Chronic Kidney Disease 1

Advances in the diagnosis and detection of chronic kidney disease

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Chronic kidney disease affects 788–844 million adults worldwide and is projected to become the fifth leading cause of death by 2040. Global burden estimates remain limited by ascertainment bias and inadequate access to testing, particularly in low-income and middle-income countries. Advances in detection include improved estimation of glomerular filtration rate (GFR) using cystatin C and the recognition of albuminuria as a key marker for screening and risk stratification. Kidney biopsy is improving diagnostic accuracy and prognostic prediction, and multiomics approaches are advancing our understanding of disease mechanisms and hold promise for precision medicine. Advanced imaging and artificial intelligence are enabling non-invasive diagnostics and case detection. Population screening strategies using estimated GFR and albuminuria are increasingly cost-effective, particularly with the availability of novel therapies. Disease-specific prediction models support individualised risk stratification and clinical decision-making. However, inequitable access, limited validation across diverse populations, gaps in biomarker standardisation, and insufficient health-care system capacity constrain implementation globally. Addressing these challenges requires coordinated investment in diagnostics, workforce training, laboratory infrastructure, and health-care system strengthening alongside continued technological advancement.

Published **Online**
June 3, 2026
https://doi.org/10.1016/S0140-6736(26)00702-6

This is the first in a **Series** of three papers about chronic kidney disease. All papers in the Series are available at www.thelancet.com/series-do/chronic-kidney-disease.

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Introduction

Chronic kidney disease (CKD) was formally defined and classified in 2002 using estimated glomerular filtration rate (eGFR) strata, recognising higher risks of kidney failure and other adverse outcomes at lower eGFR.[1] Since then, a more nuanced grading system has evolved, designed to identify and risk-stratify CKD based on cause, GFR, and albuminuria criteria. We recognise that CKD is not a diagnosis, but rather a term recognising a spectrum of abnormalities in kidney structure or function that have implications for health.

In this Series paper, we briefly review diagnostic standards for CKD, identify gaps that exist in the detection and recording of CKD globally and their implications for accurate epidemiological forecasting. We highlight major advances in the understanding of CKD causes, including increased sophistication of diagnostic tests—from underlying genetics through enhancements in molecular phenotyping (using omics)—which has underscored inflammation as an important contributor to CKD progression and adverse outcomes. Central to these advances is determining aetiology through kidney biopsy and genetic testing, which has transitioned from specialised practice to a cornerstone of comprehensive CKD evaluation, enabling earlier, mechanism-aligned interventions that target specific disease pathways rather than treating CKD as a uniform syndrome. In this context, we discuss the roles and potential utility of biomarkers to detect and risk-stratify acute kidney disease and CKD, and we discuss advances in imaging and dynamic measurements of kidney structure and function that might improve understanding. Throughout, we distinguish tools with established clinical utility from those in active translational evaluation and experimental investigational approaches. We acknowledge key diagnostic breakthroughs and how these might inform treatment

Search strategy and selection criteria

We searched PubMed and Embase for articles published in English from database inception to Dec 31, 2025, using the following terms and keywords: "chronic kidney disease" OR "CKD" OR "kidney disease" OR "renal disease" in combination with "diagnosis" OR "detection" OR "screening" OR "biomarkers" OR "cystatin C" OR "albuminuria" OR "eGFR" OR "glomerular filtration rate" OR "risk prediction" OR "KFRE" OR "kidney biopsy" OR "genetics" OR "genetic testing" OR "multi-omics" OR "proteomics" OR "metabolomics" OR "imaging" OR "MRI" OR "artificial intelligence" OR "AI" OR "digital health" OR "machine learning" OR "precision medicine" OR "epidemiology" OR "prevalence" OR "global burden" OR "low and middle income countries" OR "LMIC" OR "inequity" OR "disparity" OR "access". Priority was given to systematic reviews, meta-analyses, and consensus statements published within the past 5 years, supplemented with seminal articles and original research published within the same 5-year window. The search was done by JSL and LZ with input from all authors. We reviewed articles resulting from these searches and their references and selected those relevant to advances in diagnosis and detection of CKD. We also reviewed the Kidney Disease: Improving Global Outcomes 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease and recent Global Burden of Disease reports to frame the content of this Series paper. The selection of articles was proposed by lead authors and reviewed by all coauthors, with disagreements resolved through consensus via email discussion.

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paradigms and the gaps that remain (panel). The second paper[2] in this Series examines sex differences in CKD biology and treatment response, and the third paper[3] discusses advances in CKD treatment.

Key messages

- Chronic kidney disease (CKD) affects 788–844 million adults worldwide and remains underdetected, particularly in low-income and middle-income countries where there is minimal access to basic kidney testing
- Kidney biopsy and genetic testing are enabling individualised diagnosis and mechanism-targeted treatment
- Population-wide CKD screening using estimated glomerular filtration rate and albuminuria is cost-effective, and can reduce lifetime risk of kidney replacement therapy and cardiovascular disease
- Validated risk prediction tools, including disease-specific models and AI-based approaches, transform CKD staging from descriptive classification into potentially actionable clinical decision making
- Diagnostic and technological advances risk widening global health inequities unless matched by investment in health system capacity, particularly in under-resourced settings

Epidemiology of CKD

The estimated burden of kidney diseases worldwide is 850 million people, with CKD affecting 8–10% (788–844 million) of the adult population.[4–7] By 2040, CKD will be the fifth leading cause of death worldwide, with alarming increases in age-standardised prevalence, particularly in low-income and middle-income countries (LMICs).[7,8] Thus, with accumulating data, WHO recognised in 2025 that CKD is a non-communicable disease requiring priority attention.[9] There are many drivers of CKD—including diabetes, hypertension, obesity, and cardiovascular disease—the incidences of which increase with age. The inter-relationship between kidney disease, cardiovascular disease, and metabolic conditions has led to the recognition of CKM (cardiovascular–kidney–metabolic) syndrome, first described in 2023, as a staging framework that captures the frequent coexistence and shared pathophysiology of these conditions, substantiated with ongoing data describing prevalence and associated outcomes, with the aim of facilitating integrated recognition and management.[3,4,10]

Despite the alarming numbers and rise in incidence and prevalence, most projections have been constructed from eGFR data in administrative data sets, with minimal data on albuminuria, single eGFR thresholds of 60 mL/min per 1·73 m² (without evidence of persistence

Panel: Advances and priorities in CKD diagnosis and detection

What has changed in the past decade?

- Improved glomerular filtration rate (GFR) estimation with cystatin C for diagnosis and accurate risk prediction
- Recognition of albuminuria as a key marker for screening and risk stratification
- Prediction models incorporating multiple aspects of diseases including biopsy data and imaging
- Improved imaging techniques for non-invasive assessment of kidney structure and function
- Improved understanding of biopsy value for diagnosis, prognosis, and molecular profiling
- Systems biology approach to discovery through multiomics integration
- International consortia for precision medicine, genetics, and understanding chronic kidney disease (CKD) in underserved populations
- Artificial intelligence (AI) and digital health technologies to support accessible CKD detection and monitoring, and to facilitate patient-centred care

What should clinicians and health systems do differently now?

For clinical practice

- Use cystatin C under recommended conditions
- Screen for albuminuria according to guidelines
- Apply recommended risk prediction models during nephrology referral, patient counselling, and kidney replacement therapy preparation
- Biopsy when diagnosis uncertain: enables disease-specific therapies and molecular profiling
- Point-of-care creatinine in setting where resources are scarce
- Raise awareness and promote education early in people with CKD or at high risk of CKD

For health system and policy

- Embed CKD detection within non-communicable disease prevention and management frameworks and clinical workflows
- Adopt standardised albuminuria screening protocols
- Ensure equitable access to diagnostic tools
- Invest in point-of-care testing infrastructure in low-resource settings
- Implement AI-enabled diagnostics in primary care settings with low nephrology access

What is not ready?

- Unclear clinical utility and standardisation of emerging biomarkers
- Validation of dynamic and static imaging for diagnosis and follow-up
- Multiomics approaches for routine clinical application
- Cost-effectiveness uncertainty for advanced diagnostics
- Generalisability, transparency, and implementation barriers of AI models
- Unified and consistent recognition within national policy frameworks of the importance of CKD

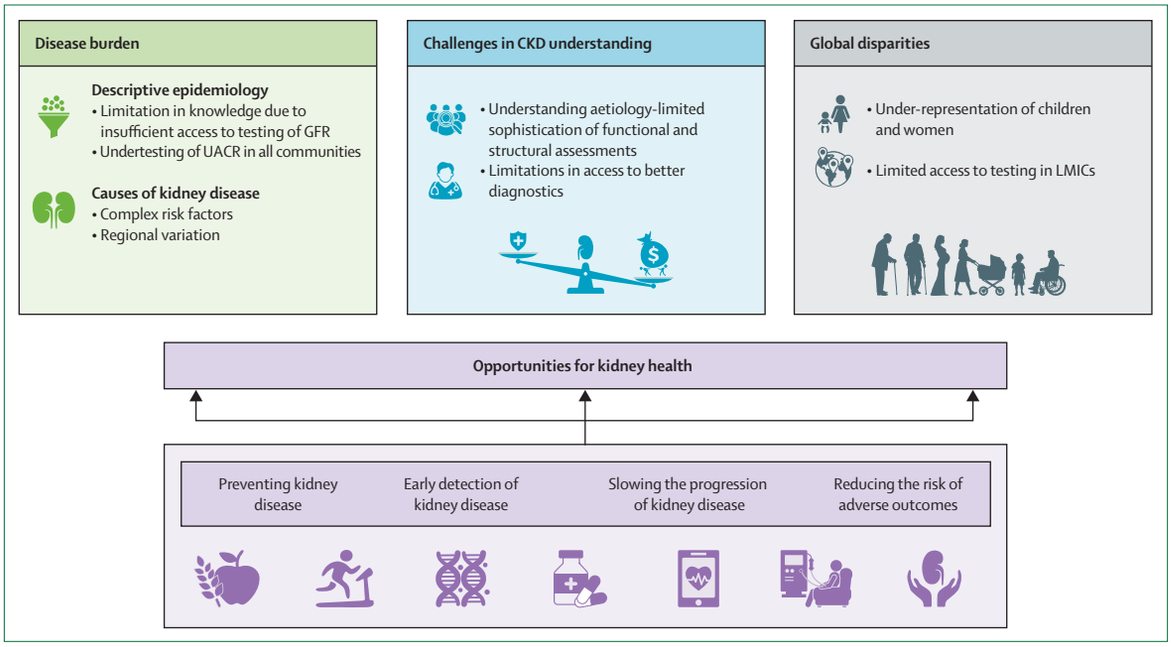

Figure 1: **Key barriers to and opportunities for kidney health**
CKD=chronic kidney disease. GFR=glomerular filtration rate. UACR=urinary albumin-to-creatinine ratio.

