



Reducing the Burden of Chronic Kidney Disease: The Role of Active Prevention and Control of Hypertension in Global Perspective

Ibama AS^{1*}, Timothy T², Oko-Jaja RI³, Amadi COA⁴

^{1,4}Federal University of Technology, Owerri, Nigeria.

²Rivers State Primary Health Care Management Board, Port Harcourt, Nigeria.

³University of Port Harcourt Teaching Hospital, Port Harcourt, Nigeria.

*Corresponding author: Ibama AS, Federal University of Technology, Owerri, Nigeria. Email: asiton.ibama@gmail.com

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Abstract

Chronic kidney disease is a health problem that consumes a lot of private and public resources in increasing pattern in the population. This review paper aimed at identifying the extent of hypertensive associated chronic kidney disease condition globally and what could epidemiologically base prevention and control of hypertension play in reducing the burden of chronic kidney disease. The methodology used was traditional review of published literatures on the subject in global perspective and identifying the burden of chronic kidney disease in terms of financial cost as well as modifiable and behavioral risk factors implicated in hypertension, which strategic prevention and intervention measures will address. Findings show that worldwide prevalence of hypertension, estimated from a 2005 systematic review of published literatures was 26%, with a projected 60% increase by 2025 and African Americans are about six times more likely than Caucasians to develop hypertension-related kidney failure. Hypertension is the second leading cause of kidney failure (28.4%), requiring either kidney transplant or dialysis to sustain life. From 1990 to 2010, treatment costs for the global maintenance of dialysis population was estimated at \$200 billion to \$1.1 trillion. Global incidence of kidney failure is on the increase and treatment is costly, therefore, the worldwide burden of illness associated with the kidney is also on the increase. Hence, by ensuring the epidemiologically based strategic prevention and control of hypertension as provided in this paper, the resources to be allocated to renal management/replacement therapy which are increasing will rather reduce by about 28%, translating to \$56 billion to \$0.3trillion overtime.

Keywords: Chronic kidney disease; hypertension; burden; cost; risk factors

Introduction

Disease burden is an aggregate reflection of impact of health problem in a given area, region or globally, and can be measured using a variety of indicators such as morbidity, mortality, or financial cost. Targeted interventions are usually geared toward arriving at estimates of avoidable burden of such disease/s thereby providing an indication of the gains in health achievable within stipulated period.

The human kidneys in 24 hours, filter about 120 to 150 quarts (126.8 to 158.5 litres) of blood to produce about 1 to 2 quarts (1.1 to 2.1 litres) of urine, composing of wastes and extra fluid [1]. The filtration unit is referred to as nephron and could be liken to be the engine room of the kidneys.

Chronic kidney disease (CKD) is in recent times, defined as abnormalities of kidney structure or function, assessed by variables such as estimated glomerular filtration rate (eGFR), thresholds of albuminuria and duration of injury [2].

Hypertension is in the group of disorders of the heart and blood vessels known as cardiovascular diseases (CVDs). A logical definition of hypertension in the purview of epidemiological principles and current state of knowledge of the benefits of blood pressure reduction is "that level of blood pressure above which treatment does more good than harm".

The American Joint National Committee (JNC-VI) classification of hypertension in adults aged 18years and above, which we consider still relevant and significant for study of comprehensive blood pressure levels all over the world is as shown in (table 1).

Variable	Blood pressure (mmHg) Range	
	Systolic	Diastolic
Blood Pressure Category		
Optimal	<120	<80
Normal (120/80mmHg)	120-129	80-84
High Normal (130/85mmHg)	130-139	85-89
Stage 1 (mild) hypertension (140/90mmHg)	140-159	90-99
Stage 2 (moderate) hypertension (180/100mmHg)	160-179	100-109
Stage 3 (severe) hypertension (180/110mmHg)	>180	>110
Hypertensive urgency (no evident organ damage) 180/130+mmHg	Usually>180	Usually>130
Hypertensive emergency (rapid increase in blood pressure or evidence of acute organ damage) 210/130+ mmHg	Usually>210	Usually>130

Table 1: Classification of Hypertension in Adults aged 18 Years and older.

Source: [3].

