Saudi Toxicology Journal (STJ)

Journal home page: https://uqu.edu.sa/s.toxicology.s/S.T.J

Review

Advancing CKD Diagnosis: Race-Free eGFR, Cystatin C, and Genetic Insights

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Citation: Albar, H. T. Advancing CKD Diagnosis: Race-Free eGFR, Cystatin C, and Genetic Insights. *STJ*, **2025**, 2, 94-107. https://doi.org/10.70957/uqu.edu.sa/s.toxicology.s/stj.2025.2.9

Received: 20 Jun 2025
Accepted: 13 Aug 2025
Published: 05 Sep 2025

Abstract: Globally, the rates of chronic kidney disease (CKD) are increasing due to the increasing incidence of hypertension, obesity, and diabetes mellitus. Early detection and treatment of kidney disease are essential in improving health outcomes. Estimate glomerular filtration rate (eGFR) is used to diagnose, stage, and manage CKD. CKD biomarkers are broadly categorized into traditional (serum creatinine), emerging (cystatin C), and disease specific (Interleukin-6). The purpose of this narrative review is to synthesize the current evidence regarding the use of eGFR in diverse populations. The initial eGFR equations included race variables, which created a controversial debate about their relevancy and has contributed to health disparities. However, evidence supports the effectiveness of race-free eGFR equation and cystatin C as emerging better alternatives to biomarker creatine. Additionally, emerging evidence supports the effectiveness of the use of genetic testing in enhancing diagnoses and management of kidney diseases. Also, point-of-care (POC) biosensors have potential solutions for rapid, accessible, cost-effective, and non-invasive kidney function diagnostics. Equity in renal health care can be enhanced through multifaceted interventions and collaboration among different stakeholders, encompassing risk assessment approaches, patient and caregiver education, integrated practices, and strategic partnerships. The emerging development, including metabolomics, fluorescent probes, and wearable sensor technologies represents a significant paradigm shift toward personalized and equitable nephrology care. To validate, scale, and ease the adoption of these technologies in clinical practice, there is a need for multidisciplinary collaboration among researchers, clinicians, and policymakers.

Keywords: Chronic kidney disease, estimated glomerular filtration rate, serum creatinine, cystatin C, race

Globally, the increase in obesity, hypertension, and diabetes mellitus rates has led to chronic kidney disease (CKD) to be the leading cause of morbidity and mortality [1]. The global prevalence of CKD ranges between 8-16% and affects one-seventh of adults aged 20 years and above [1]. With this high prevalence, early detection and treatment of kidney disease is essential. Glomerular Filtration Rate (GFR) is a key indicator for diagnosing and staging CKD, predicting outcomes, and optimizing drug dosing[2]. However, direct

measurement of GFR in routine clinical practice is impractical; therefore, it is typically estimated using equations derived from serum levels of endogenous filtration markers, most commonly creatinine and cystatin C [2,3].

There are different equations developed to estimate GRF (eGFR) using cystatin or creatinine alone or in combination, which integrates the associated factors influencing these biomarkers, such as age, gender, and muscle mass [2,4]. However, the inclusion of race in the equations has resulted in controversy, which has prompted the call for the use of race-free equations [5-9]. Additionally, the limited accuracy and sensitivity of serum creatinine and its potential misclassification of patients because of its sensitivity to different factors have recently resulted in an increased focus on cystatin C as alternative endogenous maker [3,4]. The purpose of this narrative review is to synthesize the current evidence regarding the use of eGFR in diverse populations, focusing on cystatin C, race, and the next steps.

CKD Biomarkers

The assessment and management of CKD largely depend on biomarkers. CKD biomarkers are grouped into traditional, emerging, and those specific to certain aspects of the disease based on established clinical practice, validation across population, discovery of novel biomarkers, and biological pathways related to CKD progression or complications[10]. Understanding CKD biomarkers is essential for enhancing early detection, monitoring progression, and managing treatment strategies [10]. Table 1 contains different categories of CKD biomarkers and their description and clinical relevance.

Revisiting eGFR Formulations: A Paradigm Shift from Race-Dependent Models

Critique of Creatinine-Dependent eGFR Models

Two commonly used creatinine-dependent models are the Modification of Diet in Renal Disease (MDRD) and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations (see Table 2) [11]. The MDRD and the initial CKD-EPI equations included serum creatinine, sex, age, and race variables while the revised CKD-EPI do not include race [11]. Studies have shown some benefits of MDRD such as decreasing serum phosphorus, improvement in renal functions, blood pressure control, and decreasing the risk of end-stage kidney disease [12-14]. However, the prescription of a low-protein diet regimen has been opposed by clinicians because of some evidence of an unfavorable prognosis [13]. Additionally, the MDRD equation tends to systematically underestimate GFR and overestimate the prevalence of CKD in any population [15].

The inclusion of race in the MDRD and CKD-EPI equations has been considered discriminatory. For example, at the same creatine levels, eGFR was higher in African Americans than non-Black, which would lead to delays in eligibility for the kidney transplant waiting list [15]. Lower eGFR in the Black population would increase the estimated prevalence of CKD and could enable earlier diagnoses and treatment of the condition. However, low GFR among this population could lead to missed opportunities for treatment contraindicated at low GFR [16]. On the contrary, higher eGFR in the non-Black population decreases the estimated prevalence of CKD, leading to missed diagnoses and inappropriate exposure to interventions and medications that are contraindicated at lower levels of GFR [16].

Initially, the inclusion of race variable in the CKD-EPI was based on the United States population [17,18]. However, several studies outside the United States have shown that race variable did not apply to other Black populations in Brazil, Europe, and Africa [15]. Delanaye et al. (2024) argued that the differences in serum creatinine have nothing to do with race, ethnicity, or skin color but with the population. The correction applied to MDRD and CKD-EPI equations at GFR levels was mathematically efficient but misleading because the correction should have been to the creatinine but not the GFR levels [15]. In addition, the use of race as a binary variable (Black vs non-Black) in estimating eGFR did not account for multi and biracial individuals and the admixture of the population [19,20]. Race lacks precision and is dynamic over time and in different places because it is social, not a biological construct [16]. There were concerns that including race in the equation may introduce disparities and implicit bias in medical care [16]. Considering these concerns, the CKD-EPI equation was revised in 2021 to exclude race as a variable [16]. Therefore, in 2021, the National Kidney

