Day 1
KidneyGenAfrica Workshop

Case Study

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Learning Objectives: CKD-u

You will:

Gain an overview of how disease definitions for chronic kidney disease were derived

Explore what is known about the causation of chronic kidney disease

Consider the ethical and practical challenges of investigating a subclinical disease

Receive an introduction to ongoing research regarding chronic kidney disease of unknown origin

Consider benefits and disadvantages of different epidemiological study designs in studying a subclinical condition

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Learning Objectives: CKD-u

Current definitions used in clinical care for chronic kidney disease are driven by risk analyses of biomarker measurements.

A small subset of people with very advanced kidney disease or rapidly progressing primary kidney disease will end up on dialysis.

Most people who are detected with these biomarkers are asymptomatic, and/or attribute their health problems to other conditions (e.g. diabetes, cardiovascular disease, heart failure, hypertension).

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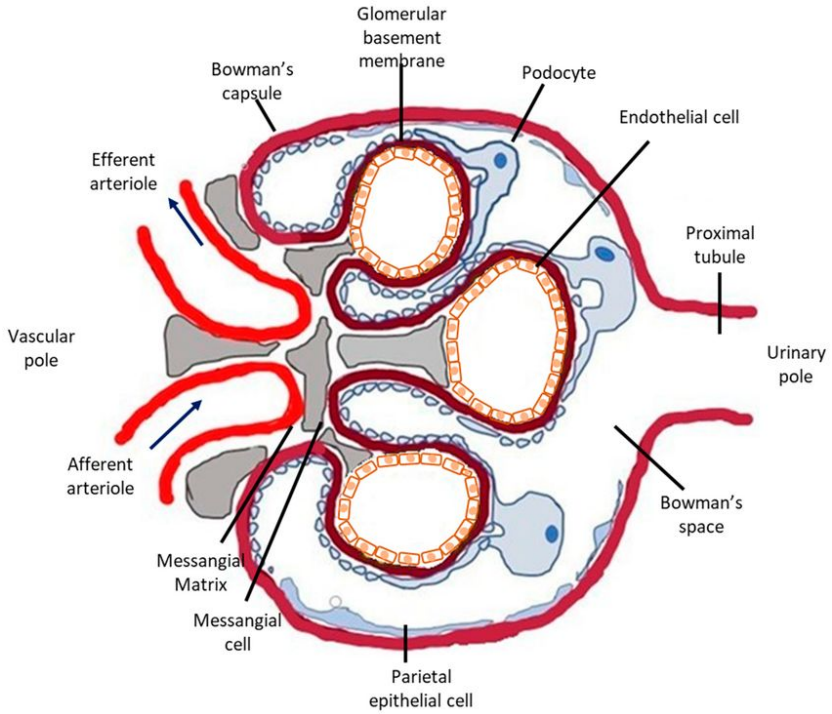
Non-invasive Biomarkers for CKD