Hypertension is promoted by modifiable risk factors like tobacco use, alcohol intake, physical inactivity and unhealthy diet. The disease can damage blood vessels in the kidneys, reducing their ability to work properly. Higher force than normal, making the blood to flow, stretches the blood vessels, just to enable blood flow more easily. Overtime, these stretching scars and weaken blood vessels throughout the body, including those in the kidneys. In cases of damage to the kidneys’ blood vessels, this may affect the wastes and extra fluid removing capacity from the body. Such extra fluid in the blood vessels, may then raise blood pressure even more, creating a dangerous cycle.

Although, kidney failures, also commonly called end-stage renal disease (ESRD) are caused by diabetes, hypertension, glomerulonephritis, cystic (fluid-filled sacs) kidney, urologic diseases among others. In all of these, the most common causes are diabetes and hypertension [4] but our focus in this paper is the hypertension related kidney failure. It is documented that kidney diseases do not have symptoms at the early stages. A person may come down with oedema, mostly in the legs, feet or ankles, which occurs because the kidneys were unable to take away extra fluid and salts from the body system. According to [1], once kidney function decreases further, symptoms can include; loss of appetite; nausea; vomiting; drowsiness or feeling tired; lack of concentration; insomnia (sleep problems); increased or decreased urination; generalized itching or numbness; dry skin; headaches; weight loss; darkened skin; muscle cramps; shortness of breath; chest pain. Similarly, most persons with hypertension do not have symptoms, but can in rare cases cause headache.

This paper seeks to identifying the extent of hypertensive nephropathy (chronic kidney disease) condition in the population and what could epidemiologically base prevention and control of hypertension play in reducing the burden of chronic kidney disease.

Burden of Chronic Kidney Disease

Patients suffering from chronic kidney disease are usually classified according to kidney function along a continuum from mild renal dysfunction to irreversible kidney failure (stages 1-5) defined by level of urinary protein excretion, estimated glomerular filtration rate (eGFR) and serum

creatinine concentration [5]. Yearly, more than 500,000 persons suffer CKD stage 5 (<15mL/min) [5] in sub-Saharan Africa alone and greater number of these patients die prematurely. The health care costs and economic burden of CKD are high and unbearable even in advanced Western countries [6]. Those coming down with kidney failure, require renal replacement therapy (RRT), either by way of kidney transplant or dialysis, to maintain life.

Globally, by the end of 2004, approximately 1.8 million patients were receiving RRT in which 77% were on dialysis and 23% were living with a functioning kidney transplant [7]. Furthermore, [7] stated that the global average prevalence for dialysis was 215 patients per million populations, although significant regional variations existed, but the worldwide incidence of kidney failure continues to rise and treatment is costly, therefore, global burden of illness is on the increase. Thus, resources allocation to RRT are seen to be increasing to ensure effectiveness.

Estimate from 1990 to 2010, indicates that treatment costs for the global maintenance of dialysis population was at \$200 billion to \$1.1 trillion [8]. According to [9], the costs of dialysis around the world can vary widely according to many local market conditions, including local production and distribution factors, import duties, the presence or absence of local suppliers and purchasing power. Haemodialysis (HD) cost is driven largely by the fixed costs of facility space and staff. HD machines typically cost approximately \$18 000 to \$30 000 each, but the machines have a 5 to 10-year life cycle, and in a weekly schedule, three to six patients can be treated on one machine. The cost of dialyzers for HD ranges from \$1000 to \$5000 per year. Other items that factor into the cost of HD are additional facility costs such as maintenance and utilities, and the costs of transportation to and from the HD facility.

In contrast, the economics of peritoneal dialysis (PD) are driven primarily by variable or disposable costs, such as the costs of solutions and dialysis tubing, and exhibits a near constant economy of scale [9,10]. Furthermore, [9,10] indicated that the cost of PD materials ranges from \$5000 to \$25 000 annually. The use of automated cyclers generally adds to the cost of PD. The machines cost \$3000 to \$10 000 each when purchased outright. However, it may be leased or provided, in which case the actual cost is bundled into the cost of solutions and materials purchased through the same

company. Therefore, comparison of supply costs alone may result in inaccurate assessment of the absolute cost of the various dialysis therapies.

