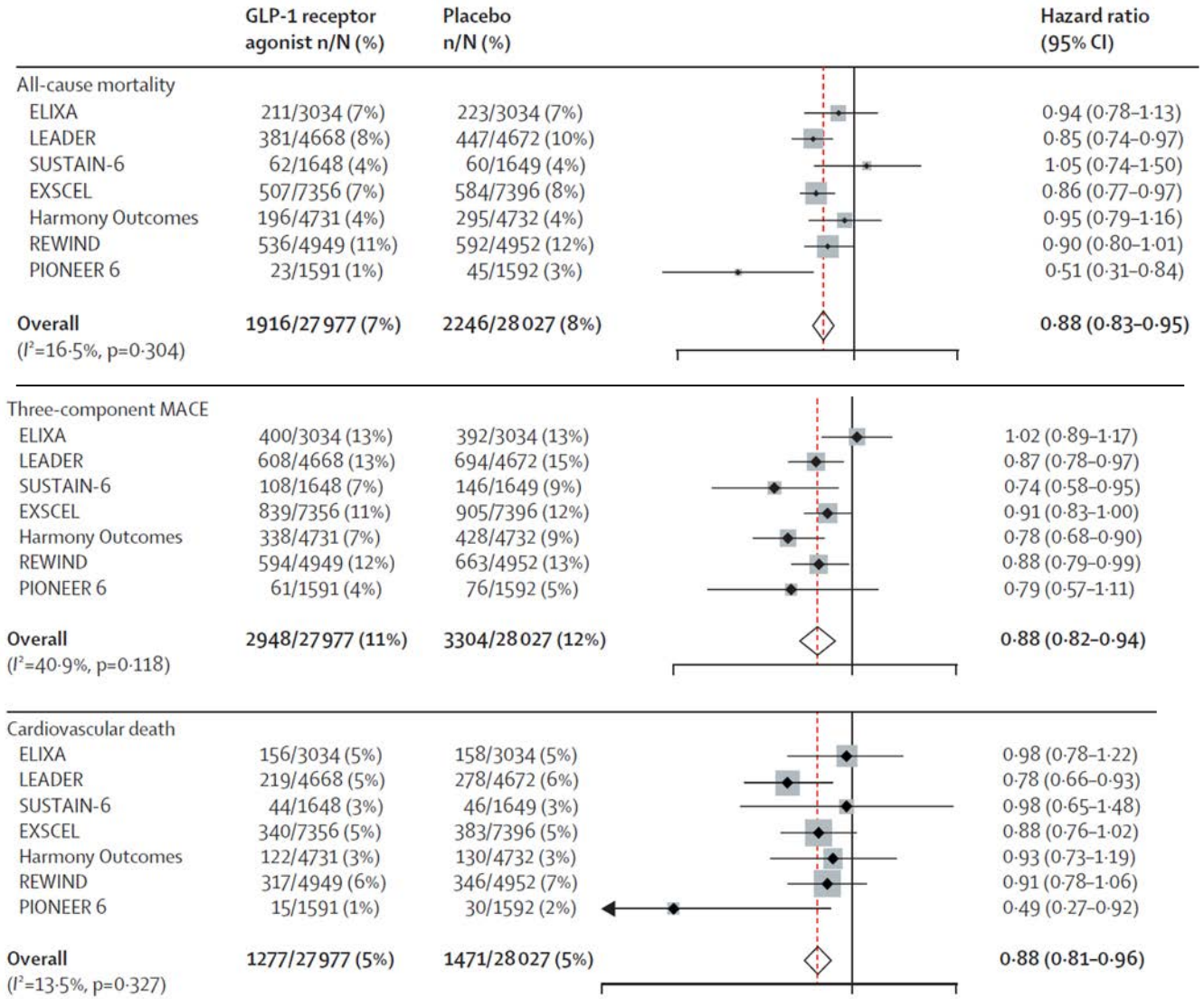
TOTAL death

↓31% RRR
p 0.0035

GLP-1 RA Recommended for Persons with Diabetes and eGFR <30 ml/min/1.73 m^2

	ELIXA[311,316]	LEADER[309,313]	SUSTAIN-6[308]	EXSCEL[310,314]	HARMONY[307]	REWIND[306,315]	PIONEER 6[317]	AWARD-7[312]
Drug	Lixisenatide	Liraglutide	Semaglutide	Exenatide	Albiglutide	Dulaglutide	Semaglutide (oral)	Dulaglutide
Total number of participants	6068	9340	3297	14,752	9463	9901	3183	577
% with CVD	100%	81.3%	83%	73%	100%	31.5%	84.7%	Not reported
eGFR criteria for enrollment (ml/min per 1.73 m²)	≥30 ml/min per 1.73 m²	Most had eGFR ≥30, but did include 220 patients with eGFR 15 to 30	Not reported	≥30	≥30	≥15	≥30 (however 0.9% had eGFR <30)	Not reported
Mean eGFR at enrollment (ml/min per 1.73 m²)	76	80	~75	76	79	76.9	74 ± 21	38
% with eGFR <60 ml/min per 1.73 m²	23	20.7 with eGFR 30 to 59 ml/min per 1.73 m², 2.4 with eGFR <30 ml/min per 1.73 m²	28.5	22.9	Not reported	22.2	26.9	100 with CKD G3a–G4
ACR	19% with micro-albuminuria and 7% with severely increased albuminuria	Not reported	Not reported	3.5% with severely increased albuminuria	Not reported	7.9% with severely increased albuminuria	Not reported	44% with severely increased albuminuria
Follow-up time	25 mo	3.8 yr	2.1 yr	3.2 yr	1.6 yr	5.4 yr	15.9 mo	52 wk
CV outcome definition	CV death, MI, stroke, or hospitalization for unstable angina	CV death, nonfatal MI, or nonfatal stroke	CV death, nonfatal MI, or nonfatal stroke	CV death, nonfatal MI, or nonfatal stroke	CV death, nonfatal MI, or nonfatal stroke	CV death, nonfatal MI, or nonfatal stroke	CV death, nonfatal MI, or nonfatal stroke	NA
CV outcome results	HR 1.02 (0.89–1.17)	HR 0.87 (0.78–0.97)	HR 0.74 (0.58–0.95)	HR 0.91 (0.83–1.00)	HR 0.78 (0.68–0.90)	HR 0.88 (0.79–0.99)	HR 0.79 (0.57–1.11)	NA
Kidney outcome (secondary end points)	New-onset severely increased albuminuria and doubling of SCr	New-onset persistent severely increased albuminuria, persistent doubling of the SCr level, ESKD, or death due to kidney disease	Persistent severely increased albuminuria, persistent doubling of SCr, a CrCl of <45 ml/min, or need for KRT	Two kidney composite outcomes: (1) 40% eGFR decline, kidney replacement, or renal death, (2) 40% eGFR decline, kidney replacement, renal death, or severely increased albuminuria	Not reported	New severely increased albuminuria ACR of >33.9 mg/mmol (339 mg/g), a sustained fall in eGFR of 30% from baseline, or use of KRT	Not reported	eGFR, ACR
Kidney outcome results	New-onset severely increased albuminuria: adjusted HR 0.81 (0.66–0.99), $P = 0.04$; Doubling of SCr: adjusted HR 1.16 (0.74–1.83), $P = 0.51$	HR 0.78 (0.67– 0.92)	HR 0.64 (0.46–0.88)	40% eGFR decline, kidney replacement, or renal death, adjusted HR 0.87 (0.73–1.04), $P = 0.13$; 40% eGFR decline, kidney replacement, renal death, or severely increased albuminuria: adjusted HR 0.85 (0.74–0.98), $P = 0.03$	Not reported	HR 0.85 (0.77–0.93) Similar for eGFR ≥60 vs. <60 ml/min per 1.73 m², no albuminuria vs. albuminuria, no ACEi/ARB vs. ACEi/ARB	Not reported	eGFR did not significantly decline (0.7 ml/min per 1.73 m²) with dulaglutide 1.5 mg or dulaglutide 0.75 mg, whereas eGFR decreased by −3.3 ml/min per 1.73 m² with insulin glargine

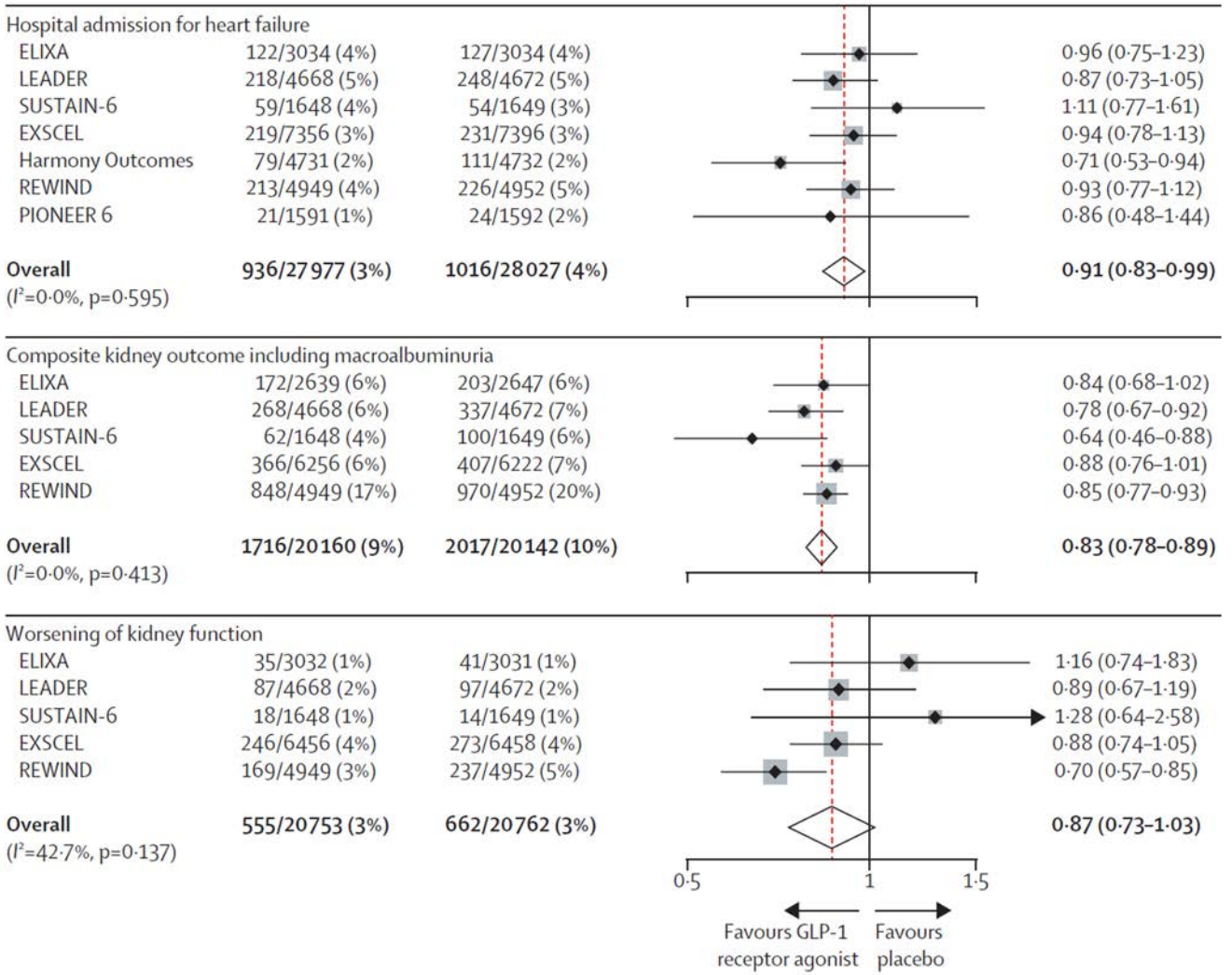
Effects of GLP-1RA on All-Cause Mortality and CV Outcomes*