Table 1 Categories of CKD Biomarkers

Category	Biomarkers	Description	Clinical Use
Traditional	Serum creatinine [1,2]	A muscle metabolism waste product measured in blood	Commonly used to estimate eGFR and evaluate kidney functions [1,2,3, 10]
	Blood Urea Nitrogen (BUN) [10]	Used to measure the amount of nitrogen in blood that comes from urea	Used in the evaluation of kidney function and hydration status influenced by the diet and protein intake[2,10]
	Urine protein and albumin[2,10]	Used to detect the presence of protein or albumin in urine	The presence of protein in urine is an early indicator of kidney damage and used to monitor disease progression and the effectiveness of treatment options [10]
Emerging	Cystatin C [1,2,10]	A kidney-filtered protein [1, 2,10]	It provides more accurate eGFR in individuals with varying muscle mass than serum creatinine [2,10]
	Neutrophil gelatinase-associated lipocalin (NGAL)	A protein related to kidney injury and inflammation[10]	Used as an early indicator of acute kidney injury and evaluating CKD progression[10]
	Kidney injury molecule-1 (KIM-1) [10]	A protein present in injured kidney tubular cells	Used as an indication of acute kidney injury and monitoring the progression of CKD[10]
	Beta-2 microglobulin[10]	A low molecular protein cleared by kidney[10]	Used to assess kidney functions. High levels indicates renal dysfunction[10]
Disease-Specific (Inflammation)	Interleukin-6 (IL-6)	A pro-inflammatory cytokine involved in immune response	Indicates the inflammation status in CKD and is associated with cardiovascular risk and disease progression[10]
	Tumor necrosis factor-alpha (TNF-alpha) [10]	A systemic inflammation cytokine	Associated with the progression of CKD and the related comorbid conditions[10]
Disease-Specific (fibrosis)	Transforming growth factor-beta 1(TGF-beta 1)	A tissue fibrosis and scarring cytokine	It is an indication of renal fibrosis associated with progression and severity of CKD [10]
	Collagen types[10]	A structural protein that contributes to the formation and organization of the extracellular matrix.	It indicates fibrotic changes in kidney tissues and used to evaluate the extend of kidney damage[10]
Disease-Specific (Oxidative stress)	Oxidative stress markers (malondialdehyde) [10]	Molecules that indicates the extend of oxidative damage and stress in the body	Used to evaluate the status of oxidative stress linked to CKD progression and its complications [10]

Note: Adapted from Gupta et al. (2024). The classification of the biomarkers is based on established clinical practice, validation across population, discovery of novel biomarkers, and biological pathways related to CKD progression or complications[10].

Table 2 Comparison of MDRD and CKD-EPI Equations

Equation	Variables
MDRD	$eGFR = 175 \times (SCr)^{-1.154} \times (age)^{-0.203} \times 0.742$ (if female) × 1.212 (if Black) [10,11]
Initial CKD-EPI	$eGFR = 141 \times \min(Scr/\kappa, 1)^{\alpha} \times \max(Scr/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018$ (if female) - 1.159 (if Black) [10,11]
NKF CKD-EPI	$eGFR = 142 \times \min(Scr/\kappa, 1)^{\alpha} \times \max(Scr/\kappa, 1)^{-1.200} \times 0.9938^{Age} \times 1.012$ (if female) [10,11]

Note: Scr = standardized serum creatinine in mg/dL, age (years), $\kappa = 0.7$ (females) or 0.9 (males), $\alpha = -0.241$ (female) or -0.302 (male), $\min(Scr/\kappa, 1)$ = minimum of Scr/κ or 1.0, $\max(Scr/\kappa, 1)$ = maximum of Scr/κ or 1.0.

Foundation NKF (2021) recommended using CKD-EPI equation without race variable [21].

The use of creatinine in the equation is also associated with some limitations, such as muscular mass variability and the impacts of the confounding variables. Serum creatinine is an imperfect biomarker of renal function in patients with prolonged hospitalization in intensive care units because of muscular mass [15]. Despite being sensitive to severe renal impairment, serum creatinine has poor sensitivity in detecting early damage [22]. Additionally, a larger amount of meat increases serum creatinine, and patients with fluid overload have lower levels of serum creatinine [22]. Additionally, serum creatinine has limitations in detecting early kidney damages and in patients with preserved renal functions [10].

Cystatin C: A Paradigm Shift in Renal Biomarkers

Evidence has emerged that cystatin C is better than creatinine in predicting kidney function outcomes [15]. Prowle et al. (2024) reported that cystatin C demonstrated a stronger association with the risk of post-operative acute kidney injury (PO-AKI) compared to creatinine. In the absence of Cystatin C, serum creatine eGFR was inadequate in distinguishing broader risk associated with mild CKD [23,24]. Cystatin C is recognized as a reliable and accurate biomarker of kidney function across diverse populations [25]. In a systematic review and meta-analysis of 12 studies that included 44,721 patients, Yan et al. (2024) found substantial variation in GFR estimation based on race and non-race-based equations. Race-based equations overestimated GFR in the Black population while cystatin C estimation equations were associated with minimal bias [26].

The 2024 Kidney Disease Improving Global Outcomes (KDIGO) recommends the use of cystatin C to confirm the diagnosis of CKD [27]. Additionally, in efforts to exclude race in the eGFR estimation, the NKF and the American Society of Nephrology (ASN) Joint task force recommended increasing the availability and use of cystatin C in clinical practices to assess kidney functions [25].

Although both serum creatinine and cystatin C are influenced by non-GFR determinants, cystatin C is influenced by fewer and less pronounced extrarenal factors compared with serum creatinine [25,28,29]. The levels of serum creatinine are influenced by sex, age, muscle mass, protein intake, nutritional status, and physical activity while adiposity, systemic inflammation, thyroid disease, and the use of steroids are non-GFR factors influencing cystatin C [10,25,30]. Unlike serum creatinine, cystatin C is more uniformly produced across diverse populations, enhancing its applicability across different populations [25].

Detecting and staging CKD is crucial for risk stratification because it determines the risk of adverse clinical outcomes, such as ESKD, cardiovascular diseases, and mortality [25]. Cystatin C is effective in identifying a subgroup of patients with a high risk of CKD who may go undetected through serum creatinine [25].