Prevalence of Hypertension and Its Association with Chronic Kidney Disease

Hypertension is a chronic disease that is increasing in prevalence worldwide with no significant variance in its distribution in race and gender lines. The worldwide prevalence of hypertension, estimated from a 2005 systematic review of published literatures was 26%, with a projected 60% increase by 2025 [7], meaning more than half (4.8 billion persons) of the estimated world population of 8.025 billion persons [11] may be hypertensive by that year. In Africa alone, the prevalence of hypertension was found to be 30.8% among adult population in year 2010 [12]. However, African Americans, are more likely than Caucasians to have high blood pressure and to develop kidney problems from it, even when their blood pressure is only mildly elevated. In fact, African Americans are about six times more likely than Caucasians to develop hypertension-related kidney failure. It was also estimated that nearly one billion people are affected by hypertension globally, and this figure is predicted to increase to 1.5 billion by 2025 [7].

Hypertension is diagnosed by a health care provider when multiple blood pressure estimations are conducted over several visits to the health care provider's service provision point/s, that showed a consistent systolic blood pressure of above 140mmHg or a consistent diastolic blood pressure of above 90mmHg with regards to age. Hypertension has been reported as one of the leading causes of kidney failure. Every year, hypertension causes more than 25,000 new cases of kidney failure in the United States alone [13].

However, the prevalence of renovascular hypertension is probably less than 1 percent in patients with mild hypertension, but it may be as high as 10 to 40 percent in patients with sudden, severe, or refractory hypertension. Atherosclerosis primarily affects patients (particularly men) over the age of 45 years. In contrast to atherosclerosis, fibromuscular dysplasia (FMD) (abnormal development of fibrous and muscular tissues) most often affects women under the age of 50 years which has similar manifestation [14].

According to [15] data, the overall prevalence of hypertension among adults aged 25 and over was about 40%. Across the income groups of countries, the prevalence of hypertension was consistently high, with low, lower middle, and upper middle countries all having rates of about 40%. The prevalence in high income countries was lower at 35%.

Study in Northeast India showed that investigating hypertension and chronic kidney disease through screening in school-age children and in adults above 30 years of age, found a remarkable prevalence of hypertension, even in underweight subjects, in both children and adult populations. A glomerular filtration rate <60 mL/min was

found in 4.1% of adult subjects significantly higher than that of 0.8% to 1.4% reported 10 years ago [4].

Hypertension is the second leading cause of kidney failure (28.4%) after Diabetes (43.7%) in the United States of America [16], meaning all other causes of kidney failure accounted for about 27.9%. However, the issue of argument is that kidney biopsies are rarely performed in hypertensive-nephropathy (HN) and many patients report to nephrologists late in their course with secondary hypertension, related to the presence of longstanding CKD [17]. This implies that, hypertensive linked CKD definitive diagnosis has not been given adequate or primary attention as a measure towards addressing the increasing cases of CKD in the population.

Relative to European Americans, African Americans are more often diagnosed with HN and hypertension-attributed ESKD. However, few African Americans with HN had documented essential hypertension with normal indices of renal function and normal urinalyses before diagnosis [17]. Rather, HN was typically a diagnosis of exclusion in non-diabetic African Americans with sub-nephrotic proteinuria and advanced CKD ([18,19]. This indicates that Nephrologists often demonstrate bias when applying this diagnosis. Physicians provide identical clinical histories of a patient with hypertension and CKD with low level proteinuria (except for differing ethnicities) diagnosed HN more often in African Americans and chronic glomerulonephritis more often in European Americans [20]. This discriminatory clinical practice regarding race/ethnic divide is capable of beclouding the extend of hypertensive linked chronic kidney disease in global perspective.

Essential hypertension is generally diagnosed between 25 and 45 years of age but overt kidney dysfunction does not develop, except if such patients so diagnosed of the condition underwent at least 10 years of uncontrolled hypertension [21]. This window period for hypertension linked chronic kidney disease forms the basis for epidemiologically based strategic prevention and control of hypertension to reducing the financial burden among others associated with chronic kidney disease.

Strategic Prevention and Control of Hypertension in Reducing Chronic Kidney Disease

Causes of Hypertension

Hypertension is a Non-Communicable Disease (NCD) with no definite causative agent but web of causation in the category of modifiable (tobacco use, alcohol abuse, physical inactivity, unhealthy diet) and non-modifiable (principally genetic and age) factors. Genetic susceptibility or predisposition is a major non-modifiable individual risk for hypertension. It poses reasonable influence on disease development but does not confer an absolute certainty that a disease will occur. Age, as another non-modifiable factor in development of chronic diseases, became more likely to be noticeable with aging. This is through conditions that permit long-term exposure to factors that lead to development of non-communicable diseases, hypertension inclusive.

