THE PREVALENCE OF CHRONIC KIDNEY DISEASE IN SOUTH AFRICA – COMPARISONS WITH SUB-SAHARAN AFRICA, AFRICA AND GLOBALLY

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Dedication

To The Supreme Absolute

To my wife Anusha, daughter Priyanka, and my Parents

Acknowledgments

Immense Gratitude to:

Professor R Bhimma

Professor AGH Assounga

Professor S Naicker

Mr. Edgar Jembere

Table of contents

List of tables

Abbreviations and Acronyms

AIDS	Acquired immune deficiency syndrome
AKI	Acute kidney injury
CGA	Cause, GFR, and Albuminuria categories
CI	Confidence interval
CKD	Chronic kidney disease
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
CKF	Chronic kidney failure
CVD	Cardiovascular disease
DALY	Disability-adjusted life years
DM	Diabetes mellitus
eGFR	estimated Glomerular Filtration Rate
GFR	Glomerular filtration rate
HIV	Human immunodeficiency virus
IDMS	Isotope-dilution mass spectrometry
IQR	Interquartile range
ISN	International Society of Nephrology
KDIGO	Kidney Disease: Improving Global Outcomes
KDOQI	Kidney Disease Outcomes Quality Initiative
KRT	Kidney replacement therapy
LMIC	Lower and middle-income countries
MDRD	Modification of Diet in Renal Disease
NCD	Non-communicable disease
RR	Relative risk
SA	South Africa
WHO	World Health Organization

Abstract

Chronic kidney disease (CKD) represents a significant global public health challenge as one of the most prevalent non-communicable diseases and a leading cause of mortality worldwide. Amidst the pandemic of non-communicable diseases, CKD's gradual progression often eludes recognition, necessitating a robust understanding of its prevalence and patterns to guide interventions.

There is no direct comparison of CKD prevalence between South Africa, Africa, and the global landscape in the available literature. This study sought to bridge this gap by systematically comparing CKD prevalence rates across these geographical regions while investigating the underlying reasons for observed differences.

A comprehensive literature search compared CKD prevalence in South Africa with sub-Saharan, African, and global studies. The review was registered with the International Prospective Register of Systematic Reviews (PROSPERO), with multiple search engines being used. The findings culminated in the publication of an original paper titled "The Prevalence of CKD in South Africa - Limitations of Comparative Studies with Sub-Saharan Africa, Africa, and Global Data" in the Biomedical Central Nephrology Journal on March 21, 2023.

The research revealed statistically significant differences in CKD prevalence rates among the studied regions. However, these differences stemmed predominantly from substantial variations in sample sizes rather than actual disparities in prevalence rates. The systematic review illuminated a spectrum of factors contributing to this variability, including divergent definitions of CKD, lack of assessment for chronicity, variations in serum creatinine calculations, disparities in formulas used to estimate glomerular filtration rate (eGFR), demographic distinctions, and differences in risk factors associated with CKD development.

This study underscores the need for a nuanced understanding of CKD prevalence and its determinants to inform targeted interventions in addressing this global health challenge.

Chapter 1

The introductory chapter will elucidate the definition and diagnostic criteria for chronic kidney disease (CKD). Subsequently, it will delve into the evolutionary journey of this definition, culminating in the current staging system and recommended clinical approach. The global ramifications and epidemiological aspects of CKD were explored, followed by an in-depth analysis of its prevalence rates and contributing factors in various geographical regions, including (South Africa)SA, sub-Saharan Africa, and the broader African context, as well as its worldwide impact.

Definition, diagnosis, and staging of CKD

CKD is defined as an abnormality of kidney structure or function, present for over three months, diagnosed by kidney damage markers, including albuminuria, urine sediment abnormalities, electrolyte and tubular abnormalities, and abnormal histology, with the second criterion being a decreased glomerular filtration rate (GFR) of less than 60 ml/min/1.73m^2 (1). This syndrome is a group of heterogeneous disorders with a variable clinical presentation related to cause, severity, and rate of progression, with health implications (1).

The definition of CKD has evolved over the past two decades. In 2002, the Kidney Disease Outcome Quality Initiative (KDOQI) group developed guidelines for CKD using new equations to calculate eGFR (2). The KDOQI working group made the first uniform definition and current five stages of CKD. The definitions allowed nephrologists to speak a common language about the management and research of CKD. The guidelines changed the clinical practice of primary care, public health communities, and nephrologists (2). In 2008, the National Institute for Health and Clinical Excellence (NICE) group in the United Kingdom suggested two new changes to the definition of CKD. They included the subdivision of Stage 3 into Stage 3a and Stage 3b (3). The suffix "P" delineated significant proteinuria at any stage (3). Significant proteinuria was equivalent to an albumin creatinine ratio of ≥ 30 mg/mmol or a protein creatinine ratio of ≥ 50 mg/mmol. The purpose of these changes was to delineate risks of adverse outcomes (3). The Kidney Disease: Improving Global Outcomes (KDIGO) working group recommends that kidney disease be classified according to the cause, GFR, and albuminuria (CGA) category (1). Since 2012, there have been five estimated GFR stages and three albuminuria categories (Table 1)(Table 2) based on the KDIGO definition of CKD (1).

The KDIGO definition of CKD is intended for use in clinical practice, research, and public health (1). The most severe stage of CKD is kidney failure (Stage 5), which requires dialysis or transplantation. Earlier stages (Stages 1 and 2) are often asymptomatic. They may be identified during the evaluation of comorbid conditions and reversible if detected and treated early (4).

The KDIGO CGA approach is used to predict the prognosis of CKD (Table 3) (1). The evaluation of the cause assists with establishing the patient's clinical context. Determining a cause includes relevant history, social and environmental factors, clinical and laboratory parameters, imaging, and histopathological

diagnosis (1). An estimated GFR (eGFR) is derived from serum creatinine, height, and a constant (1). The evaluation of albuminuria is measured by an albumin-creatinine or a protein-creatinine ratio (1).

The global impact and epidemiology of chronic kidney disease

Kidney diseases encompass a broad spectrum of syndromes characterised by varying causes, clinical trajectories, and functional severity, including acute kidney injury (AKI). As of 2017, the worldwide prevalence of CKD, AKI, and individuals undergoing kidney replacement therapy exceeded 850 million, with CKD patients constituting 844 million within the group (5). Patients suffering from kidney diseases are estimated to be twice the number of people with diabetes mellitus (DM) worldwide and more than twenty times those affected by human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) (5). This statistic underscores the global significance of kidney diseases, making CKD an undeniable priority in global public health (5, 6).

The Global Burden of Disease study ranked CKD as the 12th leading cause of death out of 133 conditions (7). The global deaths from kidney disease are estimated at 5-10 million people annually, mainly due to a shortage of kidney replacement therapy (KRT) services (8). The global all-age mortality rate from CKD increased by 41.5% between 1990 and 2017 (7). CKD is expected to be the fifth most prominent cause of years of life lost by 2040 (9). The annual estimated hospitalisation rate in CKD patients is 6.5%, and the mortality rate is 6.2% (10). CKD is associated with lower quality of life and reduced life expectancy (11). The existing clinical and research workforce is inadequate to address the current global burden of CKD, especially in low and middle-income countries (LMIC) (6).

Furthermore, the worldwide all-age prevalence of CKD has increased by 29.3% (95% CI 26.4-32.6) over the past 30 years, indicating an escalating impact (7). In 2010, 2,62 million people worldwide received KRT, and the number of people requiring KRT is expected to double to around 5.4 million people by 2030 (8). The epidemiological data is constrained because it is associated with a lack of awareness and poor access to laboratory services in lower-middle-income countries (LMIC), with the actual numbers probably underestimating the true burden of kidney disease (8).

The economic and societal ramifications of kidney disease are immense (8). High-income countries allocate 2-3% of the annual health budget to treating CKD despite chronic kidney failure (CKF) patients representing 0.03% of the total population (8). The global cost of treating milder kidney disease also appears to be greater than treating kidney failure (8). In 2010, the United States spent 41 billion dollars on CKD and 32.9 billion dollars on kidney failure, representing 24% of the total Medicare budget (12). Much of the expenditure, morbidity, and mortality attributed to hypertension and DM may also be due to kidney disease and its complications (8). The estimated disability-adjusted life years (DALYs) attributed to global kidney

disease increased from 19 million in 1990 to 33 million in 2013 (8). Reduced kidney function predicts hospitalisation and correlates with cognitive dysfunction and diminished quality of life (13). Poverty and lower socio-economic status independently heighten the risk of incident CKD and hasten its progression, magnifying the burden of poverty-related kidney disease due to infections, hazardous work, poor education, and inadequate maternal care (8).

The leading cause of CKD worldwide are hypertension and DM (7). The CKD burden in developing countries is exacerbated by factors such as HIV and exposure to toxins and heavy metals (7). The lack of adequate reporting in many countries obscures the leading causes of CKD (7). The key risk factors in developing nations for kidney disease include HIV infection, low birth weight, preterm birth, and malaria (8). Obesity also increases the lifetime risk of developing chronic kidney failure CKF (8). Nutritional factors such as increased salt intake increase mortality due to kidney disease (8). CKD is an independent risk factor for cardiovascular disease (CVD) (7). CKD is also a risk multiplier in patients with hypertension and DM for increased cardiovascular mortality (7).

While economically developed countries have studied CKD more extensively, its burden is even more significant in underdeveloped nations (13). The cost of treating CKD-associated complications, including CKF, is a challenge to health budgets and cannot be met in most developing countries (14). In 2010, 2.6 million people received some form of KRT worldwide, but nearly an equal number might have died during the same year because of a lack of access to dialysis and transplantation (15).

Unlike other major chronic diseases, such as cardiovascular and respiratory diseases, CKD's impact on mortality is rising (16). CKD has been largely unnoticed by health authorities and governments in most countries, while some countries have produced rich and very detailed CKD statistics (5). However, the degree of complexity of these statistics has not been effectively communicated to the public or policymakers (5). A concerted effort is required to simplify the research to increase awareness of kidney disease's global extent and magnitude (5).

The outcomes of CKD encompass disease progression and its complications. CKF contributes significantly to the cost of treating CKD and substantially reduces one's lifespan (1). Failing to identify CKD early results in adverse consequences and complications (1). Late referrals for advanced CKD are associated with poorer outcomes (1). Prompt identification, appropriate management, and specialist kidney disease services offer clinical and economic benefits (1). In countries where access to dialysis and transplantation is limited or

unavailable, the inevitable consequence of progressive CKD is death. A delay or prevention of progression has the potential to prolong health and save lives at a much lower cost than KRT (1).

In 2017, the International Society of Nephrology (ISN), American Society of Nephrology (ASN), and European Renal association-European Dialysis and Transplant Association (ERA-EDTA) collaborated to estimate the global prevalence of kidney diseases (5). The pragmatic estimated global prevalence of CKD of 11.1% was based on the systematic review by Mills *et al.* (12). The number affected by CKD rests on data of various qualities, approximations, and assumptions (5). There is limited information worldwide on the incidence of new-onset CKD. The purpose of monitoring the global burden of CKD is to increase awareness and acceptance by the community, policymakers, and public health groups, eventually translating into better health outcomes (5).

Therefore, CKD currently represents a monumental global health crisis, affecting millions of lives and straining healthcare systems worldwide. A multifaceted approach involving awareness, early detection, and accessible treatment is essential to mitigate its impact and improve the well-being of those affected by this debilitating condition.

Prevalence of chronic kidney disease in South Africa

SA has undergone a significant health transformation marked by a complex healthcare landscape, encompassing a burden of communicable, non-communicable, perinatal, maternal, and injury-related disorders (17). Notably, non-communicable diseases (NCDs) have emerged as a formidable challenge affecting rural and urban populations (17). The increasing burden pressures acute and chronic healthcare services (17). The impact of this shift is starkly evident in the rising mortality rates associated with diseases such as DM, CKD, prostate cancer, and cervical cancer (17). Addressing this crisis necessitates implementing targeted measures to combat the rising tide of NCDs, a trend expected to persist and intensify over the coming decades (17). According to the World Health Organisation (WHO), NCDs accounted for a significant portion, approximately 28%, of the total burden of disease measured by disability-adjusted life years (DALYs) in SA in 2004 (17). The WHO also estimates the burden from NCD in SA as two to three times higher than that in developed countries (17).

The distribution of NCD in SA exhibits stark socio-economic disparities, with the most onerous burden disproportionately affecting impoverished urban communities (17). Demographic change is a significant factor in increasing NCD in low-income countries (17). The aging demographic, a substantial factor in the surge of NCDs in low-income countries, puts older people at risk of developing chronic diseases (17). The population aged 60 years and older is projected to nearly triple, surging 18.9% from 1985 to 2025 (17). Many NCDs share common risk factors such as tobacco use, physical inactivity, and unhealthy diet, which translate into cardiovascular disease, DM, and cancer (17). Many SA adult populations harbour these potentially modifiable risk factors (17).

National prevalence data highlight a concerning shift in dietary habits, which has occurred with increasing momentum (17). This is particularly true in Black people, who constitute over three-quarters of the population (17). Fat intake has increased among Black people living in urban settings with a relative increase of 59.7% (from 16.4% to 26.2% of total energy), whereas carbohydrate intake has had a relative decrease of 10.9% (from 69.3% to 61.7%) in the past 50 years (17). Additionally, genetic and ethnic factors render specific populations more susceptible to NCDs (17). Between 1999 and 2006, SA witnessed a 67% increase in deaths attributed to CKD (17). Although accurate statistics are unavailable in SA, hypertension, and DM (in line with worldwide trends) are the

dominant diseases associated with CKF, mainly in black ethnic groups (17). Notably, hypertension not only acts as a causative factor for CKD but also exacerbates existing CKD, creating a vicious cycle (17). Other prevalent causes of CKD in SA include HIV, primary or secondary glomerular disease, congenital or inherited disease, renovascular disease, obstructive uropathy, medication toxicity, and chronic pyelonephritis (18).

The 2017 SA Renal Registry provides crucial insights into KRT data for CKF patients (19). By December 2017, 10,744 individuals with CKF received chronic dialysis or transplantation, equating to a prevalence of 190 per million population (pmp) (19). Notably, the increased incidence of KRT is attributable to a rise in patients opting for private-sector hemodialysis (19). In the private sector, the prevalence of KRT was 855 pmp, while in the public sector, serving 84% of the population, it is considerably lower at 66 pmp (19). The public sector KRT prevalence rate is lower than reported in 1994, underscoring a growing imbalance in access to KRT between the public and private sectors (19).

The South African Renal Registry additionally disclosed that kidney transplantation constituted 17.3% of all patients on KRT (19). Haemodialysis (HD) constitutes 86.5% of dialysis patients, with peritoneal dialysis accounting for the remaining 13.5% (19). The overall KRT duration was 4.4 years (interquartile range IQR 2.1-7.5 years) (19). The median age of patients on KRT was 52.6 years (IQR 41.8-62.3 years), of which 59.6% were male (19). Slightly over 50% of patients were Black (19). Hypertensive nephropathy emerged as the leading cause of CKF (35.1%), followed by unknown aetiologies (31.9%) and diabetic nephropathy (15.3%) (19). Despite these figures, SA's KRT prevalence remains remarkably low compared to countries with similar or lower gross national per capita income (19).

