

Day 1

KidneyGenAfrica Workshop

Session 1

Overview of normal kidney structure and function, kidney disease, and associated risks

Robert Kalyesubula
Introduction to kidney function & pathophysiology

June Fabian
Kidney disease and associated risk: contextualizing mechanisms of injury
and differences between global geographies



Kidney disease and associated risk: contextualizing mechanisms of injury and differences between global geographies

By the end of this session, participants should appreciate:

- Context shapes risk, presentation, and outcomes.
- Mechanisms of kidney injury across settings.
- Epidemiology and health-system capacity differences.
- Genetic and translational implications for Africa.





Reduction of NCD-related mortality by one-third by 2030

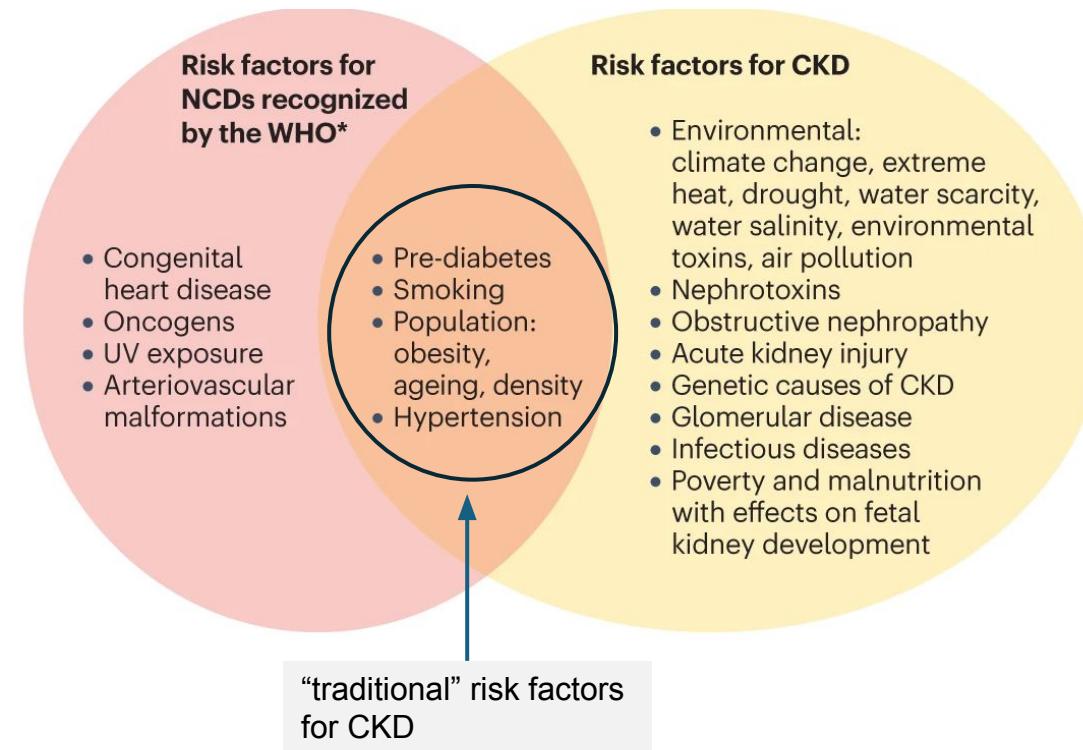
WHO = BIG FIVE = heart disease, stroke, cancer, diabetes, and chronic lung disease drive premature death and disability.

CKD = 3rd fastest-growing cause of death globally

CKD = only NCD with rising mortality and rising prevalence

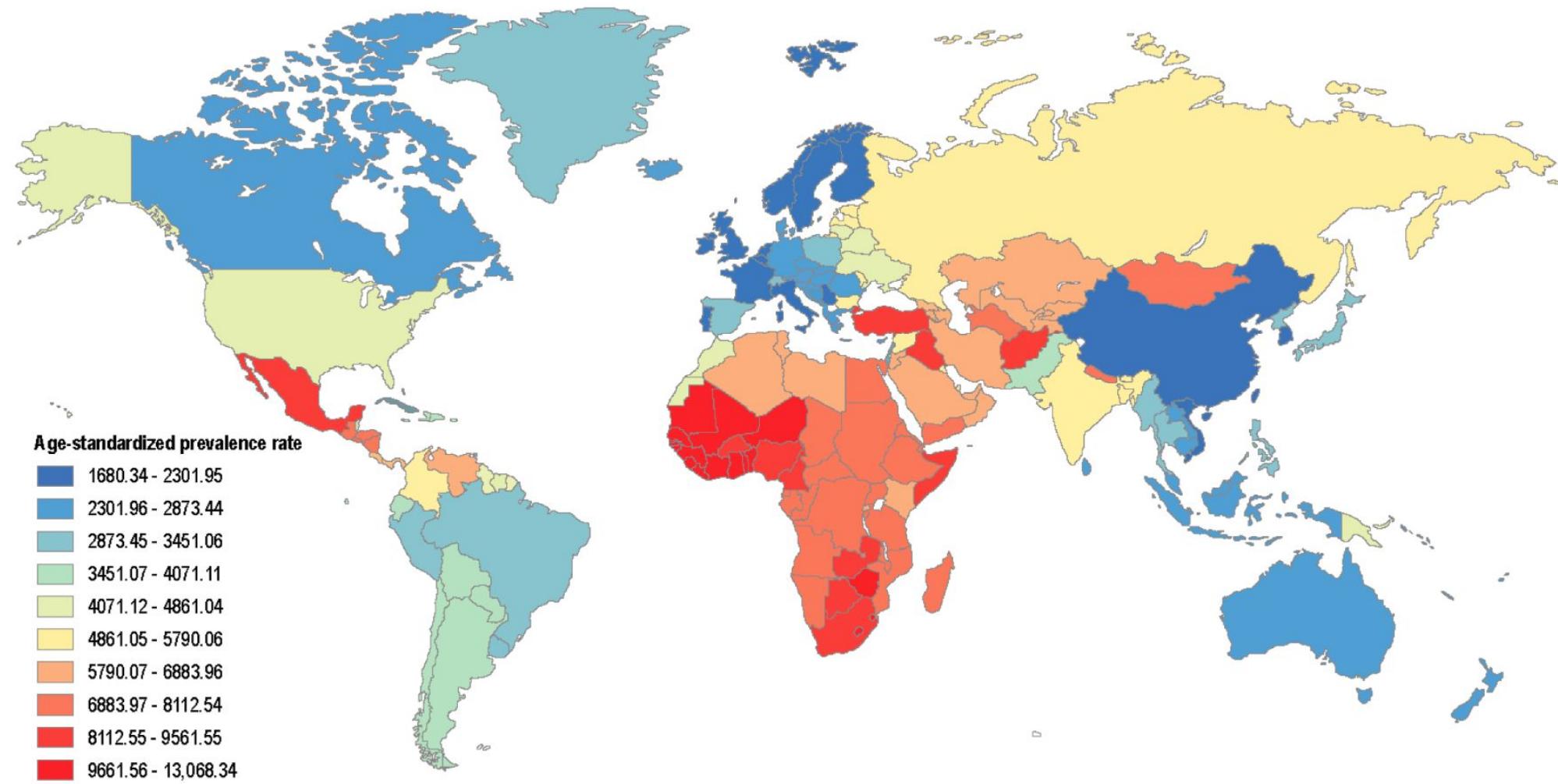
CKD = 5th highest cause of premature death by 2040