Operational Challenges in Cystatin C Implementation

Some of the operational challenges associated with the use of cystatin C in clinical practice include concerns about assay accuracy and agreement across different laboratories, cost, absence of institutional practice guidelines and policies, excessive testing, and limited clinician's awareness of and comfort using cystatin C in their routine practices [25,31]. Significant variations exist among cystatin C reagents and assays, resulting in distinct cystatin C eGFR equations with varying power functions [28]. The absence of standardization hindered data reproducibility and sharing [28]. Therefore, the International Federation of Clinical Chemistry (IFCC) and Laboratory Medicine Working

Group on Standardization of Cystatin C published internationally certified cystatin C reference material in 2010 [28]. However, the cost of cystatin C testing may decrease with its increased adoption; the cost of a cystatin C assay may be up to ten times greater than that of an enzymatic creatinine assay [31]. In the United States, only 7% of surveyed laboratories offered Cystatin C test and the cost of cystatin C was approximately $4 compared to $0.20 per test [31]. The utilization of cystatin C can be increased through team-based and multidisciplinary care models, additional training, and the development of definitive policies guiding their use in clinical practice [25,32]. The increasing availability of cystatin C testing presents an opportunity to increase its use beyond the confirmatory testing for serum creatinine. Certain clinical conditions can affect non-GFR determinants of specific filtration markers, influencing the reported eGFR (Table 3) [2]. Extreme muscle mass can lead to lower serum creatinine levels, which may mask underlying kidney functions, resulting in the underestimation of kidney functions using creatinine [2,10]. High protein, vegetarian diet, or creatinine supplements may increase the creatine levels, influencing the performance of serum creatine in e-GFR [10]. An acute alteration in GFR results in a non-steady state of endogenous filtration markers, as serum concentrations exhibit a temporal lag before equilibrating with the new level of kidney function [10]. Consequently, during this non-steady state, neither serum marker levels nor eGFR provide an accurate measure of the true GFR [10]. Some evidence indicates Cystatin C based-equations underestimate GFR among patients with morbid obesity [10].

Bridging the eGFR Disparity Gap in Heterogeneous Populations

Non-GFR endogenous filtration markers, such as cooked meat, muscle mass, sex, and age for creatinine and inflation and adiposity for cystatin C may differ significantly across the diverse global population [30]. Therefore, eGFR calculations using the Western models may not be reliable in non-Western populations with different food preferences and body compositions [30]. Inker et al. (2021) found that the new eGFR equations that combine cystatin C and creatinine while omitting race are more accurate and decrease the differences between Black and non-Black participants than the new equations without race with either cystatin C and creatinine alone [33].

Ethical and Clinical Implications of Racial Parameters in eGFR

Incorporating race into eGFR calculations carries significant clinical and ethical implications, including disparities in care access, delayed referrals to specialists, reduced eligibility for clinical trials using GFR as an inclusion criterion, and increased use of medications potentially toxic at lower GFR levels [19,20]. Additionally, including race in eGFR equations impacts surgical decision-making based on GFR, such as delays in waitlist time for kidney transplantation. [19]. For example, race-based equations assign higher GFR estimation for the Black patients, therefore, delaying their placement into the kidney transplantation waitlist [19]. Approximately 3.3 million (10.4%) more African Americans would be diagnosed with Stage 3 CKD if race is excluded in MDRD eGFR estimation [20]. The binary of race in the equation as Black and non-Black illogically suggests that Black people are uniquely and inherently distinct from all other human races [11,20,34,35]. The inclusion of race exacerbates the existing disparities and may lead to delays in preventive care and referral for kidney transplant evaluation [34]. Contrarily, omitting race in the eGFR equation enhances access and quality of care for African Americans, thereby decreasing the predominant disparities in health care [36].

Expanding the eGFR Determinants Beyond Race: Role of Genetic Factors

Understanding how genetic factors and underlying pathways influence eGFR is essential for providing insights into CKD occurrence, mechanistic pathways, and downstream complications [37]. Substantial evidence supports the contribution of ancestry-specific genetic variants in the development of CKD [3-40]. According to Zhang et al. (2021), CKD has a heritable component. Lu and Wang (2023) identified 146 cross-tissue genetic associations with kidney

Table 3 Clinical Conditions in Which Non-GFR Determinants of Some Filtration Markers May Be Influential on The Reported E-GFR

Non-GFR Determinant	Creatine	Cystatin C
Generation		
Body composition	Extreme muscle mass (body builders, muscle wasting disease, amputation)	Obesity
Health state	Chronic severe illness, frailty	Inflammation, thyroid, smoking
Diet	High protein or creatine supplements, vegetarian diet[2,10]	Not known [2]
Tubular handling		
Drugs	Cimetidine, trimethoprim, fenofibrate, tyrosine kinase inhibitors, dolutegravir,	Steroids [2]
Others	Low GFR[2]	-
Increased extra kidney elimination	Low GFR, antibiotics [2]	Not known [2]
Non-Steady state	Acute kidney disease, edematous state[2]	Dialysis, acute kidney disease, edematous state[2]

Adapted from Inker et al. (2021).

function and chronic kidney disease (CKD) using cross-tissue transcriptome-wide association studies (TWASs), Mendelian randomization (MR), summary-based MR (SMR), and molecular docking [39,42]. Over 600 genes are currently linked to monogenic kidney diseases, with known single-gene disorders accounting for up to 50% of non-diabetic CKD in pediatric patients and 30% in adults [41]. Additionally, it is estimated that common genetic variants account for up to 20% of the estimated genetic hereditability of eGFR [41]. Genetic findings are increasingly guiding the clinical management of nephropathies, enabling more accurate diagnoses, tailored therapy selection, family counseling, and targeted disease monitoring [41].

A significant problem in treating patients with CKD is that up to 90% of individuals with the disease are undiagnosed, delaying their access to health care [43]. The problem is attributed to two main factors. First is that the early stage of CKD has no overt symptoms. The second one is the limiting policy guidelines that require performing diagnostic tests only when accompanied by risk factors such as the presence of chronic disease such as hypertension and diabetes [43]. Therefore, genetic testing of CKD is essential in identifying individuals with high risk that may benefit from screening [43]. The overall diagnostic yield of massively parallel-sequence gene testing goes up to 30% in pediatrics and between 6% and 30% in adult general populations [44,45]. Rodwell et al. (2024) developed a Risk for Chronic Kidney Disease (RICK) algorithm that utilized genetic tests for CKD and clinical risk factors [43]. The algorithm identified that individuals in the top ten percentile had a 15-fold increased risk of Stage 3 CKD and that the diagnostic testing of the top decile can identify up to 43% of undiagnosed Stage 3 CKD cases [43]. These findings underscore the importance of integrating genetic testing to identify individuals with high risk of CKD, which then inform appropriate utilization of diagnostic tests to enhance early diagnoses and treatment of patients with CKD.

Strategies for Equitable Renal Health Assessment

Equity in renal health care can be enhanced through multifaceted interventions and collaboration among different stakeholders, including risk assessment approaches, patient and care-partner education, integrated practices, and strategic partnerships [46]. Technology can be also integrated to facilitate remote health care access, timely appointments, and engaging patients to enhance their treatment adherence. Equitable renal health care can also be enhanced through universal health coverage and integrating kidney disease assessment and treatment within existing health care systems and multisectoral initiatives [47]. There is also a need for collaboration

among different stakeholders and enhancing access to kidney care through approaches such as home dialysis [48]. It is also essential to improve awareness about kidney health, including diagnoses, treatment, and management in underserved and marginalized communities [21].