A regional CKD study in the Western Cape by Matsha et al. highlighted the age-adjusted prevalence of stage 3-5 CKD to be 8.7% (95 % CI 7.5-9.9) based on the Chronic Kidney Disease Epidemiology Collaboration(CKD-EPI) formula for estimated GFR (20). Women had a higher prevalence of CKD (20). The study compared various equations for estimating CKD prevalence and found that the CKD-EPI equations and Modification of Diet in Renal Diseases (MDRD), after excluding the American-derived ethnicity correction factor, performed better than the Cockcroft-Gault equations amongst African individuals (20). Hypertension was identified as a significant risk factor for prevalent CKD, doubling the risk (20). Another regional study conducted by Adeniyi et al. revealed an age-adjusted CKD prevalence of 6.4% (95% CI 3.2-9.7) in the Western Cape population (21). CKD risk factors included DM and higher

diastolic blood pressure, while the study also demonstrated a higher cardiovascular risk profile among participants (21).

Assessing SA's capacity to manage kidney disease, the ISN Global Kidney Health Atlas survey for Africa found that the country's total healthcare expenditure accounted for 8.2% of the Gross Domestic Product(22). The estimated CKD prevalence was 10.71% (95% CI 9.94-11.57) (22). The deaths attributed to CKD were 1.93%, and DALYs attributed to CKD were 1.13(95% CI 1.05-1.21) (22). Other concerning statistics include the obesity prevalence of 27%, smoking prevalence of 14.6%, and hypertension affecting 26.9% (95% CI 21.7-32.7) of the population (22). HD in SA incurs an annual per-patient cost of 10 736 US dollars, and the yearly peritoneal dialysis cost was 13 302 US dollars with an HD to peritoneal ratio of 0.81 (22). Although conservative kidney management protocols were lacking until 2018, such capacity was available (22). The country lacks registries for CKD, CKF, or AKI (22). There are 1.86 nephrologists' pmp with 0.36 trainees' pmp (22). Kidney care is through private and public funding systems (22). There is a shortage of nephrologists, transplant surgeons, laboratory access technicians, and vascular access coordinators (22).

Prevalence of chronic kidney disease in Sub-Saharan Africa

The prevalence of CKD in sub-Saharan Africa presents a multifaceted challenge. This vast and diverse region, spanning approximately 24 million square kilometers, comprises 47 countries (23). The region faces complex socio-economic conditions with a gross domestic product per person of less than US1500 dollars per year (23).

CKD in sub-Saharan Africa has diverse causes, encompassing NCDs and communicable diseases (23). The rise in NCDs, including CKD, in the region profoundly impacts economic, social, and health outcomes, particularly in resource-constrained countries with low-income populations (23). A systematic review by Stanifer et al. underscores the prevalence and potential escalation of CKD in sub-Saharan Africa (23). An analysis of 22 medium and high-quality studies revealed an average prevalence rate of 13.9% (95% CI 12.2-15.7) across the region (23).

Projections for the end of this decade anticipate a substantial increase in the prevalence of hypertension and DM, with conservative estimates suggesting that around 18.65 million people will affected by these conditions (23). Common communicable diseases such as schistosomiasis, leishmaniosis, and HIV will continue to affect the region (24). More than 22 million people in Sub-Saharan Africa live with HIV and develop chronic diseases, including CKD, further complicating healthcare management (23). The significant prevalence of CKD among HIV-positive individuals underscores the necessity for integrated management of both conditions (23). Chronic glomerulonephritis and the extensive utilization of traditional and herbal remedies are notable factors that should be considered significant contributors to CKD (23).

A population-based study by George et al. sought to determine the prevalence of markers of kidney damage and known risk factors in urban and rural areas of sub-Saharan Africa, spanning four countries: Burkina Faso, Ghana, Kenya, and SA (24). The large-scale study was the first in sub-Saharan Africa to investigate kidney damage and associated risk factors in adults from SA and countries in West and East Africa (24). The study defined CKD as an eGFR of less than 60ml/min/1.73m^2 and albuminuria of more than 3mg/mmol to define CKD (24). The overall CKD prevalence was 10.7% (95% CI 9.9-11.7), with a higher prevalence in SA sites than in West African sites (24).

Gender differences were also observed, with women demonstrating a higher prevalence of CKD of 12.0% (95% CI 10.8-13.2) compared to men of 9·5% (95% CI 8·3-10·8). Notably, women exhibited a higher prevalence of a low eGFR of 3.0% (95% CI 2.6-3.6) compared to men 1.7% (95% CI 1.3-2.3)(24).

However, gender-specific differences were not statistically different for albuminuria, with rates of 9.9% (95% CI 8.8–11.0) in women and men 8.4% (95% CI 7.3–9.7, p>0.05) (24). Risk factors associated with kidney damage included older age (relative risk (RR)1.04, 95% CI 1.03–1.05; p < 0·0001), hypertension (RR 1.97, 8=95%; CI 1.68-2.30; p <0·0001), DM (RR 2.22, 95% CI 1.76–2.78; p <0.0001), and HIV (RR1.65, 95% CI 1.36–1.99; p<0.0001)(24).

CKD prevalence variations across sub-Saharan Africa can be attributed to varying stages of regional sociodemographic and epidemiological health transitions (24). Specifically, CKD appears more prevalent in SA and Kenya than in Ghana and Burkina Faso (24). While individuals with DM, hypertension, and HIV were at the highest risk, many people with CKD did not have traditional risk factors (24). The emergence of NCDs in sub-Saharan Africa reflects complex sociodemographic transitions characterised by increased urbanisation, dietary changes, and lifestyle factors (24).

Notably, CKD patients in this study tended to be older, had an elevated body mass index (BMI) and waist circumference, and were more likely to have comorbid conditions such as HIV, DM, and hypertension (24). Hypertension doubled the risk of CKD at most sites, and DM was associated with a two-to-three threefold increased relative risk of CKD (24). Lipid profiles also differed, with higher total cholesterol and triglycerides with lower HDL cholesterol in individuals with CKD (24). Women had a higher prevalence of CKD than men, but no gender-specific differences were observed for albuminuria (24). Most comorbidities varied across sites, with the SA locations exhibiting the highest rates (24).

Despite urbanization, this population-based study found no significant difference in CKD prevalence between urban metropoles and semi-rural areas (24). More than a third of participants with CKD did not have the well-described risk factors associated with CKD, which were HIV, DM, or hypertension. The findings highlight the existence of unmeasured risk factors for CKD in sub-Saharan Africa, albeit not investigated in this study (24).

Sub-Saharan Africa, home to approximately two-thirds of its population residing in rural areas, contends with low life expectancy due to underdevelopment and poverty (25). By 2030, over 70% of the patients with CKF will be estimated to originate from regions similar to sub-Saharan Africa (25). Unfortunately, the burden and CKF in the region remain speculative due to the lack of comprehensive regional registries. (25). An intriguing aspect of CKD in sub-Saharan Africa is that it predominantly affects young and middle-aged individuals between 20 and 50 (25).

The outlook for CKF in sub-Saharan Africa is concerning, primarily due to late disease presentation and limited access to KRT (25). In most countries, healthcare workers have limited capacity to prevent kidney disease and limited awareness of preventative measures (25). Sub-Saharan Africa currently contributes less than 5% of the global KRT recipients (25).

Unfortunately, the diagnosis of CKF often carries a bleak prognosis (25). There are two outcomes of CKF: those who cannot afford KRT and are managed conservatively and those who can be dialysed or provided with a kidney transplant (25). Patients treated conservatively usually will die within the first year, but it is alarming that only 4% who commence dialysis can sustain treatment beyond 12 weeks (25). The highest rate of KRT is in SA at 37% (25). Unfortunately, the diagnosis of CKF is a death sentence for most patients in sub-Saharan Africa (25). Many patients on haemodialysis in sub-Saharan Africa receive it once or twice a week(25). Active transplant programs are only available in six sub-Saharan countries (25). Various challenges in sub-Saharan Africa include conflict, widespread poverty, inadequate planning, mismanagement of public resources, and lack of expertise, resulting in challenges to the availability and accessibility of KRT (25).

The region grapples with a high prevalence of HIV, with 68% of patients residing in sub-Saharan Africa (17). Southern Africa is the worst affected, with the national adult HIV prevalence exceeding 15% in eight southern African countries (17). While screening studies vary widely in the reported prevalence of CKD in HIV, ranging from 6-45%, this variation is due to differences in study populations, design, and CKD definitions (17).

CKD in Sub-Saharan Africa poses a complex and evolving challenge driven by a mixture of non-communicable diseases, including a substantial burden of HIV. The region faces critical issues related to early diagnosis, access to treatment, and integrated management of comorbid conditions. Additionally, CKD disproportionately affects young and middle-aged individuals, exacerbating the region's healthcare challenges. Adequate surveillance, increased awareness, and targeted interventions are essential to address sub-Saharan Africa's growing public health concern.

Prevalence of chronic kidney disease in Africa

Kaze et al. conducted a comprehensive meta-analysis of 98 studies to assess the prevalence of CKD Stages 1 to 5 in Africa, revealing an overall prevalence of 15.8% (95% CI 12.1-19.9) (26). For Stages 3 to 5, the prevalence was lower at 4.6 % (95% CI 3.3-6.1) [9]. Studies using the Cockcroft-Gault formula to calculate eGFR reported a higher prevalence than those using the MDRD or CKD-EPI equations (26). Furthermore, the prevalence was also higher in sub-Saharan Africa compared with Northern Africa (26). Consistently, studies have indicated that individuals of African descent are at increased risk of both developing CKD occurrence and progressing to CKF (26).

Abd ElHafeez et al.'s systemic review focusing on Stage 3-5 CKD revealed an average prevalence rate of 10.1% (95% CI 9.8-10.5), with a range spanning from 2% to 41% (27). The prevalence of CKD in Africa may be comparable to or even exceed that of other continents (27). Within sub-Saharan Africa, the majority of stage 3-5 CKD ranged from 2% to 14%, with a pooled prevalence of 14.02% (95% CI 13.5-14)(27).

When examining CKD in the context of HIV, untreated patients displayed a wide-ranging prevalence from 1-47%, with a pooled prevalence of 9.9% (95% CI 9.4-10.4)(27). Conversely, HIV-treated patients exhibited a lower prevalence ranging from 7 to 33% with a pooled prevalence of 5.2% (95% CI 5.0-5.4) (27).

Most of Africa is experiencing a rapid epidemiological transition characterised by a dual burden of communicable and NCD(26). Once more, younger patients in LMIC are also at risk of developing CKD, with a median age of 43.7 years (26). The simultaneous increase in hypertensive and patients with DM, combined with the HIV pandemic and the extended survival of individuals on anti-retroviral therapy, is expected to contribute to a growing CKD burden (26). Further, Africa has been consistently linked to a heightened risk of CVD mortality (26). Observational and cohort studies have highlighted that this

increased risk is apparent even in the early stages of CKD, with nearly 40% of deaths from CKD occurring before 65 years (26).

The causes of CKD in Africa are diverse and include hypertensive nephrosclerosis (16%), diabetic nephropathy (15%), chronic glomerulonephritis (13%), tubulointerstitial and obstructive uropathy (8%), primary glomerular diseases (6%), systemic lupus erythematosus (3%) and polycystic kidney disease (3%) (27). Additionally, infectious diseases, including HIV, schistosomiasis, malaria, and Hepatitis B and C, represent specific risk factors contributing to CKD in the region (27). In patients with HIV-related kidney diseases, up to 50% of causes of death are attributed to non-HIV-related diseases such as chronic glomerulonephritis and diabetic nephropathy (27).

The risk relationships of reduced eGFR rate and higher albuminuria were found to be steeper in women than in men (27). However, the risk of progression to CKF was equivalent in men and women (27). Poverty-related factors such as infectious diseases due to poor sanitation, environmental pollutants, insufficient access to safe water, and a higher prevalence of disease-transmitting vectors also play a substantial role in developing CKD in Africa (27).

Global prevalence of chronic kidney disease

The global prevalence of CKD varies across studies, reflecting its significance as a worldwide health concern. Hill et al., in a wide-ranging meta-analysis of one hundred observational studies encompassing seven million patients, estimated the global prevalence rate of CKD Stages 3-5 at 10.6% % (95% CI 9.2-12.2) for stages 3-5 (28). For all stages of CKD combined, the global mean prevalence of CKD was 13.4% (11.7–15.1%) (28). The CKD prevalence in each stage is 3.5% (95% CI 2.8-4.25%) for Stage 1, 3.9% (95% CI 2.7-5.3%) for Stage 2, 7.6% (95% CI 6.4-8.9%) for Stage 3, 0.4 %(95% CI 0.3-0.5%) for Stage 4 and 0.1%. (95% CI 0.1-0.1%) for Stage 5 (28). It is crucial to note that CKD is a prevalent health issue, with a CKD's global prevalence surpasses DM's (28, 29).

The bulk of CKD is also strongly associated with age, hypertension, and DM (28, 29). There is a gender disparity, with a higher majority of stage 3-5CKD observed in females at 12.1%, compared to males at 8.1%, highlighting a gender-specific difference in CKD prevalence (28). Additionally, there was a noticeable variation in CKD prevalence between developed and developing countries. Developed countries exhibit a higher prevalence, but it is essential to recognise that developing countries are grappling with an aging population, which may exacerbate both communicable and non-communicable diseases (28).

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In a separate study by Bikbov et al., the global prevalence of CKD Stage 1-5 was estimated at 9.1% (95% CI 8.5-9.8) in the Global Burden of Disease study (7). There were an estimated 697 million people with CKD(7). Notably, one-third of the cases were concentrated in China and India (7). The study also revealed that although females exhibited a higher prevalence, males experienced a higher mortality rate, suggesting that males progress to CKF more rapidly (7).

Further analysis indicated that 497 million individuals had Stage 1-5 CKD while 236 million had Stage 3-5 CKD (12). The prevalence of Stage 1-5 CKD was 10.4% (95% CI 9.3-11.9%) in men and 11.8% in women (95% CI 11.8-14%) (12). In LMIC, CKD prevalence was 10.6% in men (95% CI 9.4-13.1%) and 12.5% in women (95% CI 11.8-14%)(12). In high-income countries, CKD prevalence was 8.6% in men (95% CI 7.3-9.8%) and 9.6 % in women (95% CI 7.7-11.1%)(12). Noticeably, the prevalence of CKD increased with age for all stages of CKD (12).

CKD represents a significant global health challenge, with varying prevalence rates across regions, genders, and income levels. The findings underscore the need for comprehensive strategies to address CKD's impact on public health worldwide.

Summary and critical analysis with problem statement

The introductory chapter provided a comprehensive exploration of CKD, covering multiple facets, including its definition, diagnostic criteria, evolution, staging, and global impact and epidemiology of CKD. Specifically, we delved into prevalence rates and the factors contributing to CKD within various regions, focusing on SA, sub-Saharan Africa, and the continent as a whole.