LIC and LMICs account for 60% of the global burden of CKD

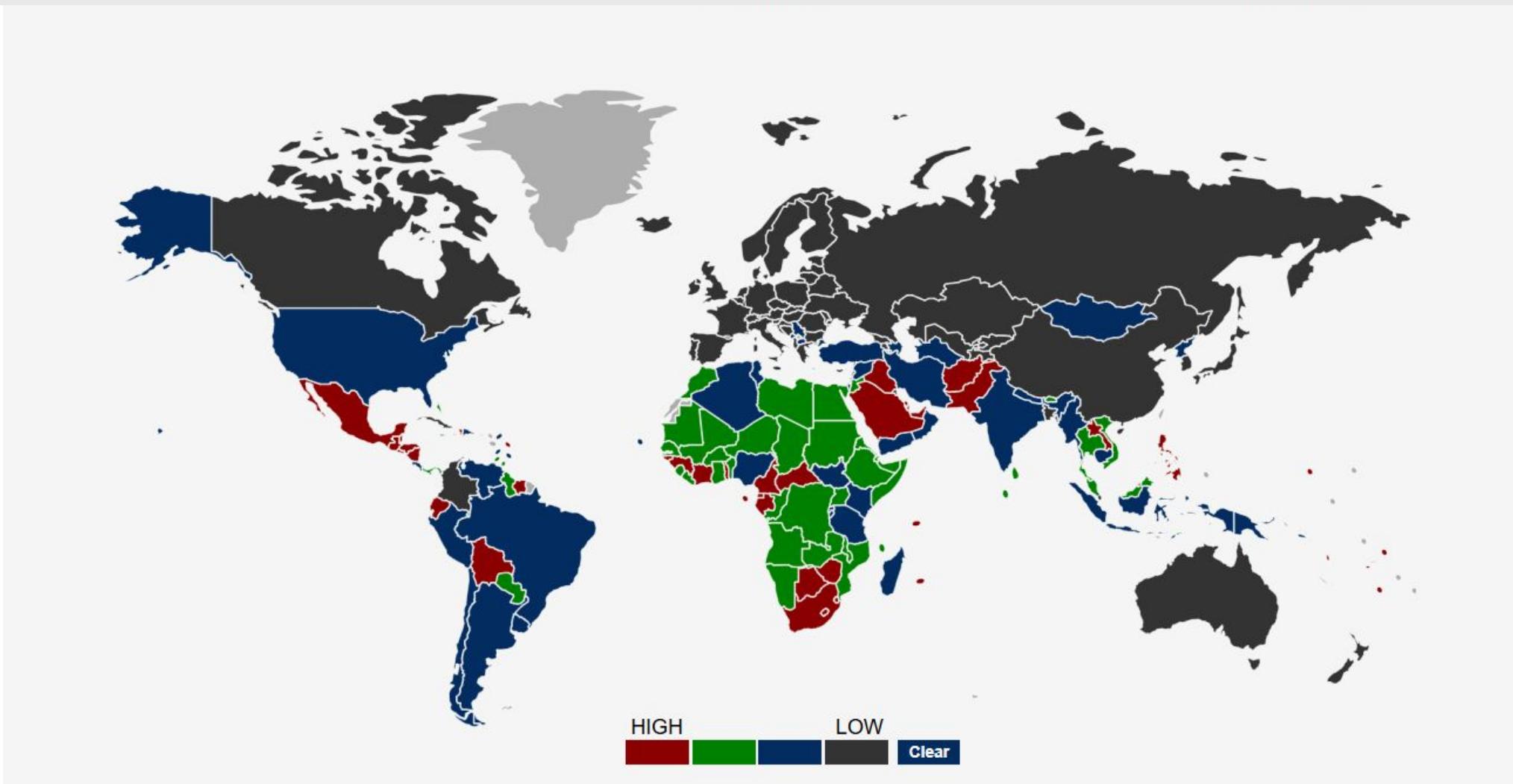


In 2025 World Health Assembly recognized CKD as a major NCD = BIG SIX

The worldwide age-standardized prevalence of CKD per 100,000 population in 2016 (adapted from GBD Study)



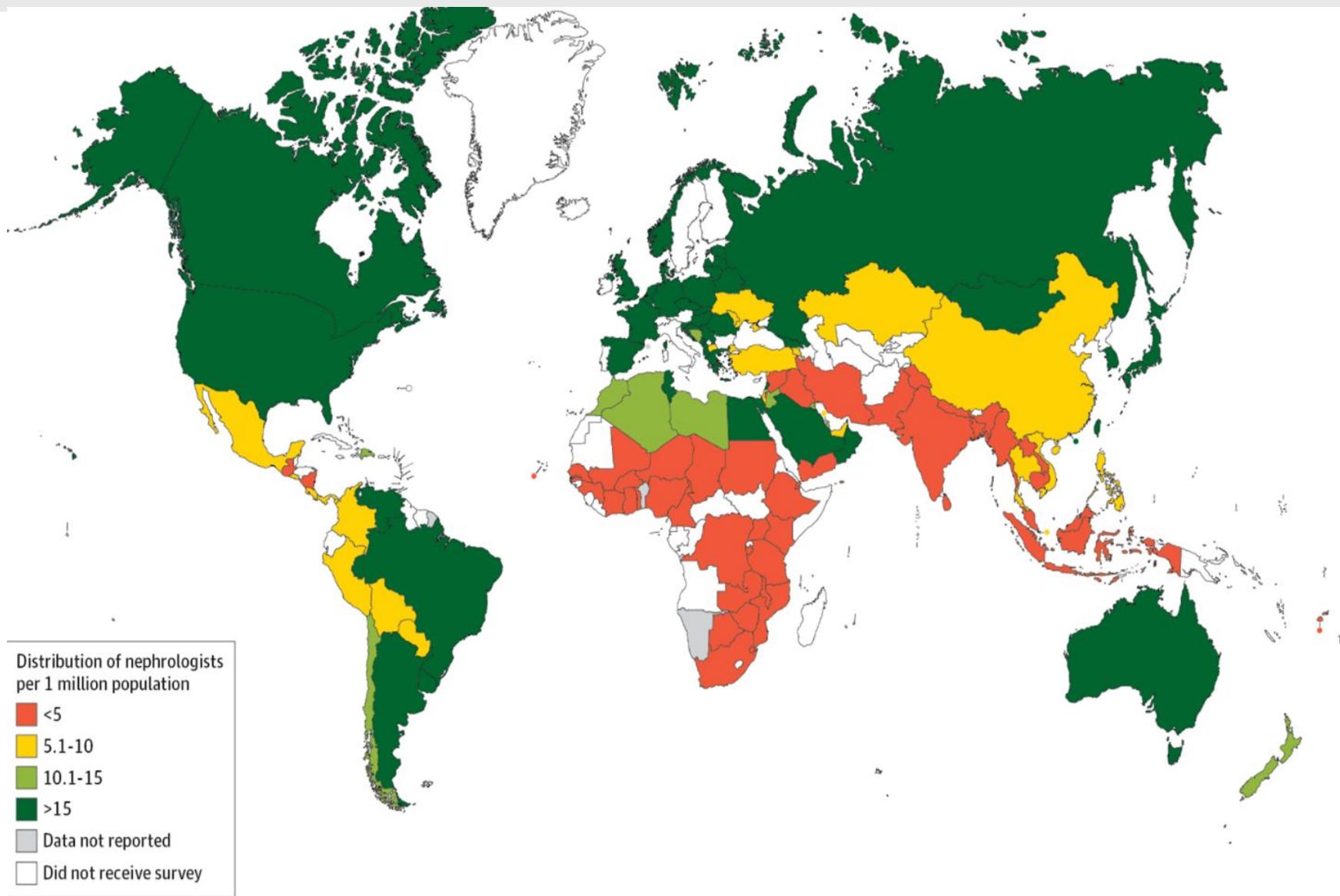
The worldwide age-standardized death rate from CKD per 100,000 population (WHO)