of the abnormality), and even fewer details on the cause of kidney disease (figure 1). The consistent sources of data include the Global Burden of Disease Study (GBD),[7] International Society of Nephrology Global Kidney Health Atlas,[11] and regional reports using laboratory data. Furthermore, the data only include patients who have had their creatinine measured (ascertainment bias), which leads to overestimation of CKD in high-resource settings,[12] and problematic underestimation of CKD in LMICs and specific populations, where creatinine testing is either not available, or might provide inaccurate estimates of GFR.[13] Selective reporting or publication of information from different regions contributes to lower understanding and awareness of CKD (eg, in Africa).[14]

The forecasts for CKD recognise the multifactorial nature of the condition but still cannot account for intercurrent events, which might increase the incidence of CKD. Life-course factors from prenatal through childhood substantially influence adult CKD risk. Prematurity and low birthweights lead to lower nephron mass, a known CKD risk.[15,16] Childhood kidney diseases—congenital anomalies, glomerulonephritis, or recurrent infections—might manifest decades later as adult CKD. Paediatric CKD diagnosis requires age-specific eGFR equations, different albuminuria thresholds, and recognition that normal paediatric creatinine might mask dysfunction; detailed guidance exists in the 2024 Kidney Disease Improving Global Outcomes (KDIGO) guidelines.[17] Reduced renal reserve increases vulnerability to environmental factors such as climate change, pollution, and occupational exposures. These stressors increase heat stress exposure and food and water insecurity, contributing to nutritional issues that further weaken resilience and growth, all of which can be compounded by infections (figure 2). In the absence of standardised testing and screening programmes, the ability to document the burden of CKD accurately in different regions remains limited and likely underestimated.[18]

Understanding aetiology and pathophysiology of CKD

In tandem with the increased appreciation of the burden of CKD, its effect on a diverse range of outcomes, foundational and translational science discoveries, and development of AI technologies, have led to a deeper understanding of systems biology and the mechanisms underlying both the initiation and progression of CKD (figure 3).

CKD encompasses a diverse set of aetiologies and pathophysiologies, with implications for different health outcomes in individuals.[19] The most common causes of CKD and kidney failure worldwide are diabetes, hypertension, and other non-communicable (inherited and immune) diseases,[7,20] but these do not account for the totality of deaths attributed to CKD.[7]

The trajectories and outcomes of individuals with CKD are influenced by both genetics and environment, which are important and measurable factors and constitute areas of active study. There are pockets in LMICs and high-income countries (HICs) with relatively higher rates of CKD caused by communicable diseases or environmental and occupational exposures. CKDu (CKD of uncertain aetiology) has been described in young adults in areas such as Sri Lanka, India, Central America, Ghana, Cameroon, and Mexico: each of these regions

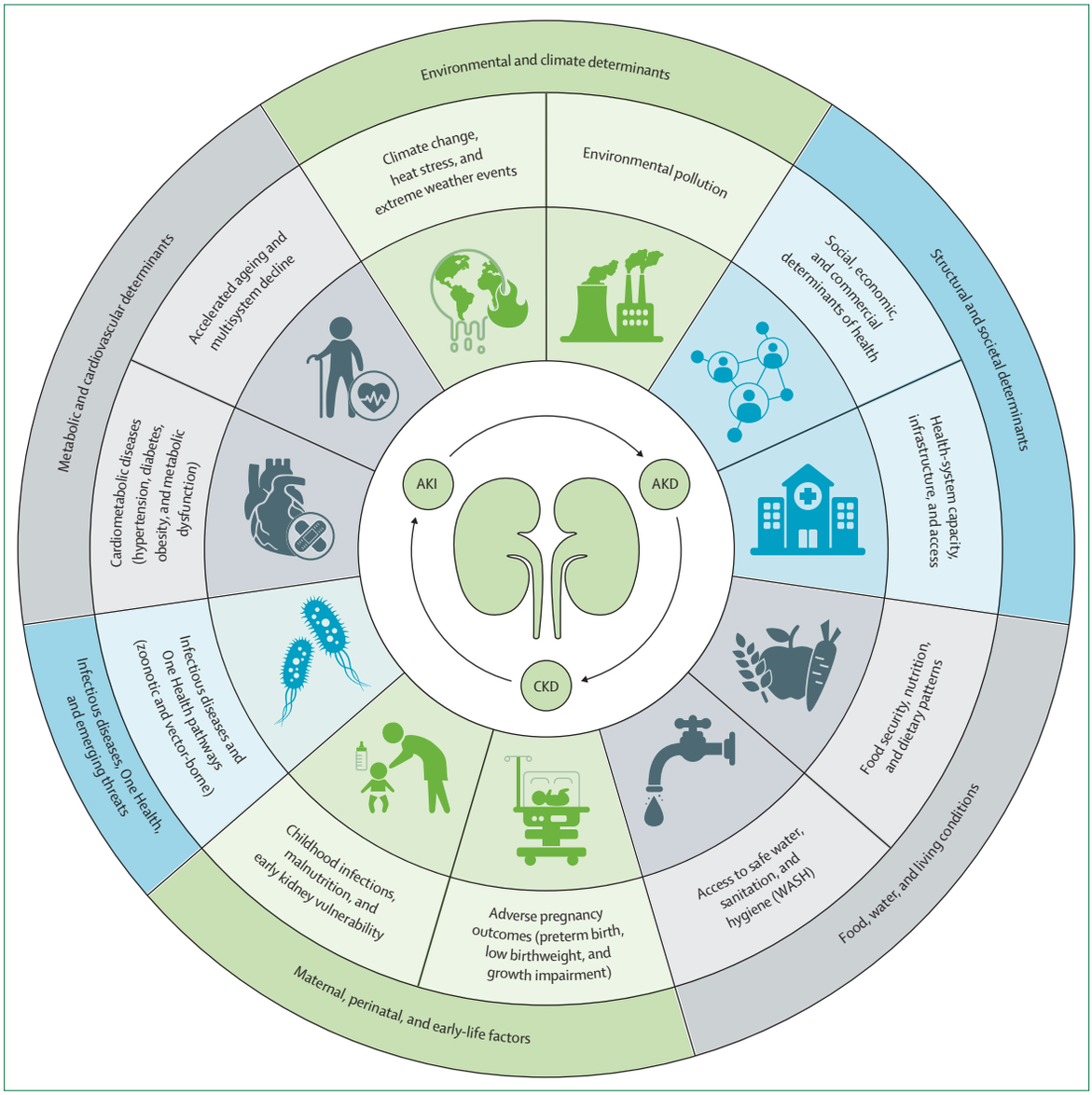

Figure 2: **Complex and inter-related social determinants contribute to the rising burden of kidney disease**
CKD=chronic kidney disease. AKI=acute kidney injury. AKD=acute kidney disease. WASH=water, sanitation, and hygiene.

have similar but not identical exposures to heat, chemical, air, and water pollutants, and similar findings (typically tubulointerstitial nephritis) on kidney biopsies, when obtained.[21] CKDu tends to affect young males, and is not commonly associated with other comorbidities such as diabetes or hypertension.[21]

The combination of variable access to testing and biopsy services, with under-resourced health-care systems, has made the study of CKDu challenging. Several initiatives, including the International Collaboration of CKDu Consortia (International Society of Nephrology),[22] the CKDu in Agricultural Communities research consortium (funded by National Institutes of Health),[23] Disadvantaged Populations eGFR Epidemiology Study,[24] and collaboration of countries (eg, Germany and Sri Lanka) might allow improved understanding of this condition, and promote new approaches to therapy. Recent genetic studies identified protective variants in the *OPCML* gene associated with reduced Mesoamerican nephropathy risk by improving tolerance to heat stress and dehydration,[25] exemplifying gene–environment interactions that drive CKD in agricultural workers exposed to extreme heat.

Beyond chronic conditions such as CKDu, the temporal spectrum between acute and chronic kidney disease has emerged as a crucial area requiring attention. Acute kidney disease (AKD)—kidney dysfunction persisting

7 days to 3 months following acute kidney injury (AKI)—represents a key transitional state offering opportunity for intervention before progression to CKD.[26] Despite the well established bidirectional relationships between AKI and CKD, AKD remains underappreciated in clinical practice and research. Current care pathways focus on short-term AKI management or long-term CKD care, with inadequate attention paid to this intermediate phase where early detection and mechanism-targeted interventions might prevent progression.

From diagnosis to precision profiling in CKD

Current guidance for diagnosis of CKD

The current definition of CKD includes individuals with abnormalities of kidney structure or function, present for a minimum of 3 months, with implications for health.[17] Abnormalities of structure can be detected with imaging or biopsies. Abnormalities of kidneys can be detected using simple blood and urine tests, including sustained eGFR less than 60 mL/min per 1·73 m², the presence of abnormal urine sediment, albuminuria, or proteinuria, or electrolyte abnormalities. The 3-month persistence requirement is frequently violated in real-world datasets, where CKD prevalence might be based on single measurements without confirmation of chronicity, leading to overestimation of disease burden in some settings and variability in reported incidence and prevalence estimates.[12,17] Diagnosis of CKD in children requires age-specific eGFR equations and albuminuria thresholds, as normal values vary with age.[17] In older adults, interpretation of reduced eGFR requires consideration of sarcopenia, which causes creatinine-based eGFR to overestimate kidney function.[17] Similarly, urinary albumin-to-creatinine ratio (UACR) could be falsely high due to falsely low creatinine in the denominator.[17] Although these criteria define the presence of CKD, classification and prognostication rely on the CGA system: cause, eGFR categories (G1–G5), and albuminuria categories (A1–A3), which together determine the risk of adverse outcomes.[17]

This simple staging system based on categories of eGFR and albuminuria, validated extensively across multiple cohorts, can be used to detect people at risk of adverse outcomes. The initial KDIGO heat maps—a colour-coded grid classifying CKD risk by eGFR and albuminuria categories, from green (low risk) to red (very high risk)—were primarily focused on detecting those at risk of kidney failure, but ongoing and extensive research has shown that these risks apply more broadly to numerous adverse health outcomes including AKI, cardiovascular disease, heart failure, peripheral vascular disease, all-cause hospitalisation, infections, and mortality.[27] Consideration of cause is often overlooked in both clinical care and population-based registries; however, it is essential to consider when making a CKD diagnosis, as the cause affects both prognosis and treatment strategies.[17]

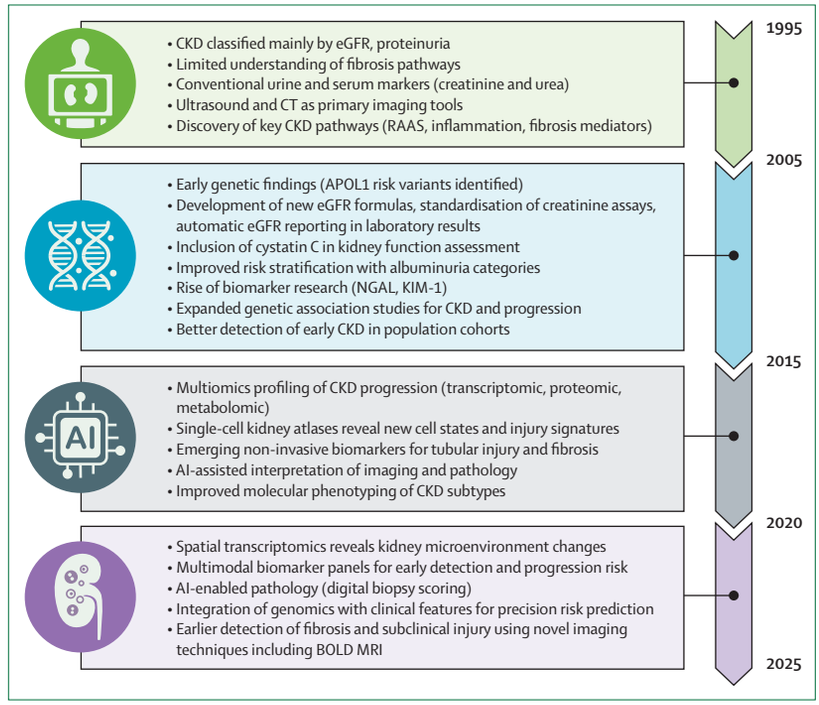

Figure 3: **Advances in CKD mechanistic understanding and diagnostics**
CKD=chronic kidney disease. eGFR=estimated glomerular filtration rate. RAAS=renin–angiotensin–aldosterone system. KIM-1=kidney injury molecule-1. AI=artificial intelligence. BOLD MRI=blood oxygen level-dependent MRI.