*based on ELIXA, EXSCEL, HARMONY, LEADER, PIONEER 6, REWIND, SUSTAIN-6

Kristensen SL et al. *Lancet Diabetes Endocrinol*. 7: 776-785, 2019

Effects of GLP-1RA on Kidney Outcomes and Heart Failure*



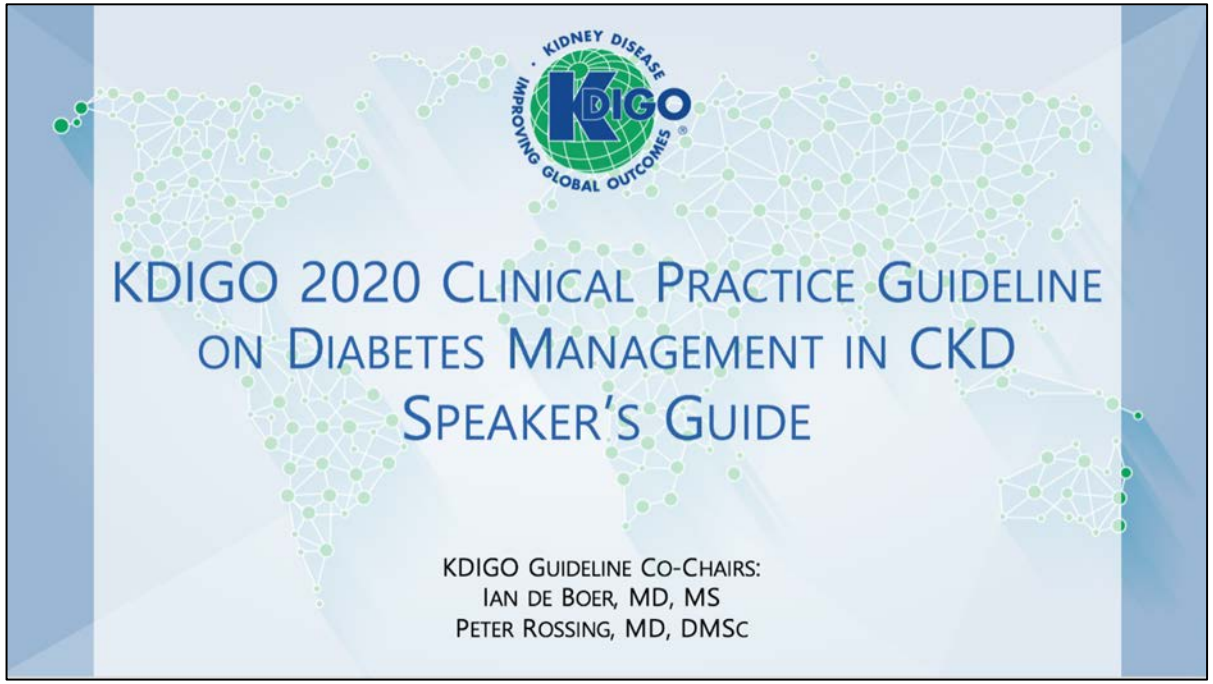
*based on ELIXA, EXSCEL, HARMONY, LEADER, PIONEER 6, REWIND, SUSTAIN-6

Kristensen SL et al. *Lancet Diabetes Endocrinol*. 7: 776-785, 2019

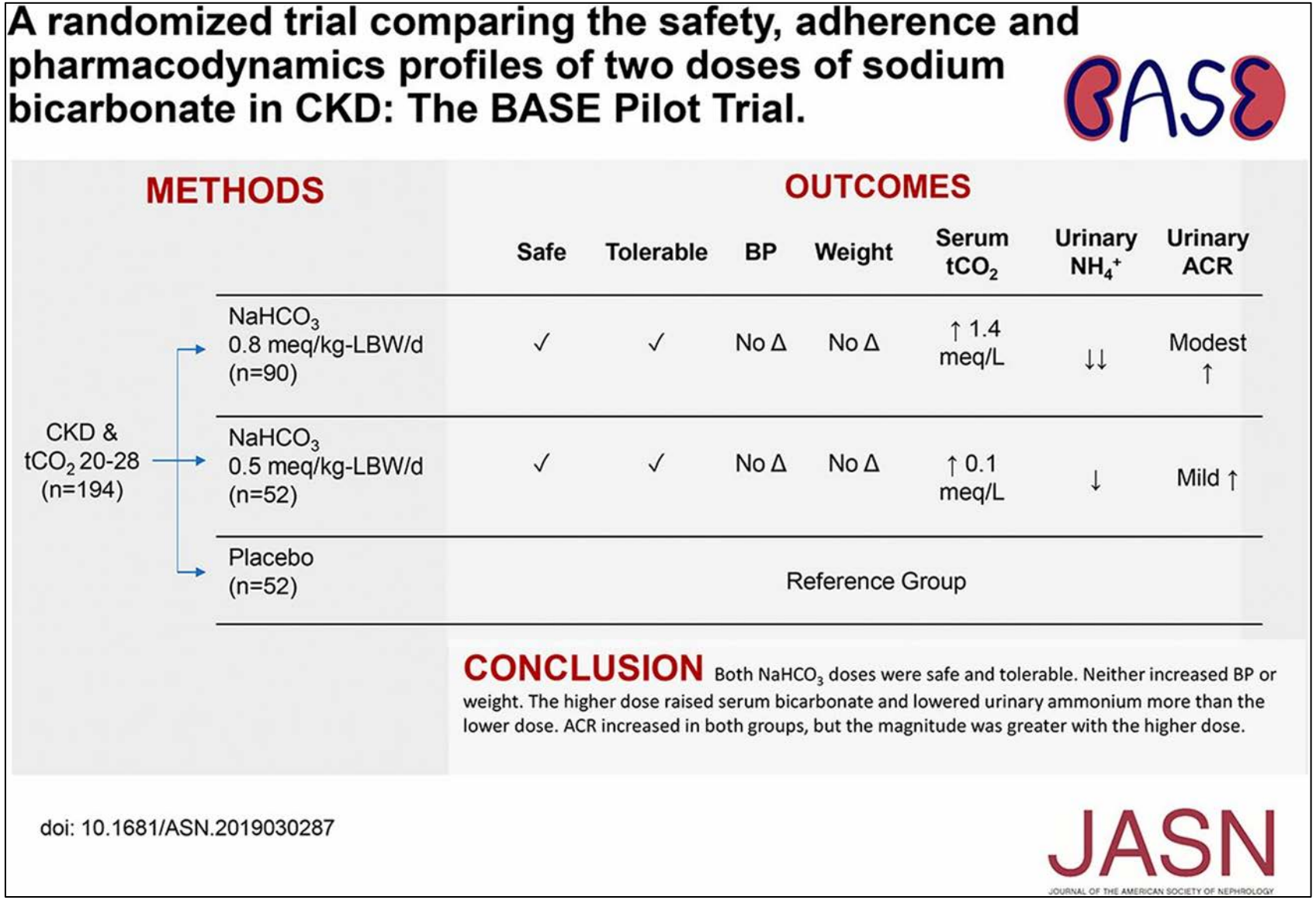
For more information on pharmacotherapies for patients with diabetes and CKD, please refer to the KDIGO Speaker's Guide noted below:

KDIGO Diabetes in CKD Guideline Website:
https://kdigo.org/guidelines/diabetes-ckd/

KDIGO Diabetes in CKD Speaker's Guide Direct Download:
https://kdigo.org/wp-content/uploads/2018/03/KDIGO-Diabetes-2020-Guideline-Speakers-Guide_Final.pptx



Management of Metabolic Acidosis



A randomized trial comparing the safety, adherence and pharmacodynamics profiles of two doses of sodium bicarbonate in CKD: The BASE Pilot Trial.