Global map of climate change risk

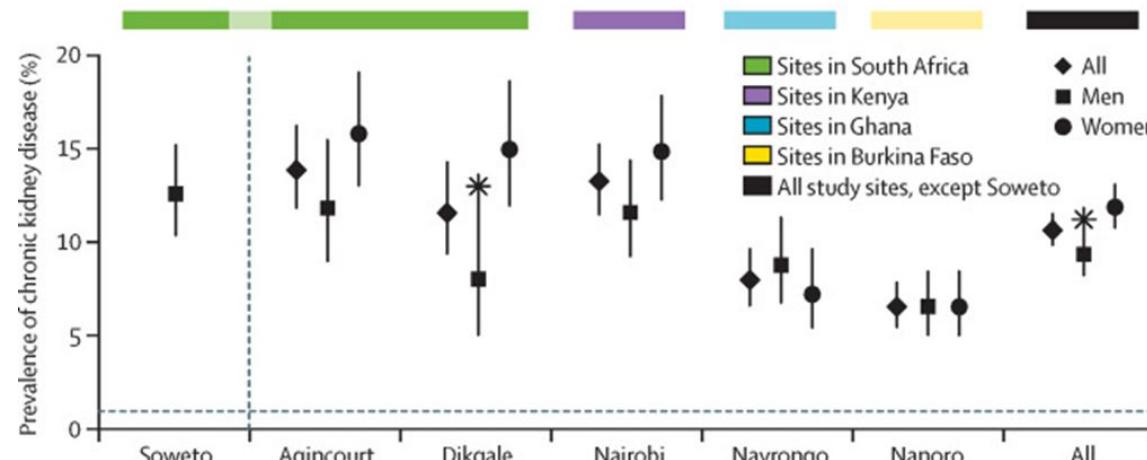


Global distribution of trained nephrologists



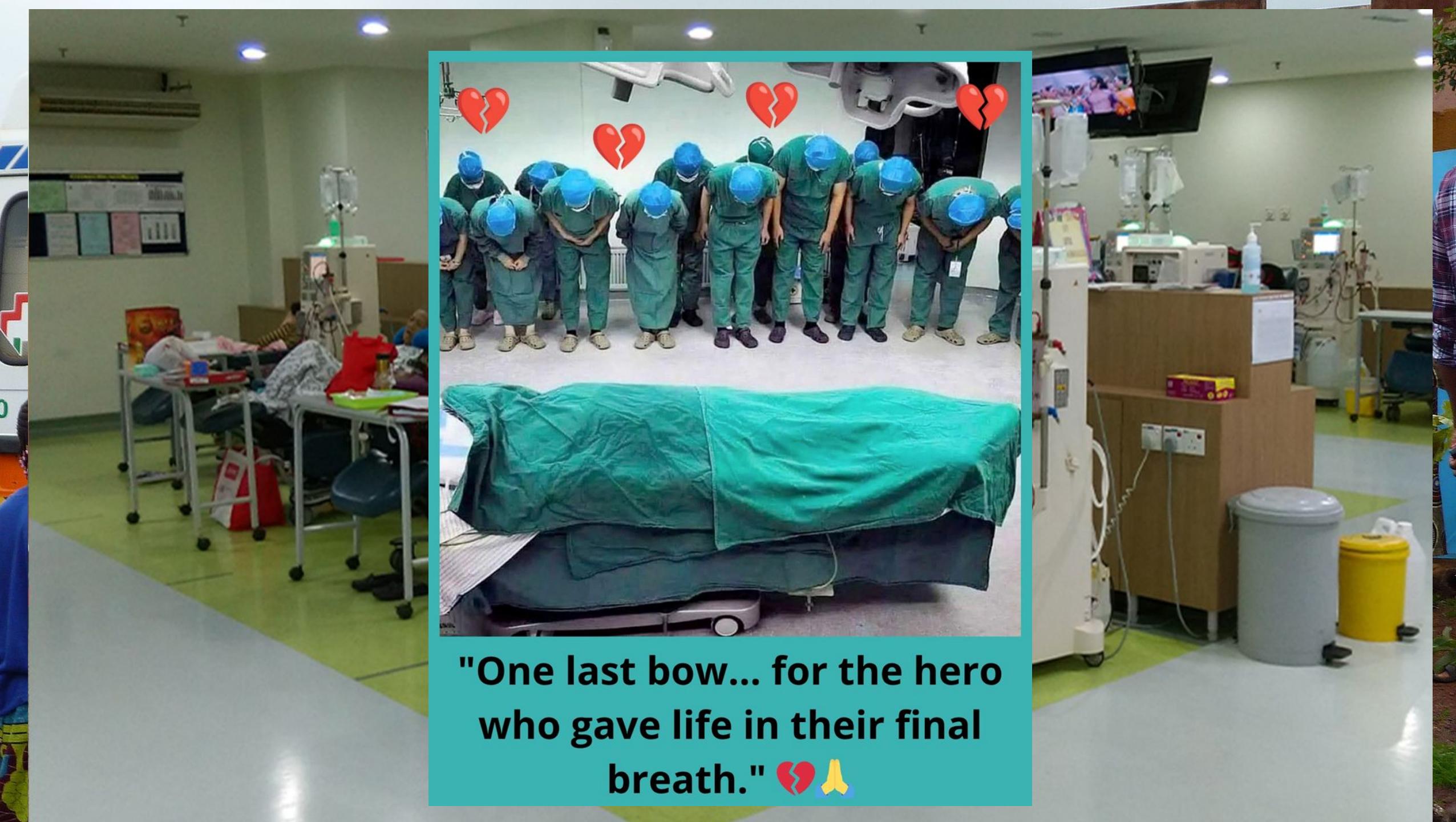
Kidney disease in African populations

- CKD presents 10-20 years earlier than HICs
- >90% of people are unaware
- Causes/risks have marked regional variation
- As many as 60% do not have “traditional” risk factors
- Of these, many more have hypertension than diabetes (contrary to HICs)
- Uganda: CKD in 12.5% in Southwestern Uganda and 3.9% in Eastern Uganda
 - Of those with CKD, two-thirds did not have HIV, diabetes, or hypertension
- AWI-GEN Study: CKD prevalence also showed marked regional variation, and by sex



Without access to treatment, kidney failure is fatal





**"One last bow... for the hero
who gave life in their final
breath."** 💔🙏

Organ harvesting syndicates prey on Kenya's desperate youth

Impoverished young men are selling their kidneys in return for cash to start their own businesses.

The price of a kidney in Kenya? Just under US\$1 000 plus a motorbike. That is how 30-year-old Joseph Japiny, from Oyugis town in Homa Bay County in western Kenya, got his *boda boda* – a motorbike taxi he uses to earn a living.

Japiny told the ENACT project that he was introduced to Jadhot, a broker recruiting young men into the kidney-harvesting underworld that operates between Eldoret, Busia and Nairobi. Jadhot said that if he donated one kidney, he would be paid US\$984 as a down payment and another US\$984 in the form of a Boxer motorcycle. This he could use as a *boda boda* taxi – a common occupation among young East African men.

Japiny agreed to the deal and was taken to a private clinic in Eldoret for tests. Two weeks later, he was back in Eldoret where he received food and accommodation, and underwent regular blood, urine and faecal tests over the next three weeks. Throughout this time, Japiny had a minder – a person hired to look after those whose kidneys were going to be harvested.

The recipient, a 57-year-old woman from Germany, needed a second kidney transplant due to a long-term disease. Facing a potential wait of 8 to 10 years in Germany, she used an agency called "MedLead" to facilitate the process in Kenya.

She admitted to paying a six-figure amount (between \$100,000 and \$200,000) for the kidney but claimed the contract "looked all right" and that she "wanted this kidney".

Institute for Security Studies





**Universal Health Care
Kidney Prevention
Programs
Public Health “Best-buys”**



**Kidney Replacement
Therapy**



Let's take a breath and recap

Contextualise mechanisms of kidney injury



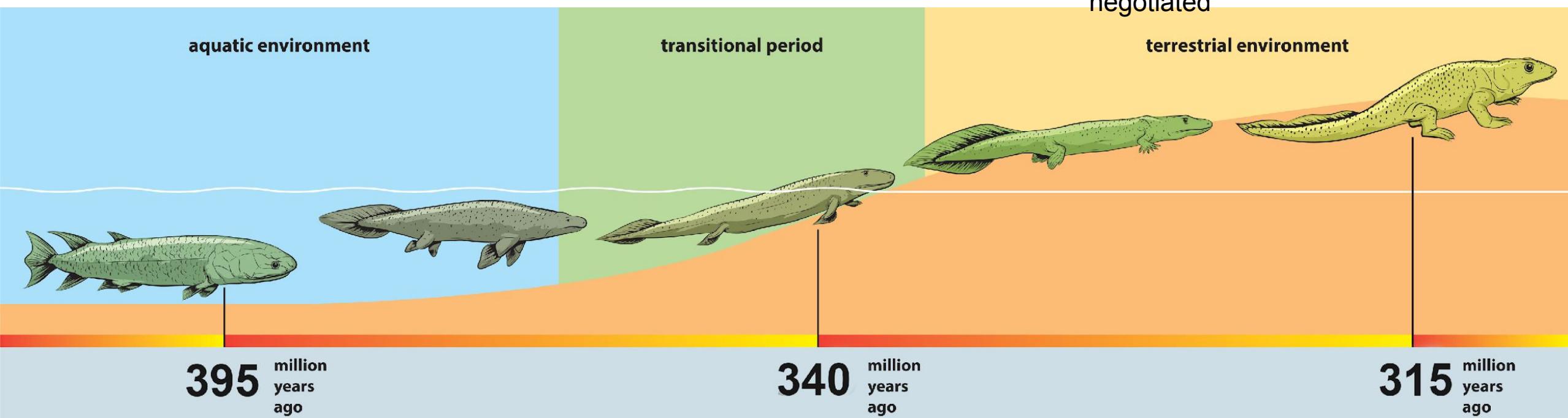
Why filter 180 L of plasma per day and then reabsorb almost all of it?

