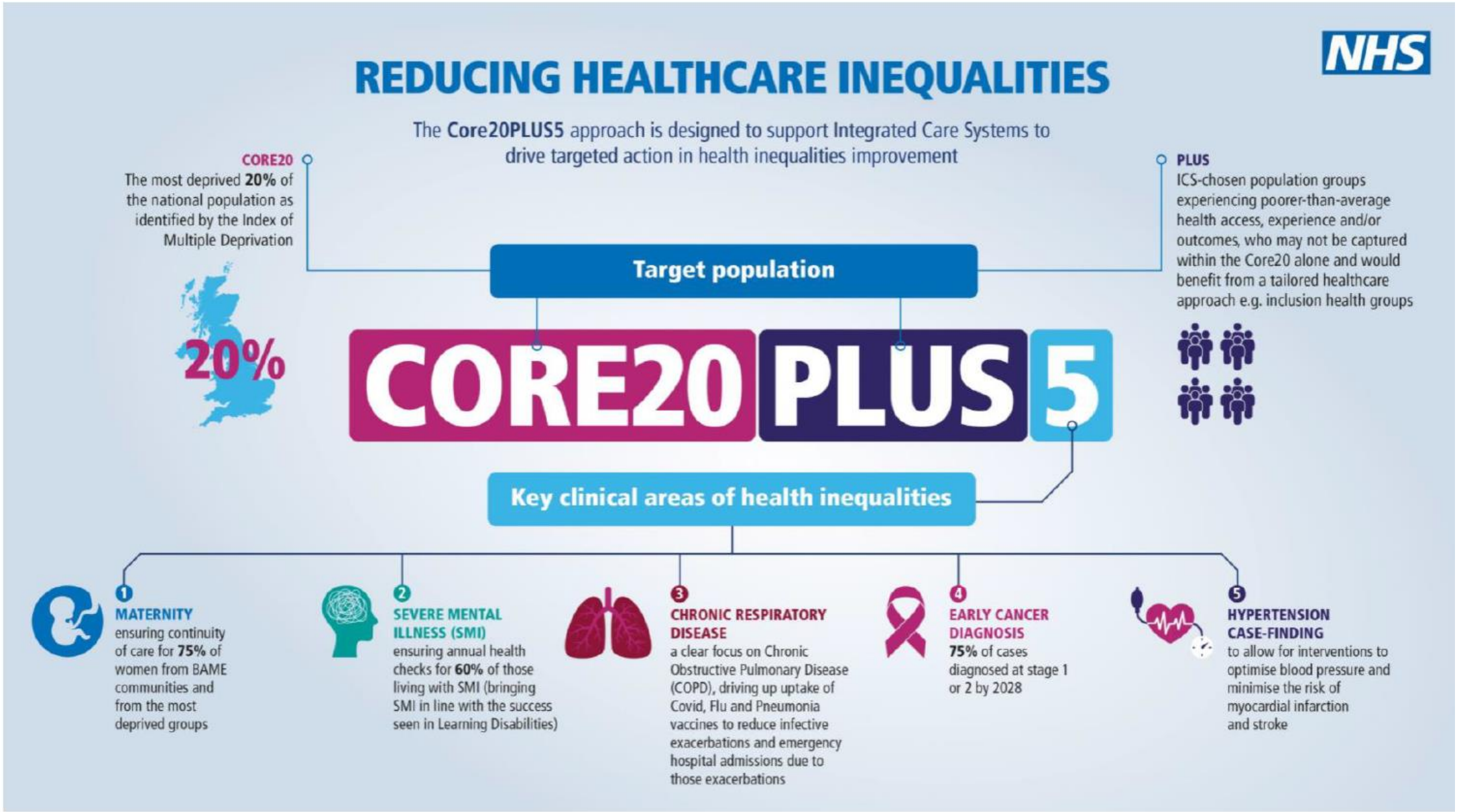
CKD: the forgotten risk factor for CVD *and* an important health equity challenge

- What is CKD and why is it a risk factor for CKD
- Epidemiology and population health of chronic kidney disease (CKD)
- Housing the kidney in cardiometabolic disease in clinical practice
- Changing the trajectory of CKD
- Quality improvement opportunities and data

We know we have a national problem with health inequalities related to CVD (and CKD)



CKD is now recognised in ‘Six High-Risk Conditions for Cardiovascular Disease’ by CVD Prevent

COHORT I – people with a coded diagnosis of at least one of the following six high-risk conditions:

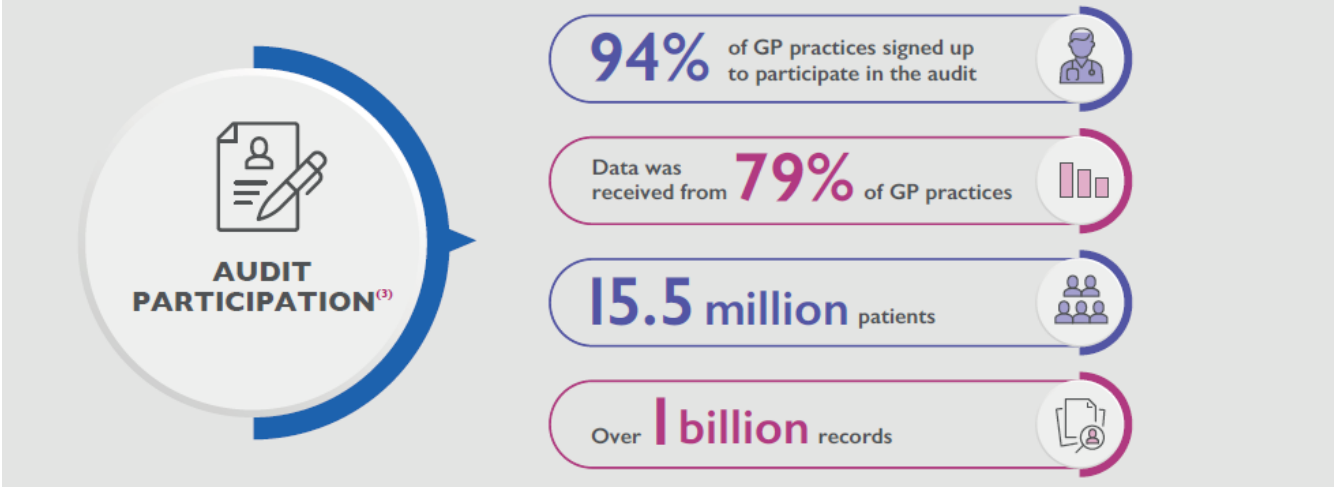
- Atrial fibrillation (AF)
- Hypertension
- Familial hypercholesterolaemia (FH) and other hyperlipidaemias
- Chronic kidney disease (CKD)
- Non-diabetic hyperglycaemia (NDH)
- Type 1 or type 2 diabetes mellitus

Data Extraction

- Coding
- Prescribing
- Management according to guidance

First Report Dec 2021

CVDPREVENT



What is Chronic Kidney Disease? (CKD)

'The presence of **kidney damage, mainly albuminuria,** and/or decreased kidney function (estimated glomerular filtration rate [eGFR] **<60 mL/min/1.73** m^2) for at least 3 months (Levey and Coresh, 2012)'

eGFR Calculated by CKD-EPI equation

Albuminuria not proteinuria testing

Recent Key Changes:
No longer use ethnicity correction for eGFR Calculation (NICE CKD Guidelines 2021)

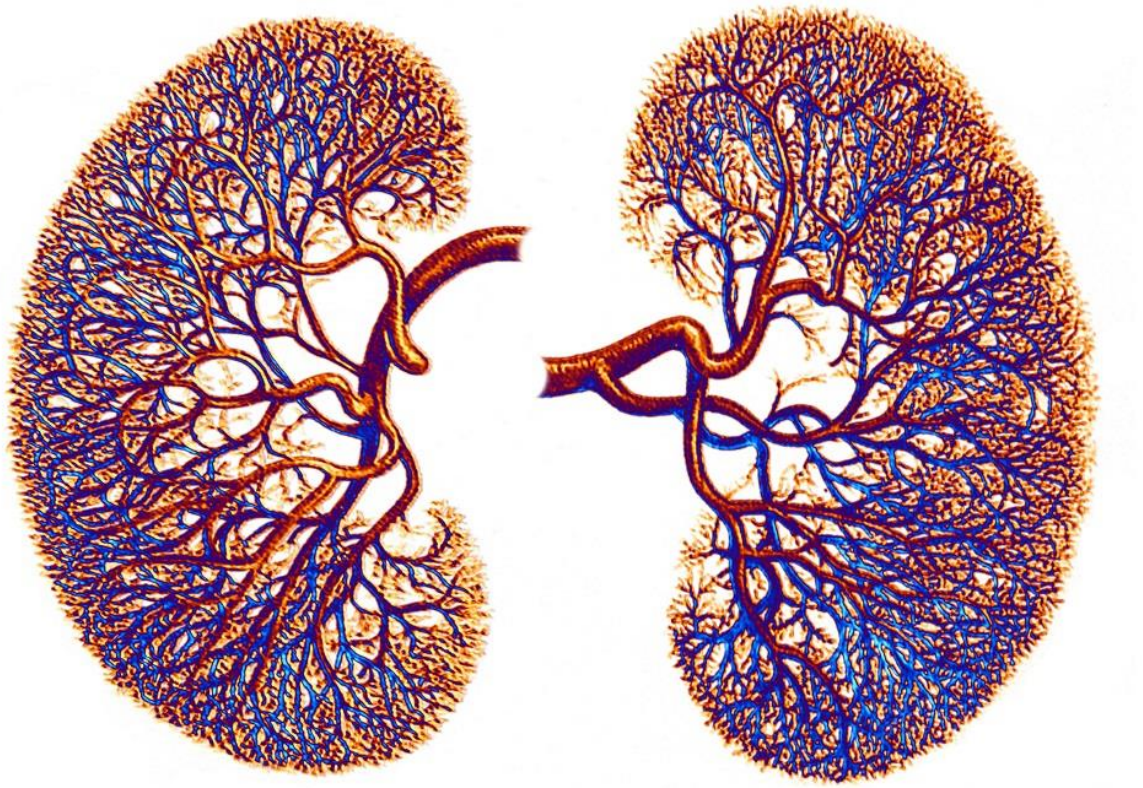
Classification of chronic kidney disease using GFR and ACR categories

GFR and ACR categories and risk of adverse outcomes			ACR categories (mg/mmol), description and range		
			<3 Normal to mildly increased	3–30 Moderately increased	>30 Severely increased
			A1	A2	A3
GFR categories (ml/min/1.73 m^2), description and range	≥90 Normal and high	G1	No CKD in the absence of markers of kidney damage		
	60–89 Mild reduction related to normal range for a young adult	G2			
	45–59 Mild–moderate reduction	G3a[1]			
	30–44 Moderate–severe reduction	G3b			
	15–29 Severe reduction	G4			
	<15 Kidney failure	G5			