BASE

METHODS

CKD & tCO_2 20-28 (n=194)

OUTCOMES

	Safe	Tolerable	BP	Weight	Serum tCO_2	Urinary NH_4^+	Urinary ACR
$NaHCO_3$ 0.8 meq/kg-LBW/d (n=90)	✓	✓	No Δ	No Δ	↑ 1.4 meq/L	↓↓	Modest ↑
$NaHCO_3$ 0.5 meq/kg-LBW/d (n=52)	✓	✓	No Δ	No Δ	↑ 0.1 meq/L	↓	Mild ↑
Placebo (n=52)	Reference Group						

CONCLUSION Both $NaHCO_3$ doses were safe and tolerable. Neither increased BP or weight. The higher dose raised serum bicarbonate and lowered urinary ammonium more than the lower dose. ACR increased in both groups, but the magnitude was greater with the higher dose.

doi: 10.1681/ASN.2019030287

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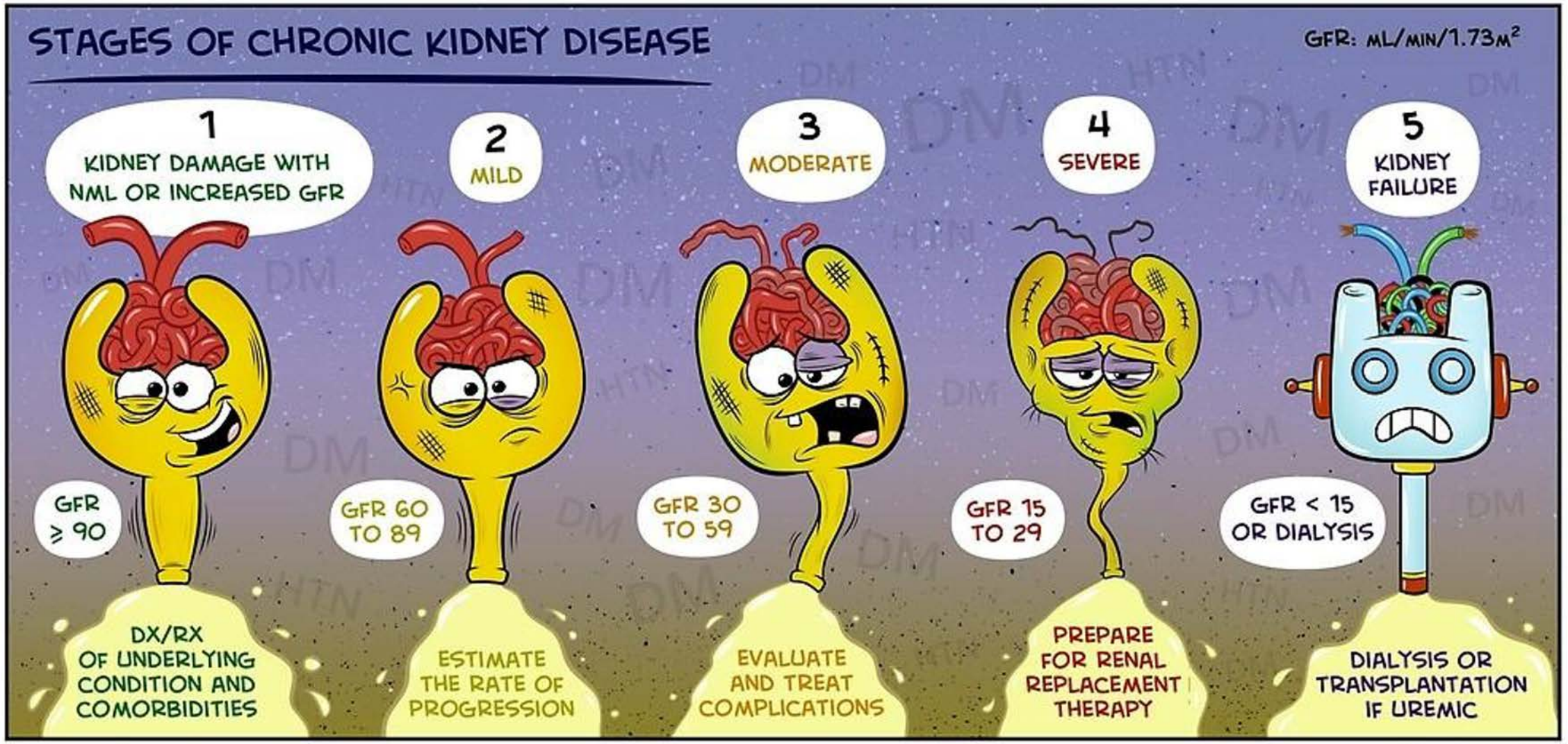
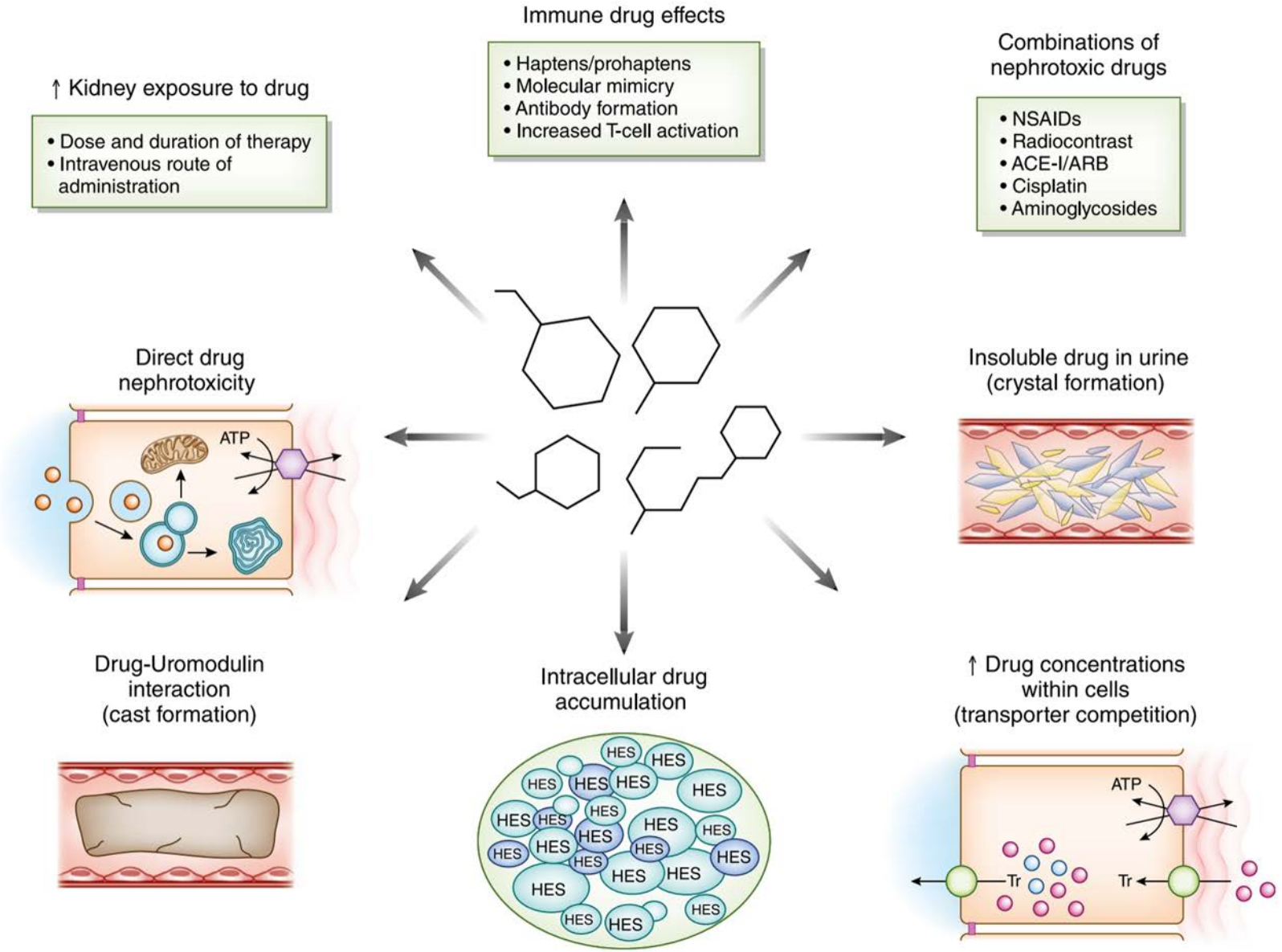
Controversies Conference Report Conclusion 8:

Accurate diagnosis and staging of CKD are necessary to utilize treatments effectively.

Conclusion 8: Accurate diagnosis and staging of CKD are necessary to utilize treatments effectively.