Advances in precision profiling in CKD

Improvements in laboratory biomarkers, better use of kidney biopsies, more accurate, accessible genetic profiling, and more sophisticated multiomics platforms and imaging techniques have substantially advanced our understanding of CKD biology.

Biomarkers

Although creatinine has been the primary filtration marker used for the diagnosis of CKD, extensive literature supports the use of cystatin C for a more accurate estimation of GFR, either alone (primarily in African populations)[13,28] or in combination with creatinine[13,29–32] (including in situations where there is a large discordance between eGFR based on creatinine alone and cystatin alone[29,31,32]). Cystatin C offers a stronger indicator of risk than eGFR based on creatinine alone,[27,28,33–36] although levels are influenced by non-GFR factors including inflammation, diabetes, and thyroid function.[17] In 2023, the CKD Prognosis Consortium described the value of GFR estimates with both creatinine and cystatin C in predicting ten outcomes, including cardiovascular and kidney events (CKD progression, kidney failure, and AKI) and mortality.[27]

As creatinine and cystatin C both have different non-GFR determinants, eGFR discordance between the different biomarkers is common. That discordance (of >30%) was most evident in inpatient monitoring (35%) compared with outpatients (11%) in a large individual patient

meta-analysis.[37] eGFR discordance has been described as a useful clinical indicator of muscle mass and sarcopenia,[38] and as a strong risk marker for a broad range of adverse clinical outcomes, including all-cause and cardiovascular mortality, atherosclerotic cardiovascular disease, heart failure, AKI, and kidney failure.[28,37,39]

Although cystatin C is not routinely available in all health-care systems, it has been part of clinical assessment in Sweden and Veteran Affairs institutions in the USA for over 10 years, and is increasingly available across National Health Service hospitals in the UK. Use of cystatin C is recommended in international guidance, particularly for individuals at extremes of body weight, amputees or patients with spinal cord injury, where reduced muscle mass and thus creatinine might be affected.[17] It is also recommended in patients with cancer, where large eGFR discordance is associated with higher rates of medication-associated adverse events,[40] and accurate GFR estimation is essential for dosing of drugs with a narrow therapeutic index.[41–43] Accurate GFR estimation is also crucial for dosing antibiotics, anticoagulants, antivirals, and cardiovascular medications, where misestimation can cause therapeutic failure or toxicity.[17,44]

The table highlights molecules that are candidates for use in clinical care and research, classified by clinical readiness: those in routine clinical use, those appropriate for selective or near-term clinical application, and those that remain research-grade. These include markers for tubular damage, glomerular damage, bone mineral disorders, and those that signal inflammation, fibrosis, podocytopathies, kidney, and cardiovascular health. Emerging studies on the value of urine exosomes (vesicles excreted by the kidney containing proteins and nucleic acids) suggest more insights might be gained from examination of urine. Specific biomarkers heralding processes such as inflammation (eg, C-reactive protein, IL-6, and TNF) and kidney tissue damage (kidney injury molecule-1, NGAL, and DKK3) are also evaluated for their clinical utility in both AKI and CKD.[45–48] As with all biomarkers, standardisation of assays across multiple platforms, understanding of variability across different

	Mechanism and function	Clinical relevance
Traditional biomarkers for routine clinical use		
Serum creatinine and eGFR	Creatinine is produced by muscles as a by-product of the breakdown of creatine; it is freely filtered in the glomerulus and in part reabsorbed by tubular structures	As GFR measurement is complex, multiple equations use creatinine levels as an indirect measure of GFR; accuracy is reduced in older patients and individuals with less or more muscle mass, obesity, exercise, diet, and AKI
Urine albumin-to-creatinine ratio	Most common proteins in the urine in kidney diseases; measured accurately even in normal levels	Values integrated in the CKD staging system; prognostic predictor of CKD risk; less prone to inaccuracies in measurement than urine protein assays
Cystatin C	Synthesised by all cells, freely filtered by the glomerulus with complete tubular reabsorption and catabolisation; no tubular secretion	Levels increase earlier and faster in AKI; equations combining serum creatinine and cystatin C give a more accurate estimate of GFR than creatinine-based equations alone; less influenced by muscle mass and gender than serum creatinine
Parathyroid hormone	Established marker of secondary hyperparathyroidism, secreted by the parathyroid gland	A predictor of CKD progression and cardiovascular morbidity and mortality
Emerging biomarkers for selective or near-term use		
β2M	Produced by all nucleated cells (MHC class 1 molecule); progressively accumulates as GFR declines	Strong predictor of kidney failure and all-cause mortality; GFR equations combining BTP and β2M predict kidney failure more accurately than traditional markers; levels are less influenced by muscle mass and gender than serum creatinine
BTP	Mainly produced by epithelial cells in the choroid plexus; catalyst in the prostaglandin pathway	Increased urinary and plasma levels correlate with serum creatinine and cystatin C levels; GFR equations combining BTP and β2M predict kidney failure more accurately than traditional markers; levels are less influenced by muscle mass and gender than serum creatinine
N-acetyl-α-D-glucosaminidase	Enzyme indicating tubular injury	Urinary levels as a marker of systemic inflammation and proteinuria
Uromodulin (Tamm–Horsfall protein)	Exclusively produced in the tubular cells; protective function in UTI; reflects tubular damage and nephron mass	Urinary and serum levels predict CKD progression; strong predictive value between serum uromodulin levels and eGFR
FGF23	Mainly produced by osteocytes and osteoblasts; major role in bone metabolism (phosphate metabolism)	Elevated early in CKD and is a major predictor of CKD progression and cardiovascular mortality
NGAL	Released during tubular injury and inflammation, produced by inflammatory cells in the liver and kidneys	Early marker of AKI and has prognostic value in CKD progression
Kidney injury molecule 1	Marker of proximal tubular injury	Mucin domain elevated in urine and plasma in AKI and CKD; correlates with urine albumin-to-creatinine ratio, inflammation, and fibrosis in the kidney; potential therapeutic target
Liver-type fatty acid-binding protein	Produced by liver and proximal tubular cells	Increased urinary levels are linked with tubulo-interstitial damage in AKI and is also associated with CKD progression
IGFBP7 and TIMP-2	IGFBP7 is secreted by proximal tubule cells, and TIMP-2 by distal tubule cells; tubular stress protein expressed with ongoing injury	Often checked together (Nephrocheck); good predictive value in the first 12 h of AKI
GDF-15	Produced in cardiac myocytes and in kidneys	Associated with progression of CKD and adverse cardiovascular outcomes; key biomarker in haemodialysis patients
Galectin-3	Produced in epithelial cells, macrophages and fibroblasts	Raised levels in CKD; predicts rapid decline in kidney function and cardiovascular mortality
Urinary soluble CD163	Shed from activated macrophages infiltrating the kidney; reflects local intrarenal macrophage activation and inflammation	Urinary levels indicate active glomerular inflammation; useful non-invasive marker of disease activity in immune-mediated kidney diseases (eg, lupus nephritis, ANCA-associated vasculitis)

(Table continues on next page)

	Mechanism and function	Clinical relevance
(Continued from previous page)		
Research-grade biomarkers		
Klotho	Reno-protective and anti-ageing molecule; predominantly expressed in the kidneys	Deficiency leads to CKD progression; positive correlation between serum and urinary levels and eGFR; potential therapeutic target
DKK3	Tubular stress protein expressed with ongoing injury	Urinary levels linked to CKD progression and proteinuria; marker indicating poor prognosis
Sclerostin	Secreted by osteocytes; inhibits bone formation and indirectly activates osteoclast activity	High levels are correlated with low GFR and a marker of CKD progression
NLRP3 inflammasome	Activates caspase-1, which cleaves pro-inflammatory cytokines (ie, IL-1β and IL-18); promotes inflammation and fibrosis	Predicts CKD progression
TNF receptors (1 and 2)	Circulating receptors of TNF, activated by binding of circulating TNF	Early biomarkers in different kidney diseases and predictive of progression in CKD and all-cause mortality
Calprotectin	Released from myeloid cells; acute phase reactant	Predictor of new-onset CKD and is a marker of vascular calcification and increased cardiovascular mortality in patients with CKD; also increased in immune-mediated kidney diseases
Ficolins	Part of the lectin pathway of the complement system	Elevated levels associated with CKD progression, poor allograft function, and increased risk of infectious complications
Soluble UPAR	Expressed at low levels in endothelial cells, podocytes, and immunologically active cells (monocytes and lymphocytes)	High levels are predictive of AKI and is also predictive of progressive kidney function decline and development of CKD
TGF-β	Cytokine involved in tissue inflammation and fibrosis	Blood levels associated with progressive kidney fibrosis and decline in function therapeutic target
Podocyte markers (podocalyxin, podocin, and nephrin)	Markers of podocyte injury in proteinuric kidney diseases	Podocalyxin urinary levels are raised in immune-mediated kidney diseases and have a prognostic value; urinary podocyte-derived markers—including podocin, podocalyxin, and nephrin—have been investigated as biomarkers for pre-eclampsia, with mixed evidence on their comparative diagnostic accuracy; nephrinuria is a biomarker in early diagnosis of proteinuric kidney disease
Testican-2	Released from podocytes	Higher levels indicate higher GFR; positive correlation with kidney health
Urinary exosomes	Vesicles excreted by the kidney that contain proteins and nucleic acids; these excreted molecules reflect the pathophysiological state of the kidney	Multiple miRNAs and other molecules (complement factor 5 and 9, ceruloplasmin, CD36, C-megalin, etc) are upregulated in various kidney disease; needs further characterisation for future clinical application

ANCA=antineutrophil cytoplasmic antibody. AKI=acute kidney injury. BTP=β trace protein. CKD=chronic kidney disease. eGFR=estimated glomerular filtration rate. miRNA=microRNA (ribonucleic acid). UTI=urinary tract infection.