Chronic non-communicable diseases which hypertension is inclusive result from genetic, behavioral, and environmental factors and the interactions between them. These factors, generally termed "risk factors," produce molecular and structural changes in organs and tissues but produce few if any, early symptoms or signs of disease. When this interaction goes on for relatively long periods of time (exposure), usually years and decades, disease manifestations and impairment of health result.

Risk factors, place an individual at a greater likelihood of developing disease. The risk factors for future disease development and early structural changes may be found during the "silent" or pre-symptomatic period before disease becomes manifest. This is the period disease screening utilizes for optimal benefit, whereby rapidly applied tests, examinations or other procedures are carried out on apparently healthy individuals, for the purpose of sorting out those who have a disease or are at greater risk of developing the disease from those who do not. We shall look at this in more detail at the section of screening in this review paper.

Summary of Risk Factors (lifestyle) that aggravate Hypertension

- High salt intake,
- Obesity,
- Lack of regular exercise,
- Excessive alcohol intake, and
- Smoking

General Principles of Prevention of Hypertension

- Definition of the risk factors and application of interventions to favourably alter risk before overt symptoms or signs develop.
- Where possible, is to prevent the development of risk factors at an earlier level through changes in the environment and personal health behaviors.
- Primary prevention of hypertension as a chronic disease is therefore an important goal, since morbidity and mortality may be averted or forestalled, and promotion of health, or "primordial prevention," is probably the foremost goal.

What is Disease Control?

Disease control in its concept implies an on-going operation or programme or activities carried out by individuals or group of individuals or professional bodies and government agencies aimed at reducing the manifestation process and effect of a disease (disability and death) in the population.

Risk Assessment Methods for Hypertension

- Screening for risk factors of hypertension: The major risk factors include- inappropriate/unhealthy diet and physical inactivity (as expressed through unfavourable lipid concentration, high body mass index and raised blood pressure, together with tobacco use [22].

The measurements of these risk factors are by;

- a) Biochemical assessment of blood sugar and blood cholesterol.
- b) Physical measurements such as height and weight, waist circumference, blood pressure, pulse rate.

- According to [23], a moderate elevates of more than one risk factor multiply the risk of diseases and its complications. The constellation of risk of diseases like dyslipidemia [hypertriglyceridemia (TG) and decreased high density lipoprotein concentration (HDL-C)], elevated blood pressure, impaired glucose tolerance and central obesity is identified as metabolic syndrome, also called syndromeX4. Metabolic syndrome is an operational definition of cardiovascular risk as it increases the risk of cardiovascular disease (CVD) of which hypertension is implicated.

- In a related development, the [24] criteria for metabolic syndrome, it is the presence of any of three (3) out of; Fasting Glucose > 100mg/dl
Waist Circumference:
Men: >102cm (40in); or 87cm (34inch) (for Asian Indians)
Women: >88cm (35in); or 80cm (32inch) (for Asian Indians)
TG ≥ 150mg/dl
HDL-C: Men: < 40mg/dl; Women: < 50mg/dl
Blood pressure > 130/ or > 85mmHg

- As documented in [25], subjects having ≥ 3 risk factors from the risk factors stated below are considered as "at risk" of developing various types of NCDs including CVDs in which hypertension is implicated. They include:
Behavioral risk factors:
Smoking or Tobacco usage
Alcohol consumption
Low fruits and vegetables intakes
Physical Inactivity
Physical measurement:
 - i. History of Hypertension and Diabetes
 - ii. High normal blood pressure (≥130/85mmHg)
 - iii. High BMI (≥24.9kg/m²)
 - iv. High waist circumference (≥90cm)

Step	Prevention & Control of Hypertension
1.Health Promotion	Awareness creation on low cholesterol diet, non-rigorous exercise, control of obesity, limiting salt intake, etc.
2.Specific Prophylaxis	*None, identified yet.
3.Early Diagnosis & Treatment	Screening, periodic medical examination, *blood pressure & cholesterol medicines among high-risk group.
4.Limitation of damage	Control and monitoring of blood pressure *at least 2weekly.
5.Rehabilitation	Complications management – eg stroke, heart failure, *Kidney failure etc.
6.Organ replacement	Appropriate transplant.

Table 2: General Stepwise Approach Strategy for Prevention and Control of Hypertension.

- Our inclusion.

Source: Adapted from [26].