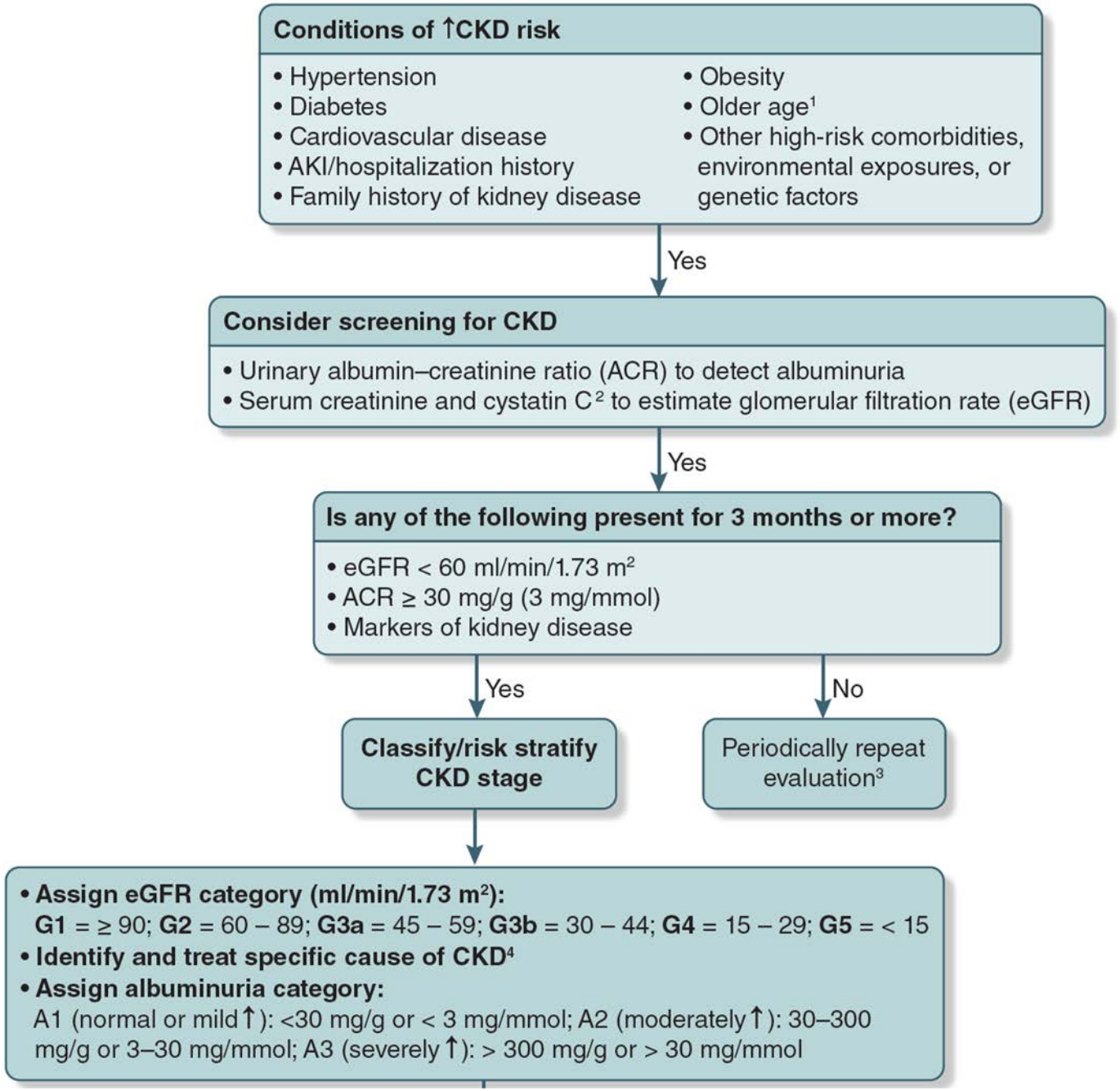


Drug Factors associated with increased risk of nephrotoxicity



SCREEN

RISK STRATIFY



Treatment

Patient safety

- **All patients eGFR < 60: patient safety risk:**
  - Dose medications based on eGFR
  - Reduce risk of AKI from volume depletion
  - Adopt "sick day rules" as needed
  - Avoid dual ACEi and ARB blockade
  - Contrast-associated AKI prevention:
    - Use lowest possible radiocontrast dose
    - Adequate hydration before, during, and after the procedure, consider isotonic saline infusion
    - Withhold ACEi or ARBs, diuretics, and other nephrotoxic agents before and after procedure
- **eGFR 45 – 59:**
  - Avoid prolonged NSAIDs
- **eGFR 30 – 44:**
  - Avoid prolonged NSAIDs
  - Use metformin with close monitoring at 50% dose
- **eGFR < 30:**
  - Avoid any NSAIDs
  - Avoid bisphosphonates
  - Avoid metformin
  - Avoid PICC lines for access preservation
  - If on warfarin: monitor PT-INR closely given increased risk of bleeding

Slowing CKD progression and reducing complications

- **Treat high blood pressure:**
  - ACEi or ARB if ACR ≥ 30mg/g or 3 mg/mmol
  - Diuretic often required
  - Dietary sodium < 2000 mg/d
- **Type 2 diabetes - target HbA1c < 6.5% to < 8.0%:**
  - For those with CKD and type 2 diabetes and eGFR > 30, start SGLT2 inhibitor and metformin
  - If glycemic target not achieved with metformin and SGLT2 inhibition, add GLP1-RA
- **CKD complications testing:**
  - Anemia – evaluate if CKD G3–G5 and Hb < 13 g/dl for men and < 12 g/dl for women Treat iron deficiency first. Consider starting erythropoiesis-stimulating agents (ESAs) if Hb 9–10 g/dl (avoid Hb > 11.5 g/dl)
  - Acidosis – correct to normal range using bicarbonate supplementation if bicarbonate < 22 mmol/l in CKD G3–G5
  - CKD - mineral bone disease – CKD G3–G5 check calcium, phosphate, 25-OH vit D, and intact PTH. Supplement vitamin D deficiency
- **Influenza vaccination**
- **Pneumococcal and hepatitis B vaccination in CKD G4–G5**
- **Screen for hepatitis C**

Reduction of CVD complications

- **CKD = ↑CVD risk**
- **Blood pressure systolic target < 120 mm Hg[5]**
  - Consider BP target of < 130/80 mm Hg in kidney transplant recipients
- **Start lipid-lowering therapy:**
  - If CKD and age ≥ 50 years, statin is recommended
  - If CKD and age 18–49 years, statin if known CAD, diabetes mellitus, prior stroke, or high ASCVD risk
- **Aspirin for secondary prevention unless bleeding risk outweighs benefits**

When to refer to nephrology:

- AKI or abrupt sustained fall in GFR
- eGFR < 30 ml/min/1.73 m²
- Consistent significant albuminuria (ACR > 300 mg/g or 30 mg/mmol)
- Progression of CKD
- Urinary red cell casts or RBC > 20 per high power field sustained and not readily explained
- CKD and hypertension refractory to treatment with 4 or more antihypertensive agents
- Persistent abnormalities of serum potassium
- Recurrent or extensive nephrolithiasis
- Hereditary kidney disease

ISN INTERNATIONAL SOCIETY OF NEPHROLOGY

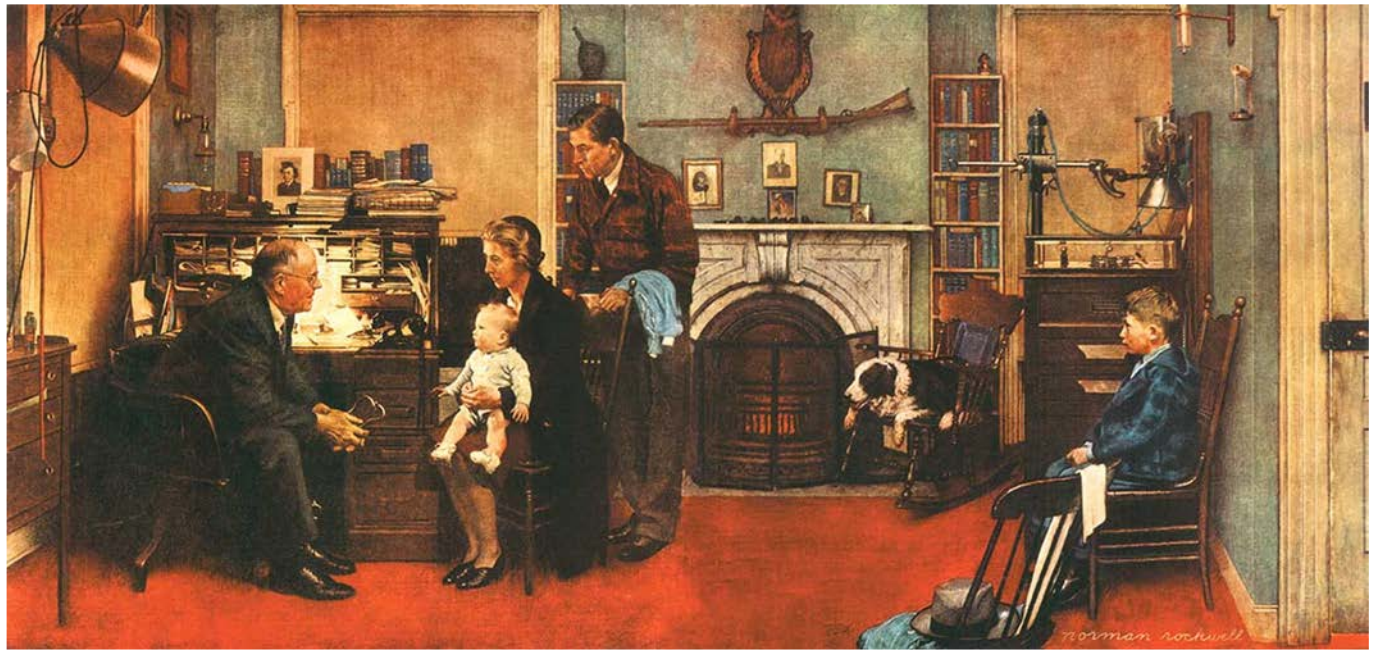
KDIGO KIDNEY DISEASE IMPROVING GLOBAL OUTCOMES

Controversies Conference Report Conclusion 9:

Patient engagement is a critical component of efforts to screen for and treat CKD.

Conclusion 9: Patient engagement is a critical component of efforts to screen for and treat CKD

Patient and family education and engagement



Potential benefits:

- Improved patient activation
- Improved access to healthcare
- Improved access and adherence to medications
- Timely nephrology referral, dietician referral, and diabetes education

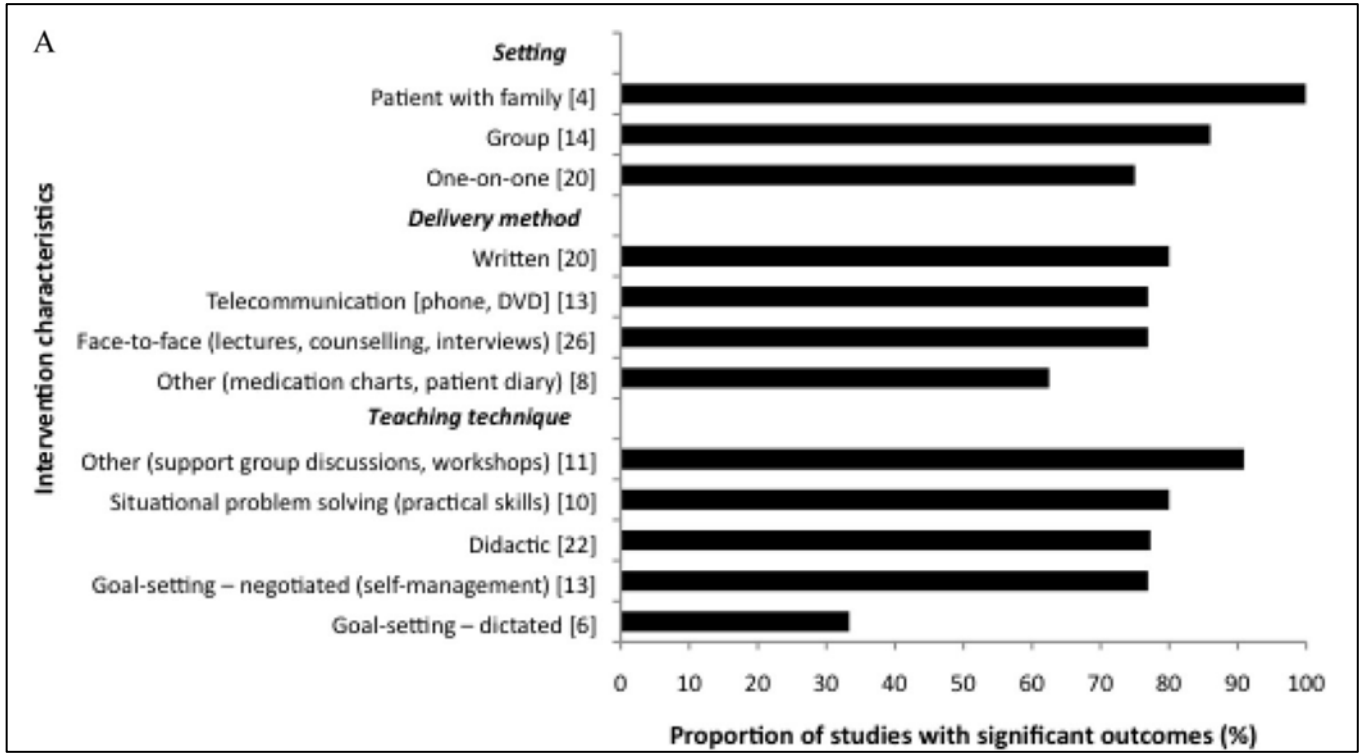
Measures for Defining Success in CKD Screening, Risk Stratification and Treatment Programs

