Knowledge about the kidney, kidney disease, prevention and therapeutic options among non-clinical Healthcare Providers at a tertiary facility in Southern Nigeria: A cross-sectional study

Original Research Article

ABSTRACT

Introduction: In Nigeria, the occurrence of kidney disease is on the rise and prevention is key. Disease awareness is low, yet knowledge of kidney in disease and health is an essential preventive measure. Information on the knowledge of the kidney, disease prevention and therapeutic options among non-clinical healthcare providers (HCPs) in hospital settings is scarce. This study is aimed to address the knowledge gap.

Study design: Cross-sectional study.

Place and Duration of study:conducted at the Rivers State University Teaching Hospital, South-South Nigeria, as part of the 2022 World Kidney Day celebrations held on March 10th 2022.

Methodology:165 consenting non-clinical HCPs were consecutively recruited. A self-administered questionnaire comprising sociodemographic characteristics and knowledge-based questions was deployed. Total knowledge scores were categorized as poor knowledge, if <50%, fair knowledge, if 50-69% and good knowledge if ≥ 70-100%. Data were analyzed and logistic regression was used to determine predictors of good knowledge using SPSS version 25. A p-value of <0.05 was considered statistically significant.

Results: Of 165 respondents recruited, 113(68.5%) were females with a mean age of 46.48 ± 14.01 years and 109(66.1%) had tertiary education. Overall, 74(44.8%) had poor, 43(26.1%) had fair and 48 (29.1%) had good knowledge about the kidney, disease prevention and therapeutic options. Tertiary education was the only significant independent predictor (aOR: 4.676; CI: 1.984; 11.023) of higher knowledge scores. No association was found between past medical/social history and knowledge of the kidney in health and disease.

Conclusion: Knowledge of the kidney, disease prevention and therapeutic options among non-clinical HCPs is poorand corroborates findings from existing literature among the general populace.There is a need for a change in educational approaches to include non-clinical HCPs during kidney health promotion activities, particularly those with lower levels of education.This includes targeting such subgroups within the hospitals and creating policies that enable risk reductive measures like permitting frequent routine screening.

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Keywords: [Kidney disease; knowledge; non-clinical healthcare providers; prevention; therapeutic options]

1. INTRODUCTION

Chronic Kidney disease (CKD) is a non-communicable disease that includes a range of different physiological disorders that are associated with abnormal renal function and progressive decline in glomerular filtration rate (GFR) [1]. CKD is defined by the Kidney Disease Improving Global Outcome (KDIGO) as kidney damage that has continued for more than three months as characterized by structural and functional abnormalities of the kidney with or without a decrease in

glomerular filtration rate [2]. It is an emerging public health issue globally and it disproportionately impacts low and middle-income countries where both prevalence and deaths due to CKD are significantly higher [3].

The increasing burden across the globe has been attributed to the rise in the prevalence of its risk factors such as obesity, hypertension, diabetes, and other cardiovascular diseases[3]. The global estimated prevalence of CKD is 13.4% (11.7% -15.1%) and patients with end-stage kidney disease needing renal replacement therapy are estimated between 4.902 and 7.083 million [4]. A large number of deaths due to poor access to renal replacement therapy and a rising number of end-stage kidney diseases in future will contribute a substantial burden to developing countries[4].

CKD increases the risk of cardiovascular disease mortality and is a risk factor for both people with diabetes and high blood pressure. These risk factors can be identified early and treated utilizing commonly accessible, low-cost methods. These therapies can enhance cardiovascular and renal outcomes and delay the onset of end-stage kidney disease (ESKD) [5]. Even in nations where data are accessible, disease awareness is low among the general public and healthcare authorities. As a result, many of these nations have underdeveloped nephrology workforces or primarily concentrate on treating patients with ESKD rather than those with early stages of CKD [6].

The financial burden involved in taking care of most CKD patients is borne by the patients and their relatives most time in developing countries and the cost of renal replacement therapy is beyond the reach of most CKD patients in Nigeria [7]. Despite the huge burden of CKD majority of Nigerians are not well informed about the disease [7–10]. There is a need to create more public awareness, especially among high-risk individuals as part of the efforts to reduce the disease burden [11].