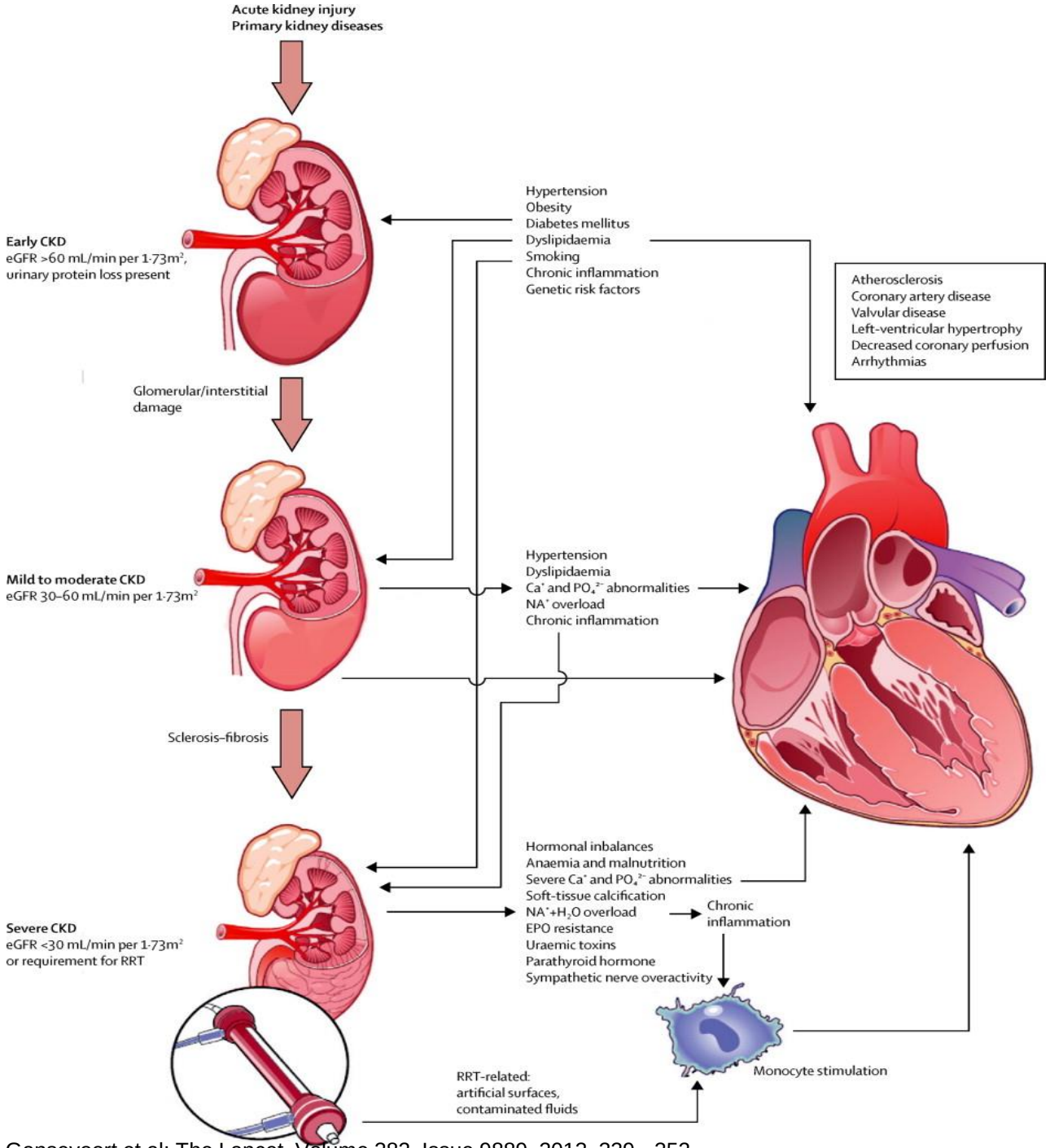
Increasing risk

Increasing risk

Kidney vasculature is a barometer of cardiovascular health

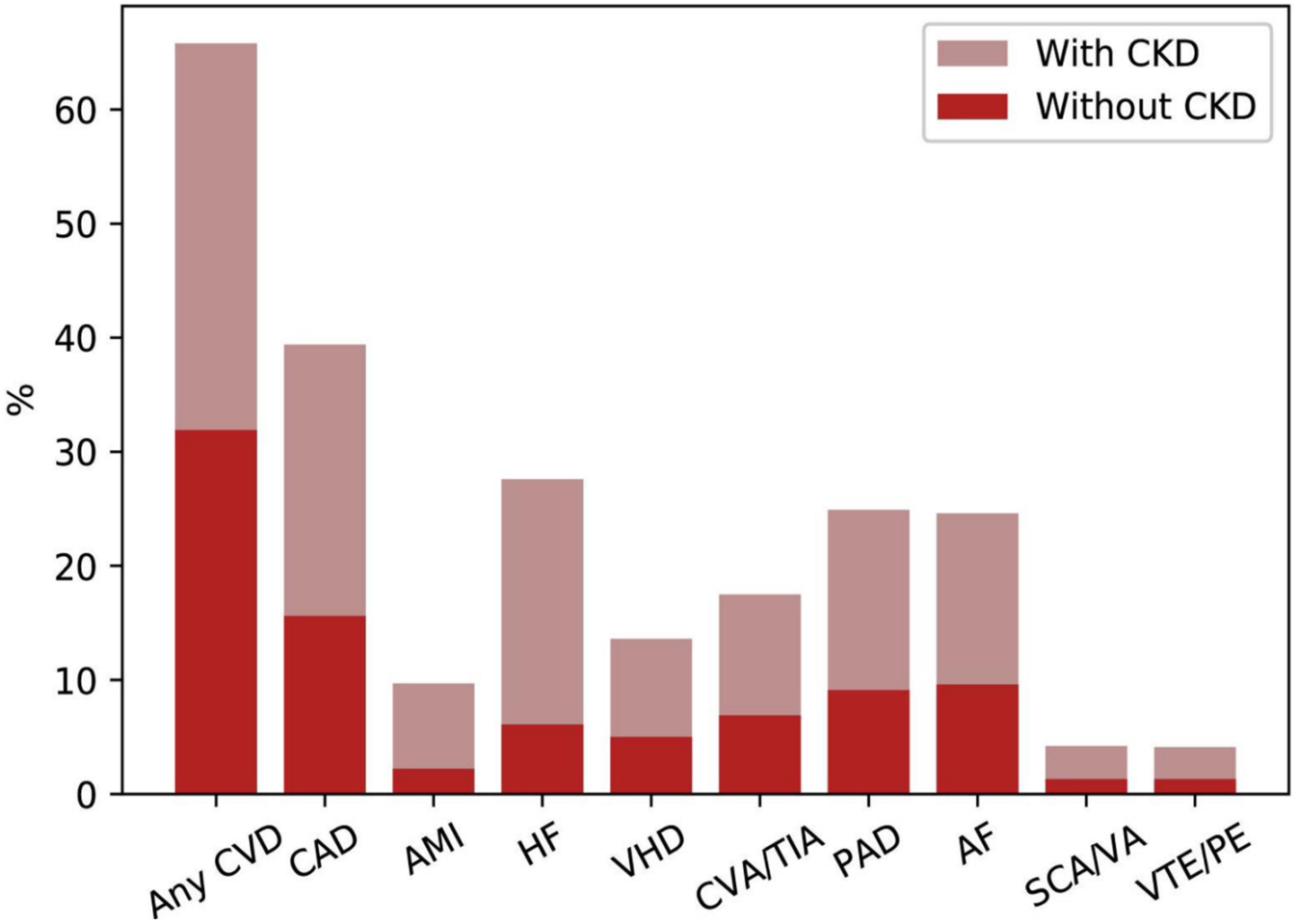


Approximately 10 km of capillaries in both kidneys



http://dx.doi.org/10.1016/S0140-6736(13)60595-4 Gansevoort et al; The Lancet, Volume 382, Issue 9889, 2013, 339 - 352

All forms of Cardiovascular Disease are more common in people with CKD

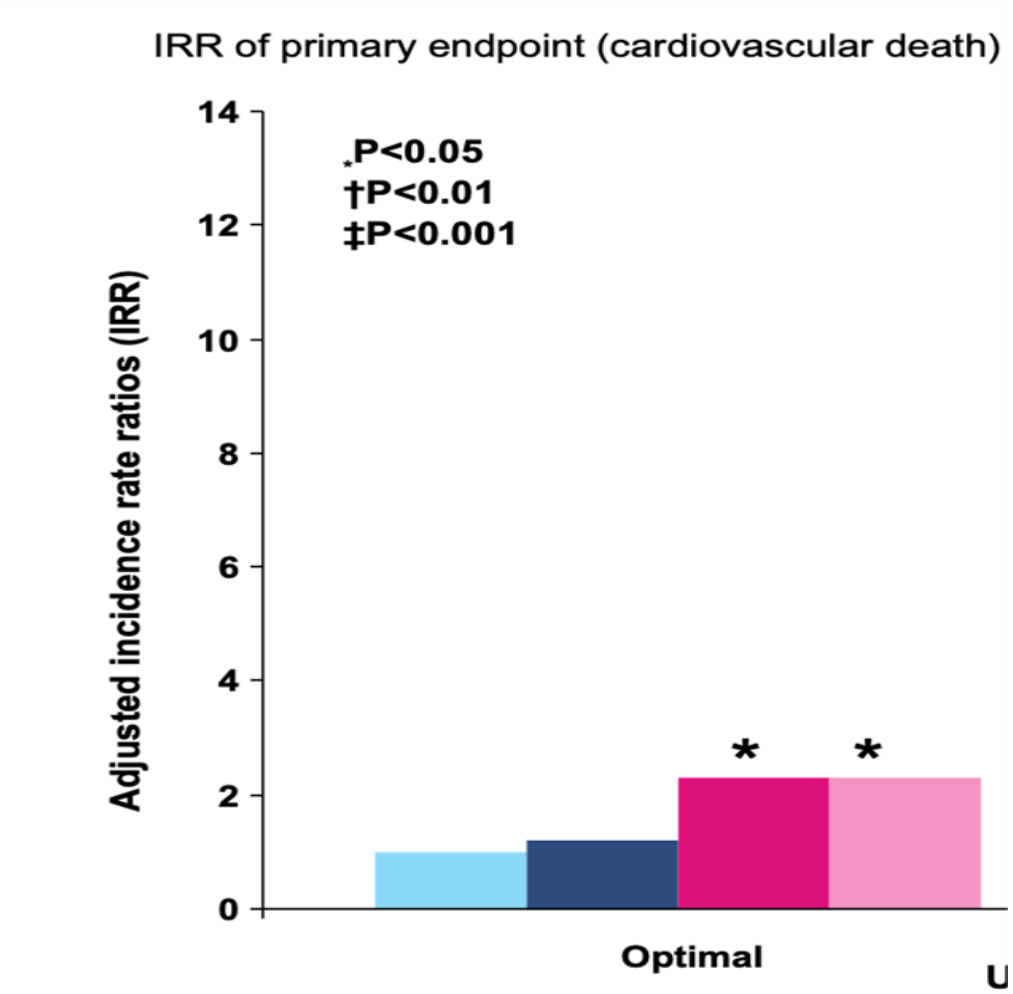


Prevalence of common cardiovascular diseases in patients with or without CKD in United States (2015)

Derived from Provenzano et al 2019
https://doi.org/10.3389/fcell.2019.00314

AF, atrial fibrillation; AMI, acute myocardial infarction; CAD, coronary artery disease; CKD, chronic kidney disease; CVA/TIA, cerebrovascular accident/transient ischemic attack; CVD, cardiovascular disease; HF, heart failure; PAD, peripheral arterial disease; SCA/VA, sudden cardiac arrest and ventricular arrhythmias; VHD, valvular heart disease; VTE/PE, venous thromboembolism and pulmonary embolism

People with reduced eGFR are more likely to die from cardiovascular disease than people with a normal eGFR