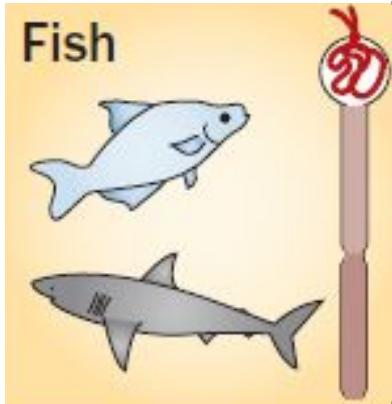


It's about our evolution

Water and salt
everywhere
Waste diffuses easily

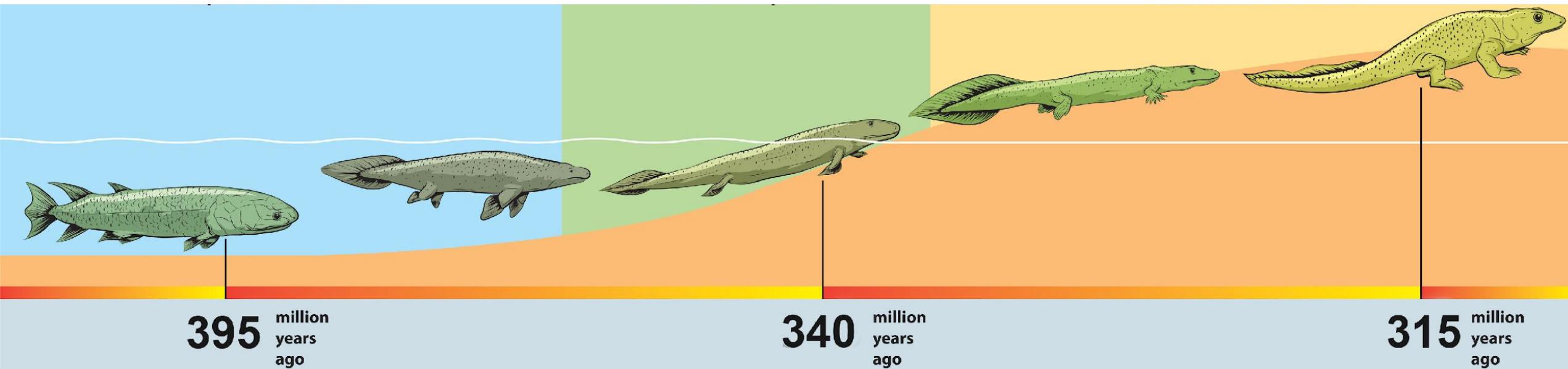
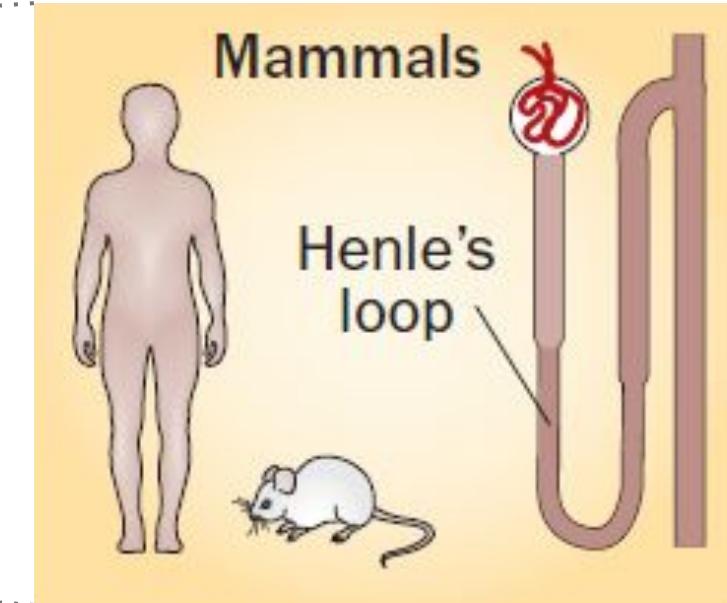
Dehydration
Salt loss
Toxins need to be excreted
Gravity needs to be
negotiated

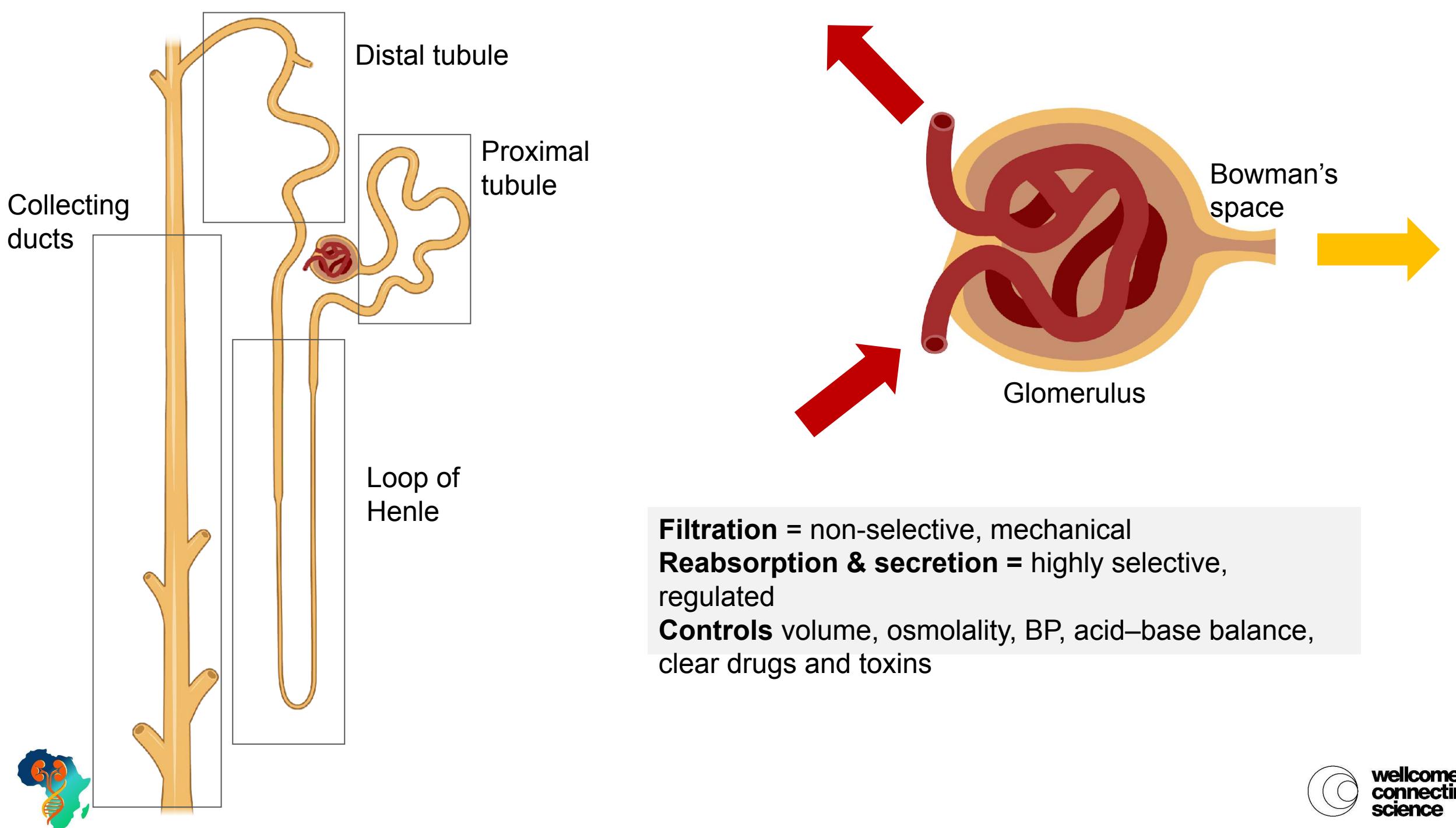




All it took was a
loop!

Loop of Henle: allows us to concentrate urine above plasma osmolality so that we survive deserts, droughts, and famine





Filtering 180 L of plasma every day is a survival advantage But what was the trade-off?