Table: **Biomarkers in CKD: from routine clinical use to research frontiers**

populations, age ranges, and sex, as well as reproducibility, require extensive study before uptake into clinical practice can be recommended. Furthermore, panels of biomarkers are increasingly recognised in all areas of medicine as more informative than single biomarkers alone, given the complexity of physiology being captured. It is beyond the scope of this Series paper to go into details of each of these biomarkers, and the list continues to emerge in both clinical care and in the research arena. The availability of many of these tests will be limited by cost in many contexts, especially LMICs.

Biopsies

Biopsies offer both diagnostic and prognostic value for people with CKD, even when clinicians believe that the underlying aetiology is evident. In the Kidney Precision Medicine Project,[49] biopsies are conducted in people with CKD and diabetes or hypertension, and in those with AKI, using rigorous research protocols.[50] Important findings to date include the acceptance and support of patients for what is seen as an invasive test, as knowing the diagnosis is believed to be of benefit, and the finding that 35% of people with diabetes receive alternative or additional diagnoses when a biopsy is done.[51] In addition to this improved diagnostic accuracy, the Kidney Precision Medicine Project team interrogates tissue to better understand pathophysiology, molecular pathways, and identify future targets for therapy. From a prognostic perspective, biopsies are valuable in glomerular diseases and have helped to characterise IgA nephropathy disease phenotypes, tailoring treatments according to where an individual lies on a continuum from active glomerular inflammation to chronic fibrotic disease.[52] Pathological findings are also being incorporated into predictive scores for IgA nephropathy[53] and antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis,[54] after kidney transplantation,[55] and used in some cases for enrolment into clinical trials (eg, chimeric antigen receptor T-cell therapy in patients with refractory lupus nephritis [NCT06897930]).

Genetics

As genetic profiling becomes more accessible and cost-effective, genetic testing in CKD is transitioning from specialist practice toward broader clinical application, although its readiness varies considerably by indication.[56,57] Integrated genomic data from polygenic and monogenic risk scores, and family-based risk factors might have a role

in disease prevention, identifying individuals at high risk of CKD or its risk factors and providing personalised clinical recommendations.[56] We can now target testing for suspected inherited conditions—including identifying the *APOL1* genotype and high-risk mutations for polycystic kidney disease—and can incorporate these mutations into prognostic scoring systems (eg, the PROPKD score).[58] Genetic testing in diverse CKD cohorts yields substantial value: a systematic review and meta-analysis of 60 studies with 10 107 adults with CKD revealed an overall diagnostic yield of 40% (95% CI 33–46%), which varied by CKD subtype, with the highest yield of 62% in cystic kidney disease.[59] With positive genetic test results, reclassification of disease occurred in 17% of individuals.[59] Multiple studies showed clinical benefits of genetic testing including cascade testing for family members and treatment changes.[59–61] Patients with CKD—often with substantial comorbidities and wide variability in response to treatments[3]—are likely to benefit greatly from advances in pharmacogenomics, where genetic profiling can be used to understand expected treatment response and propensity to adverse events at an individual level. Actualising the full clinical value of pharmacogenomics is limited by low availability and relatively high cost of testing, uncertainty of clinical utility and cost-effectiveness, minimal education among health-care professionals, and a combination of legal, ethical, and social implications.[57]

Multiomics: genomics, transcriptomics, proteomics, and metabolomics to improve understanding and inform care

Multiomics technologies have substantially advanced CKD research and represent a key step toward precision nephrology, although their current application remains largely investigational—informing disease mechanisms and identifying therapeutic targets rather than guiding routine clinical decisions. A key gap in CKD diagnostics is the inability to predict individual treatment response or identify specific disease mechanisms driving progression in patients who appear clinically similar. Multiomics addresses this gap by enabling molecular subtyping beyond clinical phenotypes.[62,63] Genomics identifies genetic predispositions; transcriptomics identifies gene regulatory pathways; proteomics identifies the key proteins; and metabolomics describes biochemical pathways that reflect kidney functions. Integration of these modalities, as illustrated by the earlier examples, enhanced by spatial profiling, is providing deeper insights into disease mechanisms and risk stratification, although translation into personalised therapies remains largely investigational. Although primarily obtained from non-invasive samples of blood or urine, the availability of tissue-based omics from kidney biopsies and the possibility to integrate rich clinical, pathological, and genetic data, puts patients with CKD in a unique position to benefit from advances in these technologies.[64] Single-cell multiomics and spatial profiling reveal four distinct kidney microenvironments (glomerular, immune, tubule, and fibrotic). Omics signatures in the fibrotic microenvironment classify kidney fibrosis and predict future CKD progression, and identify potential therapeutic targets.[62,63,65] In diabetic kidney disease, multiomics have improved the understanding of the pathophysiology of the disease, identified promising biomarkers, elucidated mechanisms of action of existing therapeutics, and identified new treatment targets.[66–68] It is beyond the scope of this Series paper to go into more depth on this subject, but we highlight the value of the emerging field on our ability to both understand important disease mechanisms in progression and injury, and to target specific therapeutic possibilities.[69–71]

Imaging techniques: static and dynamic

Established imaging modalities—ultrasound, CT, and MRI—are in routine clinical use to determine size, symmetry, and presence of parenchymal abnormalities, and are widely available, including via portable ultrasound in remote settings. In addition, nuclear renograms can be used to assess differential renal function, detect perfusion abnormalities, and help identify renal vascular disease; although they provide qualitative estimates of relative renal clearance, they do not provide a calibrated measure of absolute GFR.[72–74] These tools represent the current standard of care in kidney imaging.

Beyond established modalities, the increasing sophistication and evolution of MRI techniques now permit the evaluation of oxygenation, blood flow, and fibrosis, which has not been routinely available in clinical care. Multiparametric MRI combines different sequences; diffusion weighted-MRI, blood oxygen level dependent-MRI and magnetic resonance relaxometry offer the opportunity to improve understanding of disease states and responsiveness to therapies. These techniques provide sensitive methods for assessing perfusion, oxygenation, oedema, or fibrosis without the need for contrast injection. Improved understanding of physiology and pathophysiology, characterising renal lesions, and assessing responsiveness to different therapeutic agents might aid in more individualised decision making. The value of standardised and validated methods is under evaluation for both research and clinical purposes.[75]

PET scans have been used in oncology extensively and offer an opportunity to assess viable or metabolically active tissue. The application of this technology to kidney diseases in both research and care has been described, but remains limited.[76] PET scans delineate a precise structural and functional picture, which might be helpful in early detection and tailored treatment based on the severity of various kidney diseases, especially those with an inflammatory component. Different tracers can be used to identify the source, extent, and progression of conditions such as pyelonephritis, lupus nephritis, IgA nephropathy, and even diabetic kidney disease. Cost and availability of specific tracers and equipment limit the utility in clinical practice currently.

Dynamic testing of renal functional reserve is a promising method with research and clinical applications.[77] This is a measure of change in GFR from a baseline state to a peak value, when the kidney is stimulated by various exogenous stressors such as amino acids, protein loading (intravenous or oral), and dopamine. Although there is a strong physiological basis for the test, and the presence, absence, or amplitude of the renal functional reserve capacity should have potential to identify prognostically those with kidney dysfunction, the renal functional reserve is not used routinely in clinical practice. There are several challenges including lack of consensus on standardisation of methods to stimulate, and to measure GFR. The ability to determine organ function reserve has proven valuable in other disciplines, including cardiology and respirology, and is likely to be beneficial in numerous clinical situations. Ongoing efforts to standardise testing and to apply the results—for example, to living donor assessments, those with AKI or CKD—might lead to a change in uptake.[78]

Digital health technology and AI for diagnostics

Rapid evolution of digital health technology, including health information technology, AI, digitally enabled therapeutics, telehealth and virtual care, mobile health applications, and wearable sensors and devices,[79] creates an exciting new platform to innovate and advance precision kidney health.[80] For non-invasive diagnostics and monitoring, smartphone-based advances allow for home urine testing for albuminuria,[81] and automated digital microscopy of urine sediment closely replicates manual microscopy.[82] AI-supported interrogation of retinal images or electrocardiograms can support identification of individuals with CKD or at risk of CKD during routine health-care encounters; smartphone-based approaches in particular hold promise as scalable, low-cost screening tools applicable across resource settings.[83,84] Deep learning combined with radiomics in kidney ultrasound can non-invasively identify glomerular disease in children, supporting acute management and timely referral.[85] These approaches are in varying stages of translational development and have not yet completed the external validation required for routine clinical deployment.

Identifying CKD through screening

Beyond targeted testing in high-risk populations, efforts have been made to understand the balance of benefits of early CKD identification and initiation of guideline-directed medical therapies against the costs of population-wide eGFR and UACR screening.[3,86,87]

Studies in Spain, China, India, Mexico, Senegal, and the USA support the use of CKD case finding, using albuminuria, in high risk groups.[88–90] With the advent of novel therapies, particularly SGLT2 inhibitors, population-wide screening has become increasingly cost-effective. A more recent study from the USA showed that, under the assumption of adding SGLT2 inhibitors to renin–angiotensin system inhibitors, a one-time population-based screening for albuminuria at age 55 years increased quality-adjusted life-years, but screening every 5 years increased quality-adjusted life years more substantially and the lifetime risk of kidney replacement therapy decreased from 2·3% to 1·9%. This reduction in lifetime risk would prevent approximately 658 000 cases of kidney replacement therapy among individuals aged 35–75 years in the USA.[89] Importantly, cost-effectiveness extends beyond HICs: a study from China—representing one of the few analyses from LMICs—showed that annual screening in the general population aged 45 years and older was cost-effective, with a relative reduction of 8·2% for cardiovascular disease and 17·8% for kidney replacement therapy.[91] These findings are corroborated by a multinational microsimulation across 31 countries showing that screening general populations aged 45 years and older with combined eGFR and albuminuria testing was cost-effective in all countries studied, increasing CKD diagnosis rates from 459 to 14 392 per 100 000 persons eligible.[92] Systematic reviews confirm that screening is consistently cost-effective in populations at high risk (eg, diabetes or hypertension) and in general populations when CKD prevalence is sufficient, and screening costs are low, with treatment effectiveness being the most influential parameter.[93] Beyond slowing progression, early detection of CKD—particularly at the albuminuria stage before substantial eGFR decline—increases the likelihood of achieving disease remission, defined as normalisation of albuminuria with preserved kidney function or eGFR slopes <1 mL/min per 1·73 m² per year, especially when guideline-directed combination therapies are implemented promptly.[94] These data suggest that with novel therapies and accessible low-cost screening, population-wide screening within specific age groups (≥45–55 years) warrants stronger consideration in both high-income and middle-income settings, although implementation requires consideration of local CKD prevalence, health-care infrastructure, and treatment access.