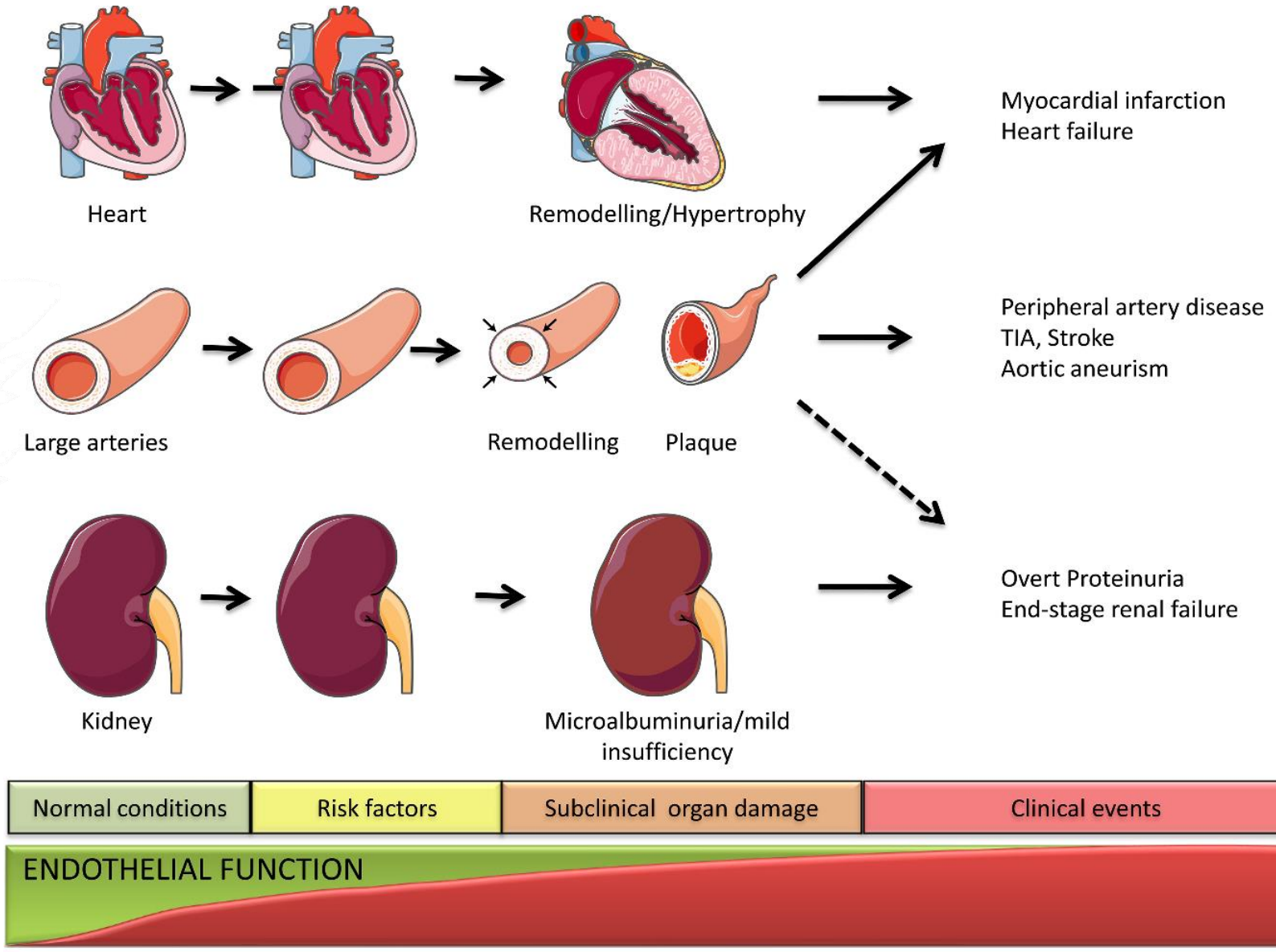
Category of eGFR, mL/min/1.73 m²	Corresponding CKD stage[2]
≥75	1 & 2
60-74	2
45-59	3a
15-45	3b & 4

2x increased risk with CKD Stage 3-5

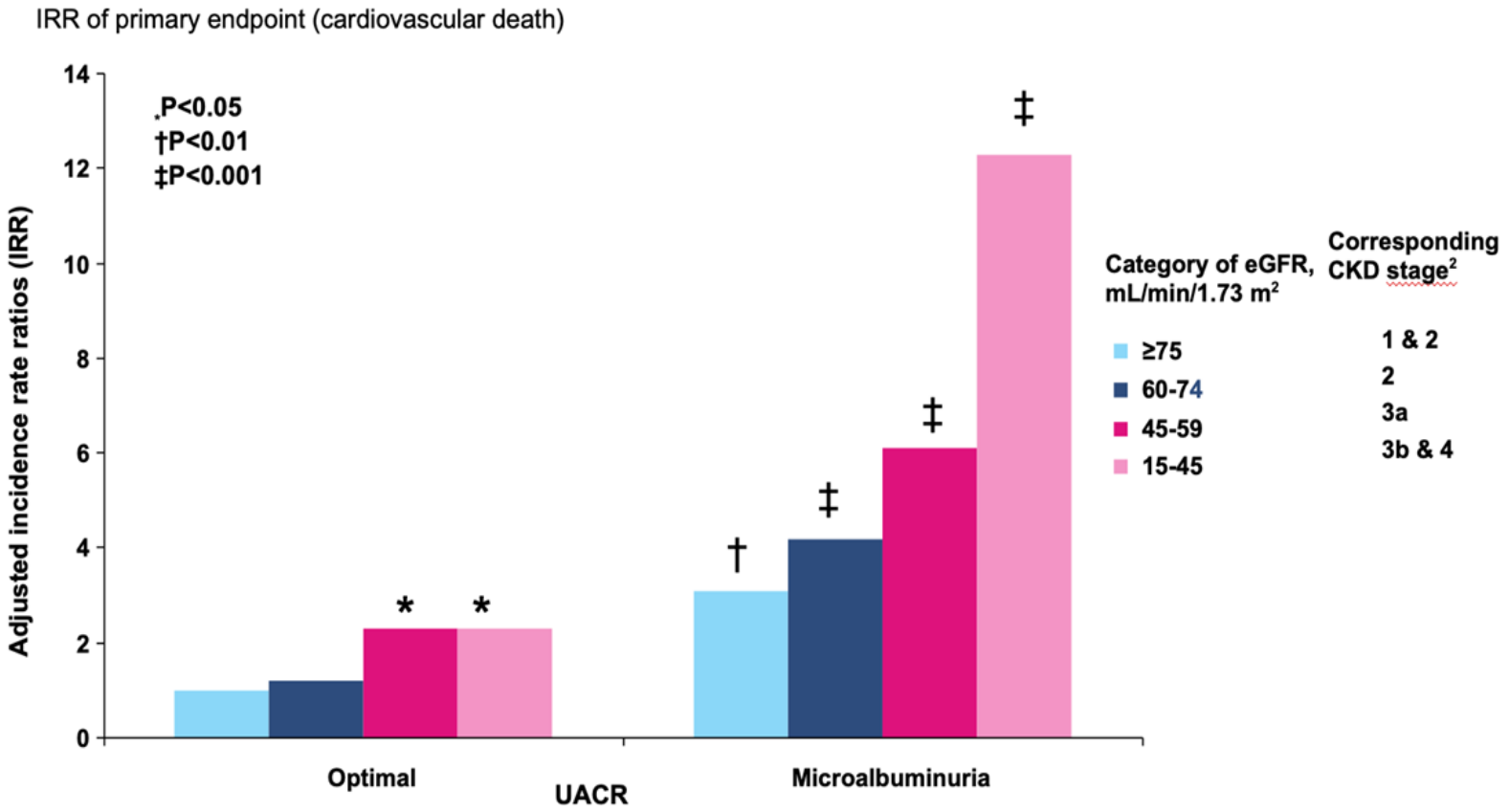
. Adapted from Hallan et al. *Archives Internal Medicine* 2007 167;22;2490-2496

2. NICE Management of CKD: *NICE*

Albuminuria is an early marker of cardiovascular disease



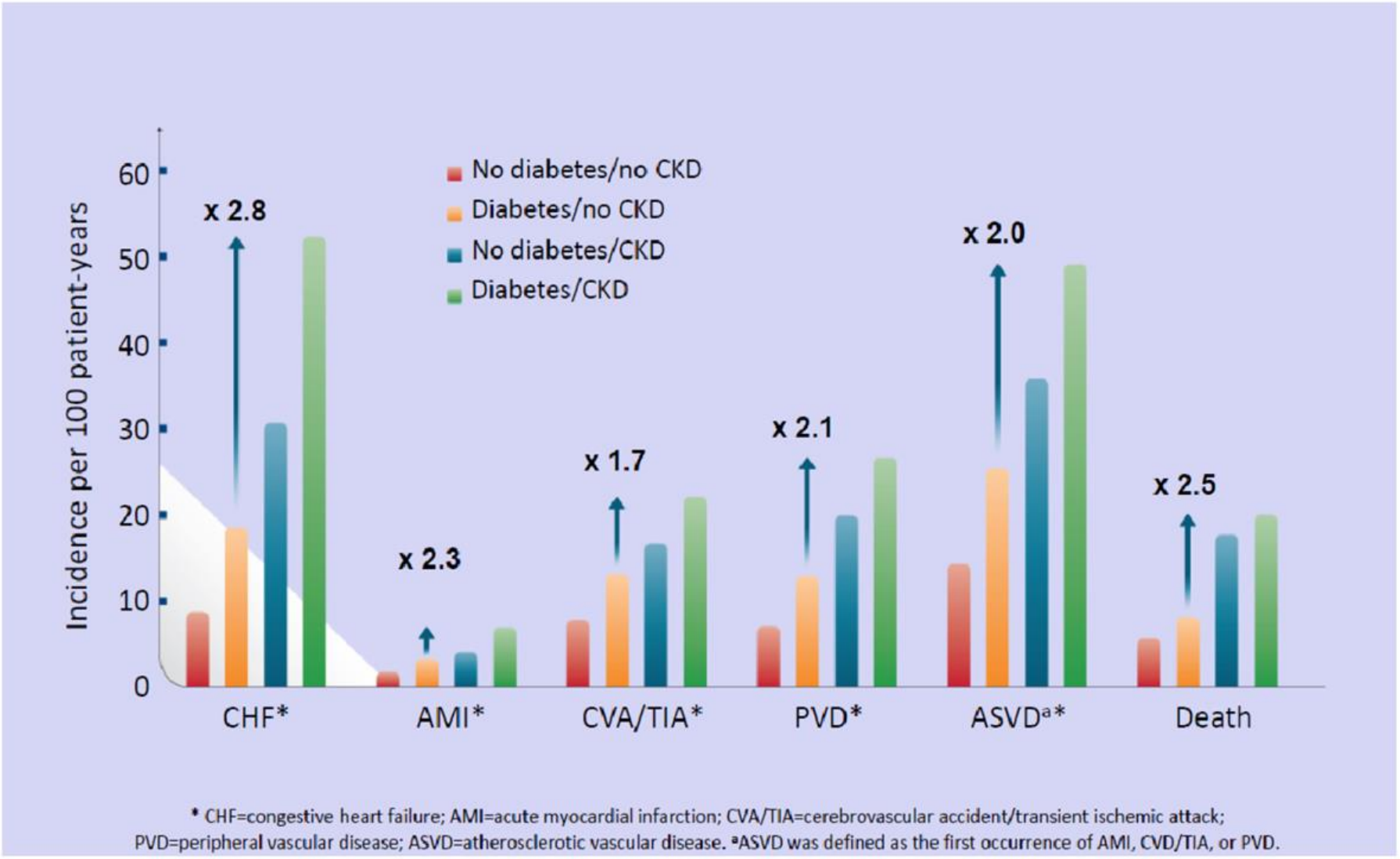
AND with microalbuminuria – risk is intensified



Microalbuminuria with eGFR >75 mls/min/1.73m^2 is associated with **higher risk** of cardiovascular death than CKD Stage 4 without albuminuria

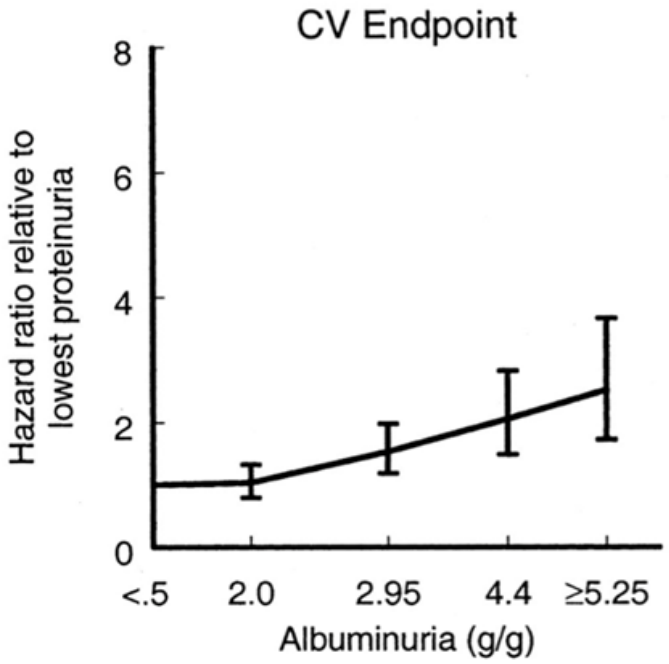
1. Adapted from Hallan et al. *Archives Internal Medicine* 2007 167;22;2490-2496
2. NICE Management of CKD: *NICE*

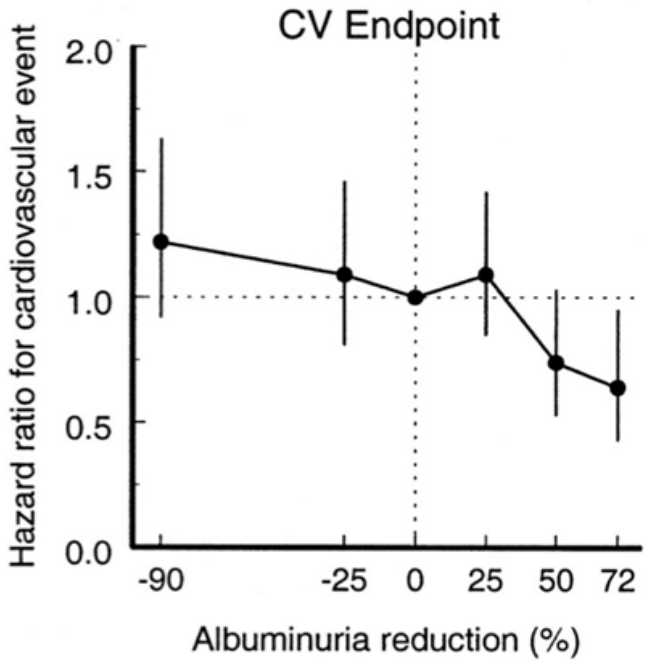
CKD is a ‘stronger’ risk factor than diabetes for ALL cardiovascular events