Non-clinical healthcare providers are defined as health coaches, patient navigators, and other personalities (ward maids, technical assistants, nurse assistants, admin staffers, etc.) who interrelate with patients but do not dispense medical advice or carry out procedures [8]. Their importance for patient and community engagement and care coordination is increasingly being recognized, in the wave of human resource crisis, as they contribute a significant workforce in the healthcare system in Africa.[12] Nevertheless, they constitute a potentially high-risk group whose health risks are often given less attention. Oftentimes, they can be easily assumed to have basic knowledge of health and disease states because of their routine work schedules in hospital care settings. Yet, they are often unintentionally missed when health promotion activities are being conducted. Since these non-clinical healthcare providers work within the hospital setting, they are more often sought out by family members, friends and individuals in the community for advice on health-related issues before presenting in the hospital [7]. Awareness of the kidneys in health and disease among these 'primary' healthcare providers is, therefore, necessary to enable them to know their CKD risks and also be effective in enlightening other people in the community.

Most studies have focused on the assessing knowledge of CKD among non-nephrology specialists and non-specialist doctors and nurses [7,13–16] as a means to improve their clinical suspicion of renal disease and prompt referral to the nephrologist when indicated. However, there is a paucity of data on the assessment of knowledge of CKD, kidney disease prevention and therapeutic options among non-clinical healthcare providers, who are also a potential source of educators to the populace. This study, therefore, aimed to address the gap by assessing the knowledge of the kidney, disease prevention and therapeutic options among non-clinical healthcare providers in a tertiary hospital in southern Nigeria as the outcomes from this study will provide the platform to further create awareness of CKD in the hospital and the community.

2. MATERIAL AND METHODS

This cross-sectional study was conducted in Rivers State, South-South Nigeria, at the Rivers State University of Port Harcourt Teaching Hospital. The RSUTH Renal Study Group (RRSG), which is made up of adult and pediatric nephrologists, nephrologists-in-training, and nephrology nurses, carried out the study. The members of the RRSG group supervised the completion of the questionnaires by consenting participants. As part of ongoing World Kidney Day celebrations, the study was carried out on March 10 of 2022. The focus was on bridging the knowledge gap for better kidney care.

A sample size calculation using the Cochran formula and a prevalence from a previous study[13] = 12%, e = 0.05%, alpha: 1.96, CI: 95% was 162. Using a Convenience sampling technique, all non-clinical healthcare providers who gave consent and made themselves available were enrolled. A total of 190 participants filled and returned the questionnaires, however, complete data were obtained from 165 of the non-clinical HCPs.

The survey tool was a standardized self-administered semi-structured questionnaire validated by the Nigerian Association of Nephrology (NAN) to be used to assess the basic knowledge of the populace. It had two parts. Section A

was for the sociodemographic and past medical variables of participants and section B was a nine-item knowledge-based set of questions. It included questions on the kidney anatomy: number, physiology: functions, risk factors of kidney disease, symptoms of kidney disease, tests to detect kidney disease, the prognosis of kidney disease and treatment options. Participants were to provide three answers to the questions that assessed kidney functions, risk factors of kidney disease, symptoms of kidney disease, tests and treatment options. One point was given to each question completely answered correctly.All questions were open-ended and participants had to provide the answers. Total scores were converted to percentages and categorised as Poor knowledge if the score was <50%, Fair knowledge if the score was between 50-69% and good knowledge if the score was ≥ 70-100%.

Data Analysis: Completed questionnaires were entered into an Excel spreadsheet and then analysed using Statistical Product and Service Solutions for Windows® version 25, SPSS Inc.; Chicago, USA. Results were presented as simple frequencies and percentages for categorical variables, and the mean and standard deviation for continuous variables A p-value of <0.05 was taken as statistically significant at a 95% confidence interval. Bivariate analysis was used to assess a relationship between participants' sociodemographic and medical and social variables and respondents' knowledge of the kidney, kidney disease prevention and treatment options. Logistic regression analysis was further conducted with the significant independent variables from the bivariate analysis to determine the predictors of good knowledge of the kidney, kidney disease prevention and treatment among the respondents. The dependent variable 'overall knowledge' was also dichotomized into good knowledge and poor knowledge – by combining fair and poor knowledge.

Ethical approval: The study was conducted following the Helsinki declaration and the details of the WKD activities and screening were approved by the Head of the Hospital before commencement.