Measures to detect kidney disease should ideally be widely accessible and affordable. Global implementation of CKD screening could be facilitated by a tiered approach that begins with accessible screening tools, such as dipstick urinalysis or point-of-care measurement of serum creatinine, to increase awareness and identify individuals requiring confirmatory testing with UACR and repeated eGFR measurements, particularly in remote regions and LMICs.[86] A study using three population-based surveys in India revealed that prediction models of CKD could be narrowed down to patient characteristics, measurement of blood pressure, and urinalysis of only albumin and glucose, without substantial reductions in sensitivity and specificity.[88] There remain ongoing discussions as to the quality of screening tools, recognising that methods to detect proteinuria vary substantially, thus affecting their sensitivity, specificity, and overall reliability.[90] The implications of this variability affect estimates of detection, and thus the benefits of screening, thus calling for

standardised screening approaches as recommended in the KDIGO guideline.[17]

In the International Society of Nephrology's Kidney Disease Data Center study, standardised screening was performed in 75 058 participants (mean age 44·5 years) and found an overall prevalence of CKD of 14·3%, with standardised screening markedly improving detection compared with non-standardised approaches.[95] Albuminuria-based screening consistently detects most individuals with CKD, irrespective of eGFR, and is increasingly advocated as a sensitive tool for screening. Given the potential low cost of this test, standardised albuminuria screening across high-risk and general population settings might be a cost-effective route to detect CKD.

Population-based research underlined that a urine dipstick analysis of proteinuria had a poor sensitivity and high false-discovery rate for UACR less than 30 mg/g (>3 mg/mmol),[96] showing that UACR is the preferred definitive test. However, in settings without laboratory capacity for quantitative UACR testing, dipstick screening can identify individuals who require further evaluation, with positive results confirmed by UACR when accessible.[96] Alternative methods to detect albuminuria might also be useful and are under investigation, with recognition that there is likely a need for country-specific approaches.[97,98]

Risk prediction for adverse outcomes

There has been a substantial evolution in risk prediction tools for adverse kidney and cardiovascular outcomes using readily available clinical information, heralding a new era in nephrology. Validated tools transform CKD staging from descriptive classification into actionable clinical decision making by estimating individualised risk and enabling appropriate triage and timely intervention.

CKD progression and kidney failure

The Kidney Failure Risk Equation (KFRE) was developed, validated, and recalibrated to multiple international settings to estimate 2-year and 5-year risk of kidney failure, time horizons that are meaningful to patients and health-care professionals. Requiring only four key parameters for the primary model (age, sex, eGFR, and albuminuria), KFRE has transformed and individualised risk stratification for kidney failure. KFRE is recommended in international guidance to support risk stratification for kidney failure, to guide referrals from primary care providers to nephrology, for patient counselling, and to prioritise preparation for kidney replacement therapy.[17]

The utility of KFRE in patients with multimorbidity and frailty has been underexplored.[99] KFRE tends to overestimate risk of kidney failure among these individuals who have high competing mortality risk.[100] This effect can be addressed by refining tools to account for competing risks,[100] or using alternative tools (such as KDPredict) where competing risks are predicted simultaneously.[101]

Individual risk prediction algorithms have been developed and validated to predict risk in individuals when the specific aetiology is known, such as glomerular or multisystem diseases: these include IgA nephropathy (International IgAN Prediction Tool)[53] and kidney failure in ANCA-associated vasculitis (ANCA Kidney Risk Score),[54] and using other parameters including imaging, clinical features and genetic information for those with polycystic kidney disease.[58,102]

Cardiovascular disease prediction

Earlier cardiovascular risk prediction tools (such as the Pooled Cohort Equations in North America; Systematic Coronary Risk Evaluation tools in Europe) did not include eGFR or albuminuria in risk stratification, although individuals with CKD were considered at high or very high cardiovascular risk.[103–105]

Evolving cardiovascular risk prediction tools now commonly integrate CKD parameters for the prediction of adverse outcomes. Most include eGFR but not UACR as important factors in predicting events. The American Heart Association Predicting Risk of Cardiovascular Disease Events equations estimate 10-year and 30-year risks for total cardiovascular disease (including atherosclerotic cardiovascular disease and heart failure).[106] The European Society of Cardiology has a suite of tools to predict primary atherosclerotic cardiovascular disease in patients with and without diabetes and incident heart failure in patients with and without pre-existing atherosclerotic cardiovascular disease, and to predict outcomes among patients with heart failure and preserved ejection fraction.[107–110] The CKD Patch—a simple multiplier derived from eGFR and UACR categories that can be applied on top of estimates from existing risk tools—offers a mechanism to refine and personalise risk estimates from previous risk prediction tools developed for the prediction of primary atherosclerotic cardiovascular disease with eGFR and UACR categories to apply a multiplication factor on top of existing risk estimates.[111,112] At the time of writing, the CKD Patch has not been widely adopted in clinical guidance or clinical practice.

Despite the recognition of albuminuria as an important predictor of outcomes, most cardiovascular risk prediction algorithms only include creatinine-based eGFR, likely due to familiarity, widespread availability, and low cost. Data are accumulating showing that albuminuria[27,111] and cystatin C —now recommended in guidelines for defined clinical indications—are better discriminators of cardiovascular disease risk,[27,33,113] whereas proteomic approaches show early promise but remain investigational and are discussed in more detail in the third paper of this Series.[3,27,33,113] Development, validation, and calibration to other geographical areas (such as LMICs) and populations (including children), are also limited and uncertain. Efforts have been made to develop, validate, and recalibrate cardiovascular disease risk prediction algorithms for LMICs, but these models do not account for the large,

growing, and often undetected burden of CKD in these regions.[7,114]

Digital health technology and AI for risk prediction

AI-based risk prediction tools analyse routinely collected data to identify individuals at risk, and several have been evaluated in clinical settings. Klinrisk uses AI technology to detect CKD and estimate the risk of CKD progression with routinely collected laboratory data, producing individualised risk estimates and recommendations based on current clinical guidance.[115] KidneyIntelX is a similar AI-based model that detects the risk of CKD progression among people with early-stage diabetic kidney disease.[115] Machine learning models for conditions such as IgA nephropathy can predict outcomes, with the potential to outperform traditional methods.[116]

Although digital health technology offers scalable and cost-effective solutions for both high-resource and low-resource settings, key challenges remain before clinical-grade deployment can be achieved. AI models require rigorous external validation across diverse populations and settings, with demonstrated fairness and calibration to avoid perpetuating or amplifying existing health-care disparities.[117] Equally important is the recognition that prediction tools without implementable care pathways could increase clinical noise rather than improve outcomes, and ongoing monitoring for calibration drift is essential as patient populations and practice patterns evolve.[118] Governance frameworks, clear accountability structures, and integration with actionable clinical workflows are prerequisites—not afterthoughts—for responsible digital health technology implementation in nephrology.[119]

Substantial gains and remaining gaps

Great strides have been made in understanding the pathophysiology of specific conditions, and in final common pathways for kidney diseases. The role of metabolic, inflammatory, and haemodynamic processes in initiation and perpetuation of injury at the tissue level is now increasingly well described and continues to be investigated. New molecules and specific mediators of processes are being discovered regularly, promising to enhance the armamentarium available for individuals, and to improve the precision with which we can identify disease, and customise therapies (figure 4; also discussed in the third Series paper).[3,120–122] A key translational consideration is that clinical readiness across these advances is not uniform: some tools—guideline-endorsed screening with UACR and eGFR, KFRE-based risk stratification, and cystatin C in certain populations—are ready for broader implementation now, whereas others—multiomics, multiparametric MRI, and most AI-based diagnostics—require validation pipelines and governance frameworks before routine clinical adoption.

Advances in CKD diagnostics and technology will not reach all populations equally and risk widening health-care disparities.[123] Implementation of diagnostic advances

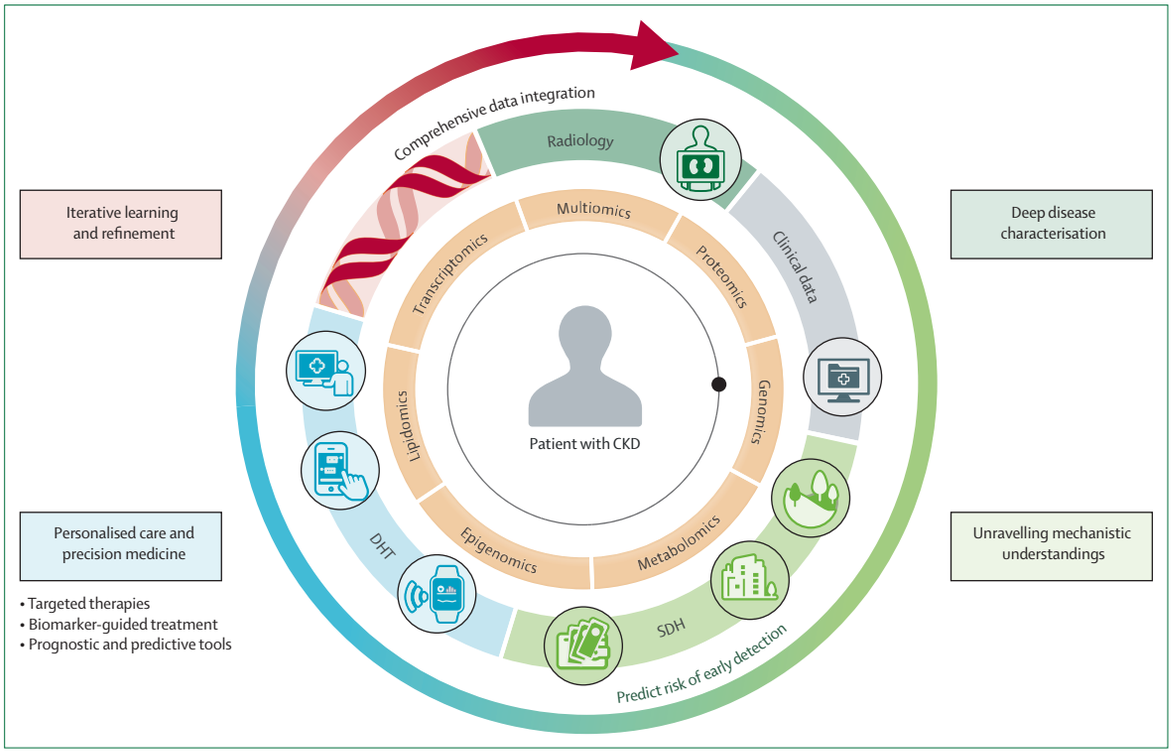

Figure 4: **Integrative, patient-centred framework for advancing CKD care**
CKD=chronic kidney disease. DHT=digital health technology. SDH=social determinants of health.

