


Predictors of Change in Weight Among People Living with HIV on Antiretroviral Treatment in West Hararghe Zone, Ethiopia: A Retrospective Longitudinal Study


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Background: Human immunodeficiency virus (HIV) remains a major global public health issue, particularly in Africa. In resource-limited settings like Ethiopia, regular weight measurement and monitoring is useful in the examination of patient response to antiretroviral therapy and in clinical decision-making. However, there is a paucity of evidence on factors that affect longitudinal weight change. Therefore, the present study was intended to identify predictors of weight change among people living with HIV (PLWH) in West Hararghe, Ethiopia.

Methods: An institutional-based retrospective cohort study was conducted among 558 PLWH aged 18 years and above from September 2013 to January 2019 at Chiro Zonal Hospital and Gelemso General Hospital in West Hararghe zone, Ethiopia. Data were entered in Epi info 7 and analyzed in R software. The linear mixed effect regression model was used to identify predictors of longitudinal change in weight. Regression coefficients with their 95% confidence intervals were used to indicate the strength and significance of the association.

Results: Weight showed improvement in follow-up periods. In this study, age of respondent (beta=0.136, 95% CI, 0.044:0.227), time since the initiation of antiretroviral therapy (ART) (beta=0.089, 95% CI, 0.075:0.104), primary educational status (beta=2.403, 95% CI, 0.540:4.266), secondary educational status (beta=4.035, 95% CI, 1.666:6.404), tertiary and above educational status (beta=3.444, 95% CI, 0.330:6.558), sex (beta= -5.514, 95% CI, -7.260:-3.768), ambulatory functional status (beta= -3.419, 95% CI, -6.169:-0.668) and baseline CD4 count (≤ 200) (beta=2.205, 95% CI, 0.593, 3.817) were significant predictors of longitudinal weight change.

Conclusion: We observed an increment in weight among PLWH who were on ART in Ethiopia. Educational status, time since the beginning of ART, age and having CD4 count above 200 have contributed positively to the change in weight, while ambulatory functional status and being female are negatively associated with longitudinal change in weight. Close monitoring is recommended for patients with ambulatory baseline functional status and for patients with baseline CD4 count ≤ 200 .

Keywords: weight change, PLWH, ART, linear mixed effect model, Ethiopia

Introduction

Human Immunodeficiency Virus (HIV) remains a major global public health issue, responsible for 770 000 deaths in 2018, of which more than two-thirds (25.7 million) are from the World Health Organization (WHO) African Region. Around 37.9 million people are living with HIV in 2019 and more than half of them

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live in Africa.¹ In Ethiopia, 690,000 were living with HIV and 11,000 people died of acquired immunodeficiency syndrome (AIDS) related illness, according to the UNAIDS report in 2019.²

People Living with HIV (PLWH) had a persistently lower subcutaneous adipose tissue compared to HIV-free participants. Most PLWH gain weight after antiretroviral therapy (ART) has started in the current ART era, despite relatively normal immune function and minimal pre-ART weight loss.^{3,4} The most pronounced increase in weight occurs in the first year after the initiation of ART. A small proportion of patients may also be underweight. Developing countries are experiencing a double burden of underweight and overweight, which may increase the risk of cardiovascular disease among PLWH.^{5,6}

Weight is one of the clinical measurements used to assess the efficacy of ART. It can be used as an open index for the monitoring and evaluation of PLWH, among other diagnostic indices, particularly in developing countries. Ensuring normal Body Mass Index (BMI) for PLWH in clinical settings is crucial in providing important insights and identifying opportunities for interventions.^{6,7}

In resource-limited settings like Ethiopia, regular weight measurement and monitoring is useful for clinicians to examine the response of patients to ART and predict the disease stage as well as clinical decision-making. Studies are needed to determine whether weight improvement prior to or at ART initiation will result in improved ART outcomes.

Despite this, there is little evidence in Ethiopia of factors affecting longitudinal weight change. Therefore, the present study was intended to identify predictors of weight change among PLWH on ART in West Hararghe, Eastern Ethiopia. The finding would be helpful for monitoring the effectiveness of ART and reducing the complication that may arise as a result of over and underweight. In addition, it would help for clinical decision-making and improving therapeutic care.