The global ramifications and epidemiological aspects of CKD are profound, cementing its status as the 12th leading cause of death worldwide. Annually, CKD claims 5-10 million lives, primarily due to the inadequacy of KRT services. Beyond its lethality, CKD takes a heavy toll on the quality of life and life expectancy of those afflicted. Notably, CKD disproportionately affects individuals of lower socio-economic status, particularly in low and middle-income countries.

In SA, CKD forms part of a burden of diseases, encompassing both communicable and non-communicable ailments. Its impact spans urban and rural populations alike, with NCD, including CKD, witnessing an alarming surge that has escalated mortality rates. Contributing to this surge are prevalent risk factors like hypertension, DM, and obesity. SA grapples with relatively high CKD prevalence, with discernible disparities in access to kidney replacement therapy between the public and private sectors.

Moving into sub-Saharan Africa, CKD emerges as a multifaceted challenge influenced by a complex interplay of non-communicable and communicable diseases, including the formidable presence of HIV. Here, CKD is compounded by issues such as late diagnosis, limited availability of kidney replacement therapy, and the intricate management of coexisting conditions.

The estimated prevalence of CKD in Africa remains elevated when considering the continent. The causative factors of CKD on this continent are diverse, encompassing hypertension, DM, infectious diseases, and genetic predispositions. Poverty-related factors, insufficient access to safe water, and substandard sanitation facilities contribute to the CKD burden.

Globally, CKD emerges as a pressing public health concern, afflicting nations across the development spectrum. Its prevalence, ranging from 10-13%, bridges the divide between developed and developing countries, although it is notably higher in the former. CKD is inextricably linked to advancing age, hypertension, and DM, with a discernible gender disparity that sees a higher prevalence among females.

These findings underscore the critical importance of CKD as a global and regional health crisis, highlighting the need for heightened awareness, early detection, and accessible treatment options. These steps are pivotal in mitigating the far-reaching impact of CKD and enhancing the well-being of those affected.

Comparative CKD prevalence rate testing in Africa with the rest of the world is uncommon, mainly due to resource constraints. The best method to determine such comparisons needs to be determined. The results of the comparison need to be rigorously evaluated. Comparative CKD prevalence rates across different geographical regions contribute significantly to public health, healthcare planning, and research (30). Research on CKD prevalence improves evidence-based decision-making related to health policies and the allocation of resources (31). Understanding variations in prevalence rates helps public health authorities and lawmakers deploy resources more effectively (31). To manage and prevent CKD, areas with high incidence rates will require more targeted interventions, screening programs, and healthcare infrastructure. The study of prevalence rates supports identifying CKD risk factors and causes (28). Prevalence comparisons across different geographical locations provide data to investigate CKD trends, epidemiology, and underlying processes (28). Identifying regions with higher prevalence rates can benefit the early detection and diagnosis of CKD, which will aid in the prevention of disease progression (28).

No comparative studies have examined CKD prevalence rates between SA, the broader African continent, and the global landscape. Consequently, it became imperative to establish a structured and comprehensive framework for collecting, analyzing, and amalgamating existing research studies and pertinent literature concerning CKD prevalence across these regions.

This systematic review was designed to contrast CKD prevalence rates among SA, sub-Saharan Africa, the entire African continent, and the global context for the general population from 2013 to 2021. Its principal aim was to furnish a thorough and unbiased synthesis of the presently accessible body of evidence.

The objectives included:

(i) Comparative prevalence of CKD

(ii) Sample size influence on differences

(iii) Participant characteristics

(iv) CKD definitions and chronicity

(v) Measurement methods for CKD indicators

Chapter 2 contains the published manuscript from the Biomedical Central Nephrology (BMC Nephrology) Journal on March 21, 2023, which is a systematic review of the comparative prevalence rates of CKD. Chapter 3 presents the synthesis, conclusions, and recommendations.

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The prevalence of chronic kidney disease in South Africa - limitations of studies comparing prevalence with sub-Saharan Africa, Africa, and globally

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Abstract

Background Chronic kidney disease (CKD) is a globally significant non-communicable disorder. CKD prevalence varies between countries and within a country. We compared the prevalence rates of CKD in South Africa with sub-Saharan Africa, Africa, and globally.

Methods We registered a systematic review with the International Prospective Register of Systematic Reviews for prevalence studies reporting CKD stages III-V from 2013 to 2021. The analysis sought to explain any significant differences in prevalence rates. The R statistical package was used for data analysis. Comparisons included measures of effect size due to the large sample sizes analysed. We also compared sex differences in prevalence rates, common aetiologies, and type of study methodologies employed.

Results Eight studies were analysed, with two from each region. The matched prevalence rates of CKD between the various regions and South Africa showed significant differences, except for one comparison between South Africa and an African study [$p = 0.09$ (95% CI −0.04–0.01)]. Both sub-Saharan African studies had a higher prevalence than South Africa. One study in Africa had a higher prevalence, while the other had a lower prevalence, whilst one Global study had a higher prevalence, and the other had a lower prevalence compared to South Africa. The statistical differences analysed using the Cramer's V test were substantially less than 0.1. Thus, differences in comparisons were largely due to differences in sample sizes rather than actual differences.

Conclusion Variable prevalence rates between regions included disparities in sample size, definitions of CKD, lack of chronicity testing and heterogeneous laboratory estimations of eGFR. Improved consistency and enhanced methods for diagnosing and comparing CKD prevalence are essential.

Keywords Prevalence, Epidemiology, Chronic kidney disease, Renal insufiency, Renal impairment, Nephropathy, Stage III-V CKD, Proteinuria, Albuminuria, Meta-analysis, Systematic reviews, Cohort, Cross-sectional, South Africa, Sub-saharan Africa, Africa, Global

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Background

The estimated number of people with chronic kidney disease (CKD) globally is approximately 844 million [1]. Patients with CKD are estimated to be twice the number of people with diabetes worldwide and more than twenty times the number of people affected by human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) [1]. Kidney diseases are among the most common global non-communicable diseases (NCDs) [1]. The worldwide all-age prevalence of CKD has increased by 29.3% over the past three decades [2]. CKD has therefore become a universal public health priority [3]. Even though CKD prevalence has been researched more widely in economically developed countries, the disease burden is even more significant in developing countries [4]. The systematic review by Mills et al. estimated the global prevalence of CKD to be 11.1% [4]. However, the numbers affected by CKD rest on data of various qualities, approximations, and assumptions [1, 5]. It is acknowledged that CKD is common, but the challenge is to define its true prevalence [5].

Non-communicable diseases (NCDs) are increasingly contributing to morbidity and mortality over the last three decades [6]. The factors contributing to NCDs rise are increasing longevity, urbanization, and cultural changes [6]. Metabolic disorders such as diabetes mellitus have contributed heavily to NCD deaths [7]. There is a projected increase of 156% in diabetes mellitus, with about 25 million more cases estimated from 2017 to 2045 [7]. The high estimated prevalence of CKD will cause a significant disruption of healthcare provision obliging fundamental infrastructural changes with increasing expenditure [8]. Comparative CKD prevalence studies involving different countries or within a continent have revealed statistically significant differences in prevalence rates [9, 10]. The variances proposed were due to actual differences and disparities in study methods [9, 10].

Due to the dearth of epidemiological data from the majority of the continent, the prevalence of CKD in Africa continues to be underestimated [11] The majority of CKD prevalence studies conducted in Africa are not optimal [11, 12] Sub-Saharan Africa comprises 85% of the African population with a higher prevalence of CKD compared to the continent's north [11]. The most frequent causes of CKD in Africa are hypertension and diabetes mellitus followed by chronic glomerulonephritis and tubulointerstitial disorders [11]. Poverty and a lower socioeconomic status are two independent risk factors for developing CKD in Africa and hasten the course of the disease [13].

The International Society of Nephrology (ISN) Global Health Atlas survey for Africa estimated the prevalence of CKD in South Africa to be 10.7% (95% CI 9.94–11.57) [14]. The distribution of NCDs in South Africa displays socioeconomic disparities, with the most onerous burden falling on poor communities in urban areas [15]. The World Health Organization (WHO) estimates that the burden of NCDs in South Africa is two to three times higher than in other developing countries [15].

The lack of comprehensive CKD registries in South Africa and the rest of Africa has resulted in limited knowledge of CKD prevalence. The ISN has underscored that the current and future burden of CKD will be concentrated in lower socioeconomic countries, which often lack systematized and coordinated policies to manage the problem [16]. Accurate CKD prevalence rates allow for efficient preparation and execution of intervention and prevention programs [17]. The purpose of this review is to compare the CKD prevalence rates in South Africa with prevalence rates in sub-Saharan Africa, Africa as a whole, and globally. The study sought to explain the causes of any substantial differences in prevalence rates if this was present.

Method

The study was registered with the International Prospective Register of Systematic Reviews (PROSPERO). The reference number for the review was CRD42022330121. Two reviewers applied the eligibility criteria independently. Decisions were checked by a third reviewer. Disagreements were resolved through discussion and reaching a consensus. The study searched for publications on CKD using Google Scholar, Scopus, Embase, and PubMed/Medline.

The search terms included "prevalence," "epidemiology," "chronic kidney disease," "renal insufficiency," "renal impairment," "nephropathy," "stage III-V CKD," "proteinuria, "albuminuria," "meta-analysis," "systematic reviews," "cohort," "cross-sectional," "population-based," "South Africa," "sub-Saharan Africa," "Africa," "global.

The current Kidney Disease Improving Global Outcomes (KDIGO) staging criteria for CKD were included (stage III-V); hence the period for the studies was limited predominantly to the last decade (2013–2021) [18]. The search included only those reporting CKD (stage III-V) prevalence as not all studies included stages I-II CKD. Inclusion criteria included adult studies and English language articles. Studies that were translated into English were also included. The search included meta-analyses, systematic reviews, cohort, and cross-sectional studies. The studies were expected to use the prevailing definition of CKD. Criteria were also limited to those directly reporting studies of CKD in South Africa, sub-Saharan Africa, and globally.

Exclusion criteria were studies with patients under 12 years of age, those with inaccessible full texts, non-English studies that were not translated into English. Studies involving specific populations such as pregnant women,

acute kidney injury or transplantation were excluded. (Fig. 1). The first reviewer developed a data extraction tool. The data extracted included author, year of study, region, the prevalence of CKD, study population, and study design. Information acquired was tabulated on an Excel Spreadsheet (Microsoft Office for Windows, version 10; Microsoft Corporation, Redmond, WA°) for analysis.

The prevalence of CKD in South African studies was compared with the prevalence in sub-Saharan Africa, Africa, and globally to determine if there were statistically significant differences. Some of the papers reviewed had studied large numbers of patients. It was hence necessary to use the effect size to assess the strength of correlations where the chi-square test of independence would have shown dependence.

The null hypothesis proposed that there was no statistically significant difference in the prevalence of CKD between South Africa and sub-Saharan Africa, Africa, and globally. The R package was used for data analysis. In R, the test for difference between two proportions and the chi-square test for independence provided the same chi-square and p values. Rejection of the null hypothesis could be interpreted as evidence that the variables being considered are statistically dependent. An alternative interpretation for the rejection was that the sample proportions being compared were significantly different.

The probability of finding a significant difference between proportions is increased with large sample sizes. The increased chi-square statistic may not represent a strong pattern of dependence between variables but reflects an increase in sample size. It was necessary to review the test of independence between two variables and use the effect size to assess whether significant differences were not due to large sample sizes. The Cramer's V test was used as an effect size measurement for the chi-square test of independence. The test measured how strongly categorical fields, regions, and CKD are associated.

Results

The analysis incorporated eight studies. (Table 1).

There were two studies each from South Africa, sub-Saharan Africa, Africa, and globally. A total of 7 665

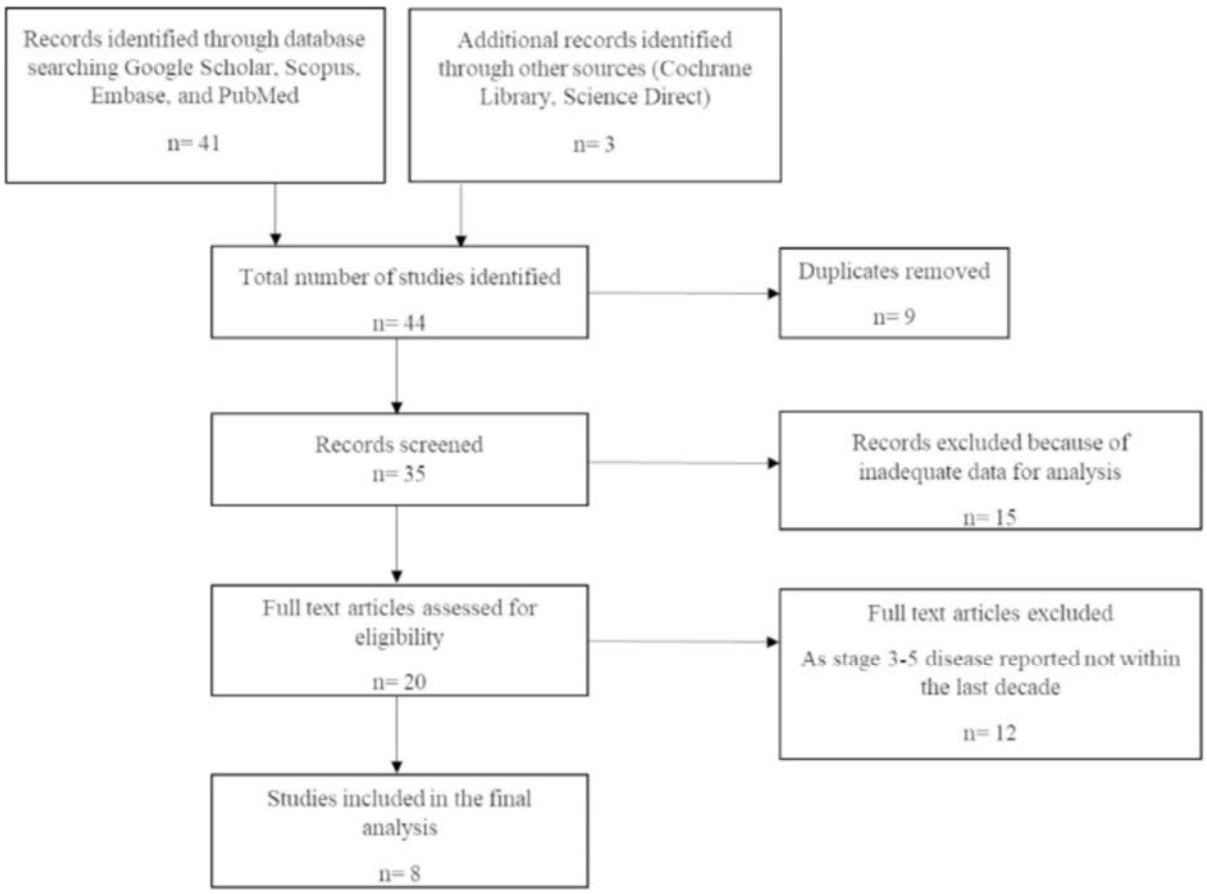

Fig. 1 Selection of papers for analysis of the prevalence of CKD from South Africa, sub-Saharan Africa, Africa and Globally

Table 1 Studies in South Africa, sub-Saharan Africa, Africa, and globally on prevalence of CKD

Author	Region	Year	Study type	95% Confidence interval	Reported CKD III-V prevalence rate	CKD number of patients	Non-CKD number of patients	Total number of patients
Matsha et al. [19]	South Africa	2013	Cohort Population based	5.0-8.5	8.7%	104	1 111	1202
Adeniyi et al. [20]	South Africa	2016	Cohort Population based	3.2–9.7	6.4%	31	458	489
George et al. [8]	Sub-Saharan Africa	2019	Cross sectional Population based	9.9–11.7	10.7%	868	7242	8110
Stanifer *et al* [22]	Sub-Saharan Africa	2014	Systematic review Population based	12.2–15.7	13.9%	8939	55,368	64,307
Kaze et al. [12]	Africa	2018	Systematic review Population and hospital based	3.3–6.1	4.6%	4528	9 3904	98 432
Abd ElHafeez et al. [11]	Africa	2018	Systematic review Population based	9.8–10.5	10.1%	15 150	134 850	150 000
Hill et al. [4]	Global	2016	Systematic review Population based	9.2–12.2	10.6%	742 000	6 258 000	7 000 000
Bikbov et al. [2]	Global	2017	Systematic review Population based	3.5–4.3	4.1%	314 262 509	7 350 676 734	7 664 939 243

961 783 participants were included: 315 034 128 (4.1%) having CKD stages III-V. The sample size of the studies ranged from 489 in a South African study [19, 20] to 7 664 939 243 in a global study [2]. The prevalence rates for CKD ranged from 6.4 to 8.7% in South Africa [19, 20], 10.7–13.9% in sub-Saharan Africa [21, 22], 4.6–10.1% in Africa [16, 17] and 4.1–10.6% globally [2, 4].