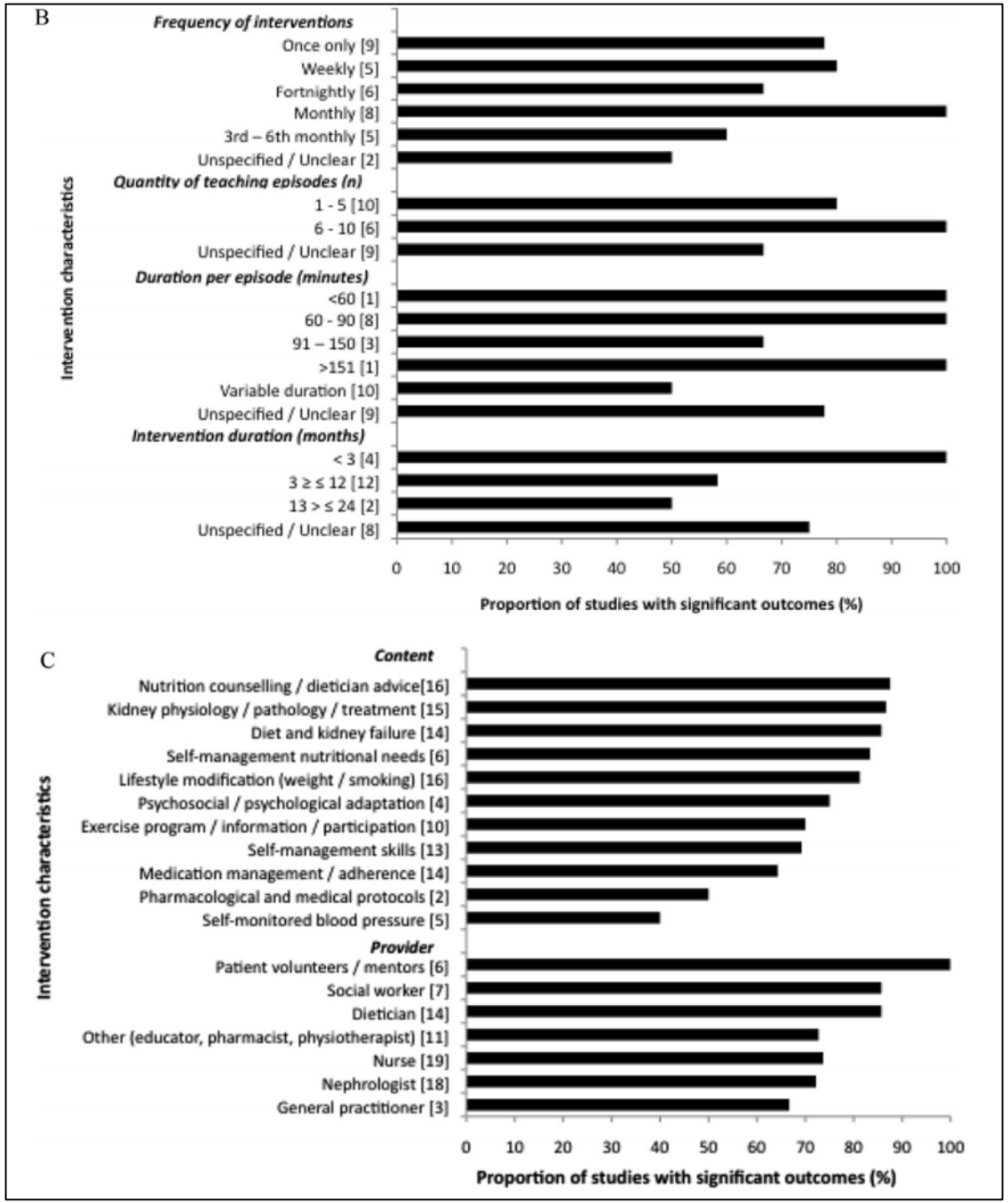
Outcomes	Indicators
Process (pertaining to health systems, providers, or patients)	• Screening with the correct tests (eGFR and UACR) • Timely and appropriate follow-up testing • Dietary, exercise, and smoking cessation counseling • Clinician CKD awareness as measured by documentation • Patient adherence to treatment plan • Appropriate nephrology/kidney transplant referrals • Availability of essential medicines and testing
Patient-centered	• Patient awareness of and attitudes toward CKD diagnosis • Patient experience and satisfaction • CKD-specific knowledge • Trust in physician • Quality of life • Shared decision-making for modality choice, including kidney replacement therapy and conservative management
Intermediate clinical	• Blood pressure control • Glycemic control • Statin use • ACEi/ARB use • SGLT2 inhibitor use • Vaccinations • Management of CKD-specific complications • Drug dosing/adverse drug events
Clinical	• CKD progression—eGFR slope, 40% decline in eGFR, doubling of serum creatinine, kidney failure • Hospitalization or emergency department visits • Cardiovascular events • Acute kidney injury events • Emergency dialysis starts • Pre-emptive transplant rates • All-cause mortality

Educational Interventions for Patients With CKD: A Systematic Review

Pamela A. Lopez-Vargas, MPH,[1,2] Allison Tong, PhD,[1,2] Martin Howell, PhD,[1,2] and Jonathan C. Craig, PhD[1,2]

Lopez-Vargas PA, et al. Am J Kidney Dis. 2016; 68: 353-370





Samples of Successful CKD Education Efforts

Reference	Patient Population	Participants (*N*)	Study Design	Education Topic(s)	Intervention	Outcome(s)
5	Patients at risk for AKI on the basis of prescription for hypertension or diabetes medications	152	Prospective cohort study	NSAID avoidance	Pharmacist–led education intervention administered during prescription pickup or pharmacy purchase	Increased knowledge of risks associated with NSAIDs; patient-reported intentions to limit NSAID use
115	Adult patients with eGFR<60 ml/min per 1.73 m^2 not on dialysis	89	Randomized, controlled clinical trial	Protein intake	Addition of nutrition education materials to a dietary counseling program	Reduced protein intake in the intervention compared with the control group; adherence rates did not differ between groups
6	Patients with progressive CKD expected to require RRT within 6–18 mo (sCr≤3.4 mg/dl)	297	Inception cohort, prospective, randomized, controlled trial	Healthy kidney function, kidney diseases, RRT modalities, diet/nutrition, medications, lifestyle changes	90-min one-on-one slide–based teaching sessions supported by a printed 60-page booklet and 10-min telephone support calls every 3 wk	Delayed dialysis initiation in the intervention group; knowledge acquisition was directly associated with time to dialysis
8	Patients with eGFR<30 ml/min per 1.73 m^2	70	Randomized, controlled trial	Self-care dialysis (*i.e.*, peritoneal dialysis, home hemodialysis)	Two–phase education program, including educational booklets and a 15-min video (phase 1) as well as a 90-min interactive small group session (phase 2)	Increase in patient-reported intention to use self-care dialysis among intervention compared with usual care group
11	Patients with progressive CKD expected to require RRT (sCr≥3.96 mg/dl and increasing)	335	Randomized, controlled trial	Normal kidney function, kidney diseases, dietary management, RRT modalities	60- to 75-min one-on-one slide lecture presentation supplemented by a 22-page booklet summarizing the presentation content	The intervention group survived an average of 8 mo longer after dialysis initiation than the usual care group
116	Patients on hemodialysis	118	Randomized, controlled trial	BP control	Nurse–led education program incorporating monitoring, goal setting, and reinforcement	The intervention group had reduced systolic and diastolic BPs compared with the control group

sCr, serum creatinine; NSAID, nonsteroidal anti–inflammatory drug.

Narva AS, et al. *Clin J Am Soc Nephrol*. 2016; 11:694-703

Role of Information Technology in CKD Care

Diamantidis and Becker *BMC Nephrology* 2014, **15**:7
http://www.biomedcentral.com/1471-2369/15/7