Foley RN, et. al. Am. Soc. Nephrol. 2005

Cardiovascular events are more common with albuminuria and less likely to occur if albuminuria is reduced





Post hoc analysis of 'RENAAL' trial (1513 patients with diabetic nephropathy – Losartan v placebo)

de Zeeuw et al Circulation 2004 DOI: 10.1161/01.CIR.0000139860.33974.28

CKD is associated with unplanned admissions

With CKD **Stage 3:**

36 unplanned admissions annually

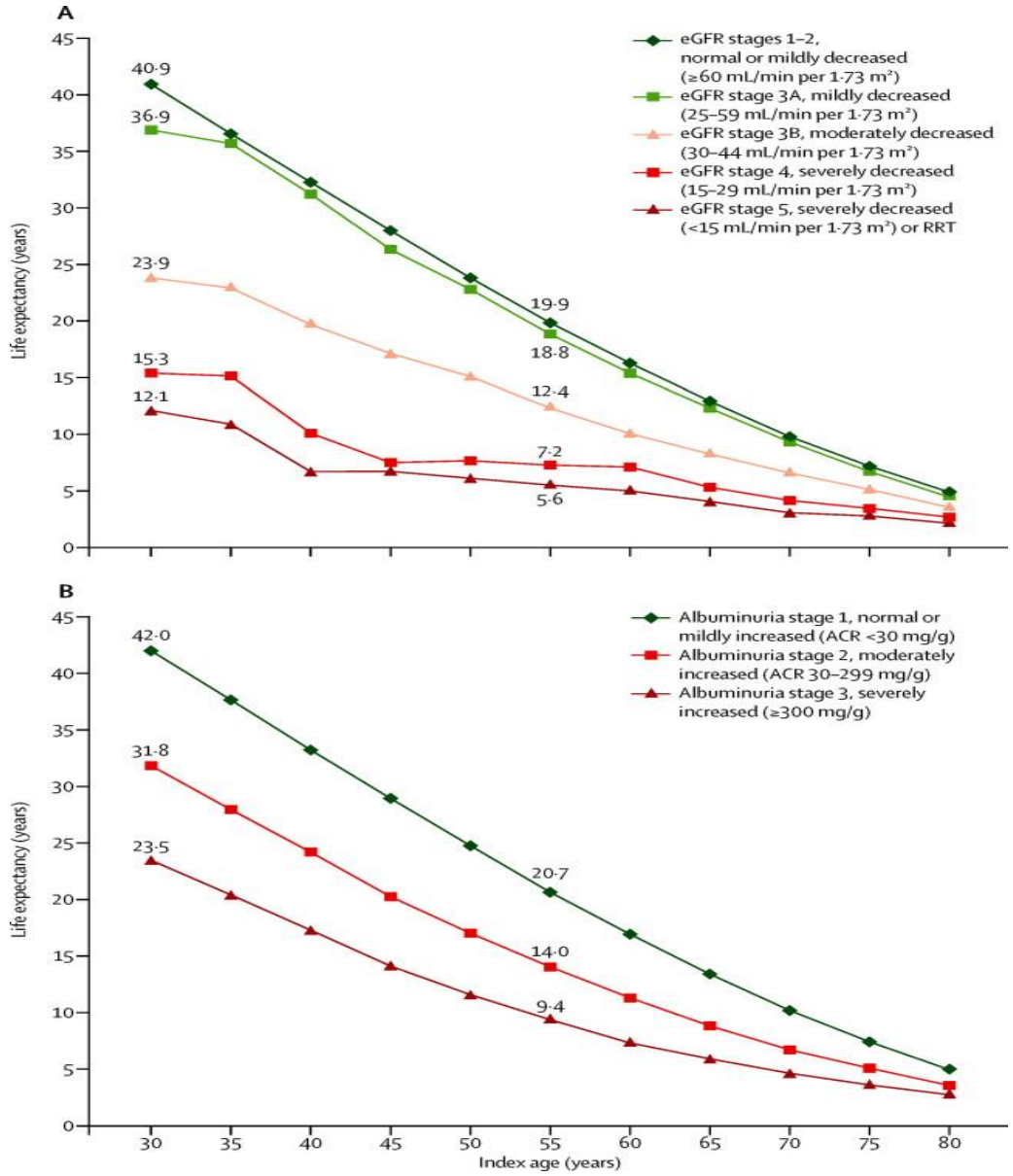
With CKD **Stage 4:**

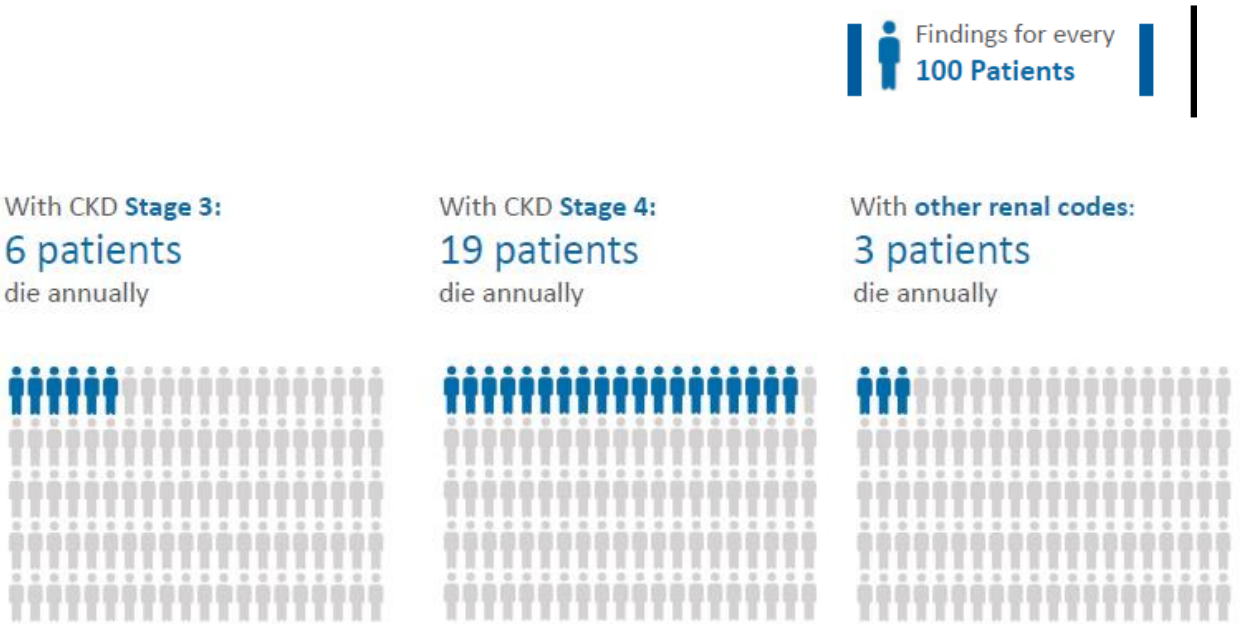
75 unplanned admissions annually

Findings for every **100 Patients**

National Chronic Kidney Disease Audit // National Report: Part 2 December 2017. https://www.lshtm.ac.uk/media/9951..

CKD is also associated with reduced life expectancy, even at early stages





National Chronic Kidney Disease Audit // National Report: Part 2 December 2017. https://www.lshtm.ac.uk/media/9951..

End Stage Kidney Disease has worse survival rates than colorectal and breast cancer