Accurate and equitable access to renal health assessment can be attained through robust risk identification and stratification using standardized and evidence-based assessment tools [49,52]. Risk assessment tools should integrate social determinants of health (SDOH), such as socioeconomic status, housing instability, and access to nutritious food [49]. Integrating SDOH into risk models, such as screening for food insecurity or transportation barriers, can enhance early detection and intervention in high-risk groups, which in turn lead to equitable access to renal care [49]. While there is no direct research showing improved health outcomes when SDOH are integrated in the risk model, sufficient evidence links unfavorable SDOH factors with both higher prevalence and poor prognosis of CKD [50,51]. These evidence suggests that integrating SDOH in risk models may increase early detection and treatment of CKD among population with unfavorable SDOH.

Equitable renal health assessment can also be enhanced by increasing investment in public awareness and educational initiatives aimed at addressing the needs of specific communities. For example, culturally appropriate education improves patient knowledge, empowers them to engage in self-management, and improves community engagement with renal health services [53]. Griffith and Umeukeje (2022) highlighted the need for culturally tailored educational programs that address knowledge gaps in underserved communities, where low health literacy often exacerbates health disparities. Community health workers and peer educators can be used to enhance public awareness about the importance of regular renal assessment, available renal services, and how individuals in the communities can access those services [48].

Revolutionizing eGFR Through Technological Advancements

The advancement in multi-omics, cytometry, and imaging alongside bioinformatics biostatistics methodologies has led to the discovery and development of novel and reproducible biomarkers for complex diseases [10]. Studies have explored perspectives across different areas of focus in biomarkers research, including the discovery of and validation of novel biomarkers, and the integration of AI (see Table 4). Although the traditional methods such as creatine, iothalamate, iohexol, and inulin clearance have provided a foundational understanding and measurement of GFR, they have notable limitations[54]. A consensus statement from 23 expert panelists determined that current clinical evidence supports using emerging biomarkers for the prevention and management of acute kidney injury [55]. Emerging technologies and biomarkers such as neutrophil gelatinase-associated lipocalin (NGAL) and kidney injury molecule-1 (KIM-1) provided enhanced diagnostic precisions and disease severity [10]. The conventional CKD classification, based on cause, GFR category, and albuminuria category, often fails to reflect the complexity of diverse outcomes, disease progression variations, and treatment responses [56]. Recent advancements in omics technologies, including proteomics, genomics, and metabolomics, have led to the discovery of novel biomarkers. These technologies have potentials identifying more specific and sensitive biomarkers for early CKD detection and prognosis [10]. Additionally, omics technologies enable high throughputs and comprehensive exploration of proteome, genome, epigenome, metabolome, and transcriptome [57]. However, these technologies are challenged by a lack of standardization in biomarker discovery methods [10]. Artificial intelligence (AI) and machine learning can be used to analyze complex biomarker datasets and enhance predictive models, resulting in accurate predictions and personalized treatment plans [10].

Point of care (POC) biosensors have potential solutions for rapid, accessible, cost-effective, and non-invasive kidney function diagnostics [75]. POC biosensors enable continuous and real-time monitoring of biomarkers, facilitating efficient management and prompt clinical measures during deviations [76]. Sweat, interstitial fluid, urine, and saliva are potential candidate biofluids for monitoring CKD using wearable sensors [76]. The development of novel

Table 4 Current Advances and Perspectives in CKD Biomarkers Research

Area of Focus	Study	Recent Advances	Challenges	Clinical Implications
Discovery of novel biomarkers	Mizdrak et al. (2022)[57]	Advanced omics technologies such as genomics, metabolomics, and proteomic have led to the identification of new novel biomarker candidates	Lack of standardization in the methods of biomarker discovery	Present opportunity to identify more specific and sensitive biomarkers for early detection and prognosis of CKD
Validation of biomarkers	Patel et al. (2021), Puthumana et al. (2021)[58,59]	Large scale clinical trials to validate CKD biomarkers	Difficulty in reproducing results across different populations and study designs	Validation of CKD biomarkers is essential in enhancing their reliability of their use in clinical practice
Biomarker panels	Bienaimé et al. (2023)[60]	Efforts to combine different biomarkers to enhance diagnostic accuracy	Complexity in interpreting combined biomarker results	Biomarker panels can enhance the accuracy of detecting CKD and differentiating the associated causes
Integration of AI	Chaudhuri et al. (2020), Alobaidi, (2024)[61,62]	AI and ML help in analyzing complex biomarkers and enhance predictive capabilities of models	Challenges in ensuring transparency and interpretability of AI-based models in clinical practice	AI and ML can provide more accurate diagnosis and predictions for CKD progression and may help in personalizing treatment plans
Personalized medicine	Ito et al. (2022)[63]	Development of biomarker-driven personalized treatment plans	High cost and complexity of personalized medicine	Personalized treatment plans enables customization of therapies for individual patients, leading to more effective management of the CKD
Discovery of non-invasive biomarkers	Rupprecht et al. (2023), Catanese et al., (2023)[64,65]	Identification of non-invasive biomarkers such as albumin, urinary NGAL	Non-invasive biomarkers may be less sensitive or specific compared to invasive biomarkers	Non-invasive biomarkers are patient-friendly for regular monitoring and management of CKD and early detection of the disease.
Longitudinal monitoring of biomarkers	Wen et al. (2023), Karger et al. (2021)[66,67]	Increased emphasis on the importance of monitoring individual patient biomarkers for CKD over time	Levels of biomarkers may fluctuate due to factors unrelated to CKD	Continuous monitoring of patient biomarkers may help in adjusting treatment plans and assess disease progression
Development of Clinical Guidelines	Graterol Torres et al., (2021), Rovin et al. (2021), Navaneethan et al. (2021)[68-70]	The development of standardize clinical guidelines for the use of biomarkers for diagnosis and management of CKD, such as KDIGO guidelines	Limited adoption of guidelines due to cost and availability of biomarkers	Clinical guidelines helps in standardization of the use of biomarkers in the management of CKD, leading to improved diagnoses ad treatment outcomes

Biomarkers for specific CKD pathways	Tejchman et al. (2020), Yuan et al. (2022)[71,72]	Identification of biomarkers specific to inflammation, oxidative stress, and fibrosis in CKD	Difficulty in differentiating CKD-related biomarker changes and those related to aging or comorbidities	Specific pathways biomarkers can help in developing targeted therapies for different stages and types of CKD
Ethical and regulatory considerations	Hoque, (2024), Patel (2025)[73,74]	Increased emphasis on ethical concerns, such as patient consent and privacy of the data in biomarker research	Regulatory challenges of approving new biomarkers for clinical use	Addressing ethical and regulatory issues is essential for upholding patient dignity and for safely and effectively using biomarkers

technologies for eGFR are still in the early stages (pre-clinical trial) and may present a paradigm shift once they are validated in clinical practice [57, 77,78].