REVIEW Open Access

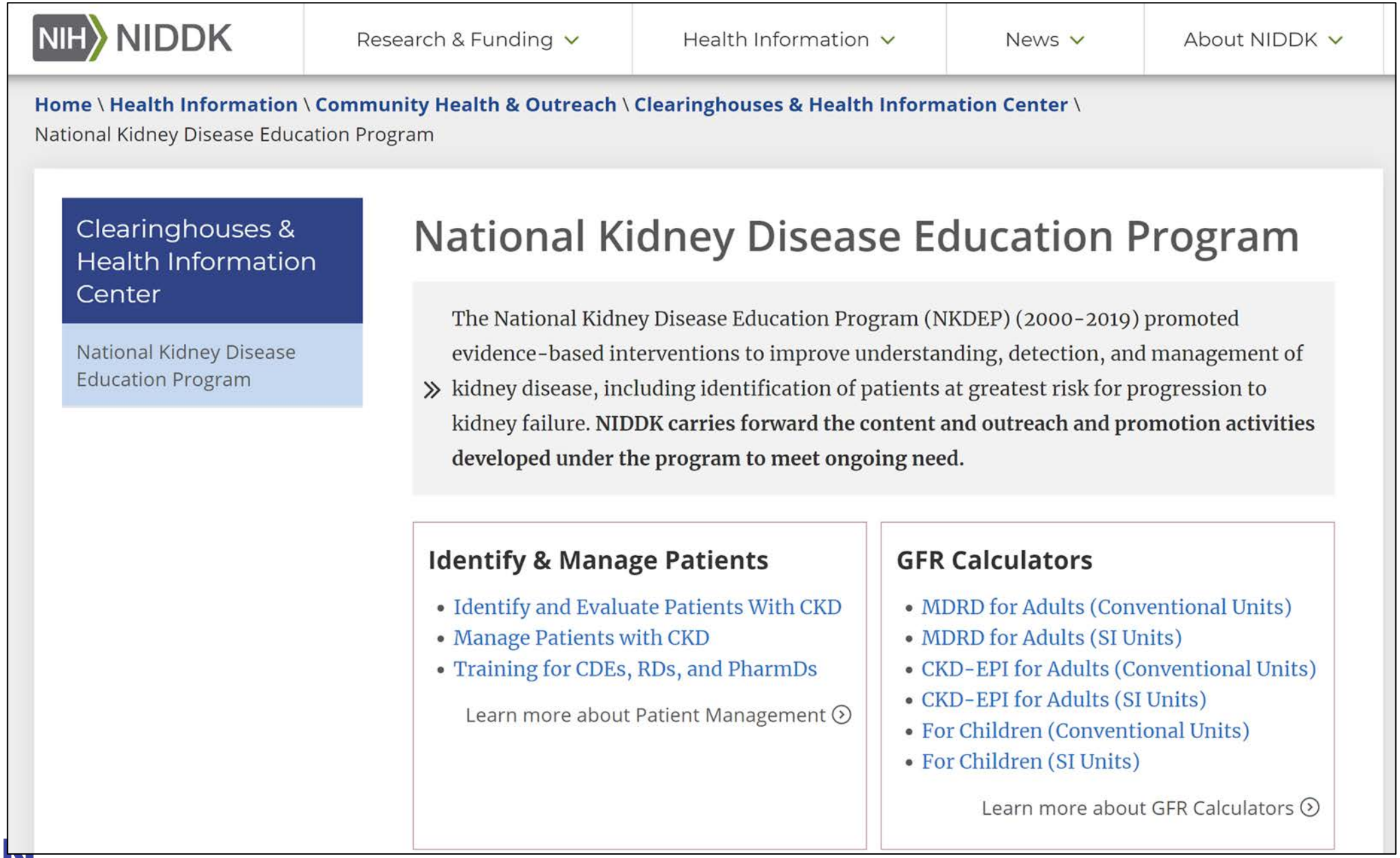
Health information technology (IT) to improve the care of patients with chronic kidney disease (CKD)

Clarissa J Diamantidis[1,2*] and Stefan Becker[3]

Abstract

Several reports show that patients with chronic disease who are empowered with information technology (IT) tools for monitoring, training and self-management have improved outcomes, however there are few such applications employed in kidney disease. This review explores the current and potential uses of health IT platforms to advance kidney disease care by offering innovative solutions to inform, engage and communicate with individuals with CKD.

Keywords: Chronic kidney disease, Health information technology, Mobile health, Patient safety



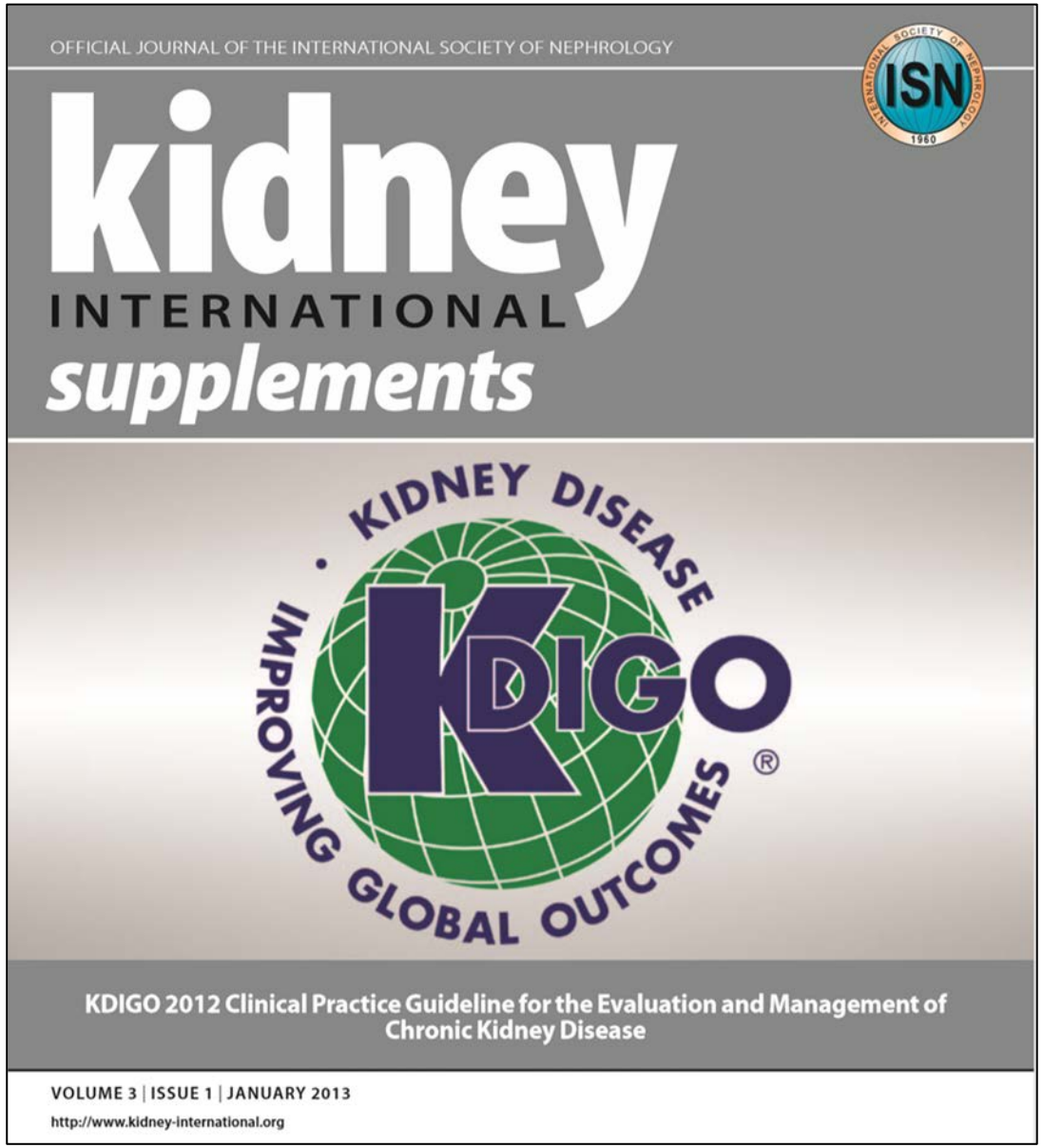
https://www.niddk.nih.gov/

Types of Telehealth Applications to Enhance CKD Knowledge and Awareness

Telehealth Application	Definition	Kolb's Learning Theory	Current Uses	Potential Future Uses
Web-based applications	Internet Web site with educational text or links to educational materials	Knowledge	Patient: education about CKD	Patient: inclusion in self-management training and risk factor education for CKD prevention
			Provider: education about CKD diagnosis and management	Provider: nephrology clinical support tools (protocols, treatment algorithms)
Videoconferencing	Synchronous discussion among peers that are physically distant, broadcast over video	Knowledge and understanding	Patient: awareness of CKD and empowerment with virtual support groups	Patient: eHealth communities for psychosocial support, including those around kidney donation
			Provider: self-efficacy for CKD management	Provider: intra-professional nephrology education during training
Text messaging	Mobile phone based text messages delivered over telephone cables or broadband	Knowledge	Patient: CKD self-management (medication adherence, appointment reminders) with 1-way communication	Patient: engagement with health team with 2-way communication
Interactive voice response	Telephone-based automated voice recognition system that delivers/captures personalized data	Knowledge; limited understanding	Patient: education about CKD and healthy lifestyles	Patient: self-management (medication titration)
Mobile applications	Wireless communication among objects that provide individualized data	Knowledge and understanding	Patient: self-management with personal data	Patient: education about community resources
Store and forward communication	Asynchronous communication using text and/or pictures	Knowledge and understanding	Provider: asynchronous eConsultation	Provider: proactive preventive consultation

Tuot DS, Boulware LE. *Adv Chronic Kidney Dis*. 2017; 24:39-45.

Health System and Economic Factors



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.

Controversies Conference Report Conclusion 10:

CKD screening and treatment efforts require multi-stakeholder implementation strategies to overcome barriers to high quality CKD care.

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Key Strategies for CKD Screening Program Development and Success

PATIENT RELATED BARRIERS

- Low patient knowledge of CKD and its associated risks, and social risk factors, such as limited financial resources and low health literacy

HEALTH SYSTEM RELATED BARRIERS

- Perceived lack of urgency for detecting early CKD among primary care clinicians
- Lack of knowledge of CKD guidelines
- Lack of incentives for CKD interventions
- Lack of CKD-specific clinical quality measures
- Suboptimal communication between specialties

Health System-Level Approaches for Improving Early CKD Identification and Management

Framework for developing initiatives

Conceptual

- Understand patient flow through the health system and identify possible tactics for engagement
- Develop risk-based approaches to identifying and treating CKD
- Integrate novel program processes with existing health services and processes
  - Augment/strengthen in view of early CKD identification and intervention
- Actively engage with:
  - Patients
  - Health care clinicians
  - Health system administrators and policy makers
- Develop monitoring and improvement strategies

Practical

- Determine population for screening based on local risk factors
- Identify existing screening programs for other diseases, such as cardiovascular
- Assess whether there is necessary political commitment
- Specify available resources (workforce/material/funding)
- Develop a technical package, strategies using the best available evidence, for CKD screening and management
- Provide specific, actionable recommendations with level of evidence
- Develop targeted versions of the guideline summary aimed at patients and primary-care providers[103,104]
- Develop visually appealing infographics and apps to aid in knowledge translation
- Integrate guideline recommendations in laboratory information systems and electronic health records with clinical decision support
- Engage medical educators to teach guideline-based CKD care in medical schools
- Engage all stakeholders—professional societies (such as ISN), patients, payers, health systems, and disease-specific foundations—in dissemination strategies
- Establish governance for monitoring, evaluation, and improvement

