



## RESEARCH ARTICLE

# Ultrasound appearance of the kidney among radiology department attendees of a tertiary centre in Malawi [version 1; peer review: 2 approved with reservations]

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## Abstract

**Background:** Diagnostic and therapeutic decisions in nephrology in low-resource settings are frequently based on ultrasound assessment of kidney size. An understanding of reference values is critical, particularly given the rise of non-communicable disease and the expanding availability of point-of-care ultrasound. However, there is a paucity of normative data from sub-Saharan Africa (SSA). We determined estimates of kidney ultrasound measures, including kidney size based on age, sex, and HIV status, among apparently healthy outpatient attendees of Queen Elizabeth Central hospital radiology department, Blantyre, Malawi.

**Methods:** We performed a cross-sectional cohort study of 320 adults attending the radiology department between October 2021 and January 2022. Bilateral kidney ultrasound was performed on all participants using a portable Mindray DP-50 machine and a 5MHz convex probe. The sample was stratified by age, sex, and HIV status. Predictive linear modelling was used to construct reference ranges for kidney size estimating the central 95 percentiles of 252 healthy adults. Exclusion criteria for the healthy sample were known kidney disease, hypertension, diabetes, BMI > 35, heavy alcohol intake, smoking and ultrasonographic abnormalities.

**Results:** There were 162/320 (51%) male participants. The median age was 47 (interquartile range [IQR] 34-59). Of those whose HIV status

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was known and positive, 138/308 (45%), 134/138 (97%) were receiving antiretroviral therapy. Men had larger average kidney sizes: mean 9.68 cm (SD 0.80 cm), compared to 9.46 cm (SD 0.87 cm) in women ( $p = 0.01$ ). Average kidney sizes in HIV-positive participants were not significantly different from those who were HIV-negative, 9.73 cm (SD 0.93 cm) versus 9.58 cm (SD 0.93 cm) ( $p = 0.63$ ).

**Conclusions:** This is the first report of the apparently healthy kidney size in Malawi. Predicted kidney size ranges may be used for reference in the clinical assessment of kidney disease in Malawi.

### Keywords

Ultrasound, Imaging, sub-Saharan Africa, Malawi, kidney size, HIV



This article is included in the [Malawi-Liverpool Wellcome Trust Clinical Research Programme gateway](#).

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## Introduction

Patients with kidney failure routinely undergo ultrasonography as part of their assessment. In low-resource settings when laboratory tests for kidney function are delayed or unavailable, therapeutic decisions are frequently made on ultrasound assessment. For example, kidney ultrasound is standard practice in Malawi as part of the assessment of acute kidney injury to identify chronic damage in the face of competition for dialysis beds. Patients with evidence of chronic kidney impairment are unlikely to be prioritized for kidney replacement therapy. Therefore, in Malawi, abnormal kidney size and appearance on ultrasound is often used as a surrogate marker for chronic kidney disease.

An understanding of reference kidney size values is critical, particularly given the rise of non-communicable disease and the expanding availability of point-of-care ultrasound in the region. A number of studies have reported reference values for kidney size in healthy adults measured by ultrasonography<sup>1-4</sup>. Data on ultrasound kidney size measurements for sub-Saharan Africa (SSA), however, are scarce. Furthermore, there are established physiological differences between populations which underlie the need for population-based estimates for examining kidney size. For example, for the same height, the vital capacity and the forced expiratory volume in one second are about 14% smaller in adults of African lineage compared to Caucasian and Asian populations<sup>5</sup>. The purpose of this study was to investigate the normal ultrasound measurements of the kidney among adults in Malawi.

## Methods

Queen Elizabeth Central Hospital (QECH) is a 1,300-bed government hospital providing free healthcare to Blantyre. QECH is the largest tertiary and teaching hospital in the country which manages severe trauma cases from the Southern and Eastern regions, and less severe cases from areas located near the hospital<sup>6</sup>. Malawi is a low-income country in South-East Africa, with an estimated adult HIV prevalence of 9%<sup>7</sup>.

At QECH, we performed a cross sectional study of adults ( $\geq 18$  years) attending the radiology department for any imaging modality, mostly relating to accidents and injury. Patients were approached for recruitment, Monday-Friday, 0700-1700. Exclusion criteria were people lacking capacity to consent with no proxy consent available. Radiology department attendees for imaging after accidents were targeted as they are less likely to have pre-existing kidney pathologies compared to other groups within the hospital. The sample was stratified by age, sex, and HIV status.