Next Steps and New Developments

Due to the known and unknown cystatin C and creatine confounders in estimating eGFR, there are current efforts to identify other GFR biomarkers. For example, Freed et al. (2019) developed a liquid chromatography (eGFRmet) that is used to quantitatively measure four serum metabolites; pseudouridine, N-acetylthreonine, tryptophan, and phenyla-cetylglutamine [28,77]. The equation, independent of cystatin C, creatinine, and demographic factors, when combined with cystatin C and creatinine, yields eGFRmet, which is more accurate than other current methods [28]. Additionally, new approaches have excluded endogenous biomarkers altogether, such as the development of fluorescent molecules to act as ideal filtration makers [78]. Instead of relying on steady-state concentration, plasma disappearance rates of exogenous makers can be measured in real time using transdermal sensors [28]. Fanous et al. (2022) found that transdermal GFR measurement using miniaturized fluorescence sensors to measure fluorescein-isothiocyanate (FITC) conjugated sinistrin was effective in evaluating renal functions in mechanically ventilated neonatal pigs [79]. Similarly, Dorshow et al. (2024) found that relmapirazin had clinical performance similar to iohexol in measuring GFR [80]. Dorshow et al. (2024) findings support the ongoing pursuit of safer, more precise, cost-effective, and scalable methodologies for direct GFR measurements [80].

Collectively, these developments depict a paradigm shift in renal function assessment. Integrating metabolomics, fluorescent probes, and wearable sensor technology represents a significant advancement toward personalized and equitable nephrology care. As they are being advanced and further developed, these technologies have the potential to revolutionize GFR estimation methodologies, leading to decreased cost, reducing disparities associated with the traditional biomarker confounders, and improving the accuracy of CKD diagnosis and monitoring across diverse patient populations. Future research should address critical implementation challenges, such as the standardization of assay protocols, cost-benefit analyses, and integration into existing clinical procedures. There is a need for multidisciplinary collaboration among researchers, clinicians, and policymakers to validate, scale, and ease the adoption of these technologies in clinical practice. Additionally, large-scale, multiethnic validation studies should be conducted to enhance the generalizability and clinical utility of these novel approaches across global healthcare settings. Both patients and healthcare professionals should be educated on the benefits and limitations of the emerging tools in the diagnosis and management of CKD. To advance eGFR and care for patients with CKD, current efforts should prioritize the following urgent next steps:

- Standardize assay protocols to ensure consistency, reproducibility, and reliability of novel GFR estimation methods across different clinical settings.
- Conduct large-scale, multiethnic validation studies to enhance the generalizability and clinical utility of these technologies across diverse global populations.
- Develop guidelines and support systems for integrating cystatin C and other novel biomarkers into existing clinical workflows to

improve accuracy and equity in CKD diagnosis and monitoring.

- Foster multidisciplinary collaboration among researchers, clinicians, and policymakers to validate, scale, and facilitate the adoption of the emerging technologies in clinical practice.

Declaration of Generative AI and AI-assisted technologies in the writing process: During the preparation of this work the author used ChatGPT 4.0 and Google Gemini in order to enhance the writing of this manuscript. After using these tools, the author reviewed and edited the content as needed and take full responsibility for the content of the publication.

Supplementary Materials: Not applicable. All data are contained within the article.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: All data and supporting materials related to this study are available within the published article.

References

1. Davis, G.; Umakanthan, S.; Pereira, L.P., Challenges for eGFR equations in the developing world. Current Medical Research and Opinion2024, 40 (11). https://doi.org/10.1080/03007995.2024.2411440

2. Inker, L. A.; Titan, S., Measurement and estimation of GFR for use in clinical practice: core curriculum 2021. American Journal of Kidney Diseases2021, 78(5). https://doi.org/10.1053/j.ajkd.2021.04.016

3. Spencer, S.; Desborough, R.; Bhandari. S,. Should cystatin C eGFR become routine clinical practice? Biomolecules 2023, 13(7). https://doi.org/10.3390/biom13071075

4. Ebert, N.; Bevc, S.; Bökenkamp, A.; Gaillard, F.; Hornum, M.; Jager, K. J.; Mariat, C.; Eriksen, B. O.; Palsson, R.; Rule, A. D.; Van Londen, M.; White, C.; Schaeffner, E., Assessment of kidney function: clinical indications for measured GFR. Clinical Kidney Journal2021, 14(8). https://doi.org/10.1093/ckj/sfab042

5. Uppal, P.; Golden, B. L.; Panicker, A.; Khan, O. A.; Burday, M. J., The case against race-based GFR. Delaware Journal of Public Health 2022, 8(3). https://pmc.ncbi.nlm.nih.gov/articles/PMC9495470/

6. Yadav, A. K.; Kaur, J.; Kaur, P.; Jha, V., Evaluation of race-neutral glomerular filtration rate estimating equations in an Indian population. Kidney International Reports2024, 9(12). https://doi.org/10.1016/j.ekir.2024.09.020

7. Diao, J. A.; Inker, L. A.; Levey, A. S.; Tighiouart, H.; Powe, N. R.; Manrai, A. K., In search of a better equation—performance and equity in estimates of kidney function. New England Journal of Medicine2021, 384(5). https://doi.org/10.1056/nejmp2028243

8. Umeukeje, E. M.; Koonce, T. Y.; Kusnoor, S. V.; Ulasi, I.. I.; Kostelanetz, S.; Williams, A. M.; Blasingame, M. N.; Epelbaum, M. I.; Giuse, D. A.; Apple, A. N.; Kaur, K.; Peña, T. G.; Barry, D.; Eisenstein, L. G.; Nutt, C. T.; Giuse, N. B., Systematic review of international studies evaluating MDRD and CKD-EPI estimated glomerular filtration rate (eGFR) equations in Black adults. Public Library of Science One 2022, 17(10). https://doi.org/10.1371/journal.pone.0276252

9. Hsu, C.;, Yang, W.; Parikh, R. V.; Anderson, A. H; Chen, T. K.; Cohen, D. L.; Go, A. S., Race, genetic ancestry, and estimating kidney function in CKD. New England Journal of Medicine 2021, 385(19). https://doi.org/10.1056/nejmoa2103753