Health System-Level Approaches for Improving Early CKD Identification and Management

Framework for continued advocacy and expansion of efforts
• Identify the full health and economic burdens of kidney diseases
• Establish kidney disease registries and use collected data to drive surveillance, feedback, and integration
• Collaborate with other guideline bodies and professional societies to maximize consistency in recommendations (e.g., primary care, cardiology, endocrinology, geriatrics)
• Develop evidence-based quality measures for CKD care
• Document real-world health and economic consequences of successful interventions and models of care
• Identify methods for sustainable financing of optimal services
• Generate and promote evidence linking health promotion to improved health and economic outcomes regarding kidney diseases
• Continue advocacy from researchers, clinicians, and policy makers for healthy environments and lives
• Focus investments and reforms to develop effective primary-care systems, including pharmaceuticals and behavioral interventions
• Invest in research to identify novel risk factors for kidney diseases
• Implement cost-effective strategies to target care to individuals at increased risk of kidney disease

Measures for Defining Success in CKD Screening, Risk Stratification and Treatment Programs

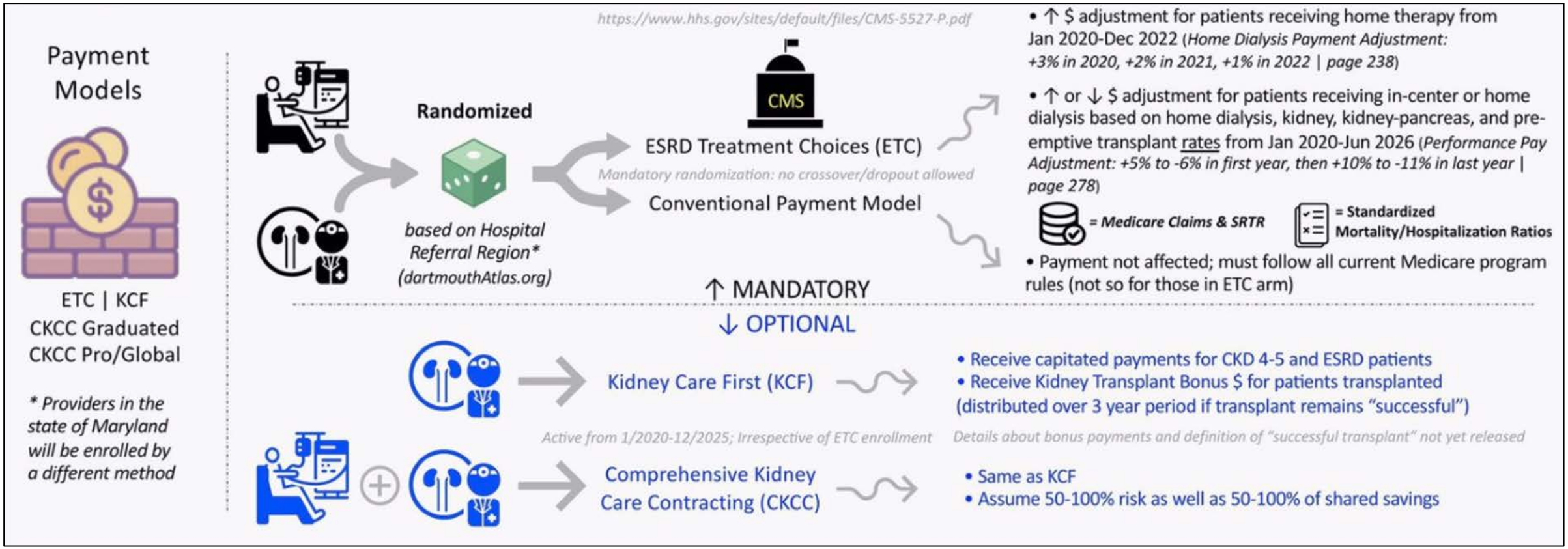
Outcomes	Indicators
Process (pertaining to health systems, providers, or patients)	• Screening with the correct tests (eGFR and UACR) • Timely and appropriate follow-up testing • Dietary, exercise, and smoking cessation counseling • Clinician CKD awareness as measured by documentation • Patient adherence to treatment plan • Appropriate nephrology/kidney transplant referrals • Availability of essential medicines and testing
Patient-centered	• Patient awareness of and attitudes toward CKD diagnosis • Patient experience and satisfaction • CKD-specific knowledge • Trust in physician • Quality of life • Shared decision-making for modality choice, including kidney replacement therapy and conservative management
Intermediate clinical	• Blood pressure control • Glycemic control • Statin use • ACEi/ARB use • SGLT2 inhibitor use • Vaccinations • Management of CKD-specific complications • Drug dosing/adverse drug events
Clinical	• CKD progression—eGFR slope, 40% decline in eGFR, doubling of serum creatinine, kidney failure • Hospitalization or emergency department visits • Cardiovascular events • Acute kidney injury events • Emergency dialysis starts • Pre-emptive transplant rates • All-cause mortality

Controversies Conference Report Conclusion 11:

Financial and nonfinancial incentives need to be aligned toward CKD screening, risk stratification, and treatment.

Conclusion 11: Financial and non-financial incentives need to be aligned toward CKD screening, risk stratification and treatment.

Advancing American Kidney Health Executive Order



Infographic courtesy of Dr. Tejas Desai

Controversies Conference Report Conclusion 12:

CKD screening in high-risk groups is likely to be cost-effective.

Conclusion 12: CKD screening in high-risk groups is likely to be cost-effective.

The Preventable Productivity Burden of Kidney Disease in Australia

Feby Savira,[1,2] Zanfina Ademi,[1] Bing H. Wang,[1,2] Andrew R. Kompa,[3] Alice J. Owen,[1] Danny Liew,[1] and Ella Zomer[1]

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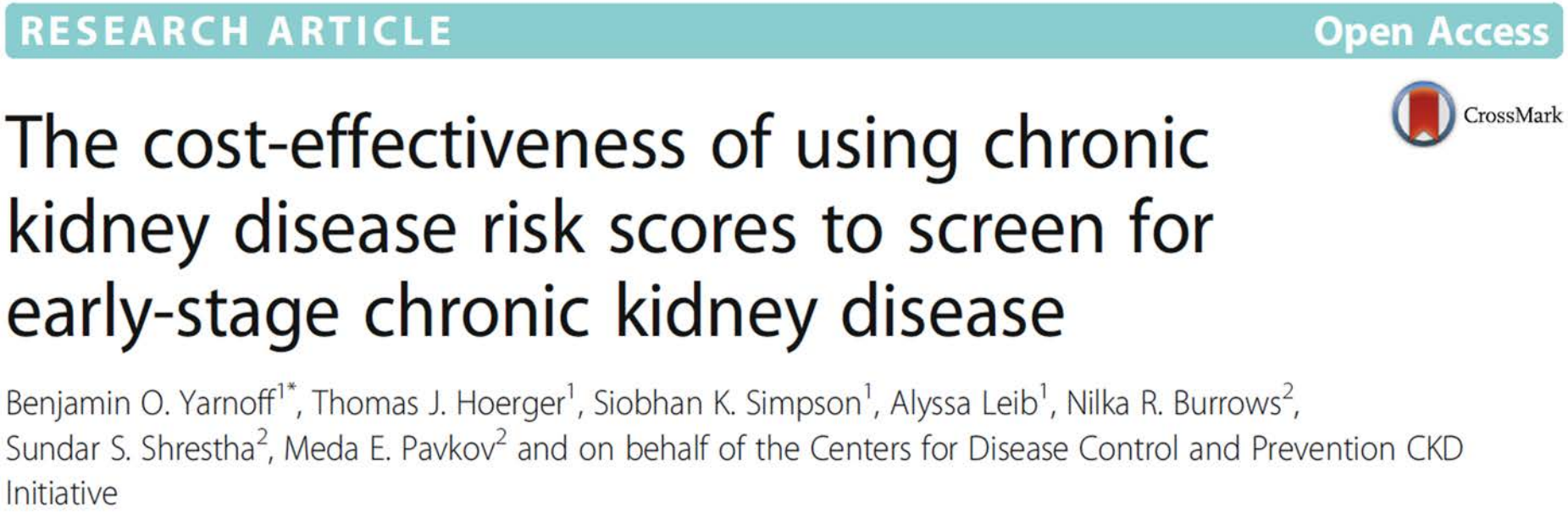
Savira et al. *JASN* 2021; doi: https://doi.org/10.1681/ASN.2020081148

This Australian study demonstrated that even a modest 10% reduction in CKD incidence translated into the prevention of 1503 cases of CKD G3, 117 cases of CKD G4-G5, and six new cases of kidney failure per year and would result in a gain of 7590 productivity-adjusted life years (PALYs), with an associated cost savings of US$1.1 billion.

Conclusion 12: CKD screening in high-risk groups is likely to be cost-effective.



RESEARCH ARTICLE Open Access

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The cost-effectiveness of using chronic kidney disease risk scores to screen for early-stage chronic kidney disease

Benjamin O. Yarnoff[1*], Thomas J. Hoerger[1], Siobhan K. Simpson[1], Alyssa Leib[1], Nilka R. Burrows[2], Sundar S. Shrestha[2], Meda E. Pavkov[2] and on behalf of the Centers for Disease Control and Prevention CKD Initiative

Yarnoff et al. *BMC Nephrology* 2017; 18:85

Using CKD risk scores may also allow clinicians to cost-effectively identify a broader population for CKD screening with testing for albuminuria and potentially detect people with CKD at earlier stages of the disease than current approaches of screening only persons with diabetes or hypertension.

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Conclusion 12: CKD screening in high-risk groups is likely to be cost-effective.