### Sampling and laboratory methods

Point-of-care HIV testing was done for those with unknown status or no recent negative test. Data on serum creatinine or estimated glomerular filtration rate were not available.

### Ultrasound

Bilateral kidney ultrasound was performed on all participants using a portable Mindray DP-50 machine and a 5MHz convex

probe. For each individual, we evaluated the left and right kidney size, presence of hydronephrosis, loss of corticomedullary differentiation, echogenicity, and any other significant abnormality (such as cysts or pyonephrosis).

The examination was performed with the patient supine and the longitudinal dimensions of the kidneys were visually estimated to represent the largest longitudinal section. Quality control was performed before and after initiation of the study. Prior to commencement, a series of test images were reviewed, and feedback was given to sonographers to optimise image acquisition. On data completion, 10% images were randomly selected for review by independent radiology experts to ensure sufficient quality.

Because kidney length is related to body height, the relative kidney length was calculated using the kidney length: body height ratio (KBR) by dividing the absolute kidney length (millimetres) by the body height (centimetres) for each kidney<sup>3</sup>.

### Exclusion

For normal size range estimates, to represent a 'healthy' population as closely as possible, participants were excluded after recruitment if they reported diabetes, current heavy smoking ( $> 20$  cigarettes/day) or heavy alcohol intake ( $> 50$  alcohol drinks/week), and if body mass index (BMI)  $> 35$ . Data did not contribute to normal range estimates where there were significant imaging abnormalities; hydronephrosis, suspected pyonephrosis, and loss of corticomedullary differentiation.

### Statistical analysis

Statistical analyses were performed using R version 4.0.2<sup>8</sup>. Summary statistics were calculated for the cohort, described using either median and interquartile range (IQR) or mean and standard deviation for continuous variables depending on data distribution, and proportions for categorical variables. Two-sample t-tests or non-parametric tests, depending on data distribution, were used to compare variables between groups.

To generate estimates of expected mean kidney size, predictive linear modelling was used to estimate the central 95<sup>th</sup> percentile for mean kidney size based on age and sex. To quantify the uncertainty of the lower and upper limits of these ranges, we fitted the same linear model to 1,000 bootstrap samples of the healthy dataset. Bootstrapped 95% confidence intervals were then constructed around the upper and lower limits of the prediction interval. Finally, a linear model was used to generate model fits of kidney size across the age ranges according to both sex and HIV status.

### Sample size

The known mean kidney bipolar length in adult males in the USA is 12.40 cm with a standard deviation of 0.90 cm<sup>9</sup>. We aimed to estimate the bipolar length in the Malawi population with a margin of error of 0.15 cm using the following formula, where  $n$  is the sample size,  $z_{\alpha/2}^2 = 1.96$  (95% confidence level),  $\sigma^2 = 0.90$  and  $d = 0.15$  cm.

$$n = \frac{(z^2_{\alpha/2} \times \sigma^2)}{d^2} = \frac{(1.96^2 \times 0.9^2)}{0.15^2} = 138$$

The number needed was inflated to 160 to cover for 15% unusable data. To recruit 50:50 HIV positive to negative, the total sample size was 320.