3. RESULTS

Socio-demographic characteristics of respondents

A total of 165 respondents were studied and 113 (68.5%) were females. Their ages ranged between 25 and 65 years, with a mean age of 46.48 ± 14.01 years. Most, 121 (73.3%) of the respondents lived in urban communities, were married 102 (61.8%), earned monthly stipend of <N30,000, 69 (41.8%) and had tertiary level of education 109 (66.1%), as shown in Table I.

Table I. Sociodemographic characteristics of respondents

	Frequency (n=165)	Percent
Sex		
Male	52	31.5
Female	113	68.5
Age (years)		
< 44	87	52.7
45-65	78	47.3
Type of community		
Rural	9	5.5
Semi-urban	35	21.2
Urban	121	73.3
Marital status		
Single	42	25.5

Married	102	61.8
Divorced/Separated	4	2.4
Widowed	17	10.3
Highest level of education		
None	2	1.2
Primary	17	10.3
Secondary	37	22.4
Tertiary	109	66.1

Medical and Social variables of respondents

A review of the medical and social variables of the respondents revealed that about a third (33.9%) had a history of hypertension, about one-fifth (17.6%) had diabetes mellitus and just above a tenth either use skin lightening cream or soap(12.1%) or take herbal concoctions(13.9%). Almost half (48.5%) take painkillers(NSAIDs)regularly (weekly for at least 1 month)and about one-third (31.5%) had been screened for kidney disease as shown in Table II.

Table II. Medical and social variables of respondents

	Frequency (n=165)	**Percent**
Have hypertension		
No	109	66.1
Yes	56	33.9
Take hypertension medication regularly		
No	121	73.3
Yes	44	26.7
Have diabetes mellitus		
No	136	82.4
Yes	29	17.6
Take diabetes mellitus medication regularly		
No	144	87.3
Yes	21	12.7
Smoke tobacco		
No	158	95.8

Yes	7	4.2
Take alcohol		
No	121	73.3
Yes	44	26.7
Use skin-lightening cream or soap		
No	145	87.9
Yes	20	12.1
Take herbal concoctions		
No	142	86.1
Yes	23	13.9
Take painkillers (NSAIDs)		
No	85	51.5
Yes	80	48.5
Have been screened for kidney disease		
No	113	68.5
Yes	52	31.5
Ever been told you have kidney disease		
No	157	95.2
Yes	8	4.8
Have any relative with kidney disease		
No	158	95.8
Yes	7	4.2
Have any other medical condition		
No	122	73.9
Yes	43	26.1

Knowledge about kidneys, kidney disease prevention and treatments

One hundred and forty-four (87.3%) of the respondents knew the number of kidneys a normal human has, 93 (56.4%) were aware that someone can live a normal life with one healthy kidney, 73 (44.2%) could state only one out of three

functions of the kidney, 62 (37.6%) could state only one out of three required risk factors of kidney disease and 83 (50.3%) could state only one of three symptom/signs of kidney disease. However, only about one-third, 52 (31.5%) of respondents were aware that chronic kidney disease has no cure. Overall, 74 (44.8%) had poor, 43(26.1%) had fair knowledge, and 48 (29.1%) had good knowledge about kidneys and disease, as displayed in Table III.

Table III. Knowledge of the kidney, kidney disease prevention and treatment

	Frequency (n=165)	Percent
How many kidneys does a normal person have?		
Wrongly answered	21	12.7
Correctly answered	144	87.3
Can someone live a normal life with one healthy kidney?		
Wrongly answered	72	43.6
Correctly answered	93	56.4
What are the functions of the kidney?		
Wrongly answered	92	55.8
Correctly answered	73	44.2
What are the risk factors of the kidney?		
Wrongly answered	103	62.4
Correctly answered	62	37.6
What are the symptoms/signs of kidney disease?		
Wrongly answered	82	49.7
Correctly answered	83	50.3
What test can be used to detect kidney disease?		
Wrongly answered	62	37.6
Correctly answered	103	62.4
How can kidney disease be prevented?		
Wrongly answered	76	46.1
Correctly answered	89	53.9
How is kidney disease treated?		
Wrongly answered	68	41.2
Correctly answered	97	58.8

Can Chronic kidney disease be cured?		
Wrongly answered	113	68.5
Correctly answered	52	31.5
Overall knowledge about Kidney and disease		
Poor (0 – 49.9%)	74	44.8
Fair (50.0 – 69.9%)	43	26.1
Good (70.0 – 100.0%)	48	29.1

Socio-demographics and knowledge of the kidney, kidney disease prevention and treatment

Of all the socio-demographic variables tested, only the level of education showed a statistically significant relationship with knowledge about kidneys and disease. This was particularly notable among respondents with a tertiary level of education (Fisher's Exact Test=26.707, p=<0.001), when compared to participants with below tertiary education, as shown in table IV.