10. 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(9). https://doi.org/10.7759/cureus.70262

11. Franks, C. E.; Scott, M. G., On the basis of race: the utility of a race factor in estimating glomerular filtration. The Journal of Applied Laboratory Medicine 2021, 6(1). https://doi.org/10.1093/jalm/jfaa128

12. Rysz, J.; Franczyk, B.; Rokicki, R.; Gluba-Brzózka, A., The Influence of Dietary Interventions on Chronic Kidney Disease–Mineral and Bone Disorder (CKD-MBD). Nutrients 2021,13(6). https://doi.org/10.3390/nu13062065

13. Hamidianshirazi, M.; Shafiee, M.; Ekramzadeh, M.; Jahromi, M. T.; Nikaein, F., Diet therapy along with nutrition education can improve renal function in

people with stages 3–4 chronic kidney disease who do not have diabetes: a randomised controlled trial. British Journal of Nutrition 2023, 129(11). https://doi.org/10.1017/s0007114522002094

14. Naber, T.; Purohit, S., Chronic kidney disease: role of diet for a reduction in the severity of the disease. Nutrients. 2021, 13(9). https://doi.org/10.3390/nu13093277

15. Delanaye, P.; Cavalier, E.; Pottel, H.; Stehlé, T., New and old GFR equations: a European perspective. Clin Kidney J 2023, 16 (9). https://doi.org/10.1093/ckj/sfad039

16. National Kideney Foundation. Frequently Asked Questions About GFR Estimates. (2022). Accessed: June 20, 2025: https://www.kidney.org/sites/default/files/441-8491_2202_faqs_aboutgfr_v5.pdf

17. Levey, A. S.; Stevens, L. A.; Schmid, C. H.; Zhang, Y.; Castro III, A. F.; Feldman.,A new equation to estimate glomerular filtration rate. Annals of internal medicine 2009, 150(9). https://doi.org/10.7326/0003-4819-150-9-200905050-00006

18. Stevens, L. A; Claybon, M. A.; Schmid, C. H.; Chen, J.; Horio, M.; Imai, E.; Levey, A. S., Evaluation of the Chronic Kidney Disease Epidemiology Collaboration equation for estimating the glomerular filtration rate in multiple ethnicities. Kidney International. 2011, 79(5). https://doi.org/10.1038/ki.2010.462

19. Skiba, J.; Bansal, A.; Palmer, O. P.; Johnstone, D., Case report: Clinical consequences of adjusting estimated GFR for black race. Journal of General Internal Medicine 2022, 37(4). https://doi.org/10.1007/s11606-021-07179-5

20. Tsai, J. W.; Cerdeña, J. P.;, Goedel, W. C.; Asch, W. S.; Grubbs, V.; Mendu, M. L.; Kaufman, J. S., Evaluating the impact and rationale of race-specific estimations of kidney function: estimations from US NHANES, 2015-2018. EClinicalMedicine 2021, 42. https://doi.org/10.1016/j.eclinm.2021.101197

21. National Kidney Foundation Advancing Equity in Kidney Health. 2022. Accessed: June 20, 2025. https://www.kidney.org/sites/default/files/kidney_health_equity_position_paper_9.12.23_final.pdf

22. Thomas, D.; Zachariah, S.; Elamin, A. E. E.; Hashim, A. L. O., Limitations of serum creatinine as a marker of renal function. Sch Acad J Pharm. 2017, 6(5). https://www.saspublishers.com/media/articles/SAJP-65168-170.pdf

23. Lees, J. S.; Rutherford, E.; Stevens, K. I.; Chen, D. C.; Scherzer, R.; Estrella, M. M.; Shlipak, M. G.,Assessment of cystatin C level for risk stratification in adults with chronic kidney disease. JAMA Network Open. 2022, 5(10).https://doi.org/10.1001/jamanetworkopen.2022.38300

24. Prowle, J. R.; Croal, B.; Abbott, T. E.; Cuthbertson, B. H.; Wijeysundera, D. N., Cystatin C or creatinine for pre-operative assessment of kidney function and risk of post-operative acute kidney injury: a secondary analysis of the METS cohort study. Clinical Kidney Journal 2024, 17(2).https://doi.org/10.1093/ckj/sfae004

25. Chen, D. C.; Potok, O. A; Rifkin, D.; Estrella, M. M., Advantages, limitations, and clinical considerations in using cystatin C to estimate GFR. Kidney360 2022, 3(10).https://doi.org/10.34067/kid.0003202022

26. Yan, A. F.; Williams, M. Y.; Shi, Z.; Oyekan, R.; Yoon, C.; Bowen, R.; Chertow, G. M., Bias and accuracy of glomerular filtration rate estimating equations in the US: a systematic review and meta-analysis. JAMA network open 2024, 7(2). Doi:10.1001/jamanetworkopen.2024.1127

27. Stevens, P. E.; Ahmed, S. B.; Carrero, J. J.; Foster, B.; Francis, A.; Hall, R. K.; Levin, A., KDIGO 2024 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney International 2024, 105(4S). https://doi.org/10.1016/j.kint.2023.10.018

28. Benoit, S. W.; Ciccia, E. A.; Devarajan, P., Cystatin C as a biomarker of chronic kidney disease: latest developments. Expert Review of Molecular Diagnostics 2020, 20(10). https://doi.org/10.1080/14737159.2020.1768849

29. Skidmore, M.; Spencer, S.; Desborough, R.; Kent, D.; Bhandari, S., Cystatin C as a Marker of Kidney Function in Children. Biomolecules. 2024, 14:938.

30. Tio, M. C., Shafi, T., The Limits of Generalizability: Pitfalls of Applying Western GFR Estimation Models to Global Populations. Kidney International Reports 2024, 9(12). https://doi.org/10.1016/j.ekir.2024.10.018

31. Stehlé, T.; Delanaye, P., Which is the best glomerular filtration marker: Creatinine, cystatin C or both? European Journal of Clinical Investigation 2024, 54(10). https://doi.org/10.1111/eci.14278

32. Lamprea-Montealegre, J. A.; Shapiro, A.; Bontrager, N. A.; Rifkin, D. E.; Jassal, S. K.; Gregg, L. P.; Wang, V., Cystatin C Use for CKD Detection in the Veterans Health Administration System: A Qualitative Study of Barriers and Facilitators. Kidney Medicine 2024, 6(7).https://doi.org/10.1016/j.xkme.2024.100830

33. Inker, L. A.; Eneanya, N. D.; Coresh, J.; Tighiouart, H.; Wang, D.; Sang, Y.; Levey, A. S., New creatinine- and cystatin C–based equations to estimate GFR without race. New England Journal of Medicine 2021, 385(19). https://doi.org/10.1056/nejmoa2102953