## Results

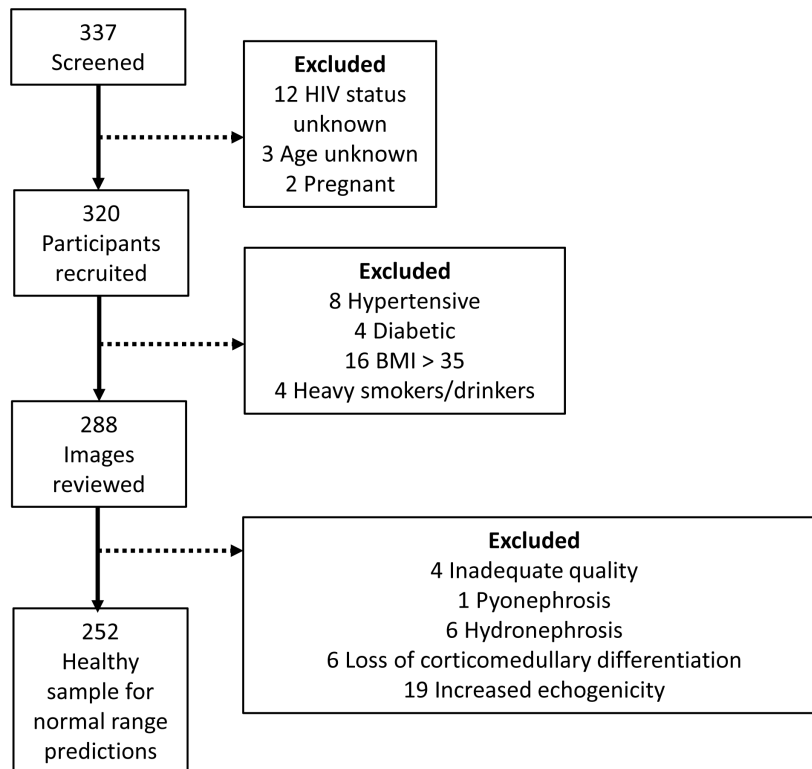
Between 27 October 2021 and 31 January 2022, 320 participants were recruited. The study flow chart is summarised in [Figure 1](#). [Table 1](#) summarises the baseline characteristics of the participants. There were 162/320 (51%) male participants. The median age was 47 (interquartile range [IQR]34-59). Of those whose HIV status was known and positive, 138/308 (45%), 134/138 (97%) were receiving antiretroviral therapy. Tuberculosis (TB) history was known for 317/320, of which 303/317 (96%) had no prior TB history, 8/317 (3%) either received prior treatment or were receiving current treatment for TB, and 6/317 (2%) were diagnosed but never treated.

Social characteristics, symptoms, and reasons for attending the radiology department are shown in [Table 2](#). Where place of residence was known 296/320, 218/296 (74%) reported living in an urban locality, 78/296 (26%) reported living

rurally. Where proximity to the lake was known (240/320), 14/240 (6%) reported living near Lake Malawi, where schistosomiasis is endemic.

Physiology and ultrasound variables are provided in [Table 3](#). The prevalence of hydronephrosis, increased echogenicity and loss of corticomedullary differentiation was low (2-7%). The mean size of the right kidney was 9.38 cm (SD 0.98 cm) in women, and 9.61 cm (SD 0.93 cm) in men. The mean size of the left kidney was 9.54 cm (SD 0.97 cm) in women and 9.76 cm (SD 0.90 cm) in men. Men had larger average kidney sizes: mean 9.68 cm (SD 0.80 cm), compared to 9.46 cm (SD 0.87 cm) in women ( $p = 0.01$ ). Average kidney sizes in HIV-positive participants were not significantly different from those who were HIV negative, 9.73 cm (SD 0.93 cm) versus 9.58 cm (SD 0.93 cm) ( $p = 0.63$ ).

Absolute and relative kidney lengths are shown in [Table 4](#). Absolute average (left and right) kidney lengths by sex and predicted range estimates with 95% confidence interval and bootstrapped upper and lower 95% prediction interval are shown in [Table 5](#). The residuals plot for the multivariable model is in the GitHub repository (*Extended data*)<sup>10</sup>. [Figure 2](#) and [Figure 3](#) show the kidney size range estimates dependent on age, sex, and HIV status.



**Figure 1.** Study flow diagram demonstrating the number of participants recruited and selected for the healthy sample for normal range predictions.

**Table 1. Baseline characteristics of participants.**

<b>TABLE 1: Baseline characteristics of included participants</b>	
Age (years), median (IQR)	47 (34-59)
Male sex, n (%)	162/320 (51%)
HIV positive, n (%)	138/308 (45%)
HIV status unknown, n (%)	12/320 (4%)
<b>Antiretroviral therapy</b>	
TDF/3TC/DTG, n (%)	125/138 (91%)
TDF/3TC/EFV, n (%)	6/138 (4%)
AZT/3TC/LPVr, n (%)	1/138 (1%)
ABC/3TC/DTG, n (%)	1/138 (1%)
AZT/3TC/ATVr, n (%)	1/138 (1%)
Not taking antiretroviral therapy, n (%)	4/138 (3%)
<b>Comorbidities</b>	
No TB history, n (%)	303/317 (96%)
Treated TB, n (%)	8/317 (3%)
Untreated TB, n (%)	6/317 (2%)
TB history not known, n (%)	3/317 (1%)
Hypertension, n (%)	8/308 (3%)
Hypertension unknown, n (%)	12/320 (4%)
Diabetes, n (%)	4/301 (1%)
Diabetes unknown, n (%)	19/320 (6%)
<b>Medications</b>	
No medication/unknown, n (%)	306/320 (96%)
NSAIDS, n (%)	10/14 (71%)
Thiazides, n (%)	3/14 (21%)
ACE inhibitors, n (%)	1/14 (7%)

TDF = tenofovir, 3TC = lamivudine, EFV = efavirenz, AZT = zidovudine, LPVr = lopinavir/ritonavir, ABC = abacavir, DTG = dolutegravir, ATVr = atazanavir/ritonavir, NSAIDS = nonsteroidal anti-inflammatories.