requires health-care system capacity beyond technology. In HICs, integration demands laboratory infrastructure, electronic health record compatibility, and workflow redesign. In LMICs, fundamental barriers include poor laboratory capacity, lack of trained personnel, and absence of basic health information systems—many community settings lack even creatinine testing. Bridging these gaps requires investment in workforce training, laboratory networks, and health system strengthening alongside technology transfer.[18,123] In low-resource settings, some developments are incredibly challenging to implement. Improvements in access to precision imaging (eg, MRI) would require overcoming issues related to funding, technology, infrastructure, and a lack of relevant clinical training.[123] Widespread genetic testing for gene variants such as *APOL1* requires implementation support for disadvantaged communities in the form of better resources, methodologies and incentives.[124] However, remote areas and low-resource settings can benefit more from point-of-care testing, which improves availability, accuracy, and clinical decision making for traditional (eg, creatinine[125] and urinary dipstick[88]) and emerging biomarkers (cystatin C[126] and NGAL[127]). There are concerns that digital health technology, with its incumbent benefits, might be confined to HICs, widening the inequities gap; however, others suggest that digital health technology could be "levelling the playing field,"[128] benefiting vulnerable populations and enhancing global precision. Given the increasingly accessible and affordable mobile applications, digital health technology might provide pragmatic, tangible solutions in settings where poor access to a highly skilled workforce and expensive diagnostics are likely to persist. Beyond technological and diagnostic advances, the limited capacity to confirm diagnoses and deliver therapies represents a crucial implementation bottleneck, particularly in LMICs where the nephrology workforce, confirmatory testing, and guideline-directed therapies remain minimal.[18,123] Increasing awareness of CKD among health-care professionals, patients, and the general public is also essential for improving kidney health outcomes. Investment in awareness, education, and health system capacity could help translate advances in diagnostics and therapeutics into improved care and outcomes across diverse populations and resource settings.

Conclusion

The current assessment of CKD burden at the population level remains hindered by a reliance on imprecise or missing laboratory measurements, and in some cases, poor access to those tests. On an individual basis, once CKD is identified, understanding of the aetiology of CKD based on laboratory biomarkers, biopsies, genetics, multiomics platforms, and imaging, is becoming increasingly sophisticated. Population-wide screening of eGFR and albuminuria is increasingly cost-effective and, combined with novel therapies, leads to meaningful reductions in lifetime risk of kidney failure and cardiovascular disease. Detection strategies should integrate not only diagnostic markers but also validated risk prediction tools that enable personalised clinical pathways, optimise resource allocation, and guide the timing of interventions based on individualised probabilities of progression rather than staging alone. The use of digital devices for monitoring and feedback, and the synthesis of all information available with AI, means that we will be in a better position to predict risk, and diagnose and treat individuals and populations accordingly over time. Translating these advances into clinical benefit requires explicit recognition of readiness tiers, rather than treating them as a uniform frontier.

Several gaps in current knowledge and practice remain, including standardisation and access to sophisticated testing, and a lack of understanding of the differential ranges, thresholds, sensitivities, and specificities of these tools by age, sex and geography. These gaps are further delineated in the second paper of this Series, where we offer an in-depth discussion on sex differences in biological processes that affect development and progression of CKD and responsiveness to treatment; and in the third paper, we discuss successful treatments, informed by advances in understanding biological processes, and the need for ongoing evidence generation to better understand best therapies and responsiveness for different subgroups of people living with CKD.

Contributors

JSL and AL conceptualised the Series theme and invited the authors. JSL, LZ, and AL conceptualised this paper, which was then discussed with all authors and agreed upon. Each author participated in writing various subsections of the paper, which were then collated and harmonised by JSL and LZ. Each iteration of the paper was reviewed and discussed by all authors, who all helped in drafting the response to the reviewers, revision, and approval of the final manuscript.

Declaration of interests

JSL is personally funded by a Wellcome Trust Early Career Award (301005/Z/23/Z); and reports personal lectureship honoraria from AstraZeneca and consulting fees from Boehringer Ingelheim, outside the submitted work. LZ is personally funded by the National Natural Science Foundation of China (No. 72125009); and reports grants from Bayer AG, outside the submitted work. AK reports grants or contracting fees from CSL Vifor and Otsuka; and consulting fees from Amgen, Argenx, AstraZeneca, Boehringer Ingelheim, CSL Vifor, Delta4, GlaxoSmithKline, Novartis, Novo Nordisk, Otsuka, Roche, Sobi, Visterra, and Walden Biosciences, all outside of the submitted work. L-AF reports speaker fees from Servier Pharmaceuticals outside the submitted work. MB reports grants from the Australian Research Council and Natural Hazards Research Australia, all outside the submitted work. AYW reports honoraria from AstraZeneca, Bayer AG, Fresenius Kabi and Vitaflo and Consun Pharma, all outside the submitted work. AL receives salary support from the University of British Columbia, and Provincial Health Services Authority in British Columbia Canada; and reports honoraria and grant funding from Bayer, AstraZeneca, NovoNordisk, Boehringer Ingelheim, Novartis, and Otsuka, all of which are donated to educational and research organisations. UA has received the National Medical and Research Council Clinical Trial Grant Singapore 2024 and funding from the Duke-NUS Khoo Bridge Funding 2025, Singapore.

Acknowledgments

We thank artists Danhong Qiu and Ziyan Song for their contributions to the design and production of the figures included in this manuscript.

References

1 National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis* 2002; **39** (suppl 1)**:** S1–266.

2 Lees JS, Stevens KI, Kotwal SS, Bruchfeld A, Levin A. Advances in understanding the impact of sex on kidney health and disease. *Lancet* 2026; published online June 3. https://doi.org/10.1016/S0140-6736(26)00654-9.

3 Lees JS, Škoberne A, Zhang L, et al. Chronic kidney disease, complex conditions, and advancing therapeutics: new hope and challenges. *Lancet* 2026; published online June 3. https://doi.org/10.1016/S0140-6736(26)00653-7.

4 Ndumele CE, Neeland IJ, Tuttle KR, et al, and the American Heart Association. A synopsis of the evidence for the science and clinical management of cardiovascular-kidney-metabolic (CKM) syndrome: a scientific statement from the American Heart Association. *Circulation* 2023; **148:** 1636–64.

5 Jager KJ, Kovesdy C, Langham R, Rosenberg M, Jha V, Zoccali C. A single number for advocacy and communication-worldwide more than 850 million individuals have kidney diseases. *Kidney Int* 2019; **96:** 1048–50.

6 Kovesdy CP. Epidemiology of chronic kidney disease: an update 2022. *Kidney Int Suppl* 2022; **12:** 7–11.

7 Mark PB, Stafford LK, Grams ME, et al, and the GBD 2023 Chronic Kidney Disease Collaborators. Global, regional, and national burden of chronic kidney disease in adults, 1990–2023, and its attributable risk factors: a systematic analysis for the Global Burden of Disease Study 2023. *Lancet* 2025; **406:** 2461–82.

8 Stanifer JW, Muiru A, Jafar TH, Patel UD. Chronic kidney disease in low- and middle-income countries. *Nephrol Dial Transplant* 2016; **31:** 868–74.

9 WHO. Agenda item 13.1: Reducing the burden of noncommunicable diseases through promotion of kidney health and strengthening prevention and control of kidney disease. May 27, 2025. https://apps.who.int/gb/ebwha/pdf_files/WHA78/A78_R6-en.pdf (accessed Nov 27, 2025).

10 Ndumele CE, Rangaswami J, Chow SL, et al, and the American Heart Association. Cardiovascular-kidney-metabolic health: a presidential advisory from the American Heart Association. *Circulation* 2023; **148:** 1606–35.

11 Okpechi IG, Luyckx VA, Tungsanga S, et al. Global kidney health priorities-perspectives from the ISN-GKHA. *Nephrol Dial Transplant* 2024; **39:** 1762–71.

12 Mazhar F, Sjölander A, Fu EL, et al. Estimating the prevalence of chronic kidney disease while accounting for nonrandom testing with inverse probability weighting. *Kidney Int* 2023; **103:** 416–20.

13 Fabian J, Kalyesubula R, Mkandawire J, et al, and the African Research on Kidney Disease Consortium. Measurement of kidney function in Malawi, South Africa, and Uganda: a multicentre cohort study. *Lancet Glob Health* 2022; **10:** e1159–69.

14 Ulasi II, Onu UC. The changing landscape of kidney health and disease in Africa. *Nat Rev Nephrol* 2025; **21:** 720–21.

15 Crump C, Sundquist J, Winkleby MA, Sundquist K. Preterm birth and risk of chronic kidney disease from childhood into mid-adulthood: national cohort study. *BMJ* 2019; **365:** l1346.

16 Luyckx VA, Brenner BM. Low birth weight, nephron number, and kidney disease. *Kidney Int Suppl* 2005; **68:** S68–77.

17 Stevens PE, Ahmed SB, Carrero JJ, et al, and the Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int* 2024; **105:** S117–314.

18 Luyckx VA, Tuttle KR, Abdellatif D, et al, and the World Kidney Day Joint Steering Committee. Mind the gap in kidney care: translating what we know into what we do. *Kidney Int* 2024; **105:** 406–17.

19 Ryu H, Hong Y, Kang E, et al, and the KNOW-CKD Study Group. Comparison of outcomes of chronic kidney disease based on etiology: a prospective cohort study from KNOW-CKD. *Sci Rep* 2023; **13:** 3570.

20 Rafferty Q, Stafford LK, Vos T, et al, and the GBD 2023 Kidney Failure with Replacement Therapy Collaborators. Global, regional, and national prevalence of kidney failure with replacement therapy and associated aetiologies, 1990–2023: a systematic analysis for the Global Burden of Disease Study 2023. *Lancet Glob Health* 2025; **13:** e1378–95.

21 Wijewickrama E, Behera S, Garcia P, et al, and the International Society of Nephrology's International Consortium of Collaborators on CKDu. Kidney biopsies among persons living in hotspots of CKDu: a position statement from the International Society of Nephrology's Consortium of Collaborators on CKDu. *Kidney Int* 2024; **105:** 464–69.

22 Smyth B, Glaser J, Butler-Dawson J, et al. Challenges and opportunities in interventions for chronic kidney disease of unknown origin (CKDu): report from the International Society of Nephrology Consortium of Collaborators on CKDu. *Kidney Int* 2023; **103:** 6–12.

23 Lebov JF, Brooks DR, Aceituno A, et al. Rationale and design of the International Prospective Study of CKD of Uncertain Etiology in Agricultural Communities. *Kidney Int Rep* 2025; **10:** 3192–201.

24 Caplin B, Jakobsson K, Glaser J, et al. International collaboration for the epidemiology of eGFR in low and middle income populations—rationale and core protocol for the Disadvantaged Populations eGFR Epidemiology Study (DEGREE). *BMC Nephrol* 2017; **18:** 1.

25 Friedman DJ, Leone DA, Amador JJ, et al. Genetic risk factors for Mesoamerican nephropathy. *Proc Natl Acad Sci USA* 2024; **121:** e2404848121.