The table 2, showing general stepwise approach strategy to prevention and control of hypertension, may give a clue to the fact that chronic disease conditions including kidney failure in the population are posing public health problem

probably because steps 1-4 were ignored or not considered as such to be given due importance/attention in the overall disease management process.

Variable	*Targeted Non-medical Intervention	Dose	Approximate impact on Systolic BP (Hypertension)	Approximate impact on Systolic BP (Normotension)
Weight loss	Weight/body fat	Ideal body weight is best goal but at least 1 kg reduction in body weight for most adults who are overweight. Expect about 1 mmHg reduction for every 1 kg reduction in body weight.	-5mmHg	-2 to -3mmHg
Healthy diet	Dietary approaches to stop hypertension (DASH) dietary pattern	Diet rich in fruits, vegetables, whole grains, and low-fat dairy products with reduced content of saturated and trans l fat	-11mmHg	-3mmHg
Reduced intake of dietary sodium	Dietary Sodium	<1,500 mg/d *(about 2-3 teaspoon) is optimal goal but at least 1,000 mg/d reduction in most adults	-5 to -6mmHg	-2 to -3mmHg
Enhanced intake of dietary potassium	Dietary Potassium	3,500-5,000 mg/d, preferably by consumption of a diet rich in potassium (*readily available is banana among others)	-4 to -5mmHg	-2mmHg
Physical activity	Aerobic *exercise (walking, cycling for about 5min)	<ul style="list-style-type: none"> • 120-150 min/week *(about 17-21min/day) • 65%-75% heart rate reserve 	-5 to -8mmHg	-2 to -4mmHg
	Dynamic Resistance *exercise (swimming, walking for longer min., cross country skiing, bicycling)	<ul style="list-style-type: none"> • 90-150 min/week *(about 12-21min/day) • 50%-80% 1 rep maximum • 6 exercises, 3 sets/exercise, 10 repetitions/set 	-4mmHg	-2mmHg
	Isometric Resistance *exercise (muscle contraction movement)	<ul style="list-style-type: none"> • 4 x 2 min (hand grip), 1 min rest between exercises, 30%-40% maximum voluntary contraction, 3 sessions/wk • 8-10 wk 	-5mmHg	-4mmHg
Moderation in alcohol intake	Alcohol Consumption	In individuals who drink alcohol, reduce alcohol† to: <ul style="list-style-type: none"> • Men: ≤2 drinks daily • Women: ≤1 drink daily 	-4mmHg	-3mmHg

Table 3: Best Proven Non-Medical Interventions for Prevention and Treatment of Hypertension and Maintenance of Normal Blood Pressure.

- Our addition.

†In the United States, one “standard” drink contains roughly 14 grams of pure alcohol, which is typically found in 12 ounces of regular beer (usually about 5% alcohol), 5 ounces of wine (usually about 12% alcohol) and 1.5 ounces of distilled spirits (usually about 40% alcohol).

Source: Adapted from [27]

The table 4, by way of evidence-based documentation has made it clearer, the importance and effect of behavioural change (lifestyle) based interventions on prevention and control of high blood pressure, therefore, raising the hope

for reducing the burden of chronic kidney disease in global perspective. The import of these proven interventions in our present discuss is that hypertension at any level, once detected through active prevention and control strategy, including identification of specific modifiable risk factors via risk assessment methods, the absolute value of the systolic hypertension may be reduced by up to 43-48mmHg. This in our consideration is auspicious and economical in reducing the burden of chronic kidney disease globally, noting that reasonable window period exists between uncontrollable hypertension and chronic kidney disease in its continuum.