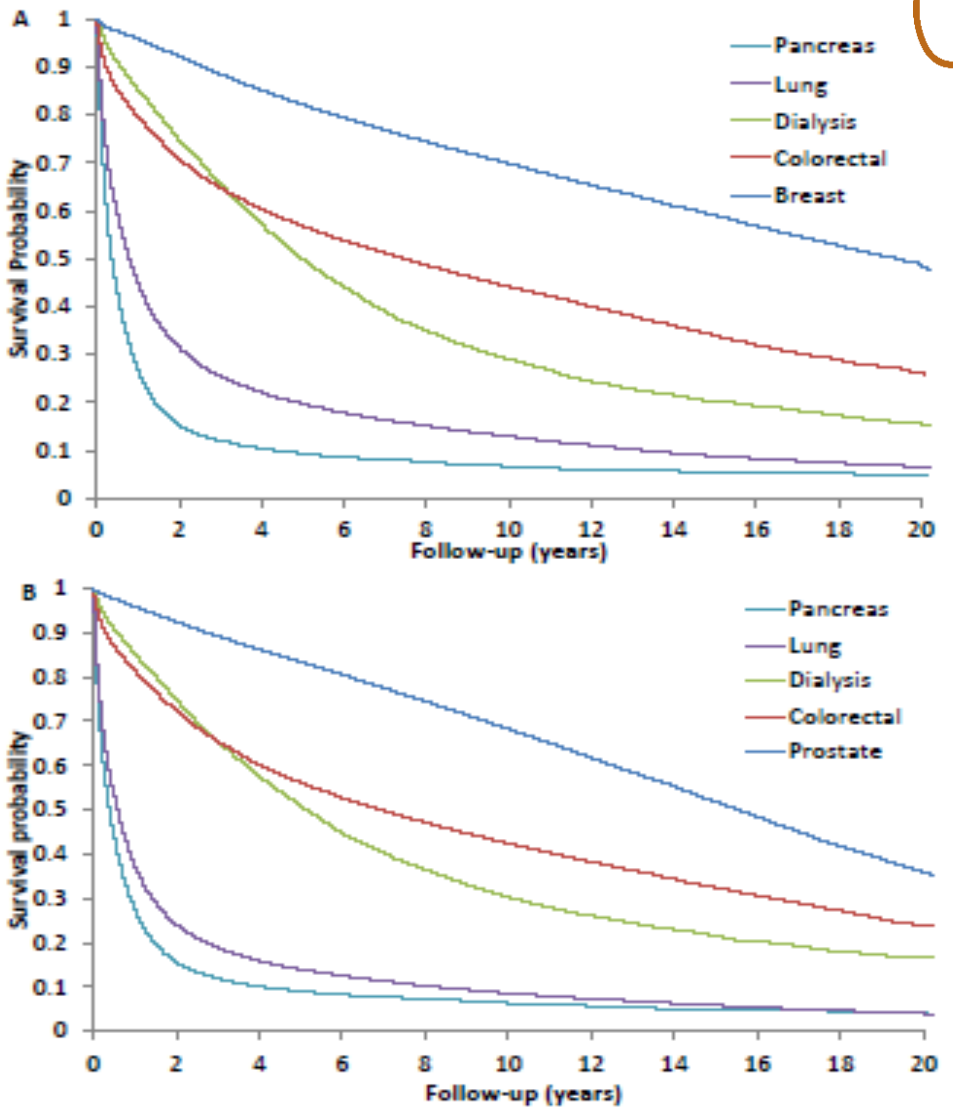
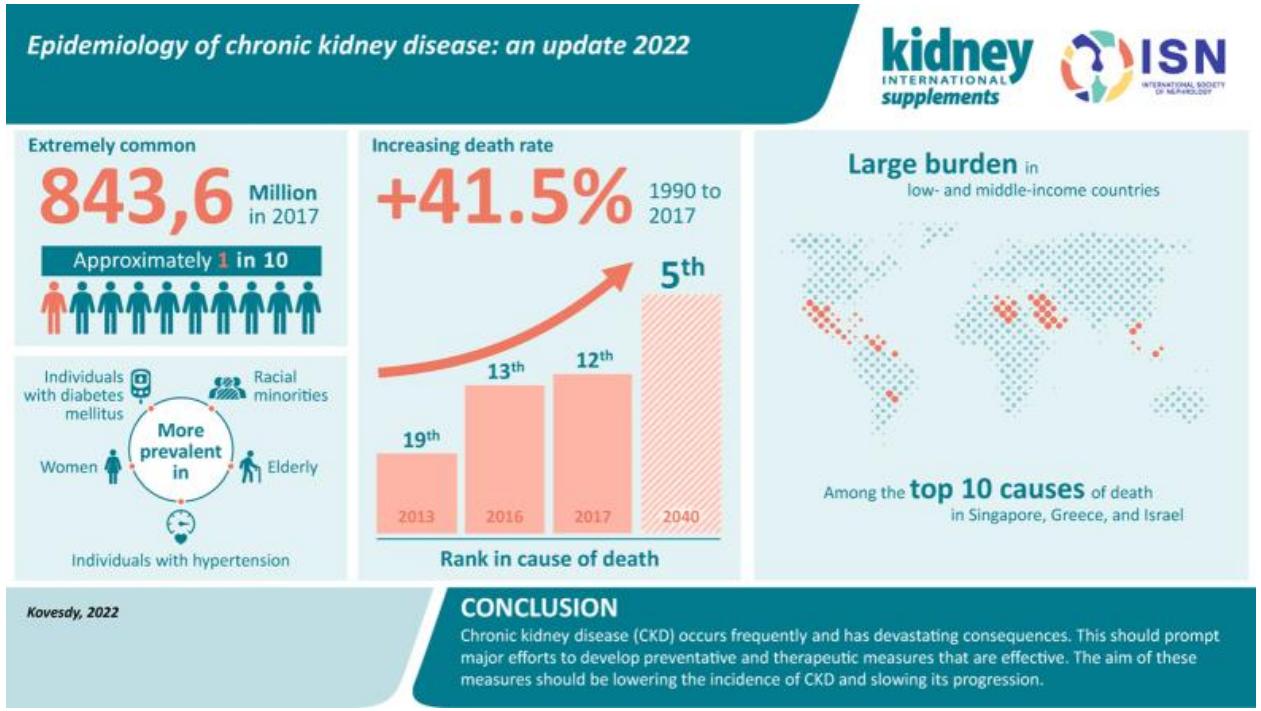
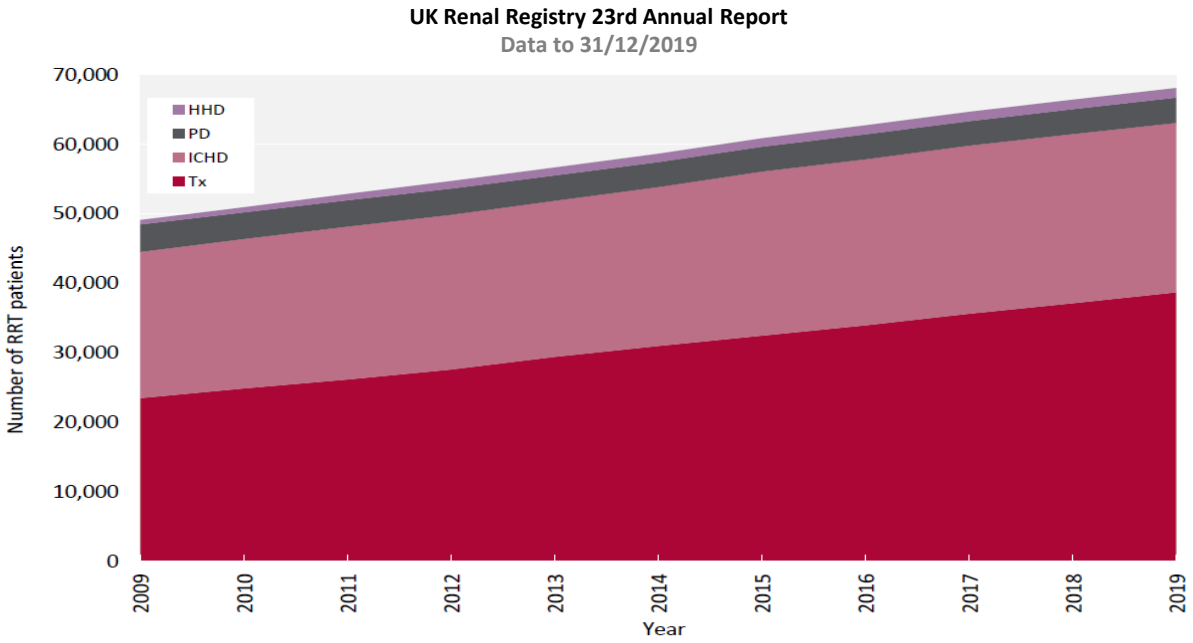


Figure 1. Survival probabilities for all-cause mortality in (A) female maintenance dialysis patients and patients with cancer (log-rank $P < 0.001$) and (B) male maintenance dialysis patients and patients with cancer (log-rank $P < 0.001$).

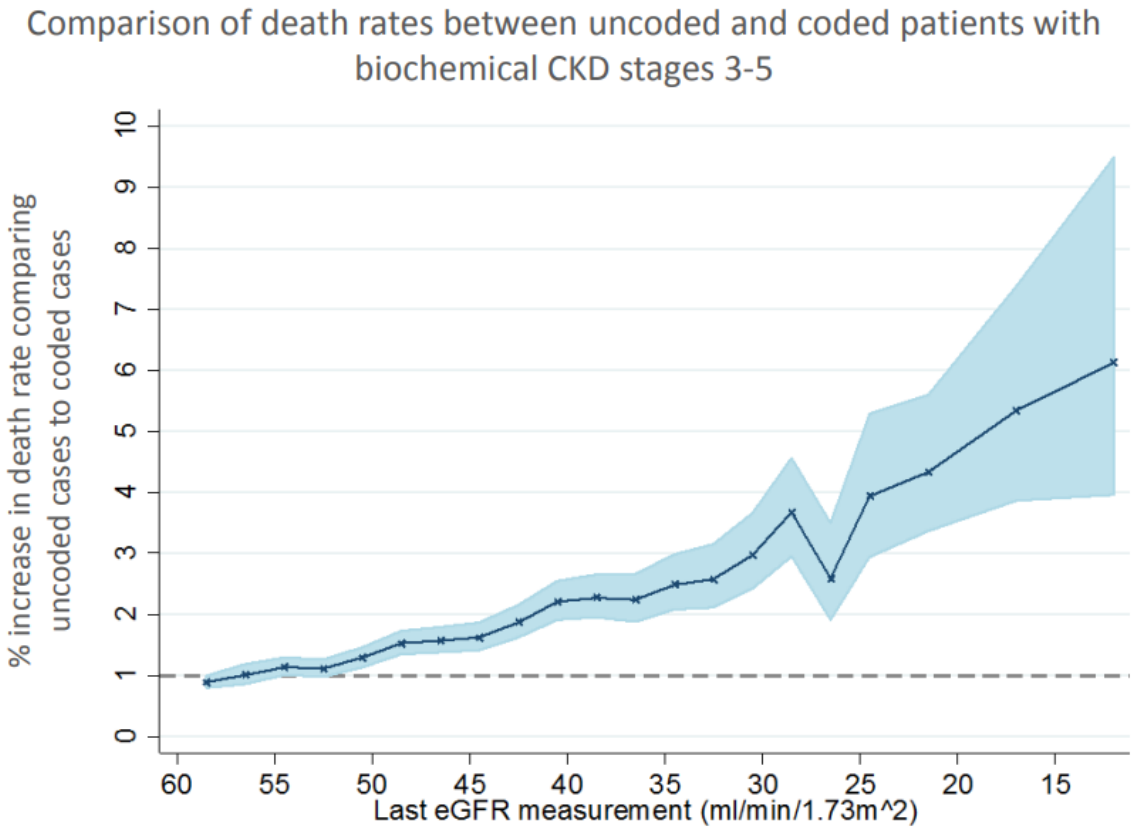
Naylor et al AJKD 2019 doi: 10.1053/j.ajkd.2018.12.011

BIG PROBLEM #1
CKD Epidemic





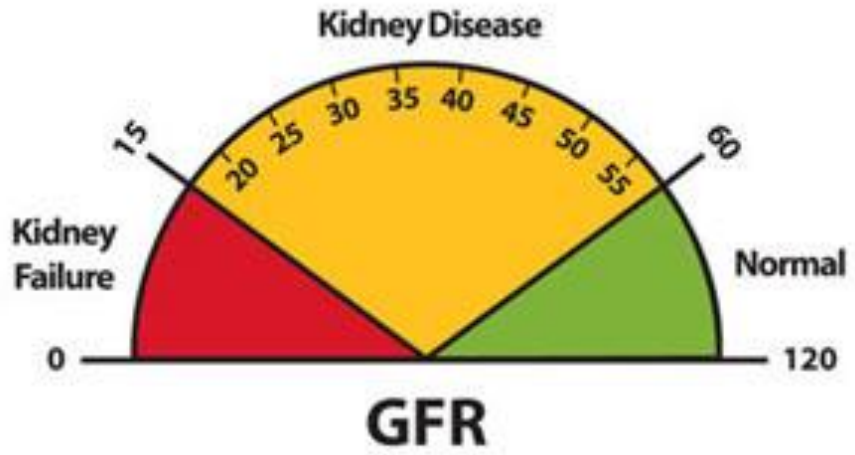
BIG PROBLEM #2
CKD is not equal

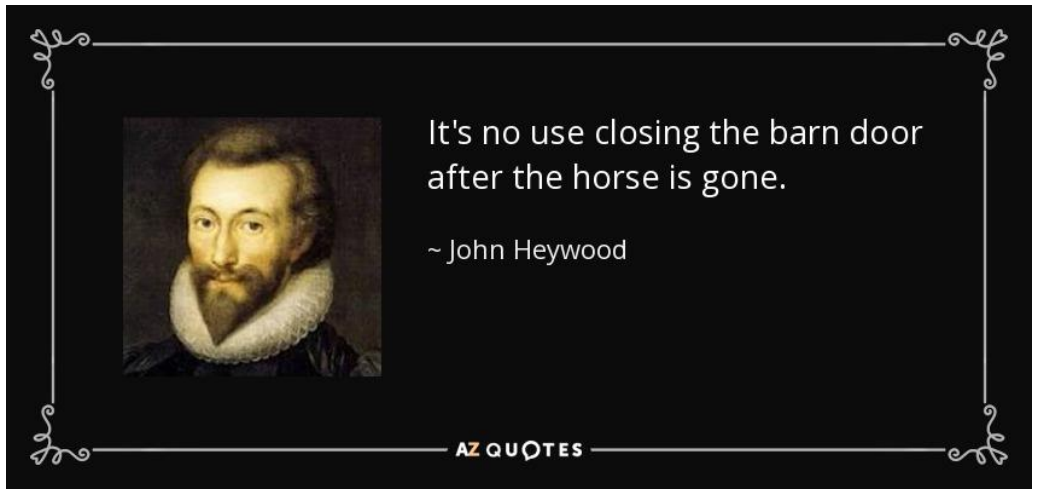


Caskey et al (2018) Kidney health inequalities in the United Kingdom: reflecting on the past, reducing in the future."

BIG PROBLEM #3
Nephrology services focus on advanced disease

NICE recommendations for referral to nephrology services GFR <30mls/min/1.73m^2





Missed opportunities for management of CKD progression / CVD prevention!

How can we impact the tidal wave of CKD?