Increasing an organ's complexity attenuates its regenerative capacity

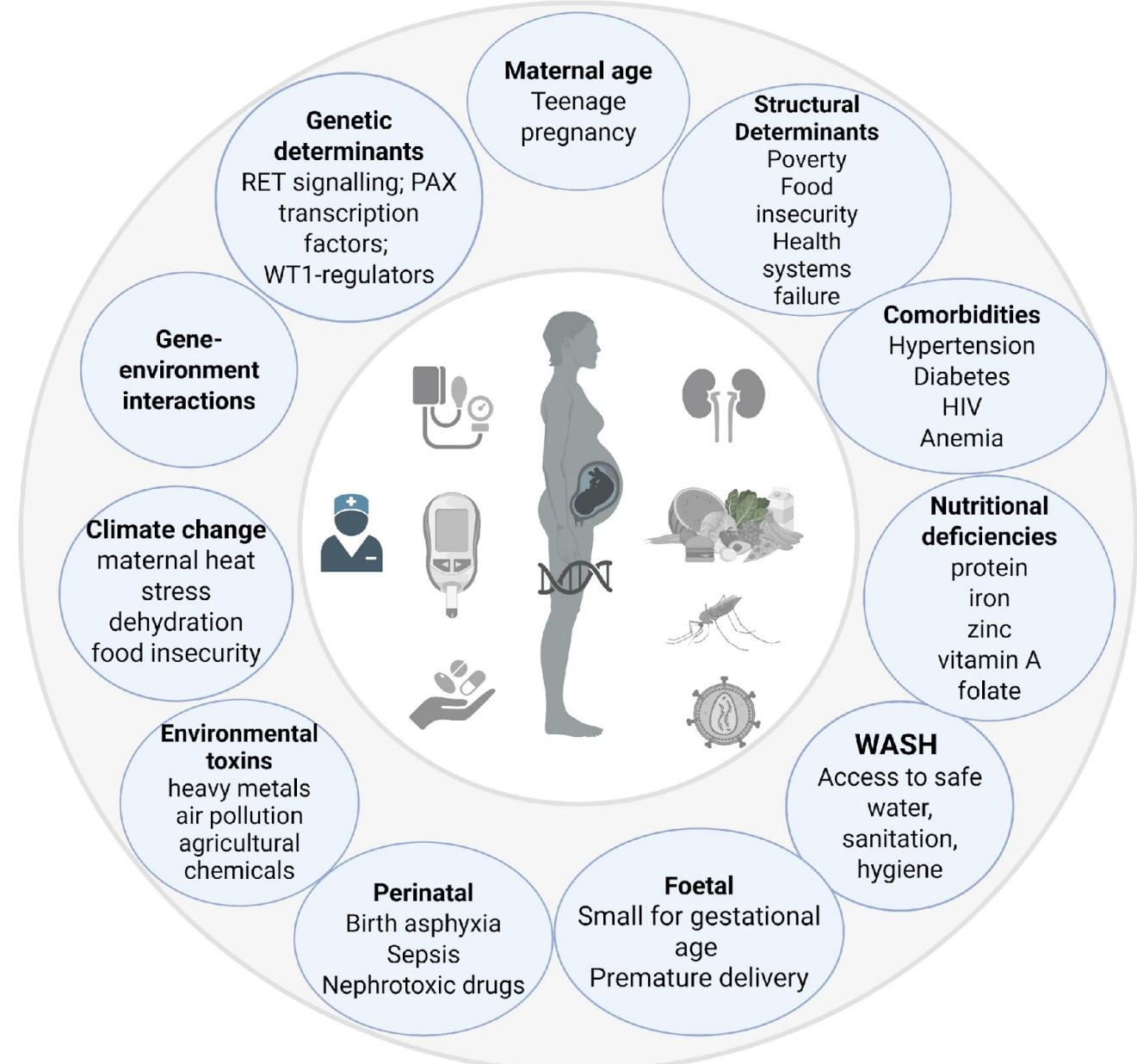
- 1. Nephron numbers are finite**
- 2. We lost the capacity for neonephrogenesis**

CKD is the price we pay for a high-performance survival system pushed beyond its limits



1. Nephron numbers are finite, determined at birth

- Nephrogenesis starts ~9–10 weeks' gestation
- Nephrogenesis ends by 34–36 weeks gestation
- No new nephrons after birth
- **Modifiable risks = focus of public health interventions**



2. Increasing our human nephron number and specialization came at the cost of neonephrogenesis

Fish, amphibians, reptiles:

Fewer nephrons, simple architecture = retain nephron neogenesis throughout life

Birds and mammals:

More nephrons, highly ordered architecture, long loops of Henle BUT nephron formation stops at birth
Thus, “cellular regeneration” is the main strategy:

Hypertrophy: existing nephrons enlarge

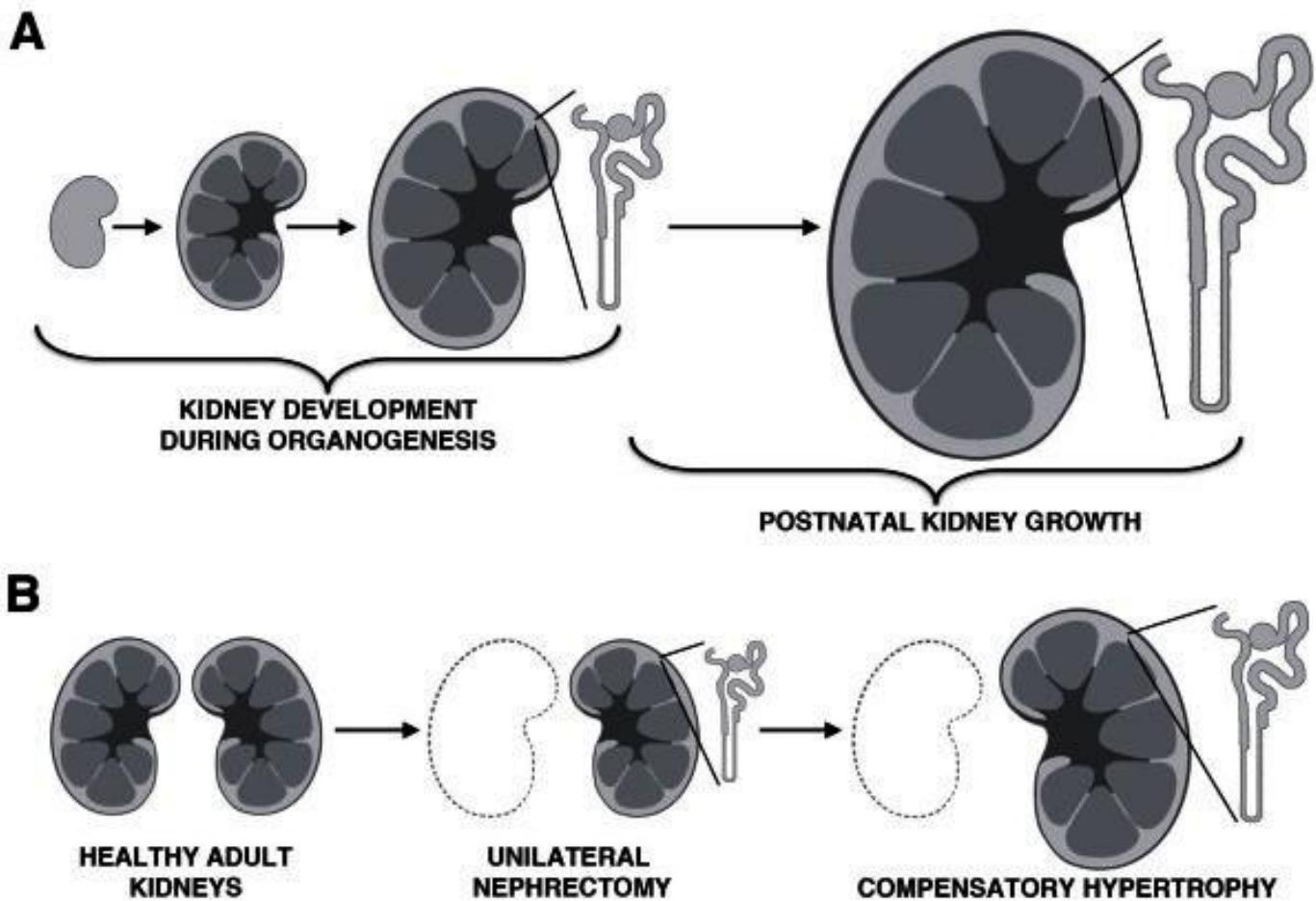
- Increase single-nephron GFR
- Early = adaptive
- Sustained = maladaptive (raised intraglomerular pressure, sclerosis, nephron loss)