Matsha et al. published a regional cohort study on CKD in the Western Cape, South Africa, in one of the two South African studies [19]. The age-standardized prevalence using the Chronic Kidney Disease Epidemiology Collaboration equation (CKD-EPI) of CKD was 8.7% (95% CI 7.5–9.9) [19]. The overall mean age of participants was 52.9 ± 14.8 years; females constituted 75.3% of the study group. The risk factors involved included hypertension (33.0%) which also doubled the risk of developing CKD [19]. The prevalence of diabetes was 26.0%, with obesity being a significant risk factor for developing diabetes mellitus [19]. The prevalence of HIV was not reported.

The second South African study was a cross-sectional survey of CKD prevalence from the Western Cape by Adeniyi et al. [20]. The age-standardized prevalence using the CKD-EPI equation for CKD was 6.4% (95% CI 3.2–9.7%) [20]. Patients had a mean age of 46.3 ±8.5 years with the majority (70.3%) being female [20]. Risk factors included hypertension and diabetes, with a prevalence of 55.2% and 20.7%, respectively, while the prevalence of HIV was not reported [20].

In the sub-Saharan African study by George et al. in 2019, using a population-based study, the authors investigated the CKD prevalence in four sub-Saharan countries, viz. Burkina Faso, Ghana, Kenya, and South Africa [21]. The overall prevalence of CKD was 10.7% (95% CI 9.9–11.7) [10]. South Africa had the highest prevalence of 12.9% (95% CI 10.6–11.5) compared to the East and West African countries [21]. The mean age of participants was 49.9 ±5.8 years [10]. Females accounted for 49.2% of the study participants [21]. Women had a higher prevalence of CKD of 12.0% (95% CI 10.8–13.2) compared to men, with a prevalence of 9.5% (95% CI 8.3–10.8) [10]. Prevalence of the risk factors of hypertension, diabetes, and HIV were 32.6% (95% CI 31.3–34), 5.6% (95% CI 5-6.2), and 15.9% (95% CI 14.9–17.1), respectively [21].

A systematic review by Stanifer et al. in 2014 of 22 medium and high-quality studies in sub-Saharan Africa reported the prevalence of CKD to be 13.9% (95% CI 13.8–19.6) [22]. The mean age in the different quality studies was 41.5± 4.1 years, with females constituting 57.5% of participants [22]. Risk factors included hypertension and diabetes, and HIV, with a median prevalence of 16.8% and 17.1%, and 11.9%, respectively [22].

In a meta-analysis of 98 CKD studies in Africa by Kaze et al. in 2018, the overall prevalence of CKD was 4.6% (95% CI 3.3–6.1) [12]. The mean age of participants was 43.0 ± 6.2 years. [12] The proportion of female participants was not reported. The main risk factors for CKD were hypertension, diabetes, and HIV [12]. The prevalence rates for the risk factors were 35.6% (95% CI 27.9–43.7), 13.3% (95% CI 10.7–16), and 17.9% (95% CI 10.9–26.1), respectively [12].

In another systematic review of 152 CKD stage III-V prevalence studies in Africa in 2018 by Abd El Hafeez et al. [11], the CKD prevalence rate was 10.1% (95% CI

9.8–10.5) [11]. The median age was 52.8 ± 11.7 years [11]. The overall proportion of female participants was 64.3% [11]. The pooled risk factor prevalence of hypertension was 34.5% (95% CI 34.0–36.0), diabetes 24.7% (95 CI 23.6–25.7), and HIV 5.6% (95% CI 5.4–5.8) [11].

The global study by Hill et al. in 2016 was a systematic review and meta-analysis of 100 observational studies involving seven million patients [4]. The estimated prevalence of CKD was 10.6% (95% CI 9.2–12.2%) [4]. The mean age of all participants was 49.0 ± 8.5 years [4]. The proportion of female participants studied was 55.0% [4]. The prevalence of CKD in males was 8.1% (95% CI 6.3–10.2) [4]. The CKD prevalence in females was 12.1% (95% CI 10.6–13.8) [4]. The median prevalence of the two major risk factors was hypertension (40.1%) and diabetes mellitus (15.1%) [4]. HIV was not reported as a risk factor.

Bikbov et al. in 2020 reported a systemic analysis of the Global Burden of Disease (GBD) study based on published literature, registration systems, chronic kidney failure registries, and household surveys [2]. The estimated prevalence in a study population for CKD stage III was 3.9% (95% CI 3.5–4.3%), 0.16% (95% CI 0.0.13–0.19%) for CKD stage IV, and 0.07% (95% CI 0.06–0.08%) for CKD stage V [2]. The mean age and proportion of female participants were not reported, but the prevalence of CKD in females was 1.29-fold (95% CI 1.28–1.3) more than in males [2]. The age-standardized prevalence of CKD in females was 9.5% (95% CI 8.8–10.2] and 7.3% (95%CI 6.8–7.9) in males [2]. Major risk factors for CKD in the study were hypertension, with a prevalence of 43.2% (95% CI 42.3–54.1), and diabetes, with a prevalence of 57.6% (95% CI 50.5–63.8) [2]. There was no reporting of HIV as a risk factor.

The first comparison was between South Africa and sub-Saharan Africa. Both sub-Saharan studies had a higher prevalence of CKD compared to Matsha et al. [19]. Once more, when compared to Adeniyi et al. [20], both sub-Saharan studies revealed a higher prevalence of CKD. .

When comparing South Africa with Africa, only one study comparing Adeniyi et al. [20](South Africa) versus Kaze et al. [12] (Africa) displayed no significant difference. The African study by Kaze et al. [12] displayed a lower CKD prevalence. Abd El Hafeez et al. [11](Africa) had a higher prevalence of CKD than both South African studies. (Table 2)

The final CKD prevalence comparison was between South Africa and global studies. The global study by Bikbov et al. [2] had a lower prevalence of CKD, while the global study by Hill et al. [4] had a higher prevalence of CKD when both were compared to the South African studies.

Table 2 shows the results of statistical tests of differences in CKD prevalence in South Africa versus sub-Saharan Africa, African and global studies

Comparative Region	Authors	Proportions	95% CI	Chi-Squared	*p*-value	Cramer's V
Sub-Saharan Africa	Matsha et al. [19] (SA)	0.07570715	-0.08: – 0.05	39.249	< 0.001	0.025
	Stanifer et al. [22]	0.13900508				
	Matsha et al. [19] (SA)	0.07570715	-0.05 : -0.01	10.78	< 0.001	0.035
	George et al. [8]	0.10702836				
	Adeniyi et al. [20] (SA)	0.06339468	-0.10 : -0.05	22.633	< 0.001	0.019
	Stanifer et al. [22]	0.13900508				
	Adeniyi et al. [20] (SA)	0.06339468	-0.07 : -0.02	8.919	< 0.001	0.033
	George et al. [8]	0.10702836				
Africa	Matsha et al. [19] (SA)	0.07570715	0.01 : 0.04	23.035	< 0.001	0.015
	Kaze et al. [12]	0.04600130				
	Matsha et al. [19] (SA)	0.07570715	-0.04 : -0.01	8.1396	0.004	0.007
	Abd ElHafeez et al. [11]	0.10100000				
	Adeniyi et al. [20] (SA)	0.06339468	-0.01 : 0.04	2.9644	0.090	0.006
	Kaze et al. [12]	0.04600130				
	Adeniyi et al. [20] (SA)	0.06339468	-0.06 : -0.01	7.1905	0.007	0.007
	Abd ElHafeez et al. [11]	0.10100000				
Global	Matsha et al. [19] (SA)	0.07570715	-0.04 : -0.01	11.321	< 0.001	0.001
	Hill et al. [4]	0.106				
	Adeniyi et al. [20](SA)	0.06339468	-0.06 : -0.02	8.9222	< 0.001	0.001
	Hill et al. [4]	0.106				
	Matsha et al. [19](SA)	0.07570715	0.02 : 0.05	35.947	< 0.001	0.00
	Bikbov et al. [2]	0.0410000				
	Adeniyi et al. [20] (SA)	0.06339468	-0.0002 : 0.04	5.6807	0.017	0.00
	Bikbov et al. [2]	0.0410000				

Overall, there were statistically significant differences in comparisons between all studies, except for one study comparing South Africa against Africa. The prevalence of CKD in both sub-Saharan studies was higher than in South African studies. One African study had a lower prevalence of CKD than the South African studies, while the other had a higher prevalence. Similarly, one global study had a lower prevalence of CKD than the South African studies, while the global study had a higher prevalence. However, the maximum Cramer's V value for all comparisons was 0.035, all considerably less than 0.1, which suggested that these statistical differences were an effect of sample size rather than actual differences.

Table 3 compares the studies analysed in each geographical region, incorporating the mean age range of participants, number of female participants, and prevalence of risk factors. In addition, the table compared whether the Kidney Disease Improving Global Outcomes (KDIGO) guidelines were used to define CKD, including whether testing for chronicity of more than three months duration was used for the diagnosis of CKD. Further comparisons included the type of serum creatinine assay used, estimating equations to calculate the estimated glomerular filtration rate (eGFR), and if ethnicity co-efficient were employed.

Most study participants in all studies assessed were in the fourth to fifth decade of life. There was a predominance of female participants in the prevalence studies. Hypertension and diabetes mellitus were the most common risk factors in all studies, with HIV identified as a common risk factor in sub-Saharan Africa and Africa.

Only George et al. [21] (sub-Saharan African study) used the KDIGO definition of CKD. None of the selected studies considered chronicity of more than three months for CKD. Matsha et al. [19], Adeniyi et al. [20] (South Africa), and George et al. [21] (sub-Saharan Africa) calculated serum creatinine with the enzyme-linked assay. Abd ElHafeez et al. [11] (Africa) and Hill et al. [4] (Global) analysed serum creatinine that was calculated using the enzyme-linked and Jaffe assays. The CKD-EPI, Modification of Diet in Renal Disease (MDRD), and Cockcroft-Gault equations were the most widely used for the estimated glomerular filtration rate (eGFR). Matsha et al. [19] (South Africa) and George et al. [21] (sub-Saharan Africa) calculated the eGFR with and without ethnicity co-efficient.

Discussion

On *prima facie* analysis, there were statistically significant differences in CKD prevalence rates between South Africa and sub-Saharan Africa, Africa, and globally in all except for one comparison. The single comparison that did not show a statistically significant difference in CKD prevalence was between the South African study by Adeniyi et al. [20] compared to the African study by Kaze et al. [12]. The prevalence of CKD in sub-Saharan studies was higher than those in South African studies. However, it could not be determined whether the prevalence of CKD in South Africa was higher or lower than the African and global prevalence.

The wide variations in sample sizes between comparative groups limited the interpretation of statistical tests such as the *p*-values and confidence intervals [23]. The significant differences in prevalence may be due to large sample sizes. The analysis of the Cramer's V effect size indicated a weak association between CKD prevalence rates and the regions. The statistically significant differences in prevalence rates across the regions may be due to differences in sample sizes rather than dependence of CKD prevalence between each geographical region. Our analysis shows a similarity to previous comparative studies between geographical regions [9, 10, 15]. Differences in prevalence rates of CKD between countries and regions have been documented, with variations being due to true differences or limitations caused by the heterogeneity of studies [15]. True variations result from high protein diets, smoking, physical activity, socioeconomic status, ethnicity, genetics, and birth weight [15]. International comparisons of CKD prevalence have been hindered by differences in age, sex distribution, sampling, and definitions of CKD [15]. Regional variations of CKD prevalence within a country are also frequent, and the degree of variations may fluctuate [15]. A rapid epidemiological transition could also explain the different prevalence of environmental changes, adoption of western lifestyles, and rapid urbanisation in Africa [12]. The clinical, demographic, and laboratory causes of variations in CKD prevalence will be discussed.

The median age of developing CKD in lower-middle-income countries was 43.7 years [12]. Observational and cohort studies in Africa have consistently shown an increased risk of cardiovascular disease mortality in the early stages, with nearly 40% of deaths from CKD occurring before 65 years [12]. The mean age of patients diagnosed with CKD in South Africa, sub-Saharan Africa, and Africa was younger, between the fourth and fifth decade, compared to the global CKD study by Hill et al. [4], where the highest prevalence was between the fifth and sixth decade. Lower kidney function was associated with a significant and progressive reduction of life expectancy in middle age for both men and women [24]. An earlier age at diagnosis heralds a worse prognosis.