26 Lameire NH, Levin A, Kellum JA, et al, and the Conference Participants. Harmonizing acute and chronic kidney disease definition and classification: report of a Kidney Disease: Improving Global Outcomes (KDIGO) Consensus Conference. *Kidney Int* 2021; **100:** 516–26.

27 Grams ME, Coresh J, Matsushita K, et al, and the Writing Group for the CKD Prognosis Consortium. Estimated glomerular filtration rate, albuminuria, and adverse outcomes: an individual-participant data meta-analysis. *JAMA* 2023; **330:** 1266–77.

28 Carrero J-J, Fu EL, Sang Y, et al. Discordances between creatinine- and cystatin C-based estimated GFR and adverse clinical outcomes in routine clinical practice. *Am J Kidney Dis* 2023; **82:** 534–42.

29 Inker LA, Eneanya ND, Coresh J, et al, and the Chronic Kidney Disease Epidemiology Collaboration. New creatinine- and cystatin C-based equations to estimate GFR without race. *N Engl J Med* 2021; **385:** 1737–49.

30 Inker LA, Schmid CH, Tighiouart H, et al, and the CKD-EPI Investigators. Estimating glomerular filtration rate from serum creatinine and cystatin C. *N Engl J Med* 2012; **367:** 20–29.

31 Pottel H, Björk J, Rule AD, et al. Cystatin C-based equation to estimate GFR without the inclusion of race and sex. *N Engl J Med* 2023; **388:** 333–43.

32 Fu EL, Levey AS, Coresh J, et al. Accuracy of GFR estimating equations in patients with discordances between creatinine and cystatin C-based estimations. *J Am Soc Nephrol* 2023; **34:** 1241–51.

33 Lees JS, Rutherford E, Stevens KI, et al. Assessment of cystatin C level for risk stratification in adults with chronic kidney disease. *JAMA Netw Open* 2022; **5:** e2238300.

34 Lees JS, Welsh CE, Celis-Morales CA, et al. Glomerular filtration rate by differing measures, albuminuria and prediction of cardiovascular disease, mortality and end-stage kidney disease. *Nat Med* 2019; **25:** 1753–60.

35 Lees JS, Ho F, Parra-Soto S, et al. Kidney function and cancer risk: an analysis using creatinine and cystatin C in a cohort study. *EClinicalMedicine* 2021; **38:** 101030.

36 Lees JS, De La Mata NL, Sullivan MK, et al. Sex differences in associations between creatinine and cystatin C-based kidney function measures with stroke and major bleeding. *Eur Stroke J* 2023; **8:** 756–68.

37 Estrella MM, Ballew SH, Sang Y, et al, and the Chronic Kidney Disease Prognosis Consortium Investigators and Collaborators. Discordance in creatinine- and cystatin C-based eGFR and clinical outcomes: a meta-analysis. *JAMA* 2025; **334:** 1915–26.

38 Liu C, Levey AS, Ballew SH. Serum creatinine and serum cystatin C as an index of muscle mass in adults. *Curr Opin Nephrol Hypertens* 2024; **33:** 557–65.

39 Liu Q, Welsh P, Celis-Morales C, Ho FK, Lees JS, Mark PB. Discordance between cystatin C-based and creatinine-based estimated glomerular filtration rate and health outcomes in adults: a systematic review and meta-analysis. *Clin Kidney J* 2025; **18:** sfaf003.

40 Hanna PE, Wang Q, Strohbehn IA, et al. Medication-related adverse events and discordancies in cystatin C-based vs serum creatinine-based estimated glomerular filtration rate in patients with cancer. *JAMA Netw Open* 2023; **6:** e2321715.

41 Costa E Silva VT, Gil LA Jr, Inker LA, et al. A prospective cross-sectional study estimated glomerular filtration rate from creatinine and cystatin C in adults with solid tumors. *Kidney Int* 2022; **101:** 607–14.

42 Lees JS, Fu EL, Faucon A-L, et al. Accuracy of glomerular filtration rate estimates among patients with cancer. *Br J Cancer* 2025; **133:** 1652–59.

43 Kitchlu A, Silva VTCE, Anand S, et al. Assessment of GFR in patients with cancer: a statement from the American Society of Onco-Nephrology. *Clin J Am Soc Nephrol* 2024; **19:** 1061–72.

44 Kitchlu A, Shapiro J, Amir E, et al. Representation of patients with chronic kidney disease in trials of cancer therapy. *JAMA* 2018; **319:** 2437–39.

45 Lu Z, Ni W, Wu Y, et al. Application of biomarkers in the diagnosis of kidney disease. *Front Med* 2025; **12:** 1560222.

46 Devarajan P. The use of targeted biomarkers for chronic kidney disease. *Adv Chronic Kidney Dis* 2010; **17:** 469–79.

47 Tonelli M, Sacks F, Pfeffer M, Jhangri GS, Curhan G, and the Cholesterol and Recurrent Events (CARE) Trial Investigators. Biomarkers of inflammation and progression of chronic kidney disease. *Kidney Int* 2005; **68:** 237–45.

48 Gupta A, Sontakke T, Acharya S, Kumar S. A comprehensive review of biomarkers for chronic kidney disease in older individuals: current perspectives and future directions. *Cureus* 2024; **16:** e70262.

49 de Boer IH, Alpers CE, Azeloglu EU, et al, and the Kidney Precision Medicine Project. Rationale and design of the Kidney Precision Medicine Project. *Kidney Int* 2021; **99:** 498–510.

50 El-Achkar TM, Eadon MT, Menon R, et al. A multimodal and integrated approach to interrogate human kidney biopsies with rigor and reproducibility: guidelines from the Kidney Precision Medicine Project. *Physiol Genomics* 2021; **53:** 1–11.

51 Fiorentino M, Bolignano D, Tesar V, et al, and the ERA-EDTA Immunonephrology Working Group. Renal biopsy in patients with diabetes: a pooled meta-analysis of 48 studies. *Nephrol Dial Transplant* 2017; **32:** 97–110.

52 Radhakrishnan J, Lafayette RA. Active glomerular inflammation versus chronicity and fibrosis: the role of targeted therapies in IgA nephropathy. *Nephrol Dial Transplant* 2025; **40:** 1811–14.

53 Barbour SJ, Coppo R, Zhang H, et al, and the International IgA Nephropathy Network. evaluating a new international risk-prediction tool in IgA nephropathy. *JAMA Intern Med* 2019; **179:** 942–52.

54 Bate S, McGovern D, Costigliolo F, et al. The improved kidney risk score in ANCA-associated vasculitis for clinical practice and trials. *J Am Soc Nephrol* 2024; **35:** 335–46.

55 Naesens M, Roufosse C, Haas M, et al. The Banff 2022 Kidney Meeting Report: reappraisal of microvascular inflammation and the role of biopsy-based transcript diagnostics. *Am J Transplant* 2024; **24:** 338–49.

56 Linder JE, Allworth A, Bland HT, et al, and the eMERGE Consortium. Returning integrated genomic risk and clinical recommendations: the eMERGE study. *Genet Med* 2023; **25:** 100006.

57 Adams SM, Crisamore KR, Empey PE. Clinical pharmacogenomics. *Clin J Am Soc Nephrol* 2018; **13:** 1561–71.

58 Cornec-Le Gall E, Audrézet M-P, Rousseau A, et al. The PROPKD score. *J Am Soc Nephrol* 2016; **27:** 942–51.

59 Schott C, Lebedeva V, Taylor C, Abumelha S, Roshanov PS, Connaughton DM. Utility of genetic testing in adults with CKD: a systematic review and meta-analysis. *Clin J Am Soc Nephrol* 2025; **20:** 101–15.

60 Dahl NK, Bloom MS, Chebib FT, et al. The clinical utility of genetic testing in the diagnosis and management of adults with chronic kidney disease. *J Am Soc Nephrol* 2023; **34:** 2039–50.

61 Groopman EE, Marasa M, Cameron-Christie S, et al. Diagnostic utility of exome sequencing for kidney disease. *N Engl J Med* 2019; **380:** 142–51.

62 Li Y, Ma T, Lu H, et al. Beyond the cell atlas: functional communities as the essential pathologic units driving kidney disease. *J Am Soc Nephrol* 2026; published online Jan 9. https://doi.org/10.1681/ASN.0000001023.

63 Lake BB, Menon R, Winfree S, et al, and the KPMP Consortium. An atlas of healthy and injured cell states and niches in the human kidney. *Nature* 2023; **619:** 585–94.

64 Eddy S, Mariani LH, Kretzler M. Integrated multi-omics approaches to improve classification of chronic kidney disease. *Nat Rev Nephrol* 2020; **16:** 657–68.

65 Abedini A, Levinsohn J, Klötzer KA, et al. Single-cell multi-omic and spatial profiling of human kidneys implicates the fibrotic microenvironment in kidney disease progression. *Nat Genet* 2024; **56:** 1712–24.

66 Wei L, Gao J, Wang L, Tao Q, Tu C. Multi-omics analysis reveals the potential pathogenesis and therapeutic targets of diabetic kidney disease. *Hum Mol Genet* 2024; **33:** 122–37.

67 Hu Y, Ni X, Chen Q, et al. Predicting diabetic kidney disease with serum metabolomics and gut microbiota. *Sci Rep* 2025; **15:** 12179.

68 Xie D, Zhu Y, Guo S, et al. The metformin mediated MAPK signaling pathway influences D-xylose regulation during diabetic kidney disease therapy. *Commun Med (Lond)* 2025; **5:** 454.

69 Alobaidi S. Emerging biomarkers and advanced diagnostics in chronic kidney disease: early detection through multi-omics and AI. *Diagnostics* 2025; **15:** 1225.

70 Elliott MD, Rasouly HM, Gharavi AG. Genetics of kidney disease: the unexpected role of rare disorders. *Annu Rev Med* 2023; **74:** 353–67.

71 Köttgen A, Cornec-Le Gall E, Halbritter J, et al, and the KDIGO Conference Participants. Genetics in chronic kidney disease: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) controversies conference. *Kidney Int* 2022; **101:** 1126–41.

72 Hephzibah J. Role of nuclear medicine in evaluation of renal system. *Curr Med Issues* 2018; **16:** 148.

73 Taylor AT, Brandon DC, de Palma D, et al. SNMMI procedure standard/EANM practice guideline for diuretic renal scintigraphy in adults with suspected upper urinary tract obstruction 1.0. *Semin Nucl Med* 2018; **48:** 377–90.

74 Taylor AT. Radionuclides in nephrourology, part 2: pitfalls and diagnostic applications. *J Nucl Med* 2014; **55:** 786–98.

75 Selby NM, Gilthorpe MS, Kalra PA, et al. Application of functional kidney magnetic resonance imaging to improve assessment of CKD: the AFiRM study. *J Am Soc Nephrol* 2024; **35**.

76 Krishnan N, Perazella MA. The role of PET scanning in the evaluation of patients with kidney disease. *Adv Chronic Kidney Dis* 2017; **24:** 154–61.