**Table 2. Table of social characteristics, symptoms, and reason for attending radiology department.**

<b>Social</b>	
Current smoker, n (%)	15/297 (5%)
Smoking unknown, n (%)	23/320 (7%)
Drinks alcohol, n (%)	62/298 (21%)

Alcohol intake unknown, n (%)	22/320 (7%)
<b>Occupation</b>	
Professionals, n (%)	45/320 (14%)
Sales and services, n (%)	13/320 (4%)
Craft and related trades, n (%)	11/320 (3%)
Labourer, n (%)	7/320 (2%)
Service workers, n (%)	6/320 (2%)
Armed forces, n (%)	5/320 (2%)
Agriculture, n (%)	5/320 (2%)
Machine operators, n (%)	3/320 (1%)
Legislators/officials/managers, n (%)	2/320 (1%)
Other/no occupation, n (%)	223/320 (69%)
<b>Place of residence</b>	
Urban, n (%)	218/296 (74%)
Rural, n (%)	78/296 (26%)
Unknown, n (%)	24/320 (8%)
<b>Reason for attending</b>	
Fall, n (%)	98/320 (31%)
Road traffic accident, n (%)	59/320 (18%)
Assault, n (%)	22/320 (7%)
Bike injury, n (%)	5/320 (2%)
Collapsed structure, n (%)	3/320 (1%)
Burn, n (%)	1/320 (0%)
Other, n (%)	132/320 (41%)
<b>Symptoms</b>	
None, n (%)	287/317 (91%)
Abdomen/Lower back pain, n (%)	8/317 (3%)
Fever, n (%)	6/317 (2%)
Chest pain, n (%)	3/317 (1%)
Cough, n (%)	2/317 (1%)
Headache, n (%)	2/317 (1%)
Other, n (%)	9/317 (3%)
Unknown, n (%)	3/317 (1%)
<b>Imaging</b>	
X-ray, n (%)	192/320 (60%)
Ultrasound, n (%)	106/320 (33%)
Other, n (%)	22/320 (7%)

**Table 3. Physiology and ultrasound variables.**

Variable	Summary measure
Height (cm)	162.40 (SD 99.01)
Weight (kg)	67.30 (IQR 57.00-76.67)
Body mass index (kg m <sup>-2</sup> )	24.00 (IQR 22.00-28.00)
Systolic blood pressure (mm Hg)	136.00 (SD 23.61)
Diastolic blood pressure (mm Hg)	80.00 (SD 12.11)
Average kidney size (cm)	9.58 (SD 0.83)
Kidney size left (cm)	9.66 (SD 0.94)
Kidney size right (cm)	9.50 (SD 0.96)
Kidney length: height right (KBR)	0.59 (SD 0.06)
Kidney length: height left (KBR)	0.60 (SD 0.06)
Loss of corticomedullary differentiation, n (%)	6/288 (2%)
Increased echogenicity, n (%)	19/288 (7%)
Hydronephrosis, n (%)	6/288 (2%)
Pyonephrosis, n (%)	1/288 (0%)

**Table 4. Absolute and relative kidney lengths\*.** Abbreviation: KBR, ratio of kidney length in millimetres to subject height in centimetres.\* Values are means ( $\pm$  2 standard deviations).

	Age, years						
	18-29 (n = 52)	30-39 (n = 55)	40-49 (n = 52)	50-59 (n = 58)	60-69 (n = 55)	70+ (n = 48)	All (n = 320)
<b>Absolute kidney length, cm</b>							
Left	9.76 (8.19, 11.34)	9.77 (8.40, 11.13)	9.68 (7.73, 11.64)	9.55 (7.49, 11.62)	9.58 (7.43, 11.73)	9.56 (7.43, 11.68)	9.65 (7.76, 11.53)
Right	9.81 (8.15, 11.46)	9.36 (7.61, 11.10)	9.66 (7.66, 11.67)	9.38 (7.50, 11.26)	9.39 (7.38, 11.40)	9.41 (7.25, 11.57)	9.50 (7.57, 11.42)
<b>Relative kidney length, KBR</b>							
Left	0.60 (0.49, 0.70)	0.61 (0.52, 0.70)	0.59 (0.48, 0.71)	0.60 (0.46, 0.73)	0.59 (0.46, 0.72)	0.58 (0.45, 0.72)	0.60 (0.48, 0.71)
Right	0.60 (0.48, 0.71)	0.59 (0.46, 0.72)	0.59 (0.47, 0.71)	0.59 (0.47, 0.70)	0.58 (0.45, 0.71)	0.58 (0.44, 0.71)	0.59 (0.46, 0.71)