The KDIGO criteria, if used to define stages of CKD, result in a considerable increase in prevalence with age and the method used to estimate GFR [25]. The threshold of 60ml/min/1.73m^2 for the diagnosis of CKD could contribute to an overestimation of CKD in older patients [26]. Elderly populations exhibit a normal "physiological"

Table 3 Comparison of eGFR equations, the mean age of participants, number of female participants, and prevalence of risk factors and laboratory methods

Author	Region	Mean age of participants (Years)	Female Participants (Percentage)	Prevalence of Hypertension	Prevalence of Diabetes	Prevalence of HIV	KDIGO CKD criteria	Test for chronicity > 3 months	Serum creatinine measurement: enzyme or Jaffe	eGFR equations studied	Ethnicity co-efficient used
Matsha et al. [19]	South Africa	52.9 ± 14.8	75.3	33.0	26.0	Not mentioned	No	No	Enzyme	CKD-EPI MDRD Cockcroft-Gault	Measured with and without ethnic co-efficient
Adeniyi et al. [20]	South Africa	46.3 ±8.5	70.3	55.2	20.7	Not mentioned	No	No	Enzyme	CKD-EPI MDRD	No
George et al. [8]	Sub-Saharan Africa	49.9 ±5.8	49.2	32.6	5.6	15.9	Yes	No	Enzyme	CKD-EPI MDRD	Measured with and without ethnic co-efficient
Stanifer et al. [22]	Sub-Saharan Africa	41.5 ± 4.1	57.5	16.8	17.1	11.9	No	No	Not mentioned	MDRD Cockcroft-Gault	No
Kaze et al. [12]	Africa	43.0 ± 6.2	Not mentioned	35.6	13.3	17.9	No	No	Not mentioned	CKD-EPI MDRD Cockcroft-Gault Cystatin C	No
Abd ElHafeez et al. [11]	Africa	52.8 ± 11.7	64.3	34.4	24.7	5.6	No	No	Enzyme and Jaffe	CKD-EPI MDRD Cockcroft-Gault	No
Hill et al. [4]	Global	49.0 ± 8.5	55.0	40.1	15.1	Not mentioned	No	No	Enzyme and Jaffe	CKD-EPI MDRD	No
Bikbov et al. [2]	Global	Not studied	Not mentioned	43.2	57.6	Not mentioned	Modelled	No	Not mentioned	CKD-EPI MDRD	No

decline in GFR with aging (renal senescence) [27]. Epidemiologic studies using a "once-off" testing of eGFR, especially with elderly participants, may also overestimate the burden of CKD in older patients [25]. The controversy of whether the decline in GFR is due to aging, as opposed to disease, has not been directly resolved [25]. A suggested method to overcome false positives would be to use the third percentile of eGFR creatinine levels and age-calibrated thresholds [26]. Alternatively, the Berlin Initiative Study 1 equation would be more suitable for subjects older than 70 years [28].

Most patients diagnosed with CKD were female, in keeping with the majority of worldwide CKD prevalence studies [29]. The prevalence of CKD in the United States of America is higher in females than males, but males have a higher prevalence of newly treated chronic kidney failure (CKF) [30]. The cause of this was indeterminate but may be multifactorial [3]. There is a possibility of overdiagnosis of CKD in older women than in men [31]. Women, on average, have lower estimated GFR and measured GFR (uncorrected for body surface area) and tend to progress to a GFR value of $<60ml/min/1.73m^2$ before men, although men progress more rapidly to CKF [31]. This physiological sex difference could contribute to an overdiagnosis of CKD in women than men as they age, especially in the absence of albuminuria [31].

The role of the social environment and economic conditions is an emerging component in the pathway from CKD risk to the development and complications of CKD and chronic kidney failure [32]. Socioeconomically underprivileged inhabitants worldwide show an unevenly high burden of CKD [32]. The burden is compounded by the inability to receive evidence-based care leading to poor clinical outcomes [32]. Lower socioeconomic status was related to a greater risk of prevalence of CKD [32].The poor with a higher kidney disease burden often have fewer resources to meet treatment costs [32]. The consequence is "catastrophic spending" (defined as out-of-pocket payments above 40% of non-food expenditure) [32]. Thus, advanced CKD could be considered a risk factor for poverty along with low education level, employment status, and ethnicity [33]. The entire family becomes affected by the reduction in resources [33]. Poverty can also directly affect adherence to medical treatment as the affected patient may be unable to access follow-up care or afford kidney replacement therapy when required [33].

Countries with a higher CKD prevalence have a higher risk factor profile [10]. Sub-Saharan Africa is estimated to have 18.65 million people with diabetes mellitus [22]. A similar number is estimated to develop hypertension by the end of this decade [22]. There would also be an estimated 22 million people living with HIV/AIDS during this time, posing a further substantial burden of CKD in this region [22]. In Africa, the dominant risk factors for developing CKD are hypertension, diabetes mellitus, and HIV [11, 12]. Africa also has the highest prevalence of HIV-1 infection [34]. There is a robust association between Apolipoprotein L1 gene variants found only on African chromosomes resulting in an increased probability of developing focal segmental glomerulosclerosis and HIV-associated nephropathy [34, 35]. Resource limitations lead to the late initiation of ARVs (antiretroviral agents), which predisposes to HIV-associated nephropathy [36]. The combination of genetic susceptibility with delayed treatment of HIV contributes to the increase in CKD prevalence and disease burden. Africa is, therefore, subject to a dual burden of non-communicable and endemic infectious diseases such as HIV leading to CKD [37].

Global studies identified hypertension, diabetes mellitus, female sex, and increasing age as the major risk factors for the development of CKD [2, 4]. International differences in the prevalence of risk factors for CKD could be affected by sample selection [10]. CKD prevalence fluctuates with time, as some international differences in CKD prevalence may be explained by differences in the study periods and the associated transition of risk factor profiles [10]. Increased prevalence within some regions compared to neighbouring areas with similar demographics may also indicate increased recognition and recording of CKD [29]. The epidemiological transition from communicable to non-communicable diseases, with significant increases in hypertension and diabetes mellitus with aging, may also account for the increased prevalence of CKD [11, 38, 39].

The estimated requirements for kidney replacement therapy will double from 2.62 million in 2010 to 5.4 million people by 2030 [40]. Global deaths due to kidney disease are projected at between 5 and 10 million people annually due to a shortage of kidney replacement therapy services [40]. Higher-income countries spend 2–3% of their annual health budget on CKF treatment for approximately 0.03% of the total population [40]. Lower-income countries are not able to provide similar resources for chronic kidney failure (CKF). They will most likely experience the societal, health, and economic burden of mostly untreated CKF.

Over the past decade, there have been substantial developments in standardising assays for serum creatinine [41]. The re-calibration of serum creatinine assays to an isotope dilution mass spectrometry reference method has resulted in more specific assays traceable to the International System of units [42]. The introduction of isotope dilution mass spectrometry calibration for serum creatinine assays has addressed the variability of serum creatinine data [42]. However, difficulties persist concerning using eGFR to assess CKD prevalence in epidemiological

studies [42]. A continuing complication is that the effect of assay calibration differs between eGFR equations [43]. Variations in calibration have a more significant effect on the MDRD equation than on the CKD-EPI equation for eGFR [43]. The variation is due to the mathematical exponent applied to serum creatinine in elevated eGFR ranges and is lower in CKD-EPI than the MDRD equation [43]. The CKD-EPI equation gives a lower prevalence of CKD due to a higher eGFR in general or specific population participants than other equations [43]. In contrast, the systematic underestimation of eGFR with the MDRD equation is associated with an overestimation of CKD prevalence in epidemiological studies [43].

The lack of standardized equations to calculate eGFR was highlighted in the studies by several authors in this paper [2, 4, 17, 20–22]. Most studies reviewed displayed an analytical heterogeneity used to measure creatinine. Evaluation of eGFR is fundamental to medical practice, research, and public health [44]. Serum creatinine is the most commonly utilized biomarker to assess eGFR [45]. However, individual values may vary due to factors that include mass, age, sex, ethnicity, and diet unrelated to CKD [45]. Measured GFR (mGFR) and gold-standard measurements using inulin clearance are, unfortunately, too cumbersome to perform in extensive epidemiologic studies [31]. In a collaborative study from Malawi, Uganda, and South Africa that prospectively measured kidney function, it was established that creatinine-based GFR-estimating equations overestimate kidney function [46]. The implication is that the burden of kidney disease may be significantly underestimated in Africa [46].

A common limitation in CKD prevalence studies is the "once-off testing" of serum creatinine (and hence eGFR). Other limitations included quantifying albuminuria; the different formulae used to calculate eGFR, the absence of proteinuria and haematuria testing, and heterogeneity in sample data used to calculate the prevalence of CKD. Once off, eGFR testing or confirming chronicity was reported here as a limitation in numerous studies [2, 4, 7, 8, 16, 20]. Glassock et al. contend that although CKD is widespread, the contention that the prevalence is increasing in many countries may be incorrect [31]. The authors maintain that using "once-off testing" of eGFR and albuminuria to define prevalence in epidemiological studies is controversial, as these "single test" studies do not adhere to the KDIGO CKD definition of three-month duration [18]. The "once-off" testing produces a false positive diagnostic rate of about 30% for eGFR and even higher for albuminuria [47]. Conversely, false-negative results, which primarily involve the younger population, arise when they have an eGFR above 60 ml/min/1.73m^2 [48]. This subset does not meet the criteria for the definition of CKD and is without proteinuria, but they have a low eGFR for their age, below the 3rd percentile for age and sex category [48].

Using ancestry coefficients, sex, and age of patients can further contribute to the limitations of prevalence studies. The ancestry coefficient is a significant constituent of the MDRD and CKD-EPI equations [31]. It was recommended to improve the understanding of the prevalence of CKD in ethnically diverse populations [31]. However, the African American coefficient results in the MDRD and CKD-EPI equations for eGFR being 21% and 15% more elevated, respectively, than the same equations without coefficients [31]. It can be contended that the use of race in eGFR equations is a social and not a biological concept [46]. The inclusion of race ignores diversity within and among racial groups [46]. Alterations in estimating equations can affect the calculation of the burden of CKD and potentially disrupt patient care [46]. It can also be debated that keeping a race term in GFR equations adversely affects access to kidney replacement therapy [49].

Alternatives to calculating eGFR without using race are currently being evaluated [50]. The estimation of GFR with the usage of cystatin C was similar to estimations using serum creatinine [50]. Cystatin C-based estimations did not use race or ancestry and were not enhanced or changed by their inclusion [50]. Most recent eGFR equations use creatinine and cystatin C without race [51]. They are more accurate in estimating GFR than either equation using creatinine or cystatin C alone [51]. This has resulted in reduced differences from measured GFR between race groups [51]. A systematic review of epidemiological studies from sub-Saharan Africa highlighted the source's potential for bias [52]. These include variability in the requirements for serum creatinine assays, appropriate choice of estimating equations to calculate eGFR, and appropriate diagnostic criteria for CKD [52]. The results were consistent with other worldwide studies [52]. The ongoing evolution of data from eGFR equations will further inform clinical practice, research, and public health considerations [52].

An essential requirement for the management of CKD is for efficient and sustainable solutions to capture high-quality population-based health data and extrapolate it into health information systems [53]. This will allow a better understanding of CKD epidemiology and variations in CKD prevalence [53]. The CKD in Africa (CKD-Africa) project is a continental collaboration network that aims to provide uniformly reliable estimates for CKD prevalence [53]. The collaboration has currently networked 12 African countries in sub-Saharan Africa, totalling 39 studies and 35 747 participants [53]. This collective health system would be able to effectively advise future health services planning and policy for CKD management in Africa [53].

The study limitations include analysing two studies from South Africa from the same region. These studies may not represent the country's prevalence of CKD because regional variations in CKD prevalence can occur within a country [15]. The South African studies had relatively small numbers of participants compared to those in sub-Saharan Africa, Africa, and globally. HIV, a significant risk factor for CKD in sub-Saharan Africa, was not investigated amongst participants in the South African studies. The population sampling was also not representative of the South African population demographics. A further limitation was the low number of studies that were eligible for inclusion in the analysis.

Conclusion

There was a statistically significant variation in the prevalence of CKD between South Africa and sub-Saharan Africa, Africa, and globally in all except one comparison. However, there was a poor correlation due to the effect size, which suggests that these differences may be due to comparing studies with large sample sizes than to actual differences in the prevalence. This review echoed the marked heterogeneity when comparing CKD prevalence from different regions. These included varying sample sizes, differences in the study methodology, the criteria for the definition of CKD, the lack of chronicity reporting, and variances in serum creatinine measurements leading to variable eGFRs. Enhanced uniformity and novel approaches are crucial for performing and reporting CKD prevalence studies to advance the accuracy of comparing the burden of the disease.

List of Abbreviations

ARV	antiretroviral
CKD	Chronic kidney disease
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
CKF	chronic kidney failure
eGFR	estimated glomerular filtration rate
GBD	Global Burden of Disease study
HIV/AIDS	Human immunodeficiency virus/acquired immune deficiency syndrome
ISN	International Society of Nephrology
KDIGO	Kidney Disease Improving Global Outcomes
MDRD	Modification of Diet in Renal Disease
mGFR	measured glomerular filtation rate
NCD	non-communicable disease
PROSPERO	International Prospective Register of Systematic Reviews
WHO	World Health Organisation

Supplementary Information

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Supplementary Table 1: Search Strategy

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Nil.

Author Contribution

SH conceptualized the project, performed the data search, and wrote the paper. RB conceptualized the project, reviewed the draft, and revised the analysis. LN reviewed the paper and was involved in its formatting. EJ was the statistician who performed the statistical analysis of the data and revised the analysis. SN reviewed the paper and revised the analysis. AA reviewed the paper and revised the analysis.

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Data Availability

Datasets generated and/or analysed during the current study are available upon request. Kindly contact the corresponding author of the study, Dr.SP Hariparshad at Sudeshphg@yahoo.com.

Declarations

Ethics approval

The study was approved by the University of KwaZulu-Natal Biomedical Research Ethics Committee with approval number BE 120/19.

Consent for publication

Not applicable.

Competing Interests

The authors have no conflict of interest.