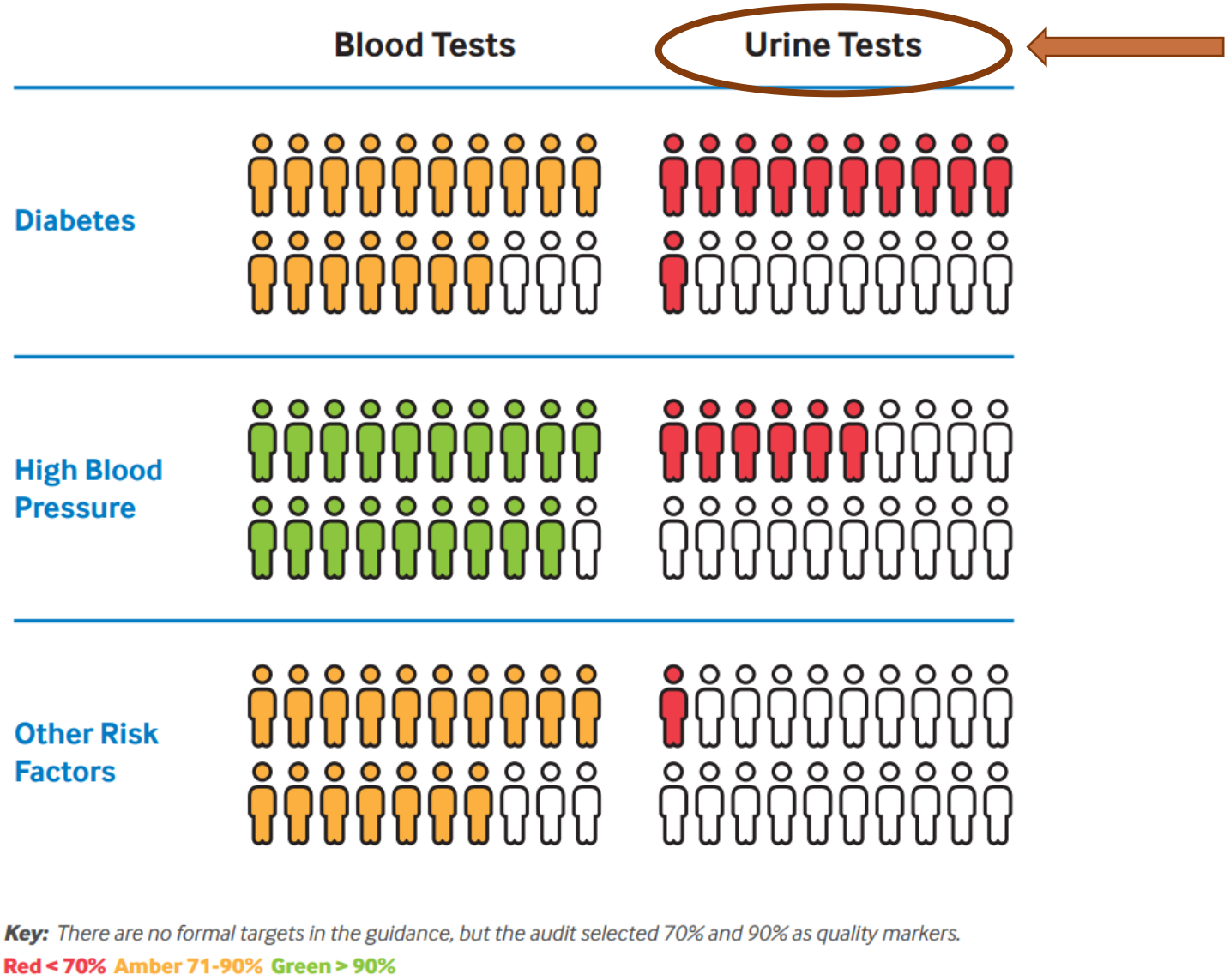
Big Problem:

An increasing number of preventable deaths associated with CKD

Solution?

Primary Care Interventions

Identification of CKD: What are the problems?



National CKD Audit – National Report (Part 1) January 2017

For people at high risk of CKD, ensure that both blood tests for eGFR and ACR are being included

Improve the coding of patients with CKD

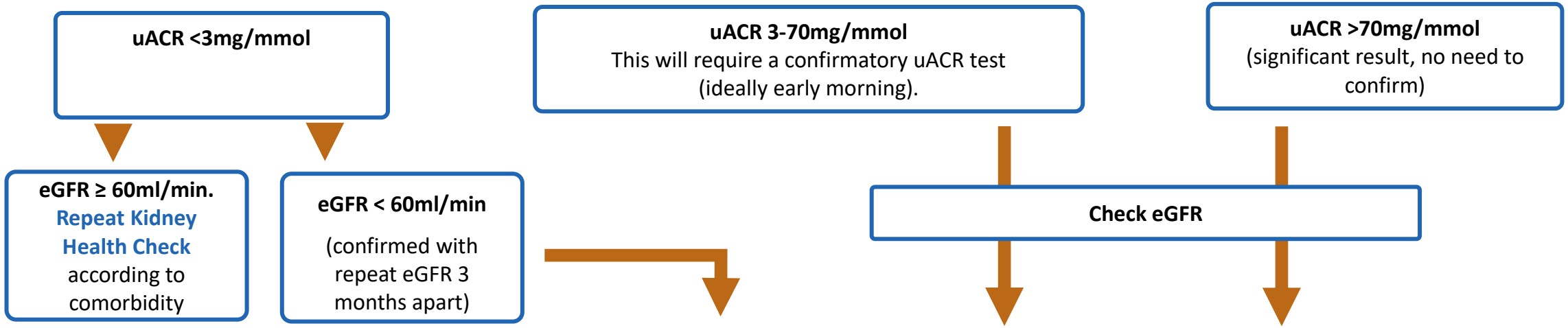
Having identified CKD, regularly review, manage high blood pressure, prescribe cholesterol lowering treatments, and perform vaccinations

The Kidney Health Check for Adults Living with Diabetes or Hypertension: How to identify Chronic Kidney Disease *early!*

What is a Kidney Health Check? It is the combination of both an **eGFR** *and* a **uACR** test

Who should have a Kidney Health Check?

1. People living with **diabetes** should have a yearly kidney health check
2. People living with **hypertension** should have a kidney health check every 1-5 years (annually for poorly controlled hypertension).
3. See NICE CKD Assessment and Management for ACR testing in other health conditions



1. INFORM the patient that they have **Chronic Kidney Disease (CKD).**
2. If eGFR is < 60ml/min, consider discussing Kidney Failure Risk equation see link: KFRE.
3. Add coding for CKD (including CKD G1 and G2) and albuminuria category, into the patient record.
4. Discuss with the person their uACR number, eGFR number, BP and HbA1c if living with diabetes.
5. Explain what each term means *and* the factors that can cause CKD or diabetic kidney disease: raised BP, raised HbA1c, obesity.
6. Give lifestyle advice and connect them with support services where suitable: weight management enhanced services, exercise, and smoking cessation (see online guidance). Offer advice on avoiding NSAIDS/sick day rules.
7. Implement the **LKN CKD Optimisation Pathways** for proteinuric CKD with and without diabetes.

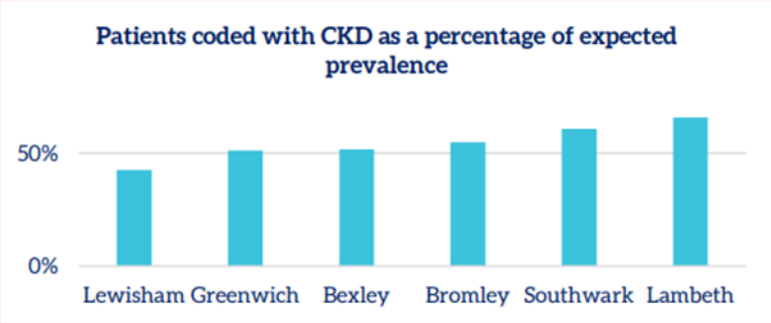
LKN London Kidney Network

Why focus on CKD in South East London?

Clinical Effectiveness South East London

CKD is not being diagnosed enough

In South East London (SEL), our CKD registers are **half** their expected size[1,2]



Patients who have CKD but are **not coded**, have **double the mortality rate** and **double the risk of being prescribed nephrotoxic drugs** compared to correctly coded patients[3]

CKD is not being managed well enough[11]

Urine ACR
2/3 of patients with CKD in SEL have **not had Urine ACR checked** in the past year

ACE-I/ARB
1/3 of patients with CKD who have proteinuria are **not on an ACE-I/ARB**

Hypertension
1/3 of patients with CKD have **uncontrolled blood pressure**

Lipid lowering therapy
1/4 of patients with CKD are not on lipid lowering therapy

Impact of CKD

CKD is associated with **reduced life expectancy**, even at early stages[4]

CKD is a stronger **risk factor for cardiovascular** events than diabetes[4]

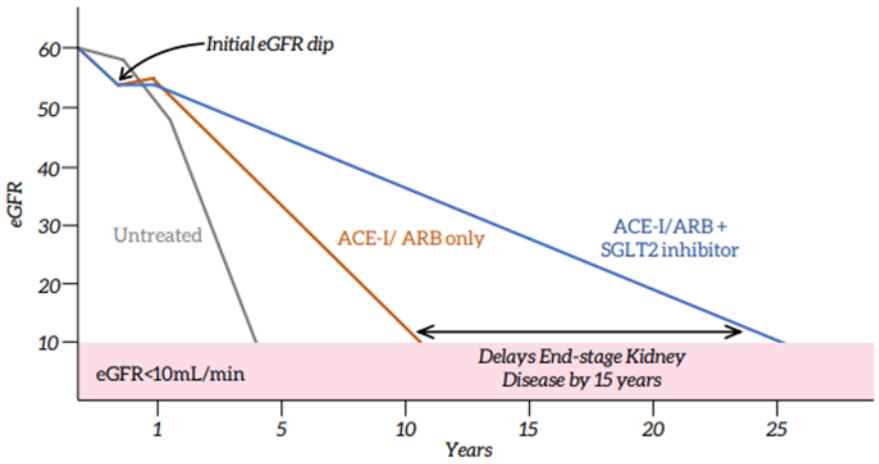
End-stage kidney disease has **worse survival rates than colorectal and breast cancer**[5]

Better treatment is now available for CKD

Dapagliflozin **reduces all cause mortality by 30%** in patients with CKD, and a 37% reduction in significant renal or cardiovascular morbidity[7]

Adding an SGLT2i for patients with diabetes and established nephropathy may **delay their progression** to end-stage kidney disease by 15 years[6]

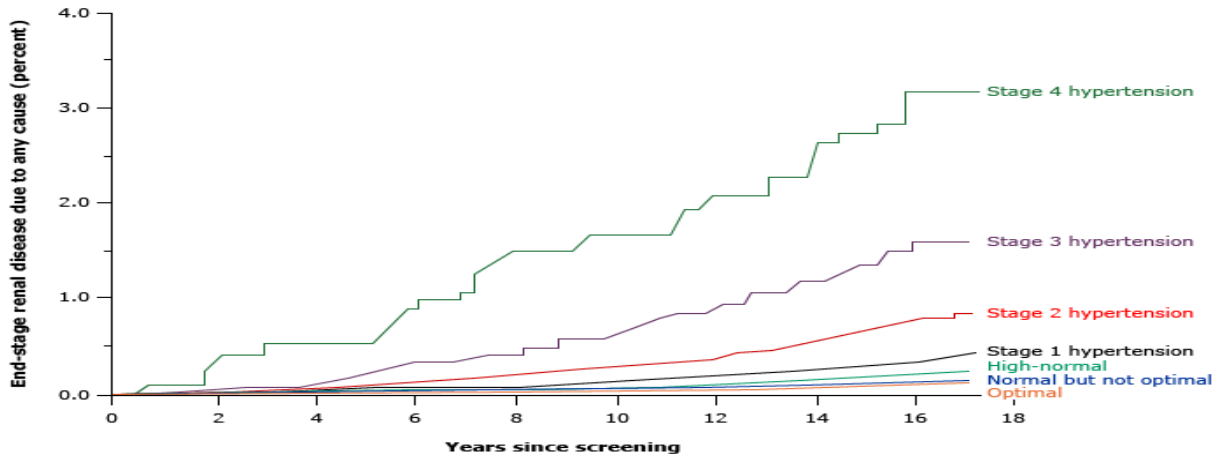
eGFR fall over time for patients with diabetes and established nephropathy[6]



https://selondonccg.nhs.uk/wp-content/uploads/dlm_uploads/2023/02/CESEL-CKD-Guide-Final-Feb-2023-1-1.pdf

RAAS blockade in CKD

Relation between hypertension and development of ESRD



Annals of Internal Medicine

Search Journal

LATEST ISSUES IN THE CLINIC JOURNAL CLUB MULTIMEDIA CME / MOC AUTHORS / SUBMIT

Articles | July 17, 2001

Angiotensin-Converting Enzyme Inhibitors and Progression of Nondiabetic Renal Disease

A Meta-Analysis of Patient-Level Data

Tazeen H. Jafar, MD, MPH, Christopher H. Schmid, PhD, Marcia Landa, MA, Ioannis Giatras, MD, ... View all authors

Author, Article and Disclosure Information

https://doi.org/10.7326/0003-4819-135-2-200107170-00007

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June 6, 2001

Effect of Ramipril vs Amlodipine on Renal Outcomes in Hypertensive Nephrosclerosis