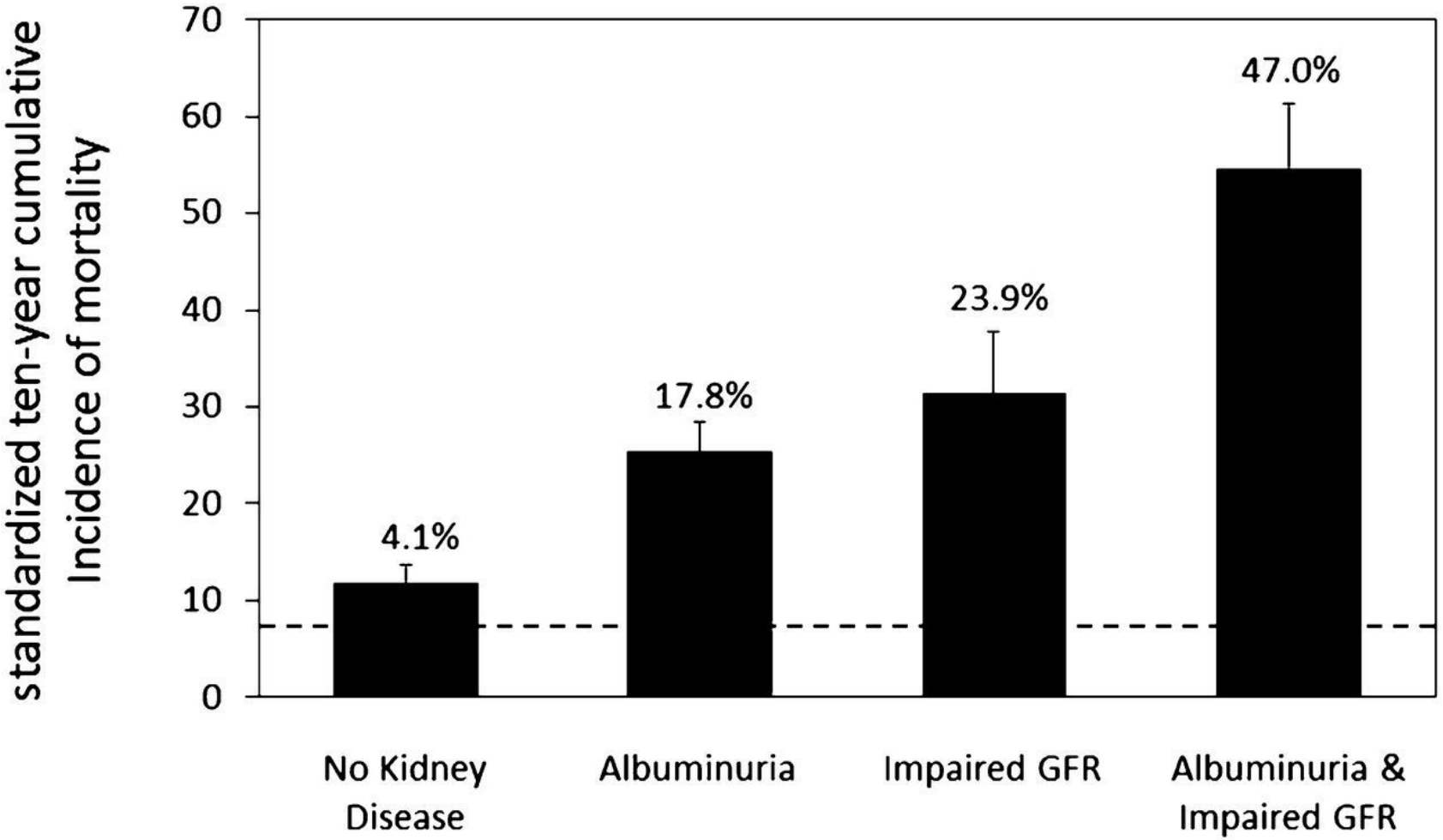
Damage to the tubule
urinary markers for research purposes only, not in routine use.

Damage to the glomerulus
Albuminuria/proteinuria (“leaking sieve”

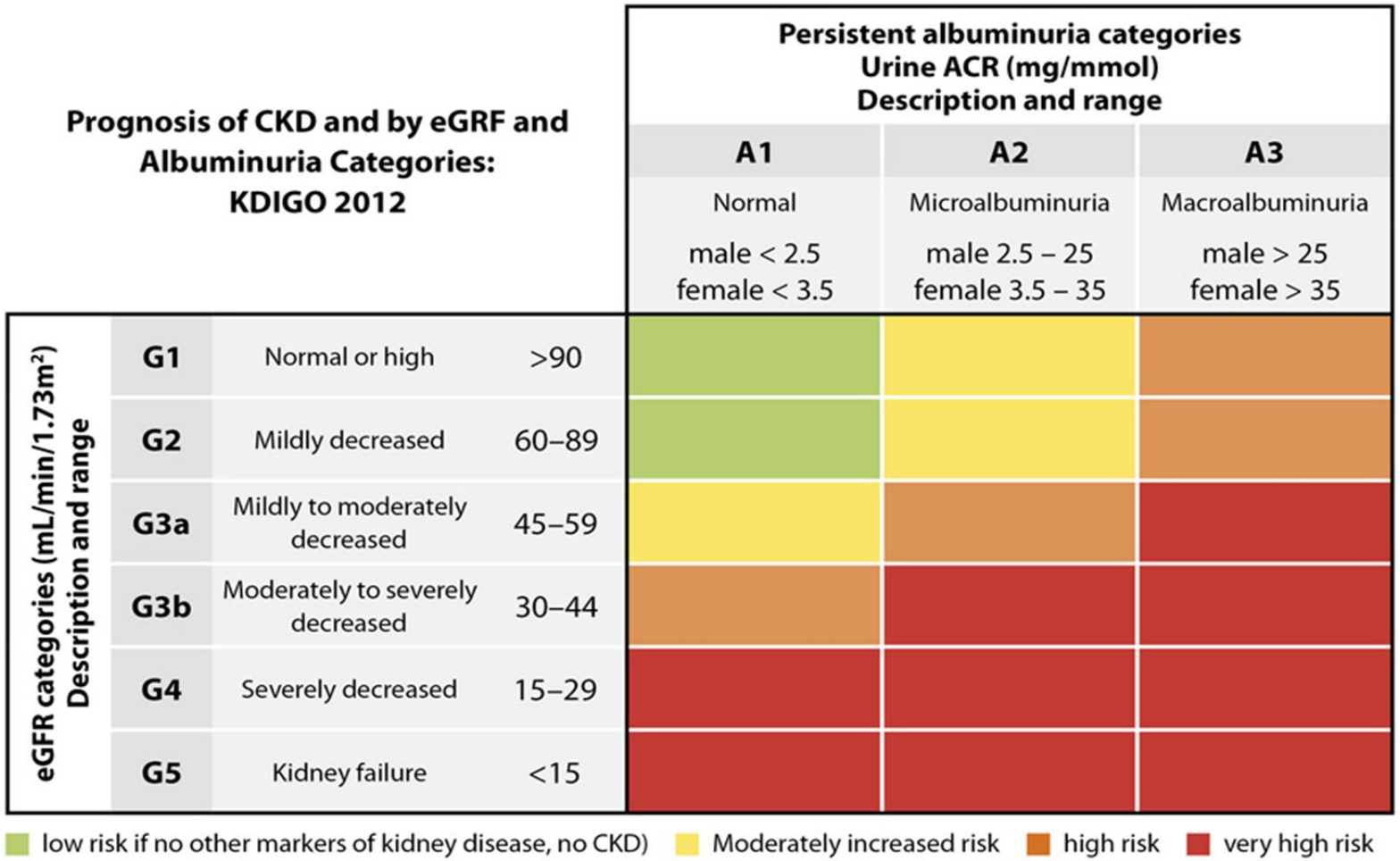
Glomerular filtration rate (GFR)
estimated GFR, based on measured serum creatinine and/or measured serum cystatin C