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References

1. 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. Oxford University Press; 2019. pp. 1803–5. https://doi.org/10.1093/ndt/gfz174
2. Bikbov B, Purcell CA, Levey AS, Smith M, Abdoli A, Abebe M, et al. Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the global burden of Disease Study 2017. The Lancet. 2020;395(10225):709–33. https://doi.org/10.1016/S0140-6736(20)30045-3
3. Levin A, Tonelli M, Bonventre J, Coresh J, Donner J-A, Fogo AB, et al. Global kidney health 2017 and beyond: a roadmap for closing gaps in care, research, and policy. The Lancet. 2017;390(10105):1888–917. https://doi.org/10.1016/S0140-6736(17)30788-2
4. Hill NR, Fatoba ST, Oke JL, Hirst JA, O'Callaghan CA, Lasserson DS, et al. Global prevalence of chronic kidney disease–a systematic review and meta-analysis. PLoS ONE. 2016;11(7):e0158765. https://doi.org/10.1371/journal.pone.0158765
5. Black C, van der Veer SN. Unlocking the value of variation in CKD prevalence. Am Soc Nephrol. 2016;1874–7. https://doi.org/10.1681/asn.2015111280
6. Matsha TE, Erasmus RT. Chronic kidney disease in sub-saharan Africa. The Lancet Global Health. 2019;7(12):e1587–e8. https://doi.org/10.1016/S2214-109X(19)30467-X

7. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, et al. Diabetes Res Clin Pract. 2019;157:107843. https://doi.org/10.1016/j.diabres.2019.107843. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas.
8. George JA, Brandenburg J-T, Fabian J, Crowther NJ, Agongo G, Alberts M, et al. Kidney damage and associated risk factors in rural and urban sub-saharan Africa (AWI-Gen): a cross-sectional population study. The Lancet Global Health. 2019;7(12):e1632e43. https://doi.org/10.1016/S2214-109X(19)30443-7
9. Wang F, He K, Wang J, Zhao M-H, Li Y, Zhang L, et al. Prevalence and risk factors for CKD: a comparison between the adult populations in China and the United States. Kidney Int Rep. 2018;3(5):1135–43. https://doi.org/10.1016/j.ekir.2018.05.011
10. Stel VS, Brück K, Fraser S, Zoccali C, Massy ZA, Jager KJ. International differences in chronic kidney disease prevalence: a key public health and epidemiologic research issue. Nephrol Dialysis Transplantation. 2017;32(suppl2):ii129–ii35. https://doi.org/10.1093/ndt/gfw420
11. Abd ElHafeez S, Bolignano D, D'Arrigo G, Dounousi E, Tripepi G, Zoccali C. Prevalence and burden of chronic kidney disease among the general population and high-risk groups in Africa: a systematic review. BMJ open. 2018;8(1):e015069. https://doi.org/10.1136/bmjopen-2016-015069
12. Kaze AD, Ilori T, Jaar BG, Echouffo-Tcheugui JB. Burden of chronic kidney disease on the african continent: a systematic review and meta-analysis. BMC Nephrol. 2018;19(1):1–11. https://doi.org/10.1186/s12882-018-0930-5
13. Nyirenda MJ. Non-communicable diseases in sub-saharan Africa: understanding the drivers of the epidemic to inform intervention strategies. Int health. 2016;8(3):157–8. https://doi.org/10.1093/inthealth/ihw021
14. Bello AK, Levin A, Lunney M, Osman MA, Ye F, Ashuntantang G, Bellorin-Font E, Benghanem GM, Ghnaimat M, Harden P. Global kidney Health Atlas: a report by the International Society of Nephrology on the global burden of end-stage kidney disease and capacity for kidney replacement therapy and conservative care across world countries and regions. Brussels: International Society of Nephrology; 2019.
15. Mayosi BM, Flisher AJ, Lalloo UG, Sitas F, Tollman SM, Bradshaw D. The burden of non-communicable diseases in South Africa. The lancet. 2009;374(9693):934–47. https://doi.org/10.1016/S0140-6736(09)61087-4
16. Working Group International Society of Nephrology ISN Framework for Developing. Dialysis Programs in low-resource settings. Brussels, Belgium. International society of Nephrology: International Society of Nephrology; 2021.
17. Brück K, Stel V, Gambaro G, Hallan S, Völzke H, Ärnlöv J. European CKD Burden Consortium: CKD prevalence varies across the european general population. J Am Soc Nephrol. 2015;27:2135. https://doi.org/10.1681/ASN.2015050542
18. Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int Suppl. 2013;3(1):1–50. https://doi.org/10.1016/j.kint.2020.06.019
19. Matsha TE, Yako YY, Rensburg MA, Hassan MS, Kengne AP, Erasmus RT. Chronic kidney diseases in mixed ancestry south african populations: prevalence, determinants and concordance between kidney function estimators. BMC Nephrol. 2013;14(1):1–10. https://doi.org/10.1186/1471-2369-14-75
20. Adeniyi AB, Laurence CE, Volmink JA, Davids MR. Prevalence of chronic kidney disease and association with cardiovascular risk factors among teachers in Cape Town, South Africa. Clin kidney J. 2017;10(3):363–9. https://doi.org/10.1093/ckj/sfw138
21. George JA, Brandenburg JT, Fabian J, Crowther NJ, Agongo G, Alberts M, Ali S, Asiki G, Boua PR, Gómez-Olivé FX, Mashinya F. Kidney damage and associated risk factors in rural and urban sub-Saharan Africa (AWI-Gen): a cross-sectional population study. The Lancet Global Health. 2019 Dec1; 7(12):e1632-43https://doi.org/10.1016/s2214-109x(19)30443-7
22. Stanifer JW, Jing B, Tolan S, Helmke N, Mukerjee R, Naicker S, et al. The epidemiology of chronic kidney disease in sub-saharan Africa: a systematic review and meta-analysis. The Lancet Global Health. 2014;2(3):e174–e81. https://doi.org/10.1016/s2214-109x(14)70002-6
23. Shreffler J, Huecker MR. Hypothesis testing, P values, confidence intervals, and significance. StatPearls [Internet] Treasure Island (FL): StatPearls Publishing; 2022 Jan–. PMID: 32491353.
24. Turin TC, Tonelli M, Manns BJ, Ravani P, Ahmed SB, Hemmelgarn BR. Chronic kidney disease and life expectancy. Nephrol Dialysis Transplantation. 2012;27(8):3182–6. https://doi.org/10.1093/ndt/gfs052
25. Glassock R, Delanaye P, El Nahas M. An age-calibrated classification of chronic kidney disease. JAMA. 2015;314(6):559–60. https://doi.org/10.1001/jama.2015.6731
26. Delanaye P, Glassock RJ, De Broe ME. Epidemiology of chronic kidney disease: think (at least) twice! Clin Kidney J. 2017;10(3):370–4. https://doi.org/10.1093/ckj/sfw154
27. Glassock RJ, Winearls C. The global burden of chronic kidney disease: how valid are the estimates? Nephron Clin Pract. 2008;110(1):c39–c47. https://doi.org/10.1159/000151244
28. Matašin M, Domislović V, Fuček M, Gellineo L, Jelaković A, Dika Ž, et al. Berlin Initiative Study 1 equation and HUGE formula for more accurate estimation of kidney function in elderly. Rad Hrvatske akademije znanosti i umjetnosti Medicinske znanosti. 2021;547(54–55):24–31. https://doi.org/10.21857/ydkx2cw8k9
29. Carrero JJ, Hecking M, Chesnaye NC, Jager KJ. Sex and gender disparities in the epidemiology and outcomes of chronic kidney disease. Nat Rev Nephrol. 2018;14(3):151. https://doi.org/10.1038/nrneph.2017.181
30. Coresh J, Selvin E, Stevens LA, Manzi J, Kusek JW, Eggers P, et al. Prevalence of chronic kidney disease in the United States. JAMA. 2007;298(17):2038–47. https://doi.org/10.1001/jama.298.17.2038
31. Glassock RJ, Warnock DG, Delanaye P. The global burden of chronic kidney disease: estimates, variability and pitfalls. Nat Rev Nephrol. 2017;13(2):104. https://doi.org/10.1038/nrneph.2016.163
32. Nicholas SB, Kalantar-Zadeh K, Norris KC. Socioeconomic disparities in chronic kidney disease. Advances in chronic kidney disease. 2015;22(1):6–15. https://doi.org/10.1053/j.ackd.2014.07.002
33. Morton RL, Schlackow I, Gray A, Emberson J, Herrington W, Staplin N, et al. Impact of CKD on household income. Kidney Int Rep. 2018;3(3):610–8. https://doi.org/10.1016/j.ekir.2017.12.008
34. Kasembeli AN, Duarte R, Ramsay M, Mosiane P, Dickens C, Dix-Peek T, et al. APOL1 risk variants are strongly associated with HIV-associated nephropathy in black South Africans. J Am Soc Nephrol. 2015;26(11):2882–90. https://doi.org/10.1681/asn.2014050469
35. Kopp JB, Nelson GW, Sampath K, Johnson RC, Genovese G, An P, et al. APOL1 genetic variants in focal segmental glomerulosclerosis and HIV-associated nephropathy. J Am Soc Nephrol. 2011;22(11):2129–37. https://doi.org/10.1681/asn.2011040388
36. Szczech LA. Renal disease: the effects of HIV and antiretroviral therapy and the implications for early antiretroviral therapy initiation. Current Opinion in HIV and AIDS. https://doi.org/10.1097/coh.0b013e328329c6462009;4(3):167-70.
37. Hodel NC, Hamad A, Praehauser C, Mwangoka G, Kasella IM, Reither K, et al. The epidemiology of chronic kidney disease and the association with non-communicable and communicable disorders in a population of sub-saharan Africa. PLoS ONE. 2018;13(10):e0205326. https://doi.org/10.1371/journal.pone.0205326
38. Cockwell P, Fisher L-A. The global burden of chronic kidney disease. The Lancet. 2020;395(10225):662–4. https://doi.org/10.1016/s0140-6736(19)32977-0
39. Madala ND, Thusi GP, Assounga AG, Naicker S. Characteristics of south african patients presenting with kidney disease in rural KwaZulu-Natal: a cross sectional study. BMC Nephrol. 2014;15(1):1–9. https://doi.org/10.1186/1471-2369-15-61
40. Luyckx VA, Tonelli M, Stanifer JW. The global burden of kidney disease and sustainable development goals. Bull World Health Organ. 2018;96(6):414. https://doi.org/10.2471/blt.17.206441
41. Piéroni L, Delanaye P, Boutten A, Bargnoux A-S, Rozet E, Delatour V, et al. A multicentric evaluation of IDMS-traceable creatinine enzymatic assays. Clin Chim Acta. 2011;412(23–24):2070–5. https://doi.org/10.1016/j.cca.2011.07.012
42. Delanaye P, Cavalier E, Cristol J-P, Delanghe JR. Calibration and precision of serum creatinine and plasma cystatin C measurement: impact on the estimation of glomerular filtration rate. J Nephrol. 2014;27(5):467–75. https://doi.org/10.1007/s40620-014-0087-7
43. White SL, Polkinghorne KR, Atkins RC, Chadban SJ. Comparison of the prevalence and mortality risk of CKD in Australia using the CKD epidemiology collaboration (CKD-EPI) and modification of Diet in Renal Disease (MDRD) Study GFR estimating equations: the AusDiab (australian diabetes, obesity and lifestyle) study. Am J Kidney Dis. 2010;55(4):660–70. https://doi.org/10.1053/j.ajkd.2009.12.011
44. Levey AS, Coresh J, Tighiouart H, Greene T, Inker LA. Strengths and limitations of estimated and measured GFR. Nat Rev Nephrol. 2019;15(12):784. https://doi.org/10.1038/s41581-019-0213-9

45. Centres for disease control and Prevention. Chronic kidney disease in the United States., 2019. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention. 2019. March,3
46. Fabian J, Kalyesubula R, Mkandawire J, Hansen CH, Nitsch D, Musenge E, et al. Measurement of kidney function in Malawi, South Africa, and Uganda: a multicentre cohort study. The Lancet Global Health. 2022;10(8):e1159–e69. https://doi.org/10.1016/s2214-109x(22)00239-x
47. Eriksen B, Ingebretsen O. The progression of chronic kidney disease: a 10-year population-based study of the effects of gender and age. Kidney Int. 2006;69(2):375–82. https://doi.org/10.1038/sj.ki.5000058
48. Gharbi MB, Elseviers M, Zamd M, Alaoui AB, Benahadi N, Trabelssi EH, et al. Chronic kidney disease, hypertension, diabetes, and obesity in the adult population of Morocco: how to avoid "over"-and "under"-diagnosis of CKD. Kidney Int. 2016;89(6):1363–71. https://doi.org/10.1016/j.kint.2016.02.019
49. Delgado C, Baweja M, Burrows NR, Crews DC, Eneanya ND, Gadegbeku CA et al. Reassessing the inclusion of race in diagnosing kidney diseases: An interim report from the NKF-ASN task force. Am J Kidney Dis. 2021 Jul; 78(1):103–115. https://doi.org/10.1053/j.ajkd.2021.03.008
50. Inker LA, Eneanya ND, Coresh J, Tighiouart H, Wang D, Sang Y, et al. New creatinine-and cystatin C–based equations to estimate GFR without race. N Engl J Med. 2021;385(19):1737–49. https://doi.org/10.1056/nejmoa2102953
51. Hsu C-y, Yang W, Parikh RV, Anderson AH, Chen TK, Cohen DL, et al. Race, genetic ancestry, and estimating kidney function in CKD. N Engl J Med. 2021;385(19):1750–60. https://doi.org/10.1056/nejmoa2103753
52. Fabian J, George JA, Etheredge HR, van Deventer M, Kalyesubula R, Wade AN, et al. Methods and reporting of kidney function: a systematic review of studies from sub-saharan Africa. Clin kidney J. 2019;12(6):778–87. https://doi.org/10.1093/ckj/sfz089
53. George C, Stoker S, Okpechi I, Woodward M, Kengne A. The Chronic Kidney Disease in Africa (CKD-Africa) collaboration: lessons from a new pan-African network. BMJ Global Health. 2021 Aug1; 6(8):e006454. https://doi.org/10.1136/bmjgh-2021-006454

Publisher's Note

Chapter 3: Synthesis, conclusions and recommendations

Synthesis

The reviewers of the published manuscript recommended altering the original title from "The prevalence of chronic kidney disease in South Africa - comparisons with sub-Saharan, Africa, Africa and globally "to "The prevalence of chronic kidney disease in South Africa – limitations of studies comparing prevalence with sub-Saharan Africa, Africa and globally." The reviewers recommended the change based on the research findings.

The results of the objectives were:

(i) Comparative prevalence of CKD:

Statistically significant differences in CKD prevalence were found when comparing SA to other geographic regions, except in one instance - an SA study versus an African study. Notably, sub-Saharan studies exhibited a higher CKD prevalence rate than SA studies. In African studies, CKD prevalence varied, with one study showing lower rates and another showing higher rates than SA studies. Similarly, global studies also displayed variable CKD prevalence rates, with one higher and one lower than SA studies.

(ii) Sample Size Influence on Differences:

These differences in prevalence rates were primarily attributed to the considerable variations in sample sizes between SA and other geographic areas rather than reflecting genuine disparities. The SA studies had smaller sample sizes than those conducted in other regions.

(iii) Participant Characteristics:

Most study participants were in their 4th to 5th decades of life, indicating a consistent age pattern. Additionally, a notable female preponderance was observed across all studies. Hypertension and DM emerged as the most prevalent risk factors in all regions, with HIV being a common risk factor in sub-Saharan Africa and Africa.

(iv) CKD Definitions and Chronicity:

Notably, only one study by George et al. adhered to the currently accepted definition of CKD in their research. Furthermore, none of the studies investigated CKD in terms of chronicity, which typically involves the condition persisting for more than three months.

(v) Measurement Methods for CKD Indicators:

Studies employed different measurement methods. Serum creatinine levels were measured using both enzyme-linked assays and Jaffe assays. Regarding estimating glomerular filtration rate (eGFR), the CKD-EPI, MDRD, and Cockcroft-Gault formulae were the most commonly utilized methods across all studies.

The study's limitations included variability in study techniques due to sample size, data collection methods, and CKD diagnostic criteria, which made direct comparisons challenging. Health data availability and quality in different regions influence CKD prevalence estimations. This arises when some locations need more or complete health information systems and need consistently accurate and up-to-date data. Due to various socio-economic, cultural, and geographic characteristics, different regions are heterogeneous. Inequalities in healthcare access can also influence CKD diagnosis and reporting. Temporal changes in health care and lifestyle affect CKD prevalence across regions. There was a significant lack of standardisation in the diagnosis and reporting of CKD, resulting in disparities in prevalence rates. A network of researchers known as the CKD in Africa Collaboration was established to evaluate CKD outcomes, standardise the evaluation of CKD prevalence, and generate more accurate prevalence estimates.

There should be consistency in study techniques, identifying potential biases, and concerted efforts to perform multicenter studies with standardised protocols. The enhanced methodology would allow more effective location comparisons to eliminate these constraints. There is a need for greater collaboration among academics, healthcare providers, and policymakers to improve data collection and reporting practices, resulting in more accurate estimates of the prevalence of CKD.