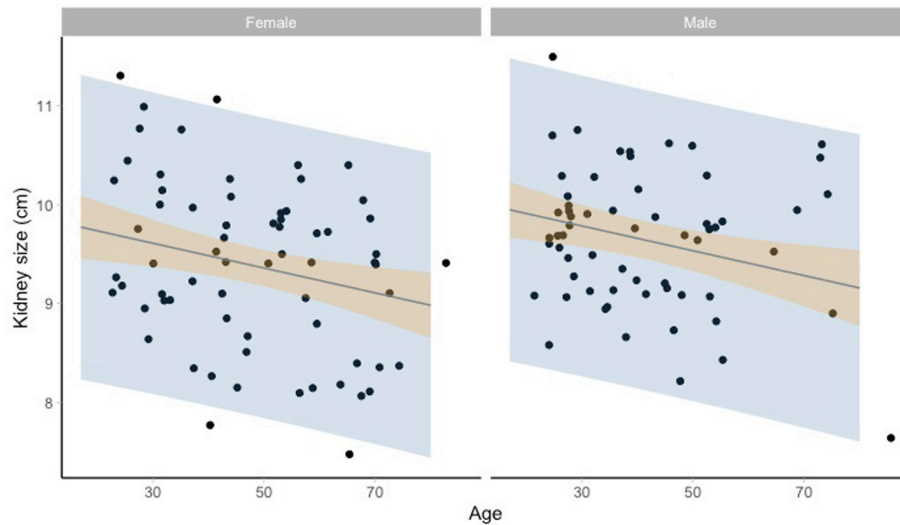
## Discussion

This is the first report of ultrasound appearances of normal kidneys in a Malawian population. In our cohort, kidneys were larger in males compared to females. Prevalence of ultrasound abnormalities such as hydronephrosis, increased echogenicity and loss of corticomedullary differentiation was low. Kidney size was not significantly different in people living with HIV versus those without HIV.

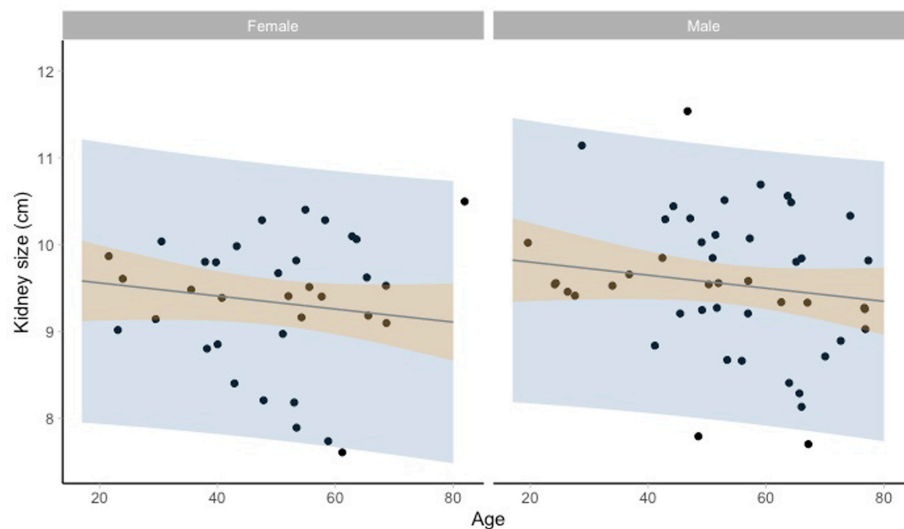
We found kidney sizes in our Malawi cohort to be smaller than in a Nigerian population, which reported 10.20 cm (SD 0.81 cm) and 9.85 cm (SD 0.90 cm) for left and right kidneys<sup>11</sup>. We also found kidney sizes in Malawi to be smaller than populations outside of SSA. For example, in the US the mean kidney bipolar length on ultrasound has been reported as 11.20 cm and 11.00 cm for left and right kidneys<sup>9</sup>, in Kuwait 10.71 cm (SD 1.00 cm) cm and 10.68 cm (SD 1.40 cm)