Methods

Study Design and Settings

An institutional-based retrospective cohort study was conducted among PLWH who are on ART between September 2013 and January 2019 at public hospitals in the West Hararghe zone of Oromia, Eastern Ethiopia. Among the five hospitals in the area, the study was conducted in Chiro Zonal Hospital and Gelemso General Hospital due to the availability of ART data. The two

hospitals are providing services to approximately 2,300,000 people in the area. At the time of the study, a total of 1120 patients from Chiro Zonal Hospital and 521 patients from Gelemso General Hospitals were on ART.

Study Population and Sample Size

The study included all PLWH aged 18 years and above who started ART between 2013 and 2019 and registered in the ART Registry of Chiro and Gelemso Hospitals. Patients who had at least two weight measurements were included in the study. Patients who had single body weight measurement, those with incomplete records, transferred in from other treatment center and pregnant women were excluded from the study. [Figure 1](#) flow chart shows how the study participants were selected. Out of PLWH who started Highly Active Anti-Retroviral Therapy (HAART) in the two selected hospitals between September 2013 and January 2019, 558 patients who met the inclusion criteria were selected.

Data Collection Procedures

The data for this study were obtained from secondary data and collected using a data extraction checklist. A baseline and follow-up weight data were identified and collected from the registration logbook of HAART attendants. In addition, socio-demographic variables, visiting times and clinical data were collected from the registration documents of patients. The data were collected by health professionals after they had been given adequate orientation.

Measurement of Study Variables

The outcome variable for this study was longitudinal weight change. Weight was measured using a standard weighing scale with graduation 0.1 kg and measuring range up to 150 kg. The scale pointer was calibrated at zero before taking measurement. Measurement of weight was recorded to the nearest 0.1 kg. Weight change refers to the difference between weight (kg) in the current visit time and weight (kg) in the visit time immediately prior to the current response.

Socio-demographic variables, baseline clinical variables (WHO Retroviral Infection (RVI) stage, baseline CD4, initial ART regimen, tuberculosis (TB) co-infection, opportunistic infection prophylaxis (OIP), baseline functional status and baseline adherence) were independent variables.

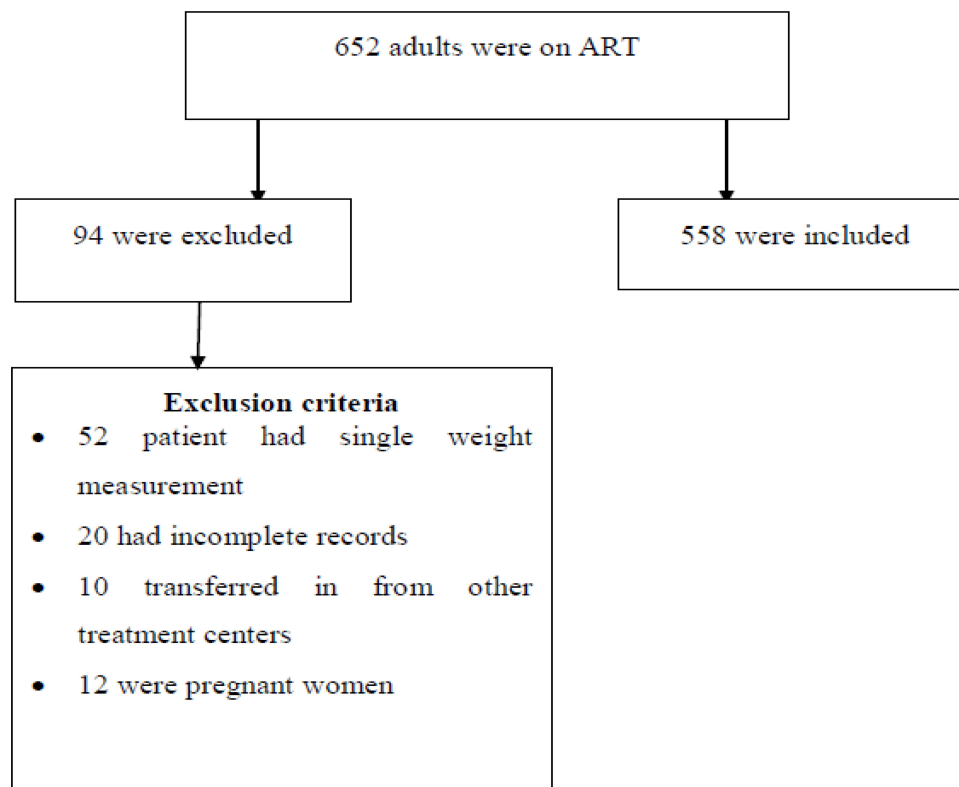


Figure 1 Flowchart depicting selection process of study participants.