Conclusions

The primary aim of this study was to conduct a systematic review of existing research to compare the prevalence rates of CKD in SA, sub-Saharan Africa, and globally. The study revealed statistically significant differences between SA and all other regions, with variations primarily attributed to disparities in sample sizes and various clinical and laboratory influences.

However, it is essential to acknowledge the limitations of this research. Firstly, the study was based on a relatively small number of papers (eight) in the final systematic analysis. Additionally, there was no analysis for significant risk factors like HIV in high-prevalence areas like SA.

The systematic review was registered with PROSPERO, and we utilised various search engines, employing appropriate statistical techniques to compare different types and sample sizes of studies. However, it remains to be seen whether including unpublished studies, conference abstracts, or grey literature might have enriched our findings. We did not contact the authors of the papers for unpublished data or perform tests to exclude publication bias.

Despite these limitations, this study successfully addressed a critical research gap by comparing SA's CKD prevalence with other regions. Furthermore, it underscores the pressing need for greater uniformity and consistency in assessing CKD prevalence and calls for novel approaches to combat this significant contributor to the global pandemic of non-communicable diseases.

Recommendations

Standardized methods should be adopted to assess CKD prevalence. Standardisation will promote consistency in data collection and reporting across regions, enabling more meaningful comparisons. We should encourage further research to address identified gaps, including a broader and more diverse range of studies, including unpublished sources that establish a comprehensive understanding of CKD prevalence.

There should be enhanced and comprehensive data collection and reporting, including testing for significant risk factors like HIV in high CKD prevalence regions. Robust data collection will contribute to more accurate and informative research outcomes.

Improved collaboration and communication among CKD researchers should be encouraged between institutions and healthcare providers. Sharing data, insights, and experiences can identify best practices and enhance global coordination.

Advanced research methods, such as "Big Data" analytics and modeling techniques, are recommended to extract robust and accurate conclusions and predict future CKD prevalence trends. Investigators can contact authors of relevant studies to obtain additional data and unpublished information, which will help fill data gaps and enhance the quality of systematic reviews.

Strategies to address CKD should be developed and implemented to tackle the high CKD prevalence rate. Policymakers, healthcare providers, and public health organisations should focus on early detection, prevention, and improving access to care and treatment.

These recommendations play a pivotal role in shaping future research endeavors and driving actions to effectively combat the challenges presented by the prevalence of CKD at both regional and globally.

References

1.Kdigo C. Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int Suppl. 2013;3(1):1-150.
2.Inker LA, Astor BC, Fox CH, Isakova T, Lash JP, Peralta CA, et al. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for the evaluation and management of CKD. Am J Kidney Dis. 2014;63(5):713-35.
3.CG182 N. Chronic kidney disease in adults: assessment and management. July; 2014.
4.Levin A, Stevens PE. Early detection of CKD: the benefits, limitations and effects on prognosis. Nature Reviews Nephrology. 2011;7(8):446-57.
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. Oxford University Press; 2019.
6.Levin A, Tonelli M, Bonventre J, Coresh J, Donner J-A, Fogo AB, et al. Global kidney health 2017 and beyond: a roadmap for closing gaps in care, research, and policy. The Lancet. 2017;390(10105):1888-917.
7.Bikbov B, Purcell CA, Levey AS, Smith M, Abdoli A, Abebe M, et al. Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. The Lancet. 2020;395(10225):709-33.
8.Luyckx VA, Tonelli M, Stanifer JW. The global burden of kidney disease and the sustainable development goals. Bulletin of the World Health Organization. 2018;96(6):414.
9.Foreman KJ, Marquez N, Dolgert A, Fukutaki K, Fullman N, McGaughey M, et al. Forecasting life expectancy, years of life lost, and all-cause and cause-specific mortality for 250 causes of death: reference and alternative scenarios for 2016–40 for 195 countries and territories. The Lancet. 2018;392(10159):2052-90.
10.Sundström J, Bodegard J, Bollmann A, Vervloet MG, Mark PB, Karasik A, et al. Prevalence, outcomes, and cost of chronic kidney disease in a contemporary population of 2· 4 million patients from 11 countries: The CaReMe CKD study. The Lancet Regional Health–Europe. 2022;20.
11.Nguyen NT, Cockwell P, Maxwell AP, Griffin M, O'Brien T, O'Neill C. Chronic kidney disease, health-related quality of life and their associated economic burden among a nationally representative sample of community dwelling adults in England. PLoS One. 2018;13(11):e0207960.
12.Mills KT, Xu Y, Zhang W, Bundy JD, Chen C-S, Kelly TN, et al. A systematic analysis of worldwide population-based data on the global burden of chronic kidney disease in 2010. Kidney international. 2015;88(5):950-7.

13.Nr H. Fatoba St, Oke JL, et al. Global prevalence of chronic kidney disease-a systematic review and meta-analysis. PLoS One. 2016;11:e0158765.
14.Naghavi M, Abajobir AA, Abbafati C, Abbas KM, Abd-Allah F, Abera SF, et al. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980–2016: a systematic analysis for the Global Burden of Disease Study 2016. The Lancet. 2017;390(10100):1151-210.
15.Liyanage T, Ninomiya T, Jha V, Neal B, Patrice HM, Okpechi I, et al. Worldwide access to treatment for end-stage kidney disease: a systematic review. The Lancet. 2015;385(9981):1975-82.
16.Wang H, Naghavi M, Allen C, Barber RM, Bhutta ZA, Carter A, et al. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015. The lancet. 2016;388(10053):1459-544.
17.Mayosi BM, Flisher AJ, Lalloo UG, Sitas F, Tollman SM, Bradshaw D. The burden of non-communicable diseases in South Africa. The lancet. 2009;374(9693):934-47.
18.Moosa M, Van der Walt I, Naicker S, Meyers A. Important causes of chronic kidney disease in South Africa. South African medical journal. 2015;105(4):320-7.
19.Davids MR, Jardine T, Marais N, Zunza M, Jacobs JC, Sebastian S. South African renal registry annual report 2017. African Journal of Nephrology. 2019;22(1):60-71.
20.Matsha TE, Yako YY, Rensburg MA, Hassan MS, Kengne AP, Erasmus RT. Chronic kidney diseases in mixed ancestry south African populations: prevalence, determinants and concordance between kidney function estimators. BMC nephrology. 2013;14(1):75.
21.Adeniyi AB, Laurence CE, Volmink JA, Davids MR. Prevalence of chronic kidney disease and association with cardiovascular risk factors among teachers in Cape Town, South Africa. Clinical kidney journal. 2017;10(3):363-9.
22.Bello A, Levin A, Tonelli M, Okpechi I, Feehally J, Harris D, et al. Global Kidney Health Atlas: a report by the International Society of Nephrology on the current state of organization and structures for kidney care across the globe. Brussels: International Society of Nephrology. 2017;2018.
23.Stanifer JW, Jing B, Tolan S, Helmke N, Mukerjee R, Naicker S, et al. The epidemiology of chronic kidney disease in sub-Saharan Africa: a systematic review and meta-analysis. The Lancet Global Health. 2014;2(3):e174-e81.
24.George JA, Brandenburg J-T, Fabian J, Crowther NJ, Agongo G, Alberts M, et al. Kidney damage and associated risk factors in rural and urban sub-Saharan Africa (AWI-Gen): a cross-sectional population study. The Lancet Global Health. 2019;7(12):e1632-e43.
25.Arogundade FA, Omotoso BA, Adelakun A, Bamikefa T, Ezeugonwa R, Omosule B, et al. Burden of end-stage renal disease in sub-Saharan Africa. Clinical nephrology. 2020;93(1):3-7.

26.Kaze AD, Ilori T, Jaar BG, Echouffo-Tcheugui JB. Burden of chronic kidney disease on the African continent: a systematic review and meta-analysis. BMC nephrology. 2018;19(1):1-11.
27.Abd ElHafeez S, Bolignano D, D'Arrigo G, Dounousi E, Tripepi G, Zoccali C. Prevalence and burden of chronic kidney disease among the general population and high-risk groups in Africa: a systematic review. BMJ open. 2018;8(1):e015069.
28.Hill NR, Fatoba ST, Oke JL, Hirst JA, O'Callaghan CA, Lasserson DS, et al. Global Prevalence of Chronic Kidney Disease - A Systematic Review and Meta-analysis. PLoS One. 2016;11(7):e0158765.
29.Group IDA. Update of mortality attributable to diabetes for the IDF Diabetes Atlas: Estimates for the year 2013. Diabetes research and clinical practice. 2015;109(3):461-5.
30.Li P, Garcia-Garcia G, Lui S-F, Andreoli S, Fung W, Hradsky A, et al. Kidney health for everyone everywhere–from prevention to detection and equitable access to care. Brazilian Journal of Medical and Biological Research. 2020;53.
31.Jha V, Garcia-Garcia G, Iseki K, Li Z, Naicker S, Plattner B, et al. Chronic kidney disease: global dimension and perspectives. Lancet. 2013;382(9888):260-72.
32.Brück K, Jager KJ, Dounousi E, Kainz A, Nitsch D, Ärnlöv J, et al. Methodology used in studies reporting chronic kidney disease prevalence: a systematic literature review. Nephrology Dialysis Transplantation. 2015;30(suppl_4):iv6-iv16.
33.Madala ND, Thusi GP, Assounga AG, Naicker S. Characteristics of South African patients presenting with kidney disease in rural KwaZulu-Natal: a cross sectional study. BMC nephrology. 2014;15(1):61.
34.Singh M, Magula NP, Hariparshad S, Assounga AG. A comparison of urban and rural patients with chronic kidney disease referred to Inkosi Albert Luthuli Central Hospital in Durban, South Africa. African Journal of Nephrology. 2017;20(1):34-8.

Appendix 1: Ethical approval

UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

29 August 2022

Dr SP Hariparshad (893288299)
School of Clinical Medicine
College of Health Sciences
sudeshph@yahoo.com

Dear Dr Hariparshad

Protocol: The prevalence and progression of chronic kidney diseases among adult patients in the public health service in KwaZulu-Natal.
Degree: MMedSc
BREC Ref No: BE120/19
New title: The prevalence of chronic kidney diseases in South Africa – comparisons with sub-Saharan Africa, Africa and Globally

We wish to advise you that your application for amendments received on 21 August 2022 to change the title to the above new title for the above study has been **noted and approved** by a subcommittee of the Biomedical Research Ethics Committee.

The committee will be notified of the above approval at its next meeting to be held on 13 September 2022.

Yours sincerely

[redacted]

Ms A Marimuthu
(for) Prof D Wassenaar
Chair: Biomedical Research Ethics Committee

UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

29 August 2022

Dr SP Hariparshad (893288299)
School of Clinical Medicine
College of Health Sciences
sudeshph@yahoo.com

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Yours sincerely

[redacted]

.....
Ms A Marimuthu
(for) Prof D Wassenaar
Chair: Biomedical Research Ethics Committee

Appendix 2: Data collection tools

Table 4: Data collection tool

Recommended methodology for comparison of CKD prevalence by the European CKD Burden Consortium (32)

Recommended tools	Details
1. General population sampling	Describe:
Sampling methods	sampling frame i.e. source to identify subjects
	Sample design i.e. method of subject selection e.g.
	Age stratified or random
Response	Report the response in percentages
2. Assessment of kidney function	
Serum creatinine assay	Describe the assay used i.e. Jaffe or enzymatic
Albuminuria assay	Describe the assay used i.e. immunoassay or dipsticks
IDMS calibration	Describe if the IDMS calibration standardization was used
CKD definition	Use the same definition of CKD
	For CKD stages 1-5
	eGFR < 60 ml/min/1.73 m^2 calculated by CKD-EPI equation and/or ACR. 30 mg/g
	For stages 3-5
	eGFR < 60 ml/min/1.73 m^2 calculated by CKD-EPI equation
3.Presentation of results	

CKD prevalence estimate	Report:
	- Unadjusted and adjusted CKD prevalence
	- 95% CI
CKD prevalence estimate by strata	Report:
	- Stratified by age groups : 20-44, 45-65 , 66-74, 75-84 years
	Stratified by DM, hypertension and obesity status
Serum creatinine determination	Indicate in tables and figures which studies use:
	- Jaffe or enzymatic assay - IDMS calibration standardization

PROSPERO reference guidance tool

NIHR | National Institute for Health Research

PROSPERO
International prospective register of systematic reviews

Registering a review on PROSPERO

PROSPERO is an international database of prospectively registered systematic reviews in health and social care. Key features from the review protocol are recorded and maintained as a permanent record in PROSPERO. The aim is to provide a comprehensive listing of systematic reviews registered at inception, to help avoid unplanned duplication. By promoting transparency in the process and enabling comparison of reported review findings with what was planned in the protocol PROSPERO also aims to minimise the risk of bias in systematic review.
PROSPERO has been developed and is managed by the Centre for Reviews and Dissemination (CRD) at the University of York and is funded by the UK's National Institute for Health Research (NIHR).

What does registration on PROSPERO involve?

Registration in PROSPERO involves the prospective submission and publication of key information about the design and conduct of a systematic review.
Registration on PROSPERO is free of charge. In return, registrants are accountable for the accuracy and updating of information submitted.

Inclusion criteria

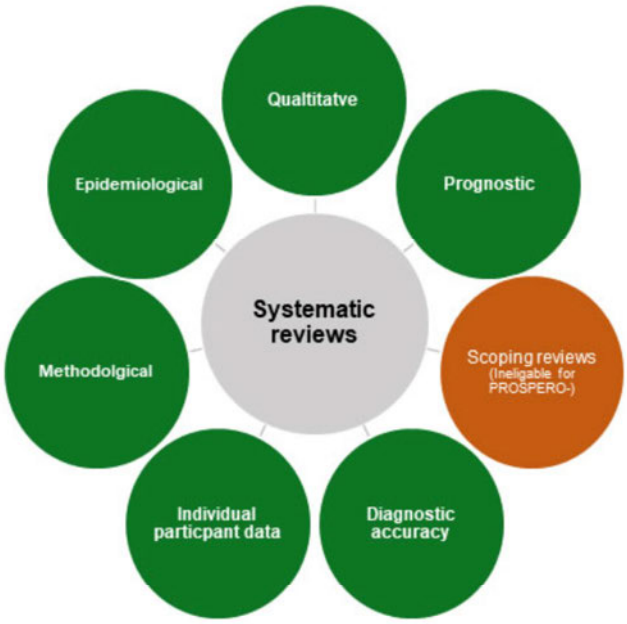
PROSPERO includes details of any planned or on-going systematic review that has a health related outcome.

PROSPERO accepts:

Systematic review protocols assessing:

- Interventions (Including qualitative and individual participant data reviews)
- Diagnostic accuracy
- Prognostic factors
- Prevention
- Epidemiological reviews relevant to health and social care
- Public health
- Service delivery in health and social care
- Methodological

Further information on protocol development specific to review types is accessible below.



Requirements for registration

- A full protocol should be ready before registering with PROSPERO
- Submissions must be made before data extraction commences (from October 2019)
- Registration forms must be complete.
- Submissions must be in English (search strategies and protocols attached to a record may be in any language).