**Table 5. Absolute average (left and right) kidney lengths and predicted range estimates with 95% confidence interval and bootstrapped upper and lower 95% prediction interval.** Absolute values are means ( $\pm 2$  standard deviations) of the complete dataset  $n = 320$ . Predicted ranges and 95% confidence intervals were generated using a linear model to predict kidney size according to sex and age category:  $\text{lm}(\text{kidneysize} \sim \text{age} + \text{sex}, \text{data} = \text{healthy})$ . The model was then fitted to a bootstrapped sample of the healthy dataset with 1,000 replicates and bootstrapped 95% confidence intervals were constructed around the upper and lower limits of the prediction interval. Abbreviation: F, female, M, male.

	Age, years						
	18-29 F = 22 M = 30	30-39 F = 27 M = 28	40-49 F = 24 M = 22	50-59 F = 36 M = 22	60-69 F = 28 M = 27	70+ F = 21 M = 27	All n = 320
<b>Absolute average (left and right) kidney length, cm</b>							
Male	9.83 (8.60, 11.06)	9.67 (8.54, 10.79)	9.78 (8.16, 11.40)	9.44 (7.52, 11.35)	9.71 (7.82, 11.61)	9.61 (7.85, 11.36)	9.68 (8.09, 11.28)
Female	9.73 (8.18, 11.28)	9.45 (8.08, 10.82)	9.55 (7.76, 11.33)	9.48 (7.70, 11.27)	9.26 (7.48, 11.05)	9.32 (7.17, 11.47)	9.46 (7.72, 11.20)
<b>Predicted ranges (95% confidence interval)</b>							
<i>Healthy sample only (n=252)</i>							
Male	8.26-11.43 (9.60-10.14)	8.16-11.30 (9.53-9.96)	8.06-11.19 (9.43-9.82)	7.95-11.08 (9.30-9.71)	7.84-10.98 (9.16-9.63)	7.71-10.88 (8.98-9.56)	7.71-11.43 (8.98-10.14)
Female	8.05-11.22 (9.38-9.94)	7.95-11.09 (9.31-9.75)	7.84-10.98 (9.21-9.62)	7.74-10.87 (9.09-9.50)	7.63-10.77 (8.95-9.41)	7.50-10.67 (8.78-9.35)	7.50-11.22 (8.78-9.94)
<b>Bootstrapped lower and upper 95% prediction interval</b>							
<i>Healthy sample only (n = 252)</i>							
Male	Lower 8.08-8.46 Upper 11.15-11.67	Lower 8.00-8.35 Upper 11.07-11.49	Lower 7.88-8.27 Upper 10.99-11.35	Lower 7.74-8.20 Upper 10.88-11.25	Lower 7.59-8.14 Upper 10.76-11.16	Lower 7.41-8.06 Upper 10.63-11.10	Lower 7.41-8.06 Upper 11.15-11.67
Female	Lower 7.83-8.31 Upper 10.92-11.48	Lower 7.74-8.19 Upper 10.84-11.30	Lower 7.65-8.09 Upper 10.77-11.16	Lower 7.52-7.80 Upper 10.67-11.04	Lower 7.39-7.94 Upper 10.57-10.95	Lower 7.23-7.87 Upper 10.45-10.88	Lower 7.23-7.87 Upper 10.92-11.48



**Figure 2. Kidney size range estimates dependent on age and sex for HIV negative participants.** Model fit (grey line) of the linear regression model:  $\text{lm}(\text{kidneysize} \sim \text{age} + \text{sex} + \text{hiv\_status}, \text{data} = \text{noHIV})$  and 95% prediction intervals (blue) and 95% confidence intervals around the mean (orange).



**Figure 3. Kidney size range estimates dependent on age and sex for HIV positive participants.** Model fit (grey line) of the linear regression model:  $\text{lm}(\text{kidneysize} \sim \text{age} + \text{sex} + \text{hiv\_status}, \text{data} = \text{HIV})$  and 95% prediction intervals (blue) and 95% confidence intervals around the mean (orange).

for left and right kidneys<sup>2</sup>, and in Copenhagen, 11.20 cm and 10.90 cm for left and right kidneys<sup>1</sup>.