A Randomized Controlled Trial

Lawrence Y. Agodoa, MD; Lawrence Appel, MD, MPH; George L. Bakris, MD; et al

Author Affiliations

JAMA. 2001;285(21):2719-2728. doi:10.1001/jama.285.21.2719

THE LANCET

ARTICLES | VOLUME 349, ISSUE 9069, P1857-1863, JUNE 28, 1997

Randomised placebo-controlled trial of effect of ramipril on decline in glomerular filtration rate and risk of terminal renal failure in proteinuric, non-diabetic nephropathy

The GISEN Group (Gruppo Italiano di Studi Epidemiologici in Nefrologia)*

Published: June 28, 1997 • DOI: https://doi.org/10.1016/S0140-6736(96)11445-8

THE LANCET

FAST TRACK — ARTICLES | VOLUME 377, ISSUE 9784, P2181-2192, JUNE 25, 2011

The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection): a randomised placebo-controlled trial

Prof Colin Baigent, FRCP • Martin J Landray, FRCP • Christina Reith, MRCP • Jonathan Emberson, PhD • David C Wheeler, FRCP • Charles Tomson, DM • et al. Show all authors • Show footnotes

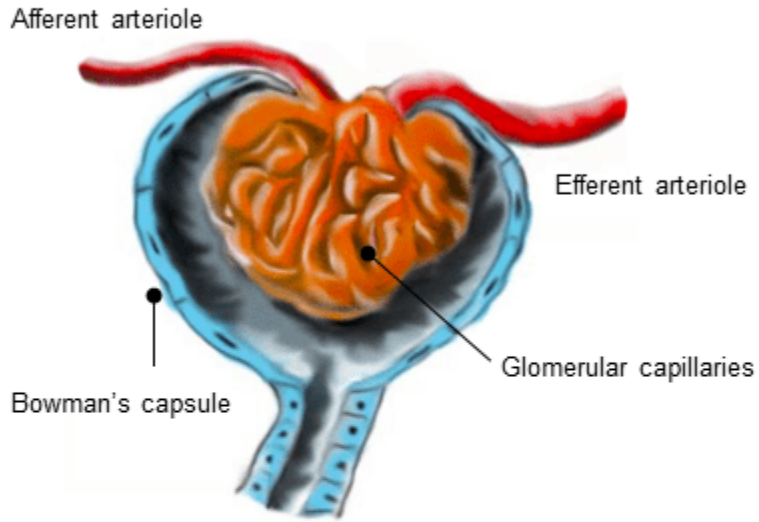
Open Access • Published: June 09, 2011 • DOI: https://doi.org/10.1016/S0140-6736(11)60739-3

SGLT2 inhibition and RAAS blockade both reduce glomerular pressure by complimentary mechanisms

SGLT2 inhibitors

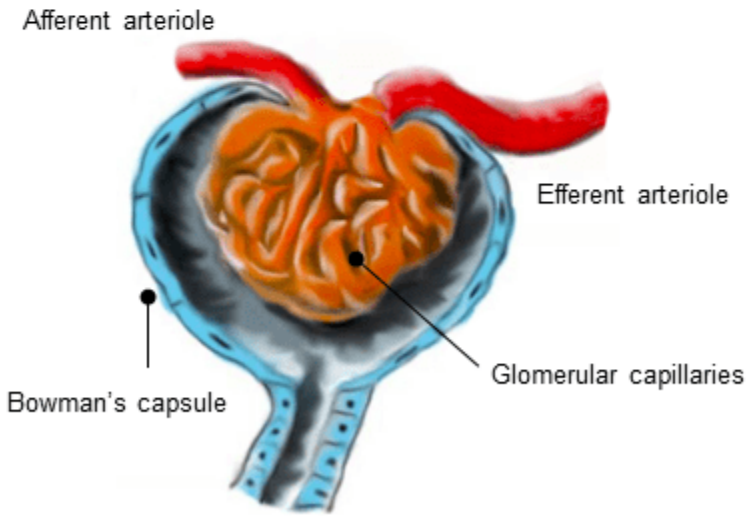
Afferent vasoconstriction

Due to increased Na+ delivery to the macula densa[1-3]



RAAS blockade

Efferent vasodilation



CLINICAL IMPLICATIONS

- **Decreased glomerular pressure**
- **Reduction in albuminuria**

- **Decreased glomerular pressure**
- **Reduction in albuminuria**

SGLT-2 inhibitors in type 2 diabetes and CKD

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)

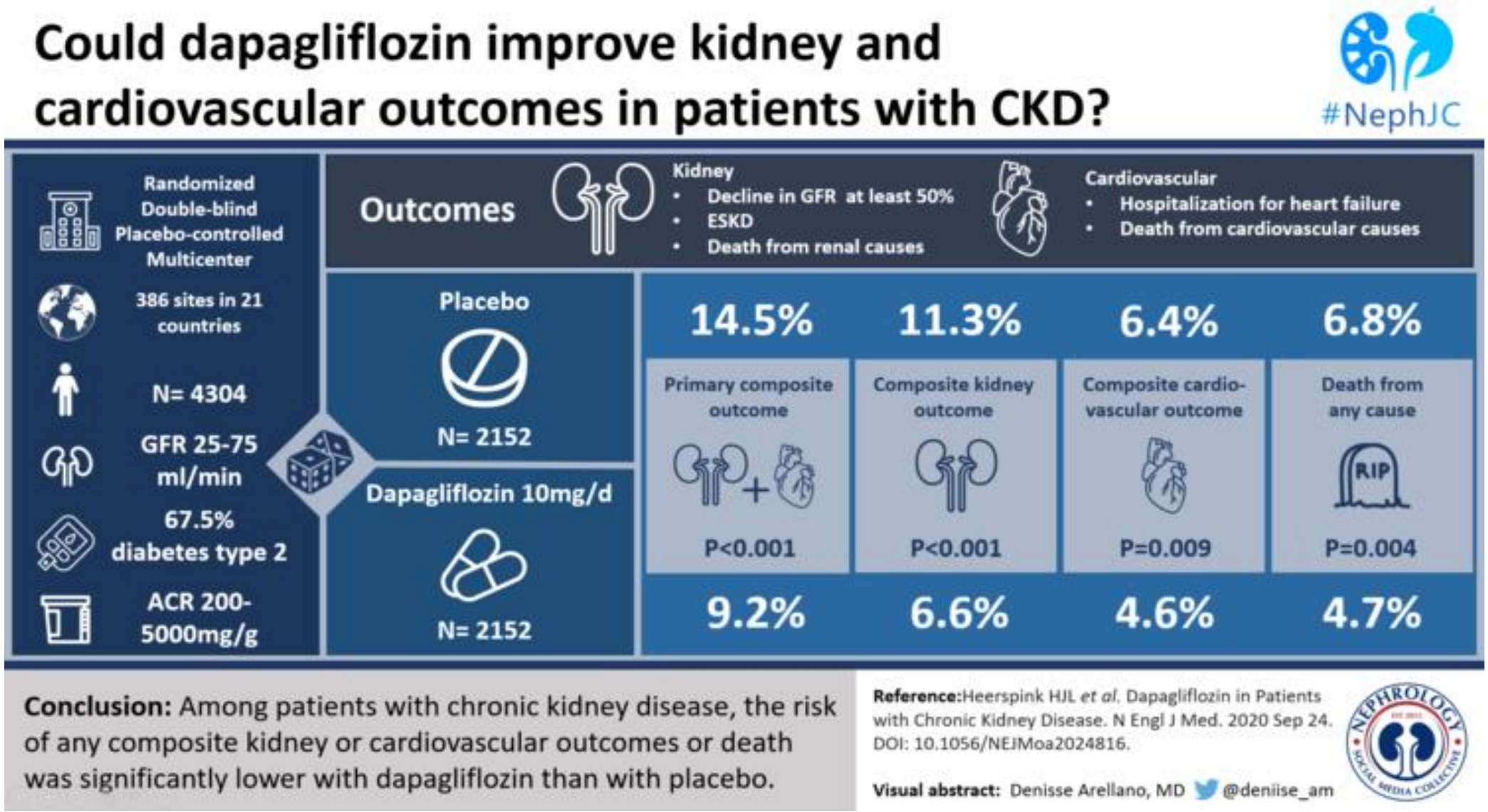
Fractures

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

An opportunity for SGLT-2 inhibitors in non-diabetic CKD



“3 within 3”

3 key actions within 3 months to save lives

LKN CKD Optimisation Pathway

In adults with Type 2 diabetes and CKD

(uACR > 3mg/mmol)

ACTION 1 (Month 1)
Maximum intensity RAS/ RAAS blockade

First, ensure the patient is on a statin, unless contraindicated.
Start ACE-inhibitor or ARB and titrate to maximum tolerated licensed dose *(NICE, NG203)* within one month

ACTION 2 (Month 2)
Initiate SGLT-2 inhibitor according to license

Consider/ counsel on risks of diabetic ketoacidosis (which may be euglycaemic), sick day rules, risk of UTI/fungal infections. Consider adjusting sulfonylureas/insulin where eGFR >45ml/min and HbA1c < 58mmol/mol to mitigate risk of hypoglycaemia.

ACTION 3 (Month 3)
Initiate further blood pressure agent to target 140/90mmHg unless uACR >70mg/mmol (then 120-129/80mmHg)

If BP remains above target initiate 2nd line BP agents as per NICE guidance (*NG203/ NG136)*

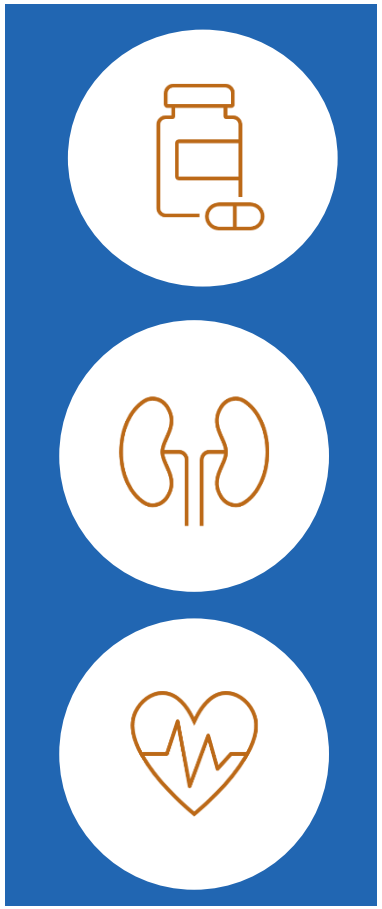
“3 within 3”

3 key actions within 3 months to save lives

LKN CKD Optimisation Pathway

In adults with albuminuria, without Type 2 diabetes

(uACR ≥ 22.6mg/mmol and eGFR 25 - 75ml/minute/1.73m^2)



ACTION 1 (Month 1)
Maximum intensity RAS/ RAAS blockade

First, ensure the patient is on a statin, unless contraindicated.
Start ACE-inhibitor or ARB unless contraindicated, and titrate to maximum tolerated licensed dose (*NICE, NG203*) within one month

ACTION 2 (Month 2)
Initiate SGLT-2 inhibitor according to license

Counsel patient on sick day rules, and the risk of UTI/fungal infection.