34. Eneanya, N. D.; Kostelanetz, S.; Mendu, M. L., Race-free biomarkers to quantify kidney function: health equity lessons learned from population-based research. National Kidney Foundation 2021,77(5). . https://doi.org/10.1053/j.ajkd.2020.12.001

35. Grubbs, V., Precision in GFR reporting: let's stop playing the race card. Clinical Journal of the American Society of Nephrology 2020, 15(8). https://doi.org/10.2215/cjn.00690120

36. Ahmed, S.; Nutt, C. T.; Eneanya, N. D.; Reese, P. P.; Sivashanker, K.; Morse, M.; Mendu, M. L., Examining the potential impact of race multiplier utilization in estimated glomerular filtration rate calculation on African-American care outcomes. Journal of General Internal Medicine 2021, 36(2). https://doi.org/10.1007/s11606-020-06280-5

37. Lin, B. M.; Grinde, K. E.; Brody, J. A.; Breeze, C. E.; Raffield, L. M.; Mychaleckyj, J. C.; TOPMed Kidney Working Group., Whole genome sequence analyses of eGFR in 23,732 people representing multiple ancestries in the NHLBI trans-omics for precision medicine (TOPMed) consortium. EBioMedicine 2021, 63. https://doi.org/10.1016/j.ebiom.2020.103157

38. Morris, A. P.; Le, T. H.; Wu, H.; Akbarov, A., J., P.; Hemani, G.; Smith, G. D.; Mahajan, A.; Gaulton, K. J.; Nadkarni, G. N.; Mychaleckyj, J. C.; Dueker, N. D.; Guo, X.; Hai, Y.; Haessler, J.; Kamatani, Y.; Stilp, A. M.; Zhu, G.; Cook, J. P.; Franceschini, N., Trans-ethnic kidney function association study reveals putative causal genes and effects on kidney-specific disease aetiologies. Nature Communications 2019, 10(1). https://doi.org/10.1038/s41467-018-07867-7

39. Lu, Y. Q.; Wang, Y., Multi-Omic Analysis Reveals Genetic Determinants and Therapeutic Targets of Chronic Kidney Disease and Kidney Function. International Journal of Molecular Sciences 2024, 25(11). https://doi.org/10.3390/ijms25116033

40. Doke, T.; Huang, S.; Qiu, C.; Liu, H.; Guan, Y.; Hu, H.; Susztak, K.,Transcriptome-wide association analysis identifies DACH1 as a kidney disease risk gene that contributes to fibrosis. The Journal of clinical investigation 2021, 131(10). https://doi.org/10.1172/jci141801

41. Köttgen, A.; Cornec-Le Gall, E.; Halbritter, J.; Kiryluk, K.; Mallett, A. J.; Parekh, R. S.; Gharavi, A. G., Genetics in chronic kidney disease: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) controversies conference. Kidney International 2022, 101(6). https://doi.org/10.1016/j.kint.2022.03.019

42. Zhang, J.; Thio, C. H.; Gansevoort, R. T,; Snieder, H.; Familial aggregation of CKD and heritability of kidney biomarkers in the general population: the lifelines cohort study. American Journal of Kidney Diseases 2021, 77(6). https://doi.org/10.1053/j.ajkd.2020.11.012

43. Rodwell, G.; Ioannidis, J. P.; Kim, S. K., A genetic and clinical risk factor algorithm to aid in identifying new cases of chronic kidney disease from the general population. medRxiv.https://doi.org/10.1101/2024.03.21.24304689

44. Knoers, N.; Antignac, C; Bergmann, C; et al., Genetic testing in the diagnosis of chronic kidney disease: recommendations for clinical practice. Nephrology Dialysis Transplantation 2022, 37(2). https://doi.org/10.1093/ndt/gfab218

45. Ottlewski, I.; Münch, J.; Wagner, T.; et al., Value of renal gene panel diagnostics in adults waiting for

kidney transplantation due to undetermined end-stage renal disease. Kidney international 2019, 96 (1). https://doi.org/10.1016/j.kint.2019.01.038

46. Brown, C. O, Pham, P. C.; Shah, A.; et al., Population health strategies for health equity in chronic kidney disease management. Current Opinion in Nephrology and Hypertension 2025, 34(1). https://doi.org/10.1097/01.mnh.0001095808.65804.8c

47. International Society of Nephrology. 10 Recommendations for Global Kidney Health. (2025). Accessed: June 20, 2025: https://www.theisn.org/in-action/advocacy/advocacy-activities/10-recommendations-for-global-kidney-health/

48. Griffith, D. M.; Umeukeje, E. M., Navigating to kidney health equity. Journal of the American Society of Nephrology 2022, 33(7). https://doi.org/10.1681/ASN.2022040421

49. Cai, X.; Li, T., Social Determinants of Health in the Development of Cardiovascular-kidney-metabolic Syndrome. Reviews in Cardiovascular Medicine 2025, 26(5). https://doi.org/10.31083/RCM26580

50. Li, K.; Chen, X.; Chen, L.; Liu, Y.; Huang, J., Li, P.; Liang, D.; Chen, J. The impact of social determinants of health on chronic kidney disease risk: Evidence from the CHARLS study. Frontiers in Public Health 2025, 13. https://doi.org/10.3389/fpubh.2025.1532372

51 Xie, C.; Wu, Q.; Xie, C., Shi, Z. Social determinants of health and chronic kidney disease in United States adults: A cross-sectional study from National Health and Nutrition Examination Survey 2003–2018. Preventive Medicine Reports 2025, 55. https://doi.org/10.1016/j.pmedr.2025.103132

52. Miano, T. A.; Barreto, E. F.; McNett, M.; et al., Toward equitable kidney function estimation in critical care practice: guidance from the Society of Critical Care Medicine's Diversity, Equity, and Inclusion in Renal Clinical Practice Task Force. Critical Care Medicine 2024, 52(6). https://doi.org/10.1097/ccm.0000000000006237

53. Porteny, T.; Kennefick, K.; Lynch, M.; et al., The need for culturally tailored CKD education in older Latino patients and their families. American Journal of Kidney Diseases 2025, 85(2). https://doi.org/10.1053/j.ajkd.2024.06.015

54. Sheikh, M. S.; Kashani, K. B., Beyond creatinine: New methods to measure renal function? European Journal of Internal Medicine 2025 134. https://doi.org/10.1016/j.ejim.2025.01.015

55. Ostermann, M.; Zarbock, A.; Goldstein, S.; et al., Recommendations on acute kidney injury biomarkers from the acute disease quality initiative consensus conference: a consensus statement. JAMA network open 2020, 3(10). https://doi.org/10.1001/jamanetworkopen.2020.19209