These differences may be explained, in part, by population differences in height; however very few studies report relative kidney size, and none in Africa. After accounting for height using kidney length: body height ratio (KBR) measurements, our data suggest smaller relative kidney sizes among Malawians compared to European populations. For example, data from Croatia suggest KBRs in adults younger than 60 without kidney disease, are between 0.60 and 0.74 for the left kidney and 0.57 to 0.72 for the right kidney<sup>3</sup>. In a Swiss autopsy series of 635 adults without diabetes or known kidney disease, mean (standard deviation) KBRs were 0.67 (0.07) for men and 0.69 (0.07) for women<sup>12</sup>.

There were limitations to our study. We were unable to determine kidney function to confirm absence of pre-existing kidney disease. However, we excluded participants with comorbidities, social behaviours, and ultrasound abnormalities likely to affect glomerular filtration rate (GFR). The lower proportion of HIV-positive participants in the younger age categories may have distorted the size estimates, however HIV status did not appear to have a significant effect on kidney size. Diabetes was not screened for within the cohort, but we relied on participants reporting a prior diagnosis. We did not collect data on CD4 count or viral load, and future studies should aim to correlate kidney size with stage of HIV infection.

We recruited participants attending a tertiary centre for imaging following accidents as they were less likely to have a pre-existing kidney disease than other hospital-based cohorts.

Future studies should aim to develop nomograms for adults and children, derived from a larger demographic sample. Ideally, these would also include GFR measurement, CD4 count and viral load for HIV positive participants.

In conclusion, we demonstrate the range of kidney sizes expected in adult Malawians without known kidney disease. We found a low prevalence of ultrasound abnormalities in our population. Our predicted size estimates within age categories can be referred to in the assessment of patients with kidney failure.

### Ethical statement

Participants gave written informed consent under ethical approvals from the College of Medicine Research Ethics Committee, University of Malawi (P.03/19/2625) and the Liverpool School of Tropical Medicine Ethics Committee (18-062). Study information including purposes, benefits and risk was provided to all participants in both English and Chichewa.

### Data availability

#### Underlying data

Zenodo: careyla/Normal-kidney: v1.0.0, <https://doi.org/10.5281/zenodo.7231616><sup>10</sup>

This project contains the following underlying data:

- baseline.csv 210.0 kB
- fulldata.csv 117.5 kB
- tidyclean2.csv 117.6 kB
- uss\_data.csv



## Extended data

Zenodo: careyla/Normal-kidney: v1.0.0, <https://doi.org/10.5281/zenodo.7231616><sup>10</sup>

This project contains the following extended data:

- Residualsplot

Data are available under the terms of the [Creative Commons Zero “No rights reserved” data waiver](#) (CC0 1.0 Public domain dedication).

## Analysis code

Analysis code available from: <https://github.com/careyla/Normal-kidney/tree/v1.0.0>

Archived analysis code at time of publication: <https://doi.org/10.5281/zenodo.7231616><sup>10</sup>

License: MIT

## Reporting guidelines

Zenodo: STROBE checklist for ‘Ultrasound appearance of the kidney among radiology department attendees of a tertiary centre in Malawi’, <https://doi.org/10.5281/zenodo.7231616><sup>10</sup>

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# Open Peer Review

Current Peer Review Status: ? ?

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## Version 1

Reviewer Report 13 December 2022

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? **June Fabian** 

Wits Donald Gordon Medical Centre, School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

Thank you for this important work which, as the authors have stated, is much needed in African populations.

The authors state that in Malawi, because of the absence of additional diagnostic capabilities, kidney size on ultrasound is often used as a proxy for determining whether there is underlying chronic kidney disease in those who need dialysis (usually presenting as acute kidney injury). However, such interpretation is hampered by the absence of population-appropriate references for normal kidney size. They also make the point that POCUS is becoming more accessible and NCDs are rising in prevalence - implying (perhaps) that kidney disease is on the rise and more clinicians will have access to POCUS. The authors screened 320 apparently healthy adults presenting at Queen Elizabeth Central hospital radiology department, Blantyre, Malawi. The authors found non-significant differences in kidney size between HIV + and HIV - participants, larger kidney sizes in men than women (expected), and relative kidney length seems to be smaller than in other studies (Nigeria, and high-income settings). They used predictive linear modelling to estimate kidney size stratified by age and sex that might be used in future.