Tubular regeneration: tubules do better

Glomerular regeneration: glomeruli do worse



Hypertrophy

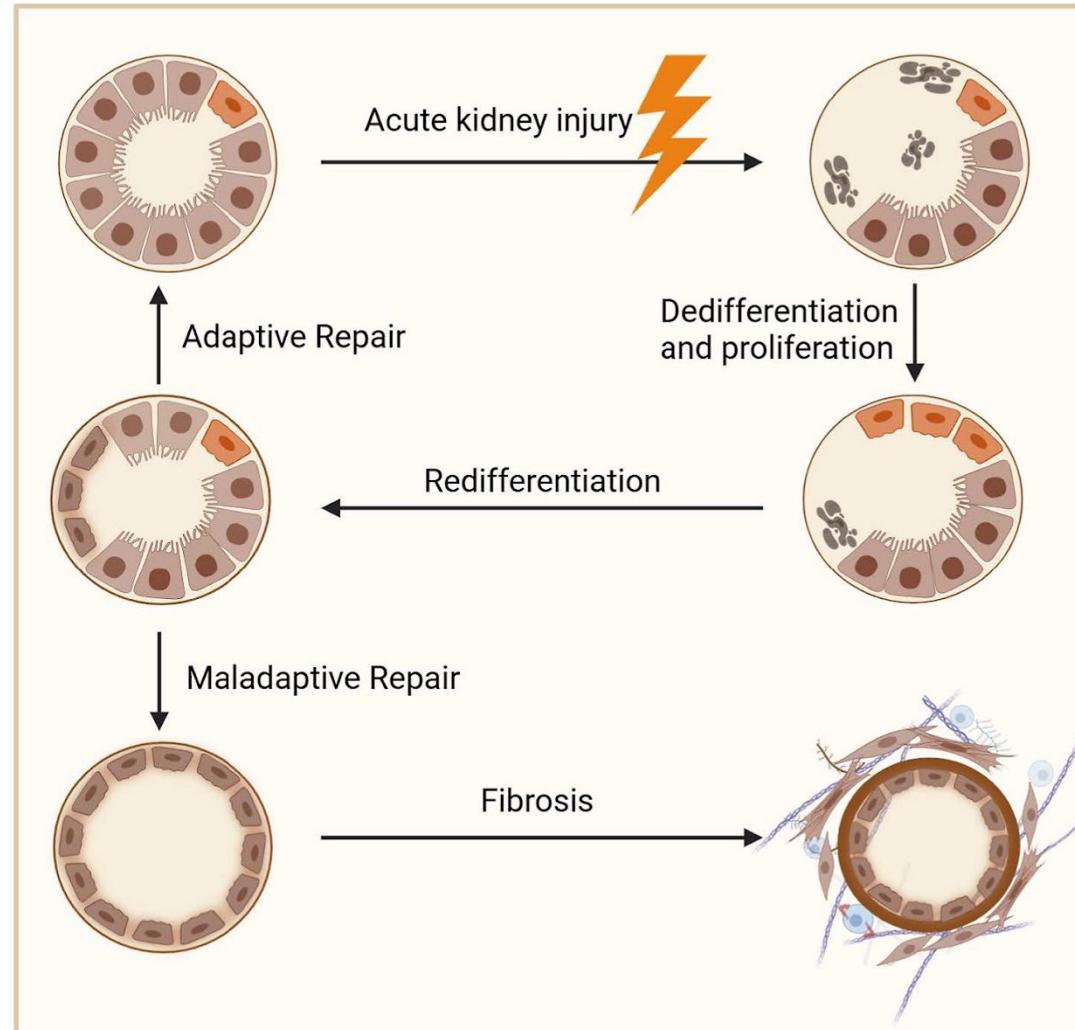


Tubular injury and regeneration

From progenitor cells and surviving proximal tubular cells

Mild injury – likely to recover
With *adaptive repair*

Repeated or severe injury leads to *maladaptive repair (fibrosis)*



Fixed Pre-existing
Progenitor Cell

Differentiated Proximal
Tubule Cell

Dead