56. Lopes, M. B.; Coletti, R.; Duranton, F.; et al., The Omics-Driven Machine Learning Path to Cost-Effective Precision Medicine in Chronic Kidney Disease. Proteomics 2024, 25(11-12). https://doi.org/10.1002/pmic.202400108

57. Mizdrak, M., Kumrić, M.; Kurir, T. T.; Božić, J., Emerging biomarkers for early detection of chronic kidney disease. Journal of Personalized Medicine 2022, 12(4). https://doi.org/10.3390/jpm12040548

58. Patel, R. B.; Ter Maaten, J. M.; Ferreira, J. P.; et al., Challenges of cardio-kidney composite outcomes in large-scale clinical trials. Circulation 2021, 143(9). https://doi.org/10.1161/circulationaha.120.049514

59. Puthumana, J.; Thiessen-Philbrook, H.; Xu, L.; et al., Biomarkers of inflammation and repair in kidney disease progression. The Journal of Clinical Investigation 2021, 131(3). https://doi.org/10.1172/jci139927

60. Bienaimé, F.; Muorah, M.; Metzger, M.; et al., Combining robust urine biomarkers to assess chronic kidney disease progression. EBioMedicine 2023, 93. https://doi.org/10.1016/j.ebiom.2023.104635

61. Chaudhuri, S.; Long, A,; Zhang, H.; et al., Artificial intelligence enabled applications in kidney disease. In Seminars in dialysis. Volume 34. Wiley Online Library 2021, 34(1). https://doi.org/10.1111/sdi.12915

62. Alobaidi, S., Emerging Biomarkers and Advanced Diagnostics in Chronic Kidney Disease: Early Detection Through Multi-Omics and AI. Diagnostics 2025, 15(10). https://doi.org/10.3390/diagnostics15101225

63. Serelli-Lee, V.; Ito, K.; Koibuchi, A.; et al., A state-of-the-art roadmap for biomarker-driven drug development in the era of personalized therapies.

Journal of Personalized Medicine 2022, 12(5). https://doi.org/10.3390/jpm12050669

64. Rupprecht, H.; Catanese, L.; Amann, K.; et al., Assessment and risk prediction of chronic kidney disease and kidney fibrosis using non-invasive biomarkers. International Journal of Molecular Sciences 2024, 25(7). https://doi.org/10.3390/ijms25073678

65. Catanese, L.; Rupprecht, H.; Huber, T. B.; et al., Non-invasive biomarkers for diagnosis, risk prediction, and therapy guidance of glomerular kidney diseases: a comprehensive review. International Journal of Molecular Sciences 2024, 25(6). https://doi.org/10.3390/ijms25063519

66. Wen, Y.; Xu, L.; Melchinger, I.; et al., Longitudinal biomarkers and kidney disease progression after acute kidney injury. Journal of Clinical Investigations Insight 2023, 8(9). https://doi.org/10.1172/jci.insight.167731

67. Karger, A. B.; Eckfeldt, J. H.; Rynders, G. P.; et al., Long-term longitudinal stability of kidney filtration marker measurements: implications for epidemiological studies and clinical care. Clinical Chemistry 2021, 67(3).https://doi.org/10.1093/clinchem/hvaa237

68. Graterol, T., F.; Molina, M.; Soler-Majoral, J.; et al., Evolving concepts on inflammatory biomarkers and malnutrition in chronic kidney disease. Nutrients 2022, 14(20). https://doi.org/10.3390/nu14204297

69. Rovin, B. H.; Adler, S.G., Barratt, J.; et al., Executive summary of the KDIGO 2021 guideline for the management of glomerular diseases. Kidney International 2021, 100(4). https://doi.org/10.1016/j.kint.2021.05.015

70. Navaneethan, S. D.; Zoungas, S.; Caramori, M. L.; et al., Diabetes management in chronic kidney disease: synopsis of the 2020 KDIGO clinical practice guideline. Annals of Internal Medicine 2021, 174(3). https://doi.org/10.7326/m20-5938

71. Tejchman, K.; Kotfis, K.; Sieńko, J., Biomarkers and mechanisms of oxidative stress—last 20 years of research with an emphasis on kidney damage and renal transplantation. International Journal of Molecular Sciences 2021, 22(15). https://doi.org/10.3390/ijms22158010

72. Yuan, Q.; Tang, B.; Zhang, C., Signaling pathways of chronic kidney diseases, implications for therapeutics. Signal Transduction and Targeted Therapy 2022, 7(2022). https://doi.org/10.1038/s41392-022-01036-5

73. Hoque, N., A Comprehensive Review of Ethical Guideline on Biomarker Application and Research. International Journal of Health and Allied Sciences 2024, 13(4). https://doi.org/10.55691/2278-344X.1103

74. Patel, D. M., Ethical considerations in biomarker research and application. The Potential of Cancer Biomarkers. Elsevier 2025. http://dx.doi.org/10.1016/B978-0-443-29279-8.00013-2

75. Liu, Y.; Zhao, X.; Liao, M.; Ke, G.; Zhang, X., Point-of-care biosensors and devices for diagnostics of chronic kidney disease. Sensors & Diagnostics. 2024. https://doi.org/10.1039/d4sd00241e

76. Han. S.; Yamamoto, S.; Jung, C.Y.; Jin, D. Y.; Lee, T.; Kim. J. S., Wearable sensors for monitoring chronic kidney disease. Communications Materials 2024, 5(153). http://dx.doi.org/10.1038/s43246-024-00606-0

77. Freed, T. A.; Coresh, J.; Inker, L. A.; et al., Validation of a metabolite panel for a more accurate estimation of glomerular filtration rate using quantitative LC-MS/MS. Clinical Chemistry 2019, 65(3). https://doi.org/10.1373/clinchem.2018.288092

78. Solomon, R.; Goldstein, S., Real-time measurement of glomerular filtration rate. Current Opinion in Critical Care 2017, 23(6). https://doi.org/10.1097/mcc.0000000000000456

79. Fanous, M. S.; Afolabi, J. M.; Michael, O. S.; Falayi, O. O; Iwhiwhu, S. A; Adebiyi, A., Transdermal measurement of glomerular filtration rate in mechanically ventilated piglets. Journal of Visualized Experiments: JoVE 2022, 187. https://doi.org/10.3791/64413

80. Dorshow, R. B.; Debreczeny, M. P.; Goldstein, S. L.; Shieh, J. J., Clinical validation of the novel fluorescent glomerular filtration rate tracer agent relmapirazin (MB-102). Kidney International 2024, 106(4). https://doi.org/10.1016/j.kint.2024.06.012