CKD and mortality



CKD and KDIGO



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Breakout 1

Consider the paper on ‘An update on the global disparities in kidney disease burden and care across countries and regions’ (https://doi.org/10.1016/s2214-109x(23)00570-3)

Questions to discuss in Breakout groups

- What are the risks and benefits of screening for kidney disease in settings where access to chronic dialysis and transplantation are severely restricted?
- How would you plan the implementation of public health screening to identify individuals with eGFR < 60 or albuminuria in a resource-limited setting?
- Specifically discuss:
  Informed consent
  Duty of care
  Risk vs benefit of point-of-care devices vs designated pathology laboratories

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CKD-u: Central America

A dramatic increase of chronic kidney disease of unknown origin (CKDu)

Unexplained by conventional risk factors such as hypertension and diabetes

Primarily affecting adult male agricultural workers, in particular sugarcane workers

Nicaragua 2002-2012:

- 46% of all male deaths were due to CKD
- 75% of deaths of men aged 35 to 55 were due to CKD.
- Mortality rate due to CKD doubled

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Challenges of estimating prevalence of CKDu

- CKDu clinically silent until it has progressed to advanced stage, so need to test asymptomatic patients to include initial stages of disease
- Lack of reliable registries for CKDu:
  - Definition of CKDu in mortality records may vary according to awareness of CKDu in the area
  - Dialysis or transplant registries not available in all regions
- No clear clinical definition of CKDu:
  - Distribution of glomerular filtration rate (GFR) may vary between regions
  - Estimates of GFR (eGFR) are affected by ethnicity and body composition