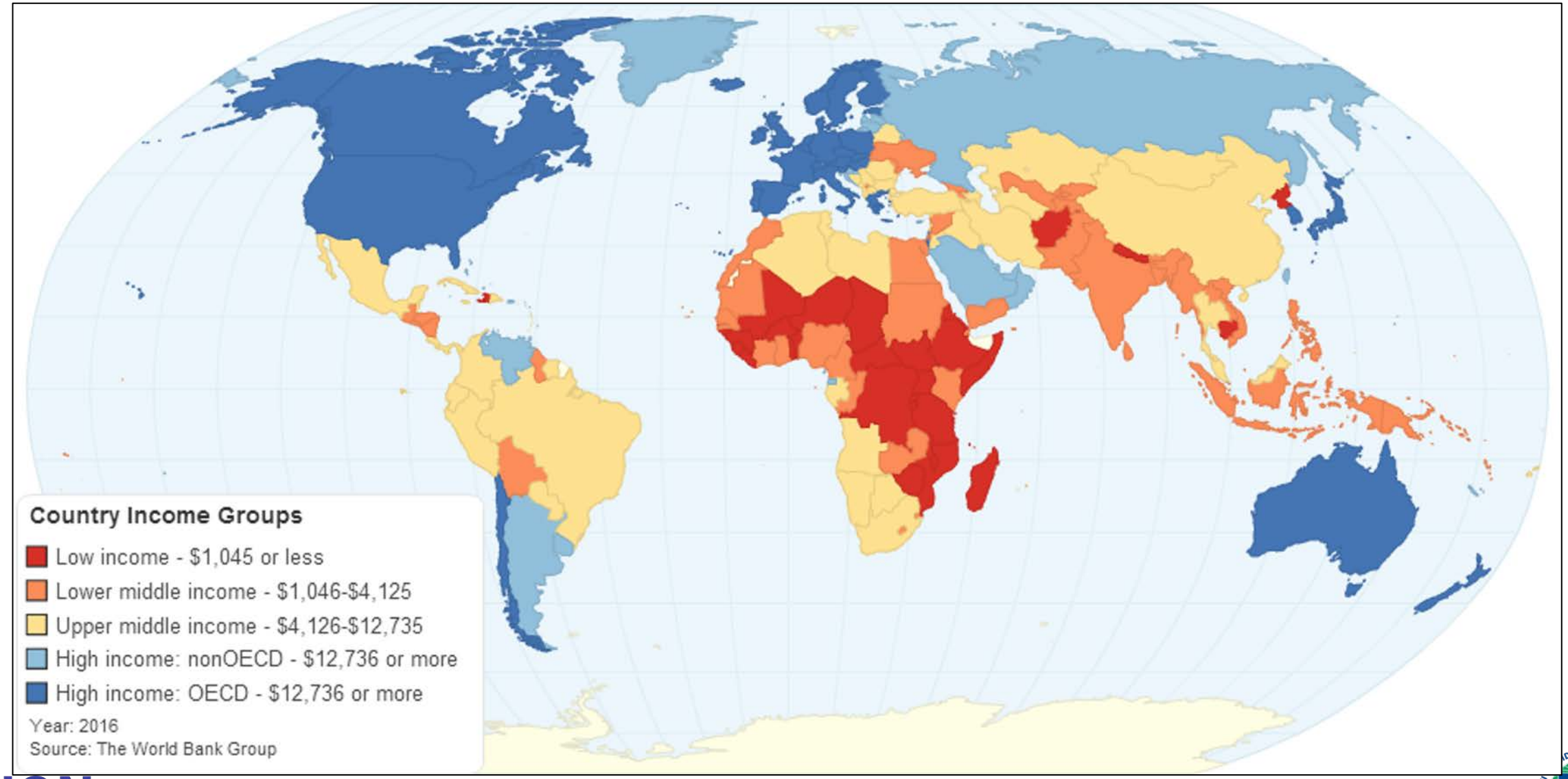
Future research direction: we need new cost effectiveness analyses to overcome limitations of prior studies.

- Predominant focus on proteinuria
- Minimal inclusion of cardiovascular outcomes: the key complication of CKD that drive hospitalizations and mortality
- Assumption of annual screening: costly and probably unnecessary
- Models did not incorporate patient perspectives and patient-reported outcomes
- Few cost-effectiveness studies included low and middle income countries (LMICs)

Controversies Conference Report Conclusion 13:

CKD screening approaches may differ in LMIC countries.

Conclusion 13: CKD screening approaches may differ in LMIC countries



http://chartsbin.com/view/2438

In Brief, Why Screen?

- ☑ CKD is highly prevalent, costly, and its worldwide disease burden is increasing.
- ☑ There are low-cost and accurate tests for CKD. Serum creatinine and cystatin C are accurate tests to estimate GFR. UACR is a sensitive measurement of kidney damage but urine dipstick proteinuria could be considered in low-resource settings.
- ☑ CKD is asymptomatic until late stages. The asymptomatic stage contributes to low awareness of CKD in patients with the diagnosis. Therefore, a screening program could shift recognition of CKD into much earlier stages relative to current practice.
- ☑ Individuals with CKD often express a preference for early communication about a CKD diagnosis.
- ☑ Treatments for recognized CKD can be initiated during early stages, are accepted, and are highly effective.
- ☑ CKD screening in high-risk groups is likely to be cost-effective.

Responses to Common Criticisms of CKD Early Detection and Treatment Proposals

Criticism	KDIGO Controversies Conference Conclusion
CKD testing is too expensive.	· The three measures recommended for CKD detection and risk stratification (creatinine, cystatin C, UACR) are all feasible on auto-analyzers, and can be measured together for less than $20 USD. Models that exclude cystatin C are acceptable for low-resource settings · Higher volume testing would further lower the costs per individual · The costs of a monitoring program are largely driven by the frequency of testing; the intervals for CKD monitoring could be tailored to the individual's prior testing and risk factor profile
All patients get a serum creatinine test anyway.	· Many persons with CKD are not actively engaged in medical care and may not have had a GFR assessment at appropriate frequency · Persons with abnormal albuminuria but preserved GFR represent a substantial proportion of the CKD population, and they are woefully under-detected in current clinical care
All CKD patients already have diabetes or hypertension, and diagnosing CKD would not change management.	· A significant proportion of patients, especially in LMIC have CKD in absence of prior diabetes or hypertension and limiting screening to those with these conditions would miss a large fraction of CKD · Persons with diabetes or hypertension are not effectively monitored with appropriate kidney measures (e.g., UACR) · CKD diagnosis may impact choice of antihypertensive agent, medication dosing, indication for statin therapy, SGLT2 inhibitor therapy, avoidance of nephrotoxins, and prognostication

Responses to Common Criticisms of CKD Early Detection and Treatment Proposals

Criticism	KDIGO Controversies Conference Conclusion
Older adults do not have "real" CKD.	· Older adults have the highest prevalence of CKD across all GFR and albuminuria stages, and CKD impacts physical and cognitive function, medication safety, and prognosis for older adults · As with all screening programs, testing must be consistent with that person's goals of care and life expectancy, but this would not justify excluding older adults from CKD detection and monitoring
There are no effective treatments for CKD, even if it is detected.	· Several available treatments can reduce CKD progression and the risk of cardiovascular disease for persons with CKD, including ACEi/ARBs, statins, BP and diabetes management, and SGLT2 inhibitors · Earlier initiation of preventive therapies may slow progression across stages and ultimately reduce both the incidence and prevalence of kidney failure and risk of future development of cardiovascular disease. Benefits have been observed for some therapies in reducing all-cause mortality and risk for heart failure.

Responses to Common Criticisms of CKD Early Detection and Treatment Proposals

Criticism	KDIGO Controversies Conference Conclusion
Notifying patients of CKD would cause more harm and anxiety than any benefit	· With proper communication about CKD staging and education regarding lifestyle and treatment options, patients with newly detected CKD can make positive choices that will reduce their risk of progression · Patient representatives have expressed their desire for early detection strategies and for prognostic information, while lamenting that their own CKD diagnosis occurred too late
The requirement for confirmatory testing at 90-days to diagnose CKD is a barrier to effective treatment	· The 90-day period might be useful to distinguish the chronicity of kidney disease, but it is not essential to establish that kidney disease is present · Persons with high-risk CKD should be treated expeditiously without waiting for confirmatory testing

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Conclusions

- The KDIGO Controversies Conference participants were unanimous that the bulk of evidence supports systematic approaches to **screen for, risk stratify, and treat persons with CKD**.
- Because interventions to slow CKD progression and reduce cardiovascular risk are evidence-based and have been shown to improve outcomes, **the focus should be on strategies to maximize deployment of CKD screening, risk stratification, and treatment efforts.**

Key conclusions from KDIGO Controversies Conference on Early Identification and Intervention

Populations for CKD screening, risk stratification, and treatment
Conclusion 1. Persons with hypertension, diabetes, or cardiovascular disease should be screened for CKD. **Conclusion 2.** CKD screening and treatment programs should also be implemented in other high-risk individuals and populations based on comorbidities, environmental exposures, or genetic risk factors. **Conclusion 3.** The initiation, frequency, and cessation of CKD screening should be individualized based on kidney and cardiovascular risk profiles and individual preferences.
Measurements for early CKD
Conclusion 4. CKD screening and risk stratification must consist of a dual assessment of estimated glomerular filtration rate (eGFR) and albuminuria (UACR). **Conclusion 5.** Accurate GFR estimation includes both creatinine and cystatin C measurements for initial diagnosis and staging. **Conclusion 6.** The combination of creatinine, cystatin C, and UACR for CKD screening is affordable in high-income settings.
Interventions for CKD
Conclusion 7. A key rationale for CKD screening is the availability of many effective interventions to delay CKD progression and reduce cardiovascular risk. **Conclusion 8.** Accurate diagnosis and staging of CKD are necessary to utilize treatments effectively. **Conclusion 9.** Patient engagement is a critical component of efforts to screen for and treat CKD.
Health system and economic factors
Conclusion 10. CKD screening and treatment efforts require multi-stakeholder implementation strategies to overcome barriers to high-quality CKD care. **Conclusion 11.** Financial and nonfinancial incentives need to be aligned toward CKD screening, risk stratification, and treatment. **Conclusion 12.** CKD screening in high-risk groups is likely to be cost-effective. **Conclusion 13.** CKD screening approaches may differ in LMIC countries.

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; GFR, glomerular filtration rate; LMICs, low- and middle-income countries; UACR, urine albumin-to-creatinine ratio.

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Future Research

- **Pragmatic trials** should be designed to test CKD early identification and intervention programs across various high-risk populations using different combinations of measures.
- Implementation efforts should engage policy makers, local clinicians, the community at large and broader stakeholders in an iterative process.
- Ultimately, **large-scale randomized controlled trials** should be conducted to evaluate the effects of CKD screening, risk stratification, and treatment programs compared with usual care on clinical endpoints.

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