Population	Adults aged 18years and above without known hypertension
Recommendation	Screen for high blood pressure; obtain measurements outside of clinical setting for diagnostic confirmation. Grade: A
Risk Assessment	<ul style="list-style-type: none"> • Persons at increased risk for high blood pressure are those who have high-normal blood pressure (130-139/85-89 mmHg), • Those who are overweight or obese, and • African Americans.
Screening Tests	<ul style="list-style-type: none"> ▪ Office measurement of blood pressure is done with a manual or automated sphygmomanometer. ▪ Proper protocol is to use the mean of 2 measurements taken while the patient is seated, allow for ≥5min between entry into the office and blood pressure measurement, use an appropriately sized arm cuff, and place the patient’s arm at the level of the right atrium. ▪ Multiple measurements over time have better positive predictive value than a single measurement. ▪ Ambulatory and home blood pressure monitoring can be used to confirm a diagnosis of hypertension after initial screening.
Screening Interval	<ul style="list-style-type: none"> ❖ Adults aged ≥40years and persons at increased risk for high blood pressure should be screened annually. ❖ Adults aged 18 to 39years with normal blood pressure (<130/85 mmHg) who do not have other risk factors should be rescreened every 3to5years.
Treatment and Interventions	<ul style="list-style-type: none"> ➤ For nonblack patients, initial treatment consists of a thiazide diuretic, calcium-channel blocker, angiotensin-converting enzyme inhibitor, or angiotensin-receptor blocker. *In addition to best proven non-medicinal interventions for modifiable risk factors. ➤ For black patients, initial treatment is thiazide or a calcium-channel blocker. Initial or add on treatment for patients with chronic kidney disease consists of either an angiotensin-converting enzyme inhibitor or an angiotensin-receptor blocker (not both). *In addition to best proven non-medicinal interventions for modifiable risk factors.
Balance of Benefits and Harms	The net benefit of screening for high blood pressure in adults is substantial.

Table 4: Timeline for Screening for Early Detection of Hypertension as Basis for Controlling Chronic Kidney Disease.

*Our addition.

Source: Adapted from [28].

Based on the existence of window period between uncontrollable hypertension and overt kidney dysfunction, the framework of timeline for screening for early detection of hypertension in the population as a tool for reducing

chronic kidney disease as reflected in table 4, would be seen as an innovation beyond the ordinary in nephrology and urology clinical management.

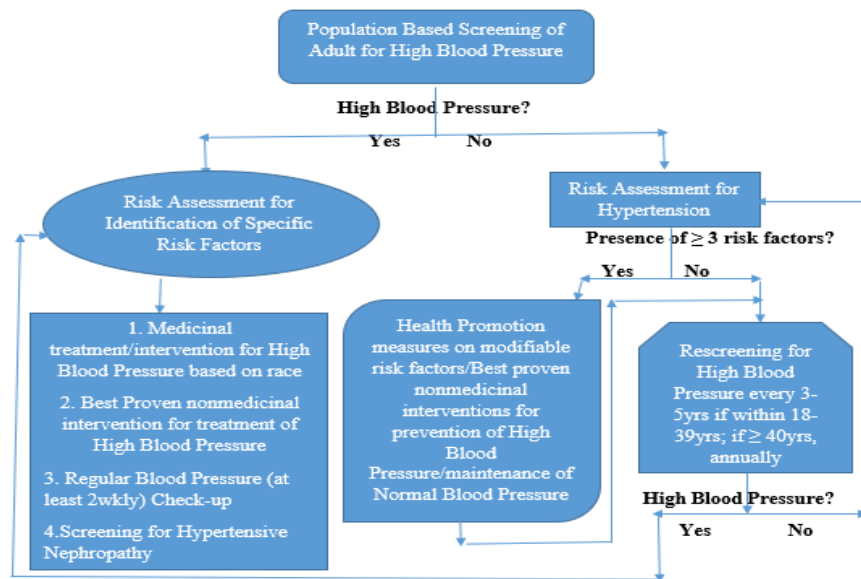


Figure 1: A flow chart for Active Prevention and Control of Hypertension (Population Based) as an Innovation beyond the Ordinary in Nephrology and Urology case management.

Figure 1 presents a pictorial illustration of summary of the strategic prevention and control measures of hypertension, as it could reduce the burden of chronic kidney disease in the population anywhere in the world.

Conclusion

Noting that globally, incidence of kidney failure is on the increase and its treatment costly, it is our believe that by ensuring the epidemiologically based strategic prevention and control of hypertension as provided in this paper, the resources to be allocated to renal management/replacement therapy which are increasing will rather supposed to reduce by up to about 28%, translating to \$56 billion to \$0.3trillion overtime as estimate of avoidable burden of chronic kidney disease, as such providing an indication of gains in health achievable within stipulated period. This should therefore, form basis for further studies in the field of nephrology and urology to improving management of cases. Also, studies should be conducted to unravel the extend of reduction in diastolic hypertension based on the best proven non-medicinal interventions for prevention and maintenance of normal blood pressure.

Recommendation

The global health team should consider taking a deep focus on the various strategies for active prevention and control of hypertension in its epidemiological point of view as an innovation beyond the ordinary in nephrology and urology clinical management, to ensure reduction in the burden of chronic kidney disease in global perspective.

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