PROSPERO does not accept:

- Systematic reviews without an outcome of clear relevance to the health of humans
- Scoping reviews
- Literature reviews that use a systematic search
- Systematic reviews assessing sports performance as an outcome
- Methodological reviews that assess ONLY the quality of reporting
- Systematic critical appraisals

Other considerations

- Cochrane protocols are automatically uploaded- To avoid duplication of records, Cochrane protocols **should not** be registered separately with PROSPERO.
- Systematic reviews of animal studies only are not eligible for registration in the section of PROSPERO dedicated to reviews of human studies. These should be registered in the section of PROSPERO for animal studies.
- Systematic reviews of in-vitro studies only are not eligible for registration on PROSPERO. We recommend registering such protocols elsewhere, for instance on Open Science Framework.

If you are in any doubt about the eligibility of your review, including the stage of progress please contact us by email using the details on the contact page for advice.

Appendix 3: The Guidelines for Authorship for BMC (Biomed Central Nephrology)

Aims and scope

BMC Nephrology is an open access journal publishing original peer-reviewed research articles in all aspects of the prevention, diagnosis and management of kidney and associated disorders, as well as related molecular genetics, pathophysiology, and epidemiology.

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Where appropriate, research papers describing in vivo studies should acknowledge the Landis 4 criteria (randomization, blinding, sample size calculation, an inclusion/exclusion criteria). Any limitations of the study should also be presented.

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BMC Nephrology strongly encourages that all datasets on which the conclusions of the paper rely should be available to readers. We encourage authors to ensure that their datasets are either deposited in publicly available repositories (where available and appropriate) or presented in the main manuscript or additional supporting files whenever possible. Please see Springer Nature's data repository guidance. Where a widely established research community expectation for data archiving in public repositories exists, submission to

a community-endorsed, public repository is mandatory. A list of data where deposition is required, with the appropriate repositories, can be found on the Editorial Policies Page.

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Preparing your manuscript

The information below details the section headings that you should include in your manuscript and what information should be within each section.

Please note that your manuscript must include a 'Declarations' section including all of the subheadings (please see below for more information).

Title page

The title page should:

- present a title that includes, if appropriate, the study design e.g.:
    - "A versus B in the treatment of C: a randomized controlled trial", "X is a risk factor for Y: a case control study", "What is the impact of factor X on subject Y: A systematic review"
    - or for non-clinical or non-research studies a description of what the article reports
- list the full names and institutional addresses for all authors
    - if a collaboration group should be listed as an author, please list the Group name as an author. If you would like the names of the individual members of the Group to be searchable through their individual PubMed records, please include this information in the "Acknowledgements" section in accordance with the instructions below
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- indicate the corresponding author

Abstract

The Abstract should not exceed 350 words. Please minimize the use of abbreviations and do not cite references in the abstract. Reports of randomized controlled trials should follow the CONSORT extension for abstracts. The abstract must include the following separate sections:

- Background: the context and purpose of the study
- Methods: how the study was performed and statistical tests used
- Results: the main findings
- Conclusions: brief summary and potential implications
- Trial registration: If your article reports the results of a health care intervention on human participants, it must be registered in an appropriate registry and the registration number and date of registration should be stated in this section. If it was not registered prospectively (before enrollment of the first participant), you should include the words' retrospectively registered'. See our editorial policies for more information on trial registration

Keywords

Three to ten keywords representing the main content of the article.

Background

The Background section should explain the background to the study, its aims, a summary of the existing literature and why this study was necessary or its contribution to the field.

Methods

The methods section should include:

- the aim, design and setting of the study
- the characteristics of participants or description of materials
- a clear description of all processes, interventions and comparisons. Generic drug names should generally be used. When proprietary brands are used in research, include the brand names in parentheses
- the type of statistical analysis used, including a power calculation if appropriate

Results

This should include the findings of the study including, if appropriate, results of statistical analysis which must be included either in the text or as tables and figures.

Discussion

This section should discuss the implications of the findings in context of existing research and highlight limitations of the study.

Conclusions

This should state clearly the main conclusions and provide an explanation of the importance and relevance of the study reported.

List of abbreviations

If abbreviations are used in the text they should be defined in the text at first use, and a list of abbreviations should be provided.

Declarations

All manuscripts must contain the following sections under the heading 'Declarations':

- Ethics approval and consent to participate
- Consent for publication
- Availability of data and materials
- Competing interests
- Funding
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- Acknowledgements
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Please see below for details on the information to be included in these sections.

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Ethics approval and consent to participate

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- The datasets generated and/or analysed during the current study are available in the [NAME] repository, [PERSISTENT WEB LINK TO DATASETS]
- The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.
- All data generated or analysed during this study are included in this published article [and its supplementary information files].
- The datasets generated and/or analysed during the current study are not publicly available due [REASON WHY DATA ARE NOT PUBLIC] but are available from the corresponding author on reasonable request.
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The datasets generated during and/or analysed during the current study are available in the [NAME] repository, [PERSISTENT WEB LINK TO DATASETS].[Reference number]

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Slifka MK, Whitton JL. Clinical implications of dysregulated cytokine production. Dig J Mol Med. 2000; doi:10.1007/s801090000086.

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Book chapter, or an article within a book

Wyllie AH, Kerr JFR, Currie AR. Cell death: the significance of apoptosis. In: Bourne GH, Danielli JF, Jeon KW, editors. International review of cytology. London: Academic; 1980. p. 251-306.

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Saito Y, Hyuga H. Rate equation approaches to amplification of enantiomeric excess and chiral symmetry breaking. Top Curr Chem. 2007. doi: 10.1007/128_2006_108.

Complete book, authored

Blenkinsopp A, Paxton P. Symptoms in the pharmacy: a guide to the management of common illness. 3rd ed. Oxford: Blackwell Science; 1998.

Online document

Doe J. Title of subordinate document. In: The dictionary of substances and their effects. Royal Society of Chemistry. 1999. http://www.rsc.org/dose/title of subordinate document. Accessed January 15 1999.

Online database

Healthwise Knowledgebase. US Pharmacopeia, Rockville. 1998. http://www.healthwise.org. Accessed September 21 1998.

Supplementary material/private homepage

Doe J. Title of supplementary material. 2000. http://www.privatehomepage.com. Accessed February 22 2000.

University site

Doe, J: Title of preprint. http://www.uni-heidelberg.de/mydata.html (1999). Accessed December 25 1999.

FTP site

Doe, J: Trivial HTTP, RFC2169. ftp://ftp.isi.edu/in-notes/rfc2169.txt (1999). Accessed November 12 1999.

Organization site

ISSN International Centre: The ISSN register. http://www.issn.org (2006). Accessed February 20 2007.

Dataset with persistent identifier

Zheng L-Y, Guo X-S, He B, Sun L-J, Peng Y, Dong S-S, et al. Genome data from sweet and grain sorghum (Sorghum bicolor). GigaScience Database. 2011. http://dx.doi.org/10.5524/100012.

Figures, tables and additional files

See General formatting guidelines for information on how to format figures, tables and additional files.

Appendix 4: Raw data

Table 5: Literature summary

Author	Year	Title	Context/ setting/ sample	Results	Limitations
Hill et al.(28)	2016	Global prevalence of chronic kidney disease- a systemic review and meta-analysis	100 observational studies with 7 million people	Stage 1-5 mean prevalence was 13.4% (95% CI) Stage 3-5 mean prevalence was 10.6% (95% CI)	Serum creatinine measurement bias was inherent in the majority of studies 95% studies did not report on 2 eGFR's more than 3 months apart Jaffe creatinine assay was the main method used and it systematically over-estimate serum creatinine to varying degrees MDRD equation used systematically over-estimates CKD prevalence Single measure eGFR results in excessive false identification of CKD

Bikbov et al (7)	2017	Global, regional and national burden of chronic kidney disease, 1990-2017: a systematic analysis for the global burden of disease study 2017	Systematic review of literature for cross-sectional or cohort studies reporting CKD prevalence using 216 studies	Global prevalence was 9.1% (95% UI)	Lack of high quality population based studies Lack of standardized equations to calculate eGFR Most data sources did not repeat serum creatinine and urine ACR measurements after 3 months which might over-estimate prevalence by 25-50%
Mills et al(12)	2015	A systematic analysis of worldwide population based data on the global burden of CKD in 2010	A systematic review of pooled data of 33 population based studies in 32 countries	Prevalence in men was 10.4% (95% CI 0.3-11.9% Prevalence in women was 11.8% (95% CI 11-2-12.6%)	Use of single creatinine measurements to calculate eGFR. Creatinine based measurements might under-estimate true GFR when more than 60 ml/min/1.73m^2 Majority of population based surveys did not follow up patients for 3 months to confirm CKD.

					Albuminuria and proteinuria were not measured in several studies.
Kaze et al(26)	2018	Burden of chronic kidney disease on the African continent : a systematic review and meta-analysis	Systematic review and meta-analysis of 98 studies and 98432 individuals	Overall prevalence of 15.8% (95% CI 12.1-19.9) CKD stage 3-5 prevalence was 4.6%	Substantial heterogeneity in prevalence estimates due to different study methodologies and populations Incomplete methodological information provided by studies Majority of studies did not follow up patients for 3 months
Abd ElHafeez et al(27)	2018	Prevalence and burden of chronic kidney disease among the general population and high-risk groups in Africa: a systematic review	Systematic review of 152 studies from throughout Africa	Pooled prevalence: 10.1% (95% CI 9.8% to 10.5%)	Analytical heterogeneity used to measure creatinine and albuminuria Serum creatinine concentrations are affected

					by intraindividual variability with over 20% changes within a 2-week period The number of studies reported using IDMS was low in Africa. Differences in sample size, demographics and clinical characteristics are all significant limitations in the systematic review The lack of information on the prevalence of CKD by age and gender in studies included in this systematic review with only 11% of the included studies reported CKD prevalence. Only 5 studies assessed chronicity criterion.

Stanifer et al.(23)	2014	The epidemiology of chronic kidney disease in sub-Saharan Africa: a systematic review and meta-analysis	Systematic review of 90 studies from 96 sites Meta-analyses of 21 medium and high quality studies from 25 sites	The overall prevalence of CKD from the 21 medium-quality and high-quality studies was 13·9% (95% CI 12·2–15·7).	Absence of reliable and validated measures of kidney function Proteinuria was poorly assessed. Variability and dearth of available data.
George et al.(24)	2019	Kidney damage and associated risk factors in rural and urban sub-Saharan Africa: a cross sectional population study	Population based study of 8110 participants between 40-60 years old from 4 rural and 2 urban sites in 4 sub-Saharan African countries	Overall age adjusted prevalence of CKD was 10.7% (95% CI 9.9-11.7) with largest relative contribution from albuminuria Overall prevalence of	Lack of validated measures of eGFR in local populations. Prevalence can vary substantially depending on the equation used. Chronicity was not demonstrated. Testing for haematuria was not done.

				CKD was higher in women with 12% (10,8-13.2) compared to men at 9.5% (8.3-10.8)	
Matsha et al.	2013	Chronic kidney disease in mixed ancestry South African populations: prevalence, determinants and concordance between kidney function estimators.	There were 1202 mixed ancestry subjects with a mean age of 52.9 years. Prevalence of stage 3-5 CKD investigated using Cockcroft-Gault, MDRD and CKD-EPI equations	The crude prevalence of stage 3-5 CKD to be 7.6 % based on the MDRD equation without correction factors. Correlations were higher between MDRD and CKD-EPI equations	Study conducted in a single geographical site. The study equations were not evaluated against the gold standard to assess their validity in estimating GFR. No estimates of albuminuria were done.

Madala et al.(33)	2014	Characteristics of South African patients presenting with kidney disease in rural KwaZulu-Natal: a cross sectional study	Cross sectional study of 302 patients (165 females/137 males) in rural KZN	Hypertension in 75.2% of sample, DM in 29.8% , HIV in 28.5% eGFR reduced with age obesity in 86.4% females and 54.5 % males 50% presented with MDRD eGFR less than 30ml/min/1.73 m^2	Cross section design has inherent limitations where causal associations cannot be determined between CKD severity and various risk factors. Selection bias from preferential referral of advanced CKD Serum creatinine values used with re-calibration to IDMS assay can introduce bias in calculating eGFR Validity in MDRD eGFR in HIV patients is uncertain
Singh et al.(34)	2017	A comparison of urban and rural patients with chronic kidney disease referred to Inkosi Albert Luthuli Central Hospital in	A retrospectiv e review of 529 patients comparing clinical characteristi c of rural	Mean age of rural patients was lower than urban participants (40.6 vs. 53.4 years respectively	Poor data capture from regional hospitals Small number of rural patients studied compared to urban

		Durban, South Africa	and urban patients	Rural participants had lower eGFR than urban participants (16.3 vs. 25.4 ml/min/1.73m^2 Rural patients had higher HIV infection rates (47.9% vs 18.3%) but lower hypertension (69.6 % vs. 83.9%) and DM (20.3% vs. 54.1%)	

Table 6 Raw data: Prevalence of CKD: Global, African, sub-Saharan Africa and South Africa

Author	Year	Region	Prevalence of CKD
Hill et al.(28)	2016	World	10.6%
Bikbov et al.(7)	2020	World	9.1%
Mills et al.(12)	2015	World	Men 10.4% Women 11.8%
Luyckx et al.(8)	2018	Africa	15.8%
Abd ElHafeez et al(27)	2018	Africa	14.2%
Stanifer et al (23)	2014	sub-Saharan Africa	13.9%
George JA (24)	2019	sub-Saharan Africa	10.7%
Bello et al(22)	2017	South Africa	10.7%
Bikbov et al.(7)	2020	South Africa	9.5 %
Hill et al(28)	2016	South Africa	7.6%
Matsha et al	2013	South Africa	Men 5.7% Women 8%
		KwaZulu-Natal	Unknown

Appendix 5: Tables

Table 1 Staging of CKD according to eGFR (1)

GFR category	GFR(ml/min/1.73m^2)	Terms
G1	More than or equal to 90	Normal to high
G2	60-89	Mildly decreased
G3a	45-59	Mildly to moderately decreased
G3b	30-44	Moderately to severely decreased
G4	15-29	Severely decreased
G5	<15	Kidney failure

Table 2 Albuminuria categories in CKD adapted from KDIGO (1)

Albuminuria category	Albumin-creatinine ratio mg/mmol	Terms
A1	<3	Normal to mildly increased
A2	3-30	Moderately increased
A3	>30	Severely increased

Table 3 Prognosis of CKD by GFR and albuminuria categories adapted from KDIGO 2012 (1)

GFR stage ml/min/1.73m^2			Persistent Albuminuria categories		
			A1	A2	A3
			Normal to mildly increased	Moderately increased	Severely increased
			<3mg/mmol	3-30 mg/mmol	>30 mg/mmol
G1	Normal to high	>90	Low risk	Moderately increased risk	Moderately increased risk
G2	Mildly decreased	60-89	Low risk	Moderately increased risk	Moderately increased risk
G3a	Mild to Moderately decreased	45-59	Moderately increased risk	High risk	Very high risk
G3b	Moderate to severely decreased	30-44	High risk	High risk	Very high risk
G4	Severely decreased	15-29	Very high risk	Very high risk	Very high risk
G5	Kidney failure	<15	Very high risk	Very high risk	Very high risk