Data Quality Assurance

The preliminary assessment of the adequacy of the checklist was carried out and the variables on which the data were not available were excluded from the checklist. Trained health professionals have been assigned as data collectors. In addition, to ensure that the data quality of the completed checklist was checked for consistency and completeness. Strict supervision has been applied by supervisors during data collection.

Data Processing and Analysis

Data entry was done using Epi Info 7 and exported to R statistical software 3.6.2 for further analysis. Descriptive statistics such as mean, median, standard deviations (SDs) and tables have been used to investigate the characteristics of the study participant. The Linear Mixed Effect Model (LMM) was used to identify predictors of weight change. Both the random intercept and slope-intercept models were examined to determine the fitness of the model. The model comparison was made using likelihood ratio test.

The predictors significantly associated with longitudinal weight change in the bi-variable analysis at p-values

below 0.2 were included in the multivariable linear mixed effect model. Regression coefficients of the final model and their 95% confidence intervals were used as a measure of association between the predictors and the outcome variable. A p-value of less than or equal to 0.05 was considered to be statistically significant.

Ethical Consideration

Ethical clearance and letter of cooperation for selected hospitals were obtained from the Institutional Review Board of the University of Gondar. Support letter was obtained from medical director of the hospitals in order to access medical records of patients. Data were fully anonymized and no personal identifiers, such as name and private information were not collected. Confidentiality during all phases of research activities was kept and data were held on secured password-protected system.

Results

A total of 558 PLWH were included in the study. The median age of the subject was 32 years IQR: (27.0–40.0). The majority of study subjects 354 (63.4%) were female, 350 (62.7%) were from urban area and more than half 303

(54.3%) were married. Of the total study participants, 470 (84.2%) had a working baseline functional status, 459 (82.3%) had TB co-infection and a majority of 358 (64.2%) had CD4 baseline status above 200. More than three-quarters (88.2%) of patients received OIP, 57 (28.1%) and 24 (4.3%) were at WHO stage III and IV, respectively (Table 1).

Exploring Longitudinal Weight Changes

A minimum of two and a maximum of 33 weight measurements were taken for ART patients during the study period. Figures 2 and 3 presents individual profile plots and mean profile plot indicating that there is variability of weight within and between patients. At baseline, patients had different starting points for weight, suggesting a random intercept model. As it can be shown from Figure 2, trajectories of weight over time show considerable heterogeneity which suggests to consider a mixed model with random slopes. The mean weight and the number of patients analyzed at each time point are shown in Table 2.

Model Comparison

The model comparison was made for the two nested models (mixed model with random intercept and mixed model with both random intercept and slope) using the likelihood ratio test and the result shows that the linear mixed effect model with both random intercept and slope was a more parsimonious model consistent with the exploratory analysis result (Table 3). Variance covariance structure showed correlation between repeated measurements diminishes over time. Therefore, a model with autoregressive (AR1) covariance structure was selected as a better model for this data.

Predictors of Longitudinal Weight Change

The Linear Mixed Effect Model was designed to identify predictors of longitudinal change in weight. Respondent sex, age, time after ART initiation, educational status, occupational status, baseline CD4 count, WHO RVI stage, baseline adherence, TB co-infection and functional status showed significant association in bi-variable analysis whereas marital status, residence and OIP had no significant association with weight change at p-value of 0.2 and therefore dropped from multi-variable model.

In multivariable analysis time since the beginning of ART (beta=0.089, 95% CI, 0.075:0.104), age of

Table 1 Baseline Characteristics of PLWH in West Hararghe Zone, Eastern Ethiopia, 2013 to 2019