I have a few questions that I would like to ask the authors for clarity:

1. The stated purpose of the study was to investigate normal US measurements in apparently healthy Malawian adults. If so, I am not sure I understand why the sample was stratified by HIV status as we know that untreated HIV can result in loss of corticomedullary differentiation or larger than normal kidney sizes. It is a valuable finding in this study that for PLWHIV who have high ART coverage, kidney sizes are not significantly different from apparently healthy Malawians. Following on from this, it feels a little incongruent that NCDs are mentioned, yet excluded when we know that hyperfiltrating diabetics can have larger than normal kidney size and hypertension is linked to kidney size in the setting of CKD. One might argue that those with HIV should have been excluded?

Perhaps asked another way, was the original study about kidney size in PLWHIV - and because no difference was found, these data could contribute to an apparently normal dataset. If so, it would be helpful to explain this in the paper and perhaps reframe it as such? Also, in clinical practice elsewhere, kidney size in the setting of HIV is/was used to ration access to short term dialysis support - perhaps this is also why the authors focused in HIV? If so, again, it would be very helpful to include this.

**2.** It would be helpful to describe the US methods in more detail that would enable replication:

- Who did the ultrasound scans - was it only sonographers - any radiologists?
- How did you account for interobserver variability?
- Can you explain what QC measures were undertaken for each sonographer prior to starting the study?

**3.** Tables 1, 3, 4 - since we describe differences in kidney size stratified by sex - can these tables describe the overall data and be stratified by sex with sample sizes for each category in the top tab for each column?

**4.** No screening was conducted (other than HIV) and it is well known that many with hypertension, kidney disease, and diabetes are unaware - so the apparently healthy population may indeed have had comorbidity. I think this is a significant limitation of the study and needs to be stated as such. Likewise, the relatively small sample sizes for predicting kidney size (by age category and sex) are also limitations that need to be stated.

One nitpicky edit (if I may): sub-Saharan Africa (SSA): the "sub" should be capitalised ("Sub-Saharan") - and using this terminology has been questioned as colonial in origin - perhaps for the authors to consider that African / African populations might suffice?

**Is the work clearly and accurately presented and does it cite the current literature?**

Yes

**Is the study design appropriate and is the work technically sound?**

Yes

**Are sufficient details of methods and analysis provided to allow replication by others?**

Partly

**If applicable, is the statistical analysis and its interpretation appropriate?**

Yes

**Are all the source data underlying the results available to ensure full reproducibility?**

Yes

**Are the conclusions drawn adequately supported by the results?**

Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Specialist physician and nephrologist, research interest is the epidemiology of kidney disease in African populations

**I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.**

Reviewer Report 25 November 2022

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**Robert Kalyesubula** 

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This is a wonderful study undertaken by Carey *et al.* in an attempt to report on the normal kidney sizes among people from Malawi. The researchers provide very useful information that would help in determination of kidney pathology in SSA.

I have a few comments that may need to be addressed:

1. The introductory statement sounds rather interesting. I would argue that most low-resource centers do not have access to ultrasound scans and therefore it is unlikely that decisions to treat kidney disease would be based on an ultrasound scan - perhaps proteinuria which is available on a dipstick. You may want to have this statement restricted to Malawi.
2. How was selection bias minimized in the selection of the participants? People who present to hospitals are sick and are therefore less likely to represent the general population.
3. The use of creatinine or proteinuria would have been of additional value in excluding those with underlying kidney dysfunction at least GFR less than 60mls/min/1.73m<sup>2</sup>. Why was this not done?
4. Please provide more details on how you did the radiography. Was the interpretation done centrally or was this as used in routine practice? What happened if there was a disagreement in the 10% of images which were randomly selected for routine control? In the exclusion criteria; was diabetes only on self report? How reliable is this in excluding DM? I believe this would be a great confounder in the size of the kidney as would HIV since the kidneys tend to be bigger. Many DM patients do not know that they have it.

5. The standardization for body size is a strong point for this study. Is there any major difference in size between the rural and urban dwellers in the study and overall in Malawi?

The STROBE guidelines for cross sectional studies were dully followed which streamlined the reporting.

**Is the work clearly and accurately presented and does it cite the current literature?**

Yes

**Is the study design appropriate and is the work technically sound?**

Yes

**Are sufficient details of methods and analysis provided to allow replication by others?**

Yes

**If applicable, is the statistical analysis and its interpretation appropriate?**

Yes

**Are all the source data underlying the results available to ensure full reproducibility?**

Yes

**Are the conclusions drawn adequately supported by the results?**

Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** I am a nephrologist working in the area of determination of kidney function among people of African origin. I am also an actively practicing clinician from Uganda, Kampala.

**I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.**

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