Proximal
Tubule Cell

Impaired Proximal
Tubule Cell



Glomerular injury and regeneration

Hemodynamic injury

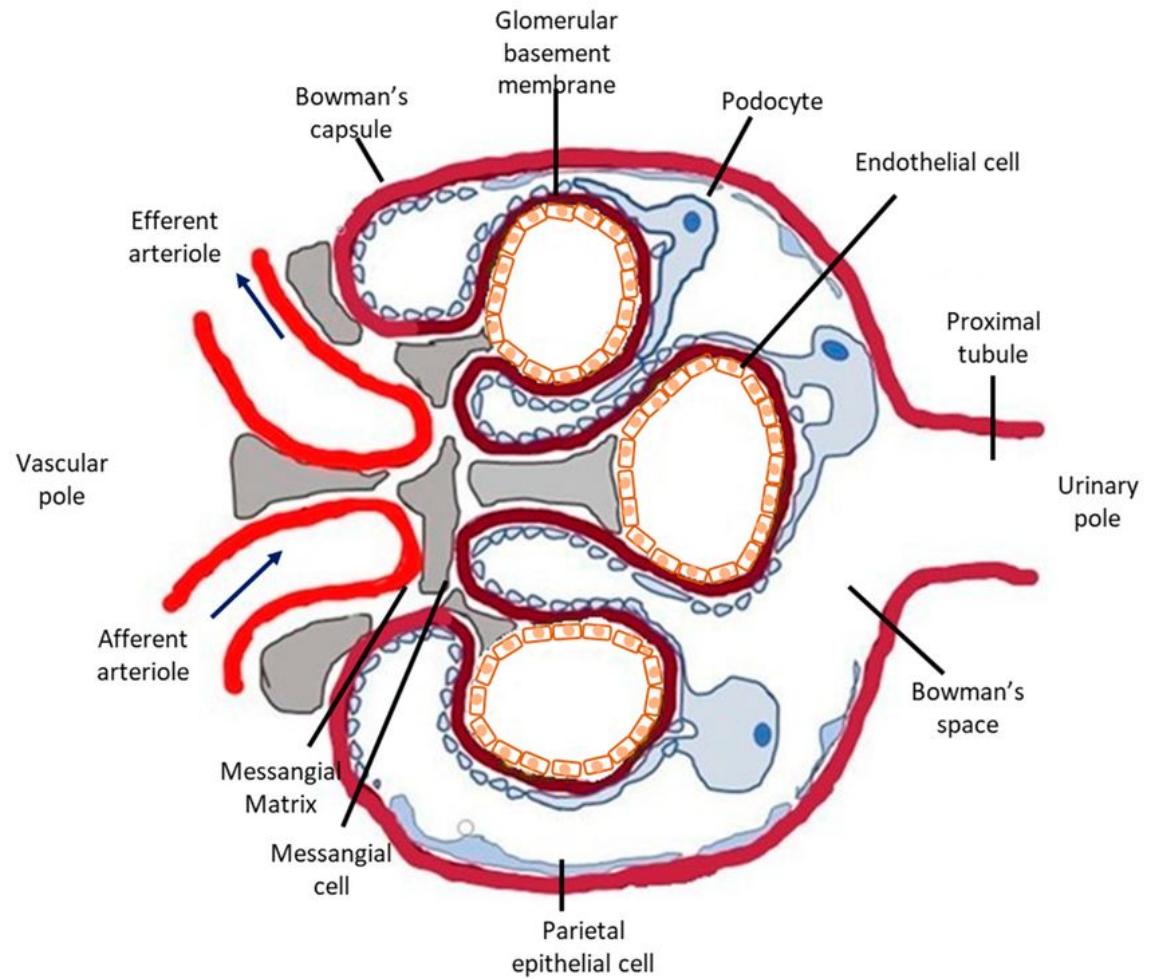
Metabolic injury

Immune-mediated injury

Infectious Injury

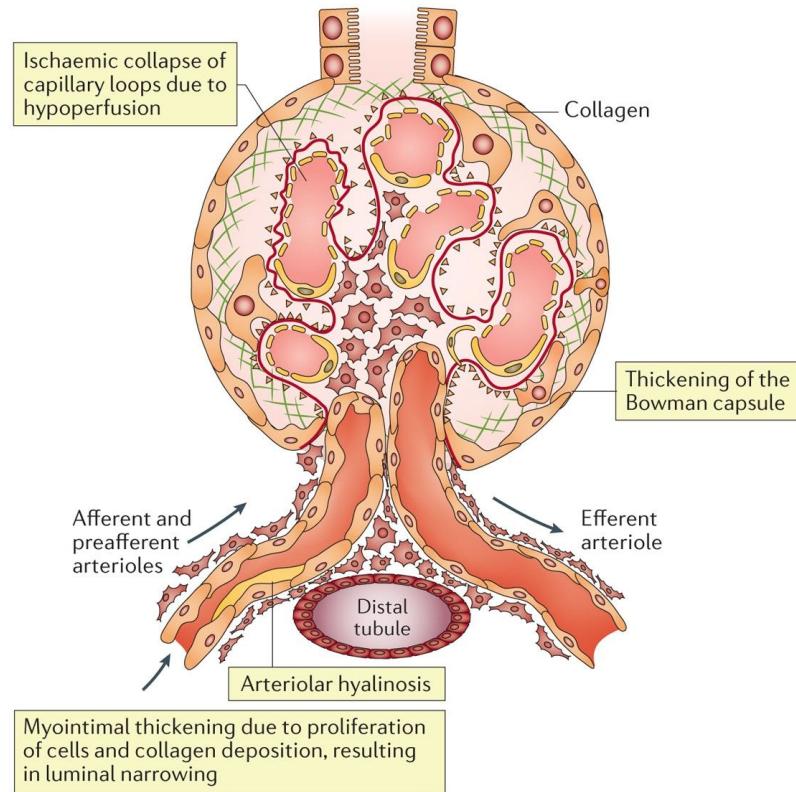
Inherited causes of glomerular injury

- **Sickle-cell disease**
- ***APOL1*-associated kidney disease**

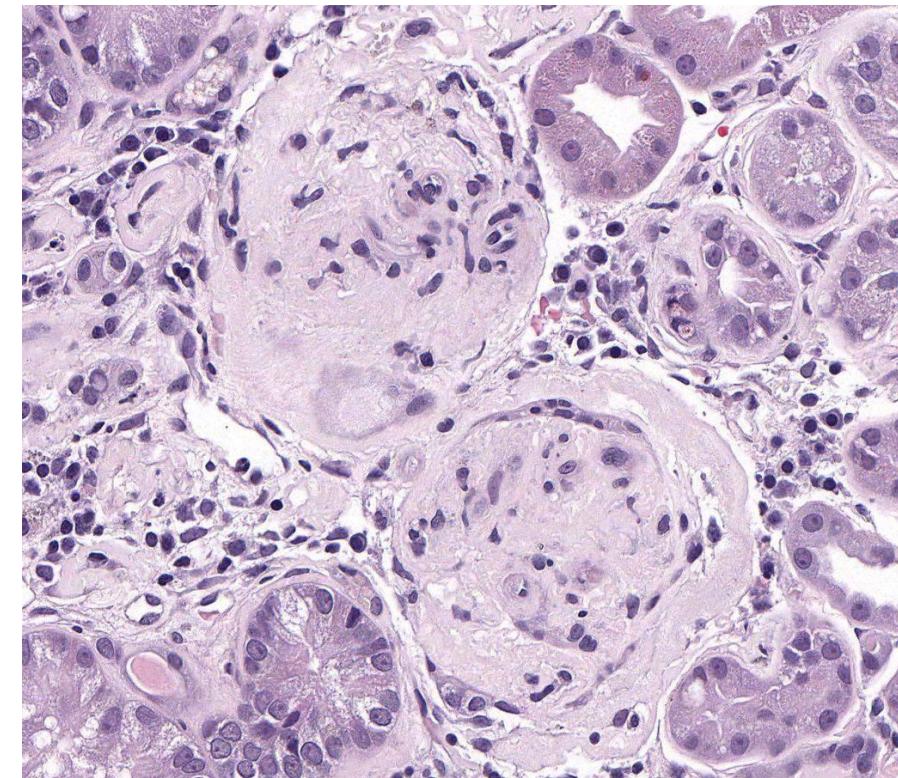
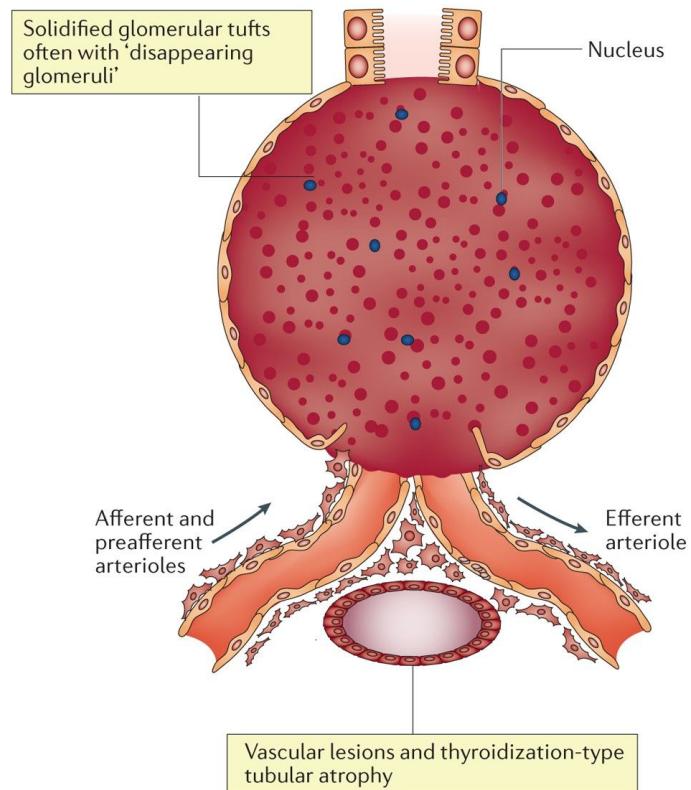