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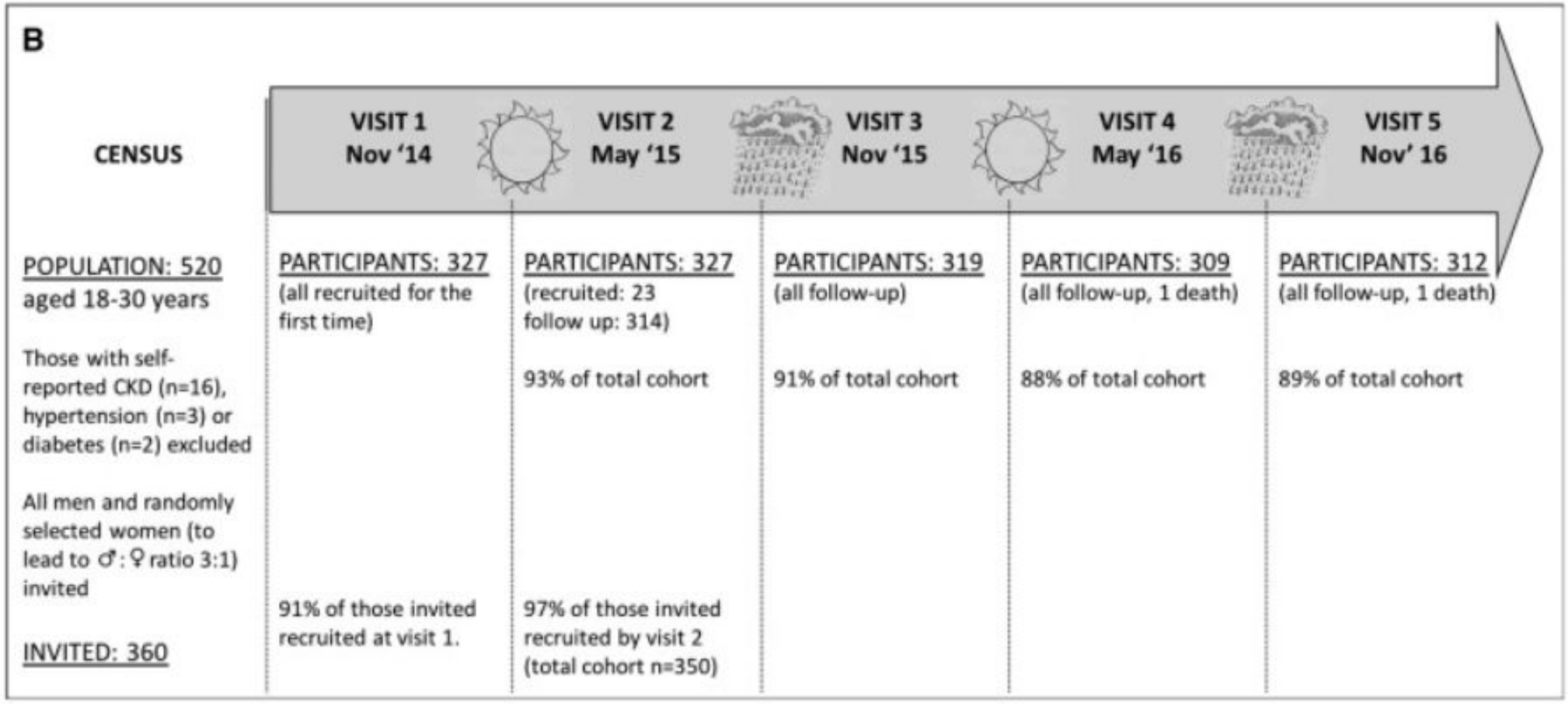
Prospective cohort study of a young population