Table IV. Socio-demographics and knowledge of kidney and disease

	Knowledge of the kidney, kidney disease prevention and treatment (n=165)							
	Poor (n=74)		**Fair (n=43)**		**Good (n=48)**			
	Freq	**%**	**Freq**	**%**	**Freq**	**%**	**X^2**	**p-value**
Sex								
Male	20	38.5%	16	30.8%	16	30.8%	1.410	0.494
Female	54	47.8%	27	23.9%	32	28.3%		
Age group								
<45 years	34	39.1%	24	27.6%	29	33.3%	2.668	0.263
45-65 years	40	51.2%	19	24.4%	19	24.4%		
Type of community								
Rural	6	66.7%	3	33.3%	0	0.0%	4.761	0.313
Semi-urban	16	45.7%	7	20.0%	12	34.3%		
Urban	52	43.0%	33	27.3%	36	29.8%		
Marital status								
Single	13	31.0%	15	35.7%	14	33.3%	6.679	0.352
Married	50	49.0%	25	24.5%	27	26.5%		

Divorced/Separated	2	50.0%	0	0.0%	2	50.0%		
Widowed	9	52.9%	3	17.6%	5	29.4%		
Monthly income								
Not applicable	0	0.0%	1	33.3%	2	66.7%	12.723	0.139[#]
<N30,000 (USD 65)	36	52.2%	18	26.1%	15	21.7%		
N30,000-N74,999 (USD 66 – 165)	27	47.4%	12	21.1%	18	31.6%		
N75,000-N149,999 (USD 165 – 330)	10	34.5%	8	27.6%	11	37.9%		
N150,000-N200,000 (USD 330 – 440)	0	0.0%	3	75.0%	1	25.0%		
>N200,000 (> USD 440)	1	33.3%	1	33.3%	1	33.3%		
Highest level of education								
None	2	100.0%	0	0.0%	0	0.0%	26.707[#]	**<0.001***
Primary	13	76.5%	3	17.6%	1	5.90%		
Secondary	25	67.6%	8	21.6%	4	10.8%		
Tertiary	34	31.2%	32	29.4%	43	39.4%		

*=Statistically significant at p<0.05; [#]=Fishers Exact Test used

Medical and social variables of respondents and knowledge of the kidney, kidney disease prevention and treatment

There was a significant association between having a history of hypertension(p=0.042) and taking pain medications (p=0.007)and respondents' knowledge of the kidney, kidney disease prevention and treatment respectively. Good knowledge was higher among those that were not hypertensive (35.1%) compared to their hypertensive counterparts (16.7. Similarly good knowledge scores were higher among those who did not take pain medications(33.7%)compared to those that did(23.7%), as seen in table V.

Table V: Medical and social variables and knowledge of kidney, kidney disease prevention and treatment

	Knowledge about kidney, kidney disease, prevention and treatment (n=165)							
	Poor (n=74)		Fair (n=43)		Good (n=48)			
	Freq	%	Freq	%	Freq	%	X^2	p-value
Have hypertension								
No	47	42.3%	25	22..5%	39	35.1%	6.363	**0.042***
Yes	27	50.0%	18	33.3%	9	16.7%		
Take hypertension medication regularly								
No	54	45.0%	31	25.8%	35	29.2%	0.012	0.994
Yes	20	44.4%	12	26.7%	13	28.9%		
Have diabetes mellitus								
No	61	45.2%	33	24.4%	41	30.4%	1.181	0.554
Yes	13	43.3%	10	33.3%	7	23.3%		
Take diabetes mellitus medication regularly								
No	66	47.1%	33	23.6%	41	29.3%	3.294	0.193
Yes	8	32.0%	10	40.0%	7	28.0%		
Smoke tobacco								
No	70	44.0%	41	25.8%	48	30.1%	0.991#	0.667
Yes	4	66.7%	2	33.3%	0	0.0%		
Take alcohol								
No	52	41.2%	37	29.4%	37	29.4%	3.770	0.152
Yes	22	56.4%	6	15.4%	11	28.2%		
Use skin-lightening cream or soap								
No	66	46.1%	33	23.1%	44	30.8%	0.739	0.691
Yes	8	36.3%	10	45.5%	4	18.2%		
Take herbal concoctions								
No	63	43.8%	37	25.7%	44	30.6%	1.197	0.549