77 Mueller TF, Luyckx VA. Potential utility of renal functional reserve testing in clinical nephrology. *Curr Opin Nephrol Hypertens* 2024; **33:** 130–35.

78 Palsson R, Waikar SS. Renal functional reserve revisited. *Adv Chronic Kidney Dis* 2018; **25:** e1–8.

79 Han S, Yamamoto S, Jung C-Y, Jin DY, Lee T, Kim J-S. Wearable sensors for monitoring chronic kidney disease. *Commun Mater* 2024; **5:** 153.

80 Kashani KB, Awdishu L, Bagshaw SM, et al. Digital health and acute kidney injury: consensus report of the 27th Acute Disease Quality Initiative workgroup. *Nat Rev Nephrol* 2023; **19:** 807–18.

81 Shore J, Green M, Hardy A, Livesey D. The compliance and cost-effectiveness of smartphone urinalysis albumin screening for people with diabetes in England. *Expert Rev Pharmacoecon Outcomes Res* 2020; **20:** 387–95.

82 Oyaert M, Delanghe J. Progress in automated urinalysis. *Ann Lab Med* 2019; **39:** 15–22.

83 Holmstrom L, Christensen M, Yuan N, et al. Deep learning-based electrocardiographic screening for chronic kidney disease. *Commun Med* 2023; **3:** 73.

84 Sabanayagam C, Xu D, Ting DSW, et al. A deep learning algorithm to detect chronic kidney disease from retinal photographs in community-based populations. *Lancet Digit Health* 2020; **2:** e295–302.

85 Kou J, Li Z, You Y, Wang R, Chen J, Tang Y. Automatic identification and classification of pediatric glomerulonephritis on ultrasound images based on deep learning and radiomics. *J Big Data* 2024; **11:** 165.

86 Levin A, Okpechi IG, Caskey FJ, Yang C-W, Tonelli M, Jha V. Perspectives on early detection of chronic kidney disease: the facts, the questions, and a proposed framework for 2023 and beyond. *Kidney Int* 2023; **103:** 1004–08.

87 Shlipak MG, Tummalapalli SL, Boulware LE, et al, and the Conference Participants. The case for early identification and intervention of chronic kidney disease: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) controversies conference. *Kidney Int* 2021; **99:** 34–47.

88 Bradshaw C, Kondal D, Montez-Rath ME, et al. Early detection of chronic kidney disease in low-income and middle-income countries: development and validation of a point-of-care screening strategy for India. *BMJ Glob Health* 2019; **4:** e001644.

89 Cusick MM, Tisdale RL, Chertow GM, Owens DK, Goldhaber-Fiebert JD. Population-wide screening for chronic kidney disease: a cost-effectiveness analysis. *Ann Intern Med* 2023; **176:** 788–97.

90 Hodel NC, Rentsch KM, Paris DH, Mayr M. Methods for diagnosing proteinuria—when to use which test and why: a review. *Am J Kidney Dis* 2025; **85:** 618–28.

91 Wen F, Wang J, Yang C, et al. Cost-effectiveness of population-based screening for chronic kidney disease among the general population and adults with diabetes in China: a modelling study. *Lancet Reg Health West Pac* 2025; **56:** 101493.

92 Tangri N, Oh K-H, Choo JCJ, et al. Inside CKD: cost-effectiveness of multinational screening for CKD. *Kidney Int Rep* 2025; **10:** 1087–100.

93 Rokhman MR, Alkaff FF, van Dorst PWM, et al. Economic evaluations of screening programs for chronic kidney disease: a systematic review. *Value Health* 2024; **27:** 117–28.

94 Tangri N, Neuen BL, Cherney DZ, Tuttle KR, Perkovic V. From progression to remission: a new paradigm for success in chronic kidney disease. *Kidney Int* 2026; **109:** 17–21.

95 Ene-Iordache B, Perico N, Bikbov B, et al. Chronic kidney disease and cardiovascular risk in six regions of the world (ISN-KDDC): a cross-sectional study. *Lancet Glob Health* 2016; **4:** e307–19.

96 Park JI, Baek H, Kim BR, Jung HH. Comparison of urine dipstick and albumin:creatinine ratio for chronic kidney disease screening: a population-based study. *PLoS One* 2017; **12:** e0171106.

97 Vanness DJ, Lomas J, Ahn H. A health opportunity cost threshold for cost-effectiveness analysis in the United States. *Ann Intern Med* 2021; **174:** 25–32.

98 Pouwels XGLV, van Mil D, Kieneker LM, et al. Cost-effectiveness of home-based screening of the general population for albuminuria to prevent progression of cardiovascular and kidney disease. *EClinicalMedicine* 2024; **68:** 102414.

99 Walker H, Day S, Grant CH, et al. Representation of multimorbidity and frailty in the development and validation of kidney failure prognostic prediction models: a systematic review. *BMC Med* 2024; **22:** 452.

100 Walker H, Carrero J-J, Sullivan MK, et al. Frailty in adults with CKD and validation of the kidney failure risk equation in frailty subgroups. *Clin J Am Soc Nephrol* 2025; **20:** 1051–62.

101 Liu P, Sawhney S, Heide-Jørgensen U, et al. Predicting the risks of kidney failure and death in adults with moderate to severe chronic kidney disease: multinational, longitudinal, population based, cohort study. *BMJ* 2024; **385:** e078063.

102 Caliskan Y, Yildiz A, Aypek H, et al. Comparative validation of the Mayo Clinic imaging classification and PROPKD score for predicting ADPKD progression across diverse ethnic cohorts. *J Nephrol* 2025; **38:** 1469–77.

103 Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines. *J Am Coll Cardiol* 2019; **74:** e177–232.

104 Cosentino F, Grant PJ, Aboyans V, et al, and the ESC Scientific Document Group. 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD. *Eur Heart J* 2020; **41:** 255–323.

105 Visseren FLJ, Mach F, Smulders YM, et al, and the ESC National Cardiac Societies, and the ESC Scientific Document Group. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. *Eur Heart J* 2021; **42:** 3227–337.

106 Khan SS, Matsushita K, Sang Y, et al. Development and validation of the American Heart Association's PREVENT equations. *Circulation* 2024; **149:** 430–49.

107 Pennells L, Kaptoge S, Østergaard HB, et al. SCORE2-diabetes: 10-year cardiovascular risk estimation in type 2 diabetes in Europe. *Eur Heart J* 2023; **44:** 2544–56.

108 Reitsma TH, Lim C-E, Gynnild MN, et al. Prediction of incident heart failure in established atherosclerotic cardiovascular disease: the SMART2-HF model. *Eur Heart J* 2026; published online March 11. https://doi.org/10.1093/eurheartj/ehag153.

109 Kaptoge S, Keene SJ, Reitsma T, et al. Prediction of incident heart failure in individuals without prior cardiovascular disease: the SCORE2-HF risk model. *Eur Heart J* 2026; published online March 11. https://doi.org/10.1093/eurheartj/ehag154.

110 Reitsma TH, Savarese G, Kuźma Ł, et al. Risk prediction in patients with heart failure with preserved ejection fraction: the LIFE-Preserved model. *Eur Heart J* 2026; published online March 11. https://doi.org/10.1093/eurheartj/ehag182.

111 Matsushita K, Jassal SK, Sang Y, et al. Incorporating kidney disease measures into cardiovascular risk prediction: development and validation in 9 million adults from 72 datasets. *EClinicalMedicine* 2020; **27:** 100552.

112 Matsushita K, Kaptoge S, Hageman SHJ, et al. Including measures of chronic kidney disease to improve cardiovascular risk prediction by SCORE2 and SCORE2-OP. *Eur J Prev Cardiol* 2023; **30:** 8–16.

113 Ho FK, Mark PB, Lees JS, et al. A proteomics-based approach for prediction of different cardiovascular diseases and dementia. *Circulation* 2025; **151:** 277–87.

114 Kaptoge S, Pennells L, De Bacquer D, et al, and the WHO CVD Risk Chart Working Group. World Health Organization cardiovascular disease risk charts: revised models to estimate risk in 21 global regions. *Lancet Glob Health* 2019; **7:** e1332–45.

115 Tangri N, Sabanayagam C. Artificial intelligence approaches to enable early detection of CKD. *Nat Rev Nephrol* 2025; **21:** 153–54.

116 Noda R, Ichikawa D, Shibagaki Y. Machine learning-based diagnostic prediction of IgA nephropathy: model development and validation study. *Sci Rep* 2024; **14:** 12426.

117 Chin MH, Afsar-Manesh N, Bierman AS, et al. Guiding principles to address the impact of algorithm bias on racial and ethnic disparities in health and health care. *JAMA Netw Open* 2023; **6:** e2345050.

118 Finlayson SG, Subbaswamy A, Singh K, et al. The clinician and dataset shift in artificial intelligence. *N Engl J Med* 2021; **385:** 283–86.

119 Cruz Rivera S, Liu X, Chan A-W, et al, and the SPIRIT-AI and CONSORT-AI Working Group. Guidelines for clinical trial protocols for interventions involving artificial intelligence: the SPIRIT-AI extension. *Lancet Digit Health* 2020; **2:** e549–60.

120 Stenvinkel P. Inflammation: a key driver in the progression of CKD. *Am J Kidney Dis* 2025; **86:** 296–97.

121 Yuan Q, Tang B, Zhang C. Signaling pathways of chronic kidney diseases, implications for therapeutics. *Signal Transduct Target Ther* 2022; **7:** 182.

122 Maringhini S, Zoccali C. Chronic kidney disease progression—a challenge. *Biomedicines* 2024; **12:** 2203.

123 Murali S, Ding H, Adedeji F, et al. Bringing MRI to low- and middle-income countries: directions, challenges and potential solutions. *NMR Biomed* 2024; **37:** e4992.

124 Giudicelli GC, De Souza CMB, Veronese FV, Pereira LV, Hünemeier T, Vianna FSL. Precision medicine implementation challenges for *APOL1* testing in chronic kidney disease in admixed populations. *Front Genet* 2022; **13:** 1016341.

125 Gama RM, Griffiths K, Beencke N, et al. A pilot point-of-care kidney disease clinic in primary care to pharmacologically optimise people with chronic kidney disease (PROTECT KIDNEY). *Fam Pract* 2025; **42:** cmaf083.

126 Bikkarolla SK, Venkatesan K, Revathy YR, Parameswaran S, Krishnakumar S, Dendukuri D. The quantitative detection of cystatin-C in patient samples using a colorimetric lateral flow immunoassay. *Biosensors* 2024; **14:** 30.

127 Dent CL, Ma Q, Dastrala S, et al. Plasma neutrophil gelatinase-associated lipocalin predicts acute kidney injury, morbidity and mortality after pediatric cardiac surgery: a prospective uncontrolled cohort study. *Crit Care* 2007; **11:** R127.

128 Graham-Brown MPM, Smith AC, Greenwood SA. Digital health interventions in chronic kidney disease: levelling the playing field? *Clin Kidney J* 2022; **16:** 763–67.