Variables	Category	Frequency (n=558)	Percent (%)
Sex	Male	204	36.6
	Female	354	63.4
Marital status	Single	71	12.7
	Married	303	54.3
	Divorced	87	15.6
	Widowed	62	11.1
	Separated	35	6.3
Occupational status	Government employed	58	10.4
	Non-government employed	138	24.7
	Farmer	106	19.0
	Jobless	162	29
	Others	94	16.8
Place of residence	Urban	350	62.7
	Rural	208	37.3
Educational status	Uneducated	167	29.9
	Primary	204	36.6
	Secondary	110	19.7
	Tertiary and above	77	13.8
RVI stage	Stage I	285	51.1
	Stage II	92	16.5
	Stage III	157	28.1
	Stage IV	24	4.3
Functional	Working	470	84.2
	Ambulatory	70	12.5
	Bedridden	18	3.2
Adherence	Good	482	86.4
	Fair	30	5.4
	Poor	46	8.2
TB co-infection	Yes	459	82.3
	No	99	17.7
OIP	Yes	492	88.2
	No	66	11.8
CD4 Count	Less than or equal to 200	200	35.8
	Greater than 200	358	64.2
ART regimen	AZT, 3TC, NVP	30	5.4
	AZT, 3TC, EFV	24	4.3
	TDF, 3TC, NVP	18	3.2
	TDF, 3TC, EFV	486	87.1

Note: Others = Daily laborer, Driver, Merchant.

Abbreviations: AZT, zidovudine; 3TC, lamivudine; NVP, nevirapine; EFV, efavirenz; PLWH, people Living with HIV; RVI, retroviral infection; TB, tuberculosis; OIP, opportunistic infection prophylaxis; ART, antiretroviral therapy.

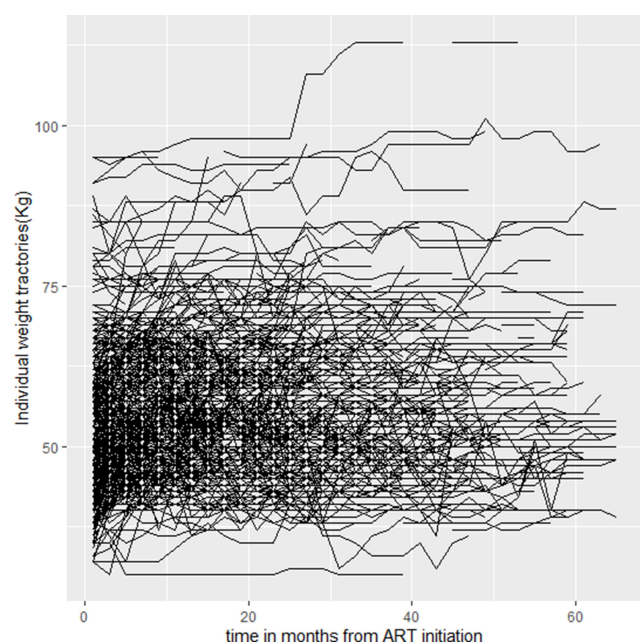


Figure 2 Individual profile plot for longitudinal weight trajectory among PLWH at public hospitals in west Hararghe zone, Eastern Ethiopia, 2013 to 2019.

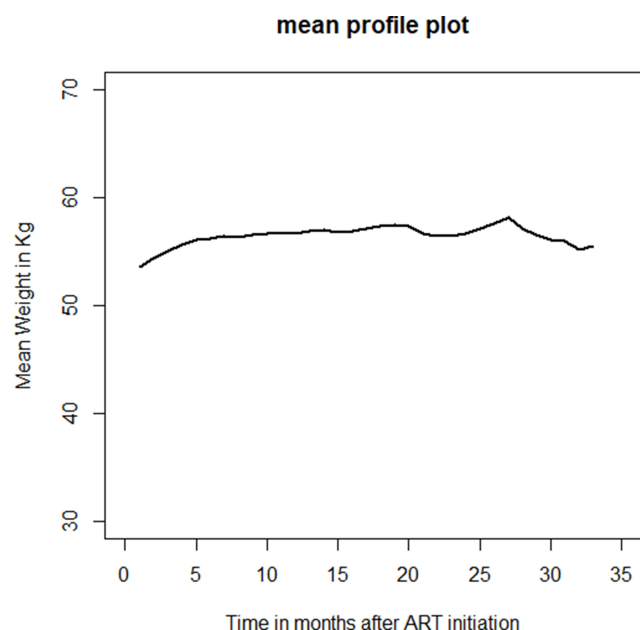


Figure 3 Overall mean weights for PLWH in West Hararghe Zone, Eastern Ethiopia 2013 to 2019.