Yes	11	53.4%	6	28.6%	4	19.0%		
Take painkillers routinely								
No	36	40.4%	23	25.8%	30	33.7%	9.788	**0.007***
Yes	38	50.0%	20	26.3%	18	23.7%		
Have been screened for kidney disease								
No	50	43.9%	27	23.7%	37	32.5%	2.315	0.314
Yes	24	47.1%	16	31.4%	11	21.6%		
Ever been told you have kidney disease								
No	71	45.5%	41	26.3%	44	28.2%	1.107	0.575
Yes	3	33.3%	2	22.2%	4	44.4%		
Have any relative with kidney disease								
No	71	44.9%	43	27.2%	44	27.8%	1.459[#]	0.545
Yes	3	42.9%	0	0.0%	4	57.1%		
Have any other medical condition								
No	55	45.4%	25	20.7%	41	33.9%	4.066	0.131
Yes	19	45.2%	16	38.1%	7	16.7%		

*=Statistically significant at p<0.05; [#]=Fishers Exact Test

On logistic regression analysis, as shown in Table VI, it was revealed that participants' highest level of education was significantly (p = 0.001) associated with having a good knowledge of kidney, and kidney disease prevention and treatment. Participants with a tertiary level of education were 4.676 times more likely (aOR: 4.676; CI:1.984; 11.023) to have good knowledge when compared to participants below a tertiary level of education. Although bivariate analysis suggested otherwise, regression analysis showed that there was no significant association between taking pain medications aOR: 0.589 (CI: 0.286; 1.217) or not being hypertensive aOR: 1.151 (CI: 0.520; 2.548) and having good knowledge of kidney, kidney disease prevention and treatment, after adjusting for all other confounding variables.

Table VI: Logistic regression showing the strength of association of significant demographic, medical and social variables and knowledge of kidney, kidney disease prevention and treatment

			95% CI for OR		
	B	**aOR**	**Lower Limit**	**Upper Limit**	**p-value**
Take pain killers					
Good knowledge	-.529	0.286	1.217	0.589	**0.153**
Poor knowledge	0[b]				
Have Hypertension					
Good knowledge	0.141	1.151	0.520	2.548	**0.729**
Poor knowledge	0[b]				
Highest level of education					
Good knowledge	1.543	4.676	1.984	11.023	**<0.001***
Poor knowledge	0[b]				

aOR=Odds Ratio; Reference category (b)= Poor knowledge; b=Parameter set at 0 because it is redundant

DISCUSSION

Chronic kidney disease is a common and increasing problem globally[8,18,19]. There is evidence that a huge aspect of the populace has insufficient awareness of the disease[3,20–22]. This study assessed the knowledge of the kidney, kidney disease prevention and therapeutic options among non-clinical healthcare providers at a tertiary hospital in Southern Nigeria.

The study participants had an overall poor knowledge about kidneys, disease prevention and therapeutic options. The fact that these non-clinical healthcare providers had inadequate knowledge despite rendering some form of care in the hospital community including the medical and nephrology outpatients' clinics suggests that physicians' existing education strategies do not necessarily meet the needs of these cohorts of healthcare staffers. Our finding, has invariably, identified and highlighted a gap through the World Kidney Day activities in 2022, which focused on - 'bridging the knowledge gap for better kidney care' among non-clinical HCPs in our setting. It is plausible that these non-clinical healthcare providers are not receiving adequate education from their clinical counterparts and are more often than not, missing out despite being within the hospital. This research highlights the need for a change in educational approaches, such that even non-medical staffers are included during the health promotions and education about the kidney in health and disease. Similar to our findings were reported from other studies within Nigeria[9,23,24] and outside Nigeria[25,26] which found low levels of knowledge of kidneys, kidney disease prevention and therapeutic options among the general populace of adults. In contrast, however, studies by Ibitoba et al[27] conducted among motorcyclists in Ado-Ekiti State, and Adejumo et al[28] among nurses in Akure, Ondo State, found that only 35.5% and 37% had poor knowledge of kidney disease respectively. Our rather higher prevalence of poor knowledge found can be possibly explained by the fact that the general awareness of kidney disease and health promotions often occur outside of the hospitals and are often within clinical healthcare providers, somehow overlooking the non-clinical HCPs.