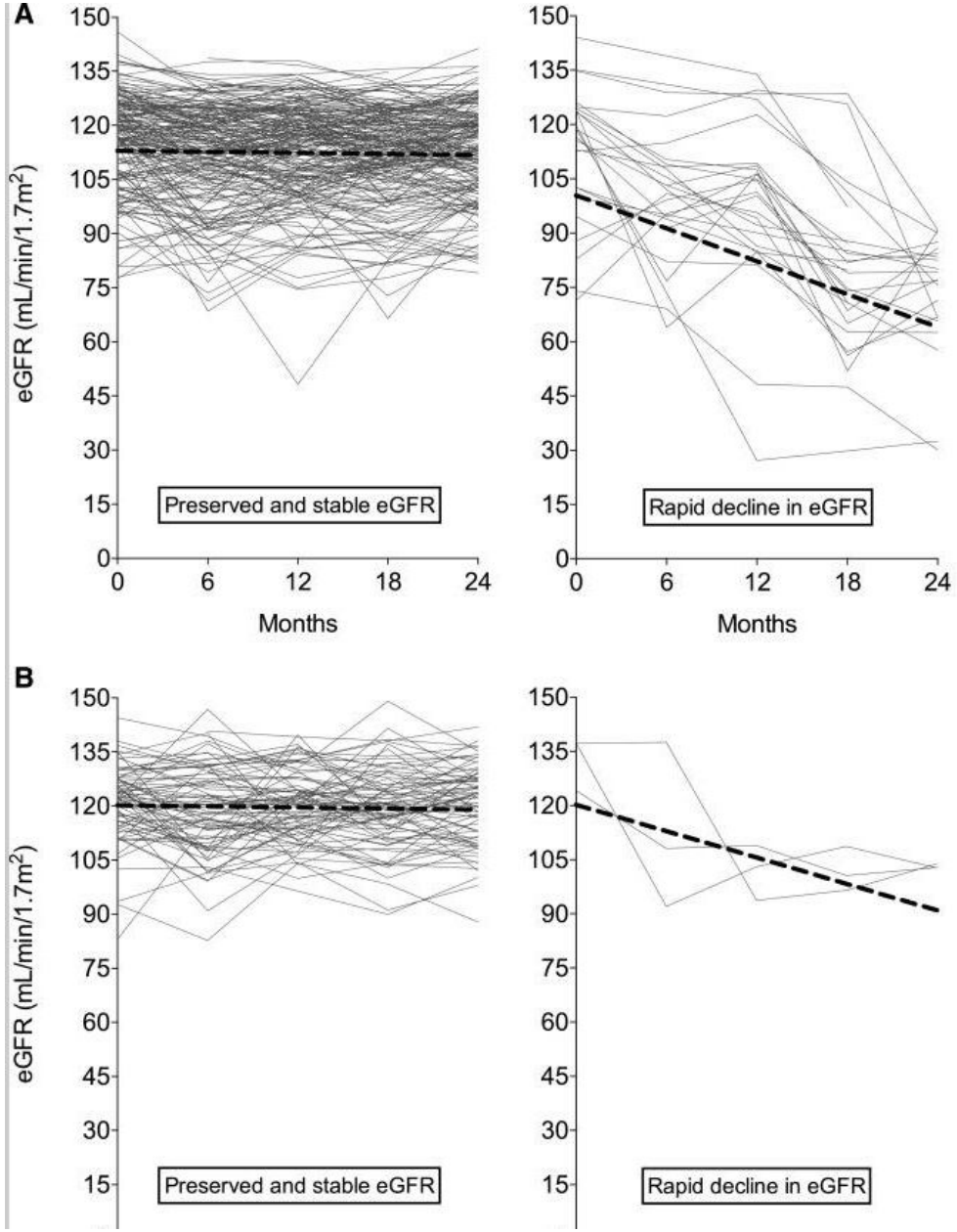


Even after excluding those with self-reported CKD, 9.5% of the apparently healthy men (but no women) in the study had evidence of baseline renal dysfunction.

J Am Soc Nephrol. 2018; 29(8): 2200–2212

MEN

WOMEN



Rapid loss of eGFR from normal baseline levels was found in 9.5% of men and 3.4% of women.

Among men, risk factors at baseline for rapid decline included working outdoors, agricultural work, and lack of shade availability

J Am Soc Nephrol. 2018; 29(8):

? Occupational or Environmental ?

Balkans (1920) - “Balkan Nephropathy” from aristolochic acid in wheat

Japan (1910 – 1960) – “Itai Itai Disease” from cadmium in waster water

Japan – “Mercury Nephropathy” from eating fish contaminated with organic mercury

Tunisia – CKDu from a mycotoxin contaminant in food (Ochratoxin)

International prevalence patterns of low eGFR in adults aged 18-60 without traditional risk factors from a population-based cross-sectional disadvantaged populations eGFR epidemiology (DEGREE) study

OPEN

Charlotte E. Rutter[1], Mary Njoroge[1], Philip J. Cooper[2,3], Dorairaj Prabhakaran[4], Vivekanand Jha[5,6,7], Prabhdeep Kaur[8], Sailesh Mohan[4], Ravi Raju Tatapudi[9], Annibale Biggeri[10], Peter Rohloff[11], Michelle H. Hathaway[12], Amelia C. Crampin[13,14], Meghnath Dhimal[15], Anil Poudyal[15], Antonio Bernabe-Ortiz[16], Cristina O'Callaghan-Gordo[17,18,19,20], Pubudu Chulasiri[21], Nalika Gunawardena[22], Thilanga Ruwanpathirana[23], S.C. Wickramasinghe[24], Sameera Senanayake[25], Chagriya Kitiyakara[26], Marvin Gonzalez-Quiroz[27,28,29], Sandra Cortés[30], Kristina Jakobsson[31,32], Ricardo Correa-Rotter[33,34], Jason Glaser[32], Ajay Singh[35], Sophie Hamilton[36], Devaki Nair[28,37,38], Aurora Aragón[29], Dorothea Nitsch[39], Steven Robertson[40], Ben Caplin[28] and Neil Pearce[1]; and the DEGREE Study Group[41]