ACTION 3 (Month 3)
Initiate further blood pressure agent to target <140/90mmHg unless uACR >70mg/mmol (then <130/80mmHg)

If BP remains above target initiate 2nd line BP agents as per NICE guidance (*NG203/ NG136)*

And the 4th step: Finerenone in type 2 diabetes

NICE TA877

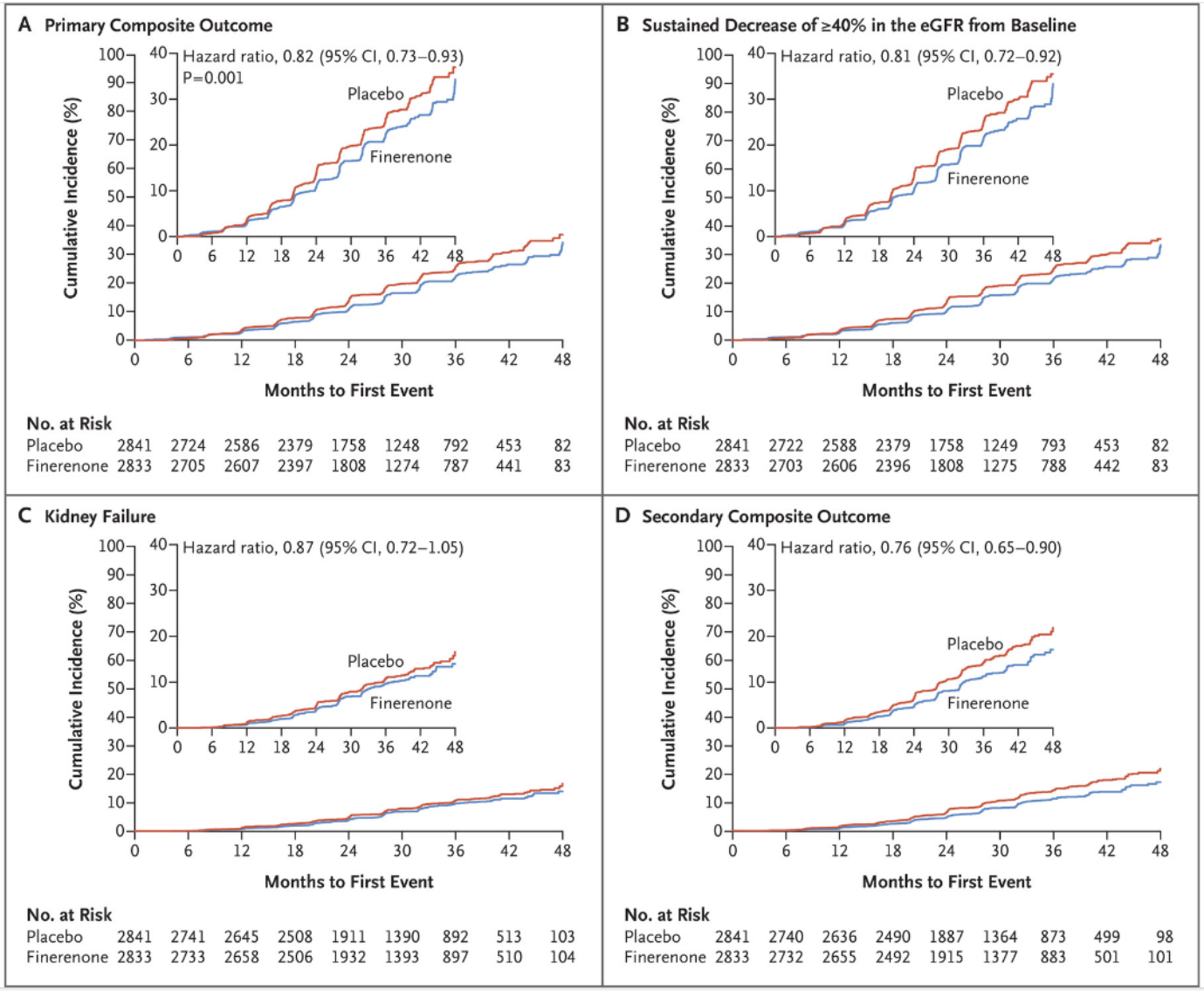


Figure 1. Kidney Outcomes.

Outcomes were assessed in time-to-event analyses. Panel A shows the primary composite outcome of kidney failure, a sustained decrease of at least 40% in the estimated glomerular filtration rate (eGFR) from baseline, or death from renal causes in the finerenone and placebo groups. Panel B shows a sustained decrease of at least 40% in the eGFR from baseline maintained for at least 4 weeks (a component of the primary composite outcome). Panel C shows kidney failure (defined as end-stage kidney disease or a sustained eGFR of <15 ml per minute per 1.73 m^2 of body-surface area, confirmed by a second measurement ≥4 weeks after the initial measurement); end-stage kidney disease was defined as the initiation of long-term dialysis or kidney transplantation. Panel D shows the secondary composite kidney outcome of kidney failure, a sustained decrease of at least 57% in the eGFR from baseline (equivalent to a doubling of the serum creatinine level) maintained for at least 4 weeks, or death from renal causes. Insets show the same data on an enlarged y axis. CI denotes confidence interval.

Effect of finerenone on CKD outcomes in Type 2diabetes Bakris et al
NEJM 2020 383:2219-2229

Geography of the London Kidney Network

NHS
Royal Free London
NHS Foundation Trust

NHS
Barts Health
NHS Trust

NHS
Imperial College Healthcare
NHS Trust

NHS
King's College Hospital
NHS Foundation Trust

NHS
St George's University Hospitals
NHS Foundation Trust

NHS
Guy's and St Thomas'
NHS Foundation Trust

NHS
Epsom and St Helier
University Hospitals
NHS Trust

Guernsey

Tunbridge Wells

- ✓ 7 adult renal units
- ✓ 6 ICS systems (5 London + Surrey)
- ✓ Tertiary referrals

London renal activity >25% England

London's Renal Centres and Satellite Units

London Integration Transformation Collaborative: Renal Pathway Transformation

May 3rd 2023

London Renal Collaborative programme

A partnership between
NHS England, London ICBs and
London Kidney Network

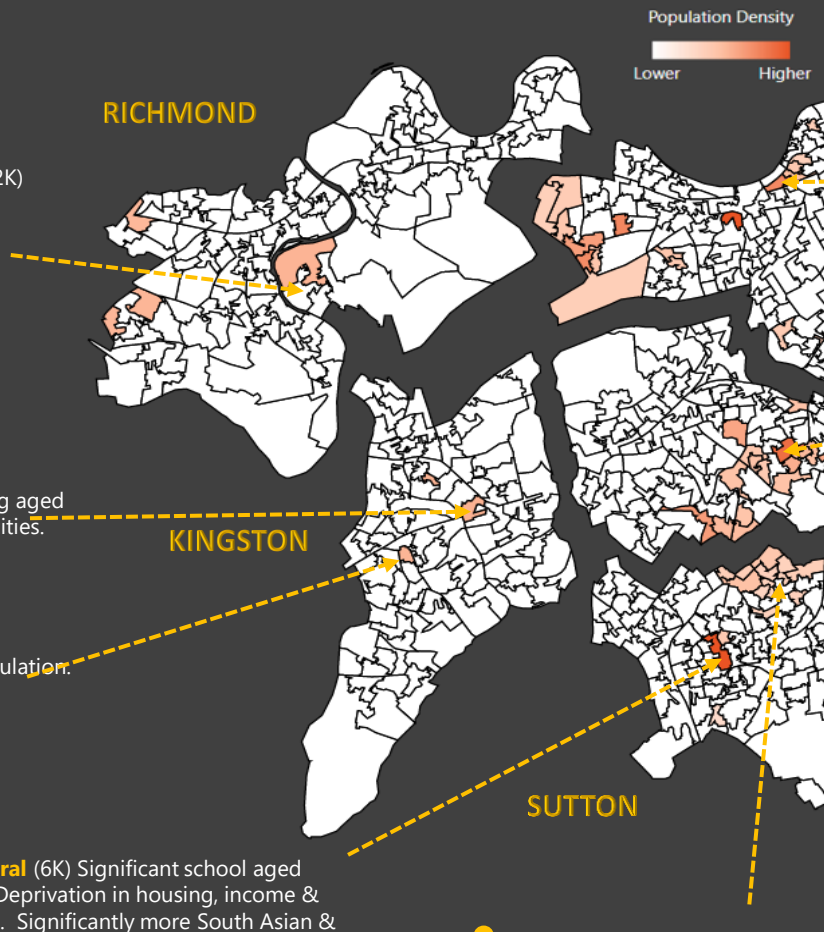
How can we use this data locally? Learning from SWL

In partnership with South West London Health & Care Partnership

Where are the SWL Core20 population of 340k located?

NHS

Main features of population:



Ham, Petersham and Richmond Riverside (2K) Older population. Significant White British population.

Beverley (2K) More school and young working aged population. More of the Asian & Mixed ethnicities.

Berrylands (2K) More young working age population. More of the Arab/Middle Eastern ethnicities.

Sutton Central (6K) Significant school aged population. Deprivation in housing, income & environment. Significantly more South Asian & Chinese ethnicities.

St Helier & Wandle Valley (14K) More school & retirement aged population. Significantly more White British and Eastern European ethnicities.

Queenstown (9K) Young adult to working age population (15-44). Significantly more Black & Chinese ethnicities. Barriers to housing and living environments

Latchmere (14K) Younger working age population. More Black ethnicities. Barriers to housing

East Merton (29K) Deprivation in housing and environment. Significant school aged and older working age (44-64) population. Ethnically diverse.

Croydon North (89K) School and working aged population. Significantly more Black & Asian ethnicities. Barriers to housing.

Addington (24k) High school aged population. Very high deprivation driven by income, employment, education and barriers to housing. Significantly White British and Black African

Fairfield (21k) Young adult to working age (15-44), adversity in living environment, housing & crime. Significant Indian ethnicities.

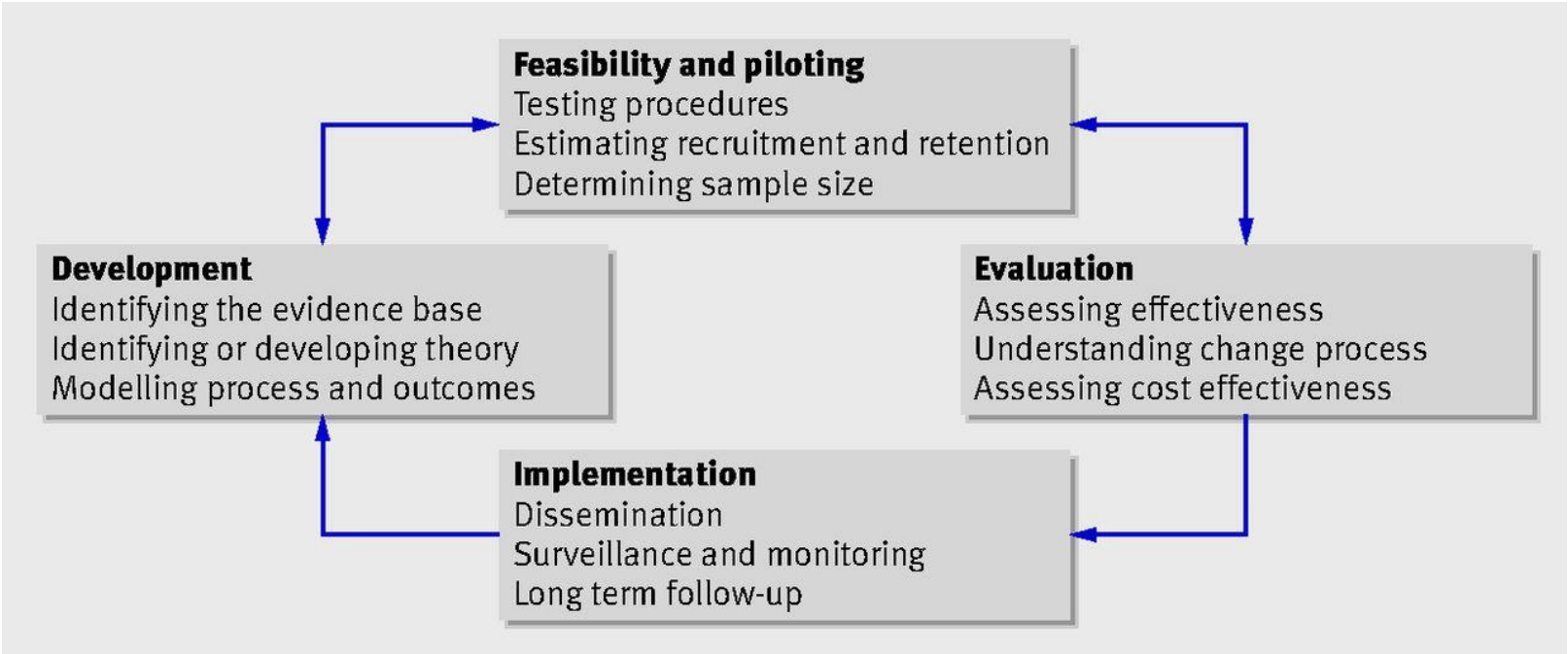
Opportunity for change KEY: High Medium Low

Summary of key learning points

- CKD is common
- CKD is associated with high rates of CVD, hospital admissions and mortality
- Strong associations between CVD and CKD risk and outcomes
- Prevention of CKD progression can reduce CVD, End Stage Kidney Disease and mortality
- Both ACR and eGFR testing are important for early identification.

Summary of key learning points

- We need to understand our own local population, and see where health inequalities exist
- A change in our approach is needed, to engage with people at greatest risk of CKD
- The greatest benefit lies in both improving detection *and* optimising treatment in these at-risk groups
- The time to act is now!



Peter Craig et al. BMJ 2008;337:bmj.a1655