Despite a majority of respondents having poor knowledge, there were some items on the survey tool on which they scored fairly well. Particularly, 87.3% of the participants knew the anatomical location and the number of kidneys, 56.4% knew that a person could live a normal life with only one kidney, 50,3% could mention at least one symptom of kidney disease, 58.8% knew at least one modality of treatment for kidney disease. This was in contrast to findings from a study in Akwa-Ibom by Akpan and Ekrikpo,[9] where only 43.3% knew the correct location of the kidneys. However, less than half of the respondents in this study could mention only one of any three vital functions of the kidney. A greater majority could not answer beyond one of the required three items per question. Our study was similar to findings from other

Nigerian studies where respondents had low knowledge of the functions and symptoms of kidney disease. Risk factors for kidney disease and the possibility of curing chronic kidney disease were also areas with low levels of knowledge, found in this study.

Also, it was found that of all the sociodemographic, medical and social variables tested, only the level of education showed a statistically significant relationship with knowledge about the kidney, kidney disease prevention and treatment. This was similar to the findings done in Maiduguri, Ado Ekiti, Lagos, Saudi Arabia and Brazil [2,10,21,27,30]. This underscores the well-established fact that improvement in social determinants of health such as educational status improves health outcomes [31]. The educated are more likely to understand and follow up on their health statuses as has been demonstrated in the already existing literature [10].

As regards the medical history of the respondents, it was found that about one-third either had a history of hypertension (33.9%) or diabetes mellitus (29%) and about one-tenth (9%) either knew a relative with kidney disease or had kidney disease themselves. It was also rather an unexpected finding that there was no significant relationship between respondents with a past medical history of hypertension, diabetes and other risk factors and their knowledge of kidney disease. It would rather have been expected that those with existing risk factors would know more, this albeit, was not the case among the non-clinical healthcare providers. These further stresses the importance of health education, promotion and physician-patient communication.

Worthy of note are other risk factors known to be linked with kidney disease identified among non-clinical healthcare providers in this study. Almost half (48.5%) reported using painkillers like nonsteroidal anti-inflammatory drugs (NSAIDs) regularly, almost one-quarter (26.7%) take alcohol and just over a tenth (13.9%) of non-clinical HCPs use herbal concoctions. Our findings differed from studies in Nigeria conducted among non-clinical healthcare provider populations, where herbal concoctions were the most commonly identified risk factor for kidney disease followed by alcoholic beverages and NSAIDs[32,33]. This could be because painkillers are more readily available over the counter and would naturally be the go-to drug for non-clinical HCPs in clinical settings.

Limitations:

Despite being able to achieve our main aim to determine the knowledge of the kidney, kidney disease prevention and therapeutic options among non-clinical healthcare providers in our setting, our study was limited due to the study design, a considerably small sample size, and being single-centred.

4. CONCLUSION

Knowledge of the kidney, disease prevention and therapeutic options among non-clinical HCPs is unsatisfactory. There is a need for change in educational approaches to ensure kidney and CKD-targeted health education and promotional activities are also towards non-clinical HCPs, particularly those with lower levels of education. This includes targeting such subgroups within the hospitals and creating policies that enable risk reductive measures like permitting frequent routine screening.This is essential as they are a potential, yet a crucial source of educators for kidney health promotion in the community.

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COMPETING INTERESTS

The authors have declared that no competing interests exist.

AUTHORS' CONTRIBUTIONS

Author DCB, EBJ designed the study. DCB performed the statistical analysis and managed the analysis, wrote the protocolandwrote the first draft of the manuscript. Authors 'MI, NTI, OE, and DCB'' managed the literature searches. 'Author EBJ wrote the abstract, EBJ and PMD proofread for intellectual content' All authors were involved in data collation, read and approved the final manuscript.

CONSENT

All authors declare that informed consent was obtained from the participants before the commencement of the study.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki."

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