Kidney International (2025) **107,** 541–557

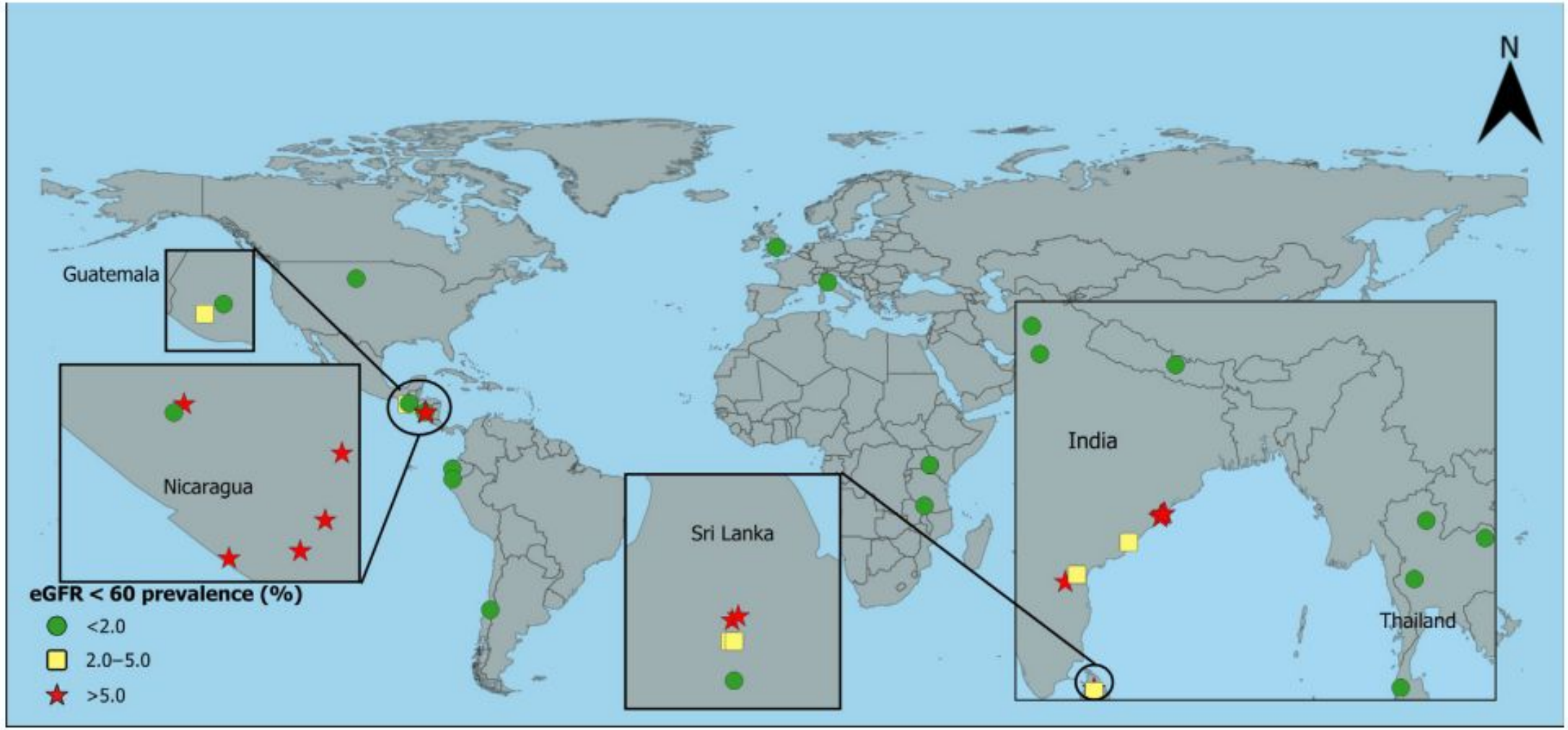


Figure 1 | Age-standardized prevalence of creatinine-based estimated glomerular filtration rate (eGFR) <60 ml/min per 1.73 m^2 in rural[a] men without hypertension, diabetes, or heavy proteinuria. [a]USA includes rural and urban together.

Breakout 2

Questions to discuss in Breakout groups

Why do you think CKD-u is a risk in African populations?

What studies would you design to determine the prevalence of CKD-u in African countries?

What studies would you design to understand what causes CKD-u in African countries?

- For each of these questions, please suggest a study design, target populations, baseline/follow-up assessments, duration, and size of study.

What would you advise your local Ministry of Health to do about CKD-u?

Each group should assign a colleague to provide feedback on the group's suggested answers.

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