Glomerular injury and regeneration

a Arteriolar nephrosclerosis



b APOL1-associated glomerulosclerosis

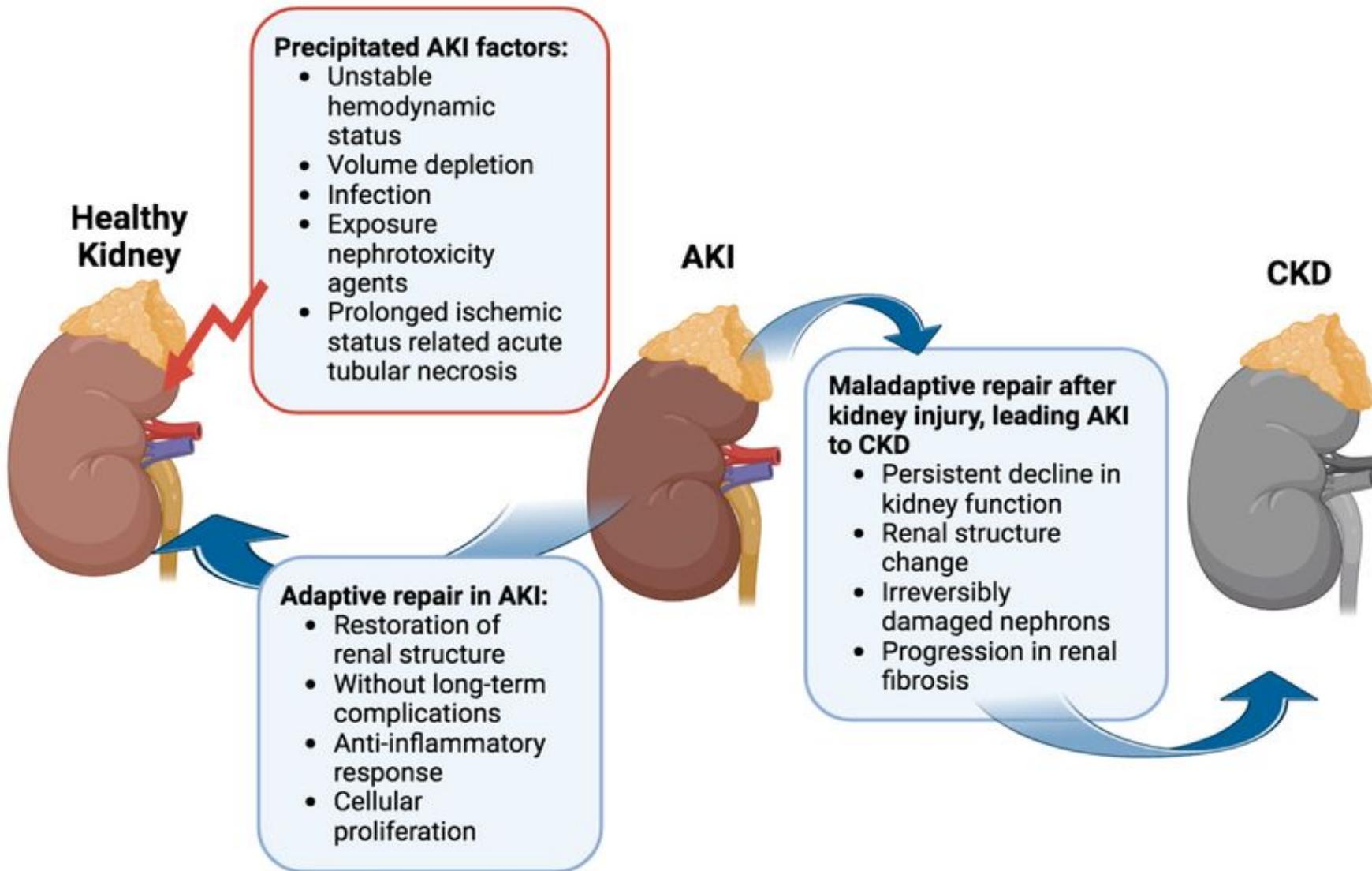


Nature Reviews | Nephrology



wellcome
connecting science

The link between AKI/AKD as a risk for CKD is largely underestimated



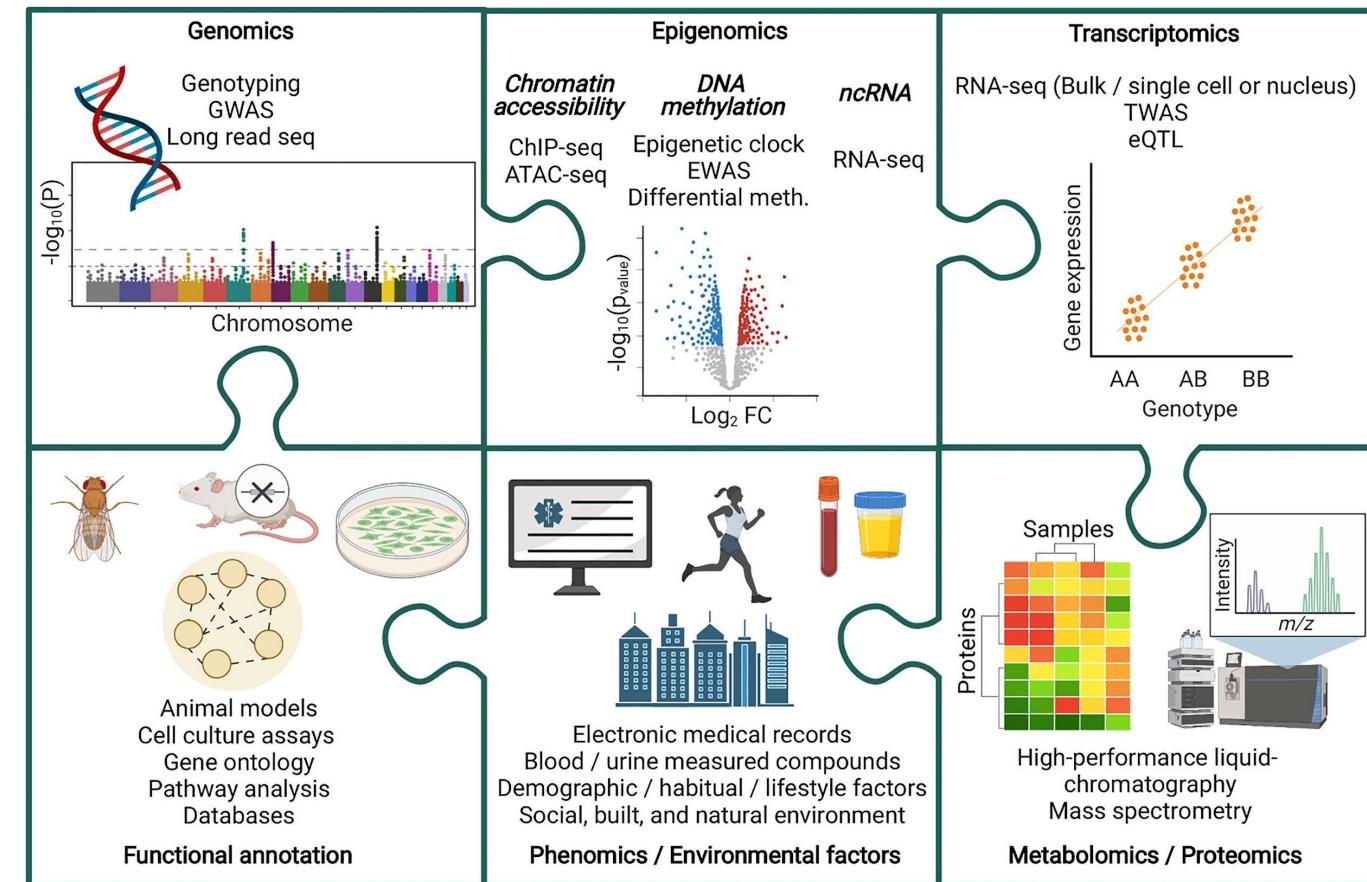
The evolutionary trade-off for a kidney-enabled transition from water to land was a finite nephron mass at birth, and no capacity for neonephrogenesis.

Thus, we have limited options in response to injury. These are hypertrophy and cellular regeneration.

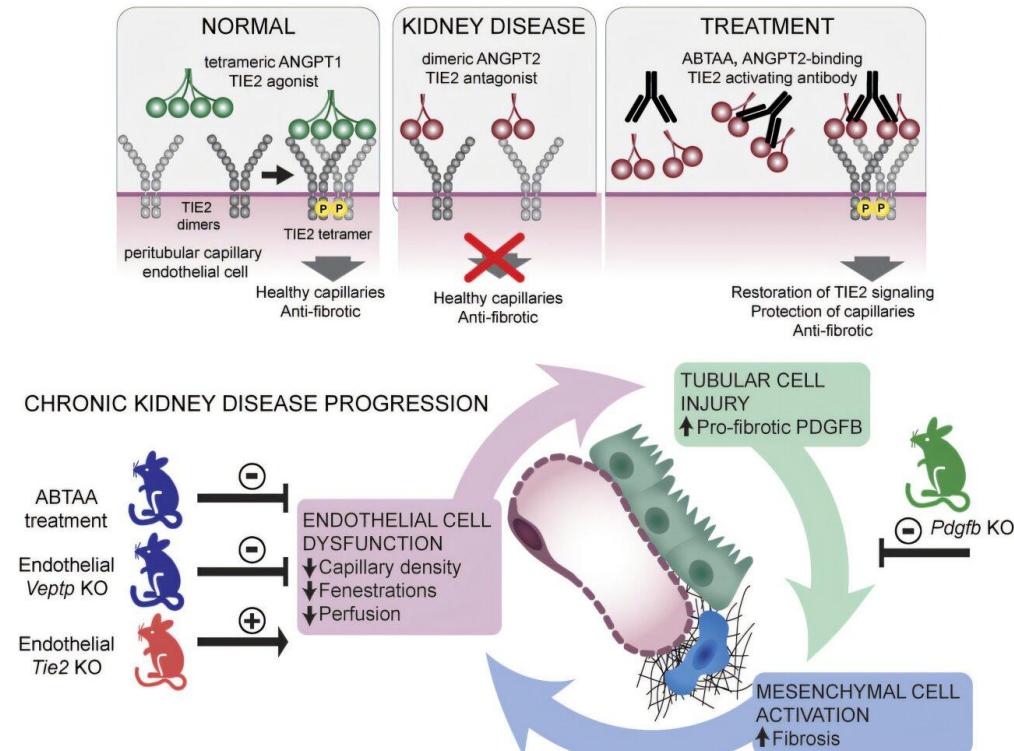
The final common pathway of maladaptive repair is fibrosis and scarring



Technological advances are giving us new ways to understand kidney disease and treat it



TIE2 activation by antibody-clustered endogenous angiopoietin-2 prevents capillary loss and fibrosis in progressive kidney disease



**Thank
you**

Q & A