respondent ($\beta=0.136$, 95% CI, 0.044:0.227), primary educational status ($\beta=2.403$, 95% CI, 0.540:4.266), secondary educational status ($\beta=4.035$, 95% CI, 1.666:6.404), tertiary and above educational status ($\beta=3.444$, 95% CI, 0.330:6.558), sex ($\beta=-5.514$, 95% CI, -7.260:-3.768), ambulatory functional status ($\beta=-3.419$, 95% CI, -6.169:-0.668) and baseline CD4

Table 2 Average Baseline and Follow-Up Values of Weight for PLWH in West Hararghe Zone, Eastern Ethiopia 2013 to 2019

Follow-Up Period	Weight in Kilograms	
	N	Mean (\pm SD)
Baseline	558	53.54 (10.30)
3rd month	558	54.40 (9.89)
5th month	550	55.08 (9.86)
7th month	531	55.59 (9.88)
9th month	510	56.04 (9.86)
11th month	493	56.16 (9.78)
13th month	471	56.38 (9.94)
15th month	458	56.28 (10.14)
17th month	439	56.57 (10.20)
19th month	417	56.68 (10.35)
21st month	406	56.67 (10.39)
23rd month	376	56.70 (10.56)
25th month	356	56.89 (10.99)
27th month	327	56.97 (11.39)
29th month	301	56.75 (11.28)
31st month	281	56.84 (11.37)
33rd month	269	57.11 (11.62)
35th month	259	57.39 (11.53)
37th month	235	57.44 (11.91)
39th month	210	57.41 (12.18)
41st month	194	56.69 (11.46)
43rd month	181	56.48 (11.68)
45th month	169	56.46 (11.49)
47th month	149	56.64 (11.78)
49th month	121	57.07 (13.20)
51st month	99	57.61 (13.68)
53rd month	89	58.14 (14.09)
55th month	78	57.14 (11.96)
57th month	62	56.60 (12.50)
59th month	52	56.08 (12.13)
61st month	36	55.94 (13.14)
63rd month	21	55.19 (13.91)
65th month	10	55.50 (13.79)

Table 3 Model Comparison for Longitudinal Models Using Likelihood Ratio Test

Model	Log-Likelihood	LR	P-value
Random intercept model	-24585.04	2348.316	< 0.001
Random intercept and slope model	-23410.89		

Abbreviation: LR, likelihood ratio.

count (≤ 200) ($\beta=2.205$, 95% CI, 0.593, 3.817) were significant predictors of longitudinal weight change (Table 4).

Table 4 Linear Mixed Effect Model for Predictors of Longitudinal Changes in Weight Over Time for PLWH, 2013 to 2019

Variables	Category	Beta	P-value	95% CI
Intercept	–	51.036	<0.001	44.748, 57.323
Time	–	0.089	<0.001	0.075, 0.104
Sex	Male Female	Ref. –5.514	Ref. <0.001	Ref. –7.260, –3.768
Age		0.136	0.004	0.044, 0.227
Educational status	Uneducated Primary Secondary Tertiary and above	Ref. 2.403 4.035 3.444	Ref. 0.012 0.001 0.030	Ref. 0.540, 4.266 1.666, 6.404 –0.330, 6.558
Occupational status	Government employed Non-government employed Farmer Jobless Others	Ref. 0.023 –0.435 –1.281 2.548	Ref. 0.989 0.809 0.439 0.159	Ref. –3.202, 3.248 –3.958, 3.089 –4.527, 1.965 –1.000, 6.096
RVI stage	Stage I Stage II Stage III Stage IV	Ref. –1.393 –1.325 –0.626	Ref. 0.194 0.199 0.778	Ref. –3.497, 0.712 –3.349, 0.700 –4.989, 3.737
Functional	Working Ambulatory Bedridden	Ref. –3.419 –2.656	Ref. 0.015 0.285	Ref. –6.169, –0.668 –7.531, 2.219
Adherence	Good Fair Poor	Ref. –2.144 –1.247	Ref. 0.223 0.432	Ref. –5.593, 1.305 –4.364, 1.870
TB co-infection	No Yes	Ref. –1.922	Ref. 0.093	Ref. –4.164, 0.319
Baseline CD4	≤200 >200	Ref. 2.205	Ref. 0.007	Ref. 0.593, 3.817
ART regimen	AZT, 3TC, NVP AZT, 3TC, EFZ TDF, 3TC, NVP TDF, 3TC, EFZ	Ref. 3.324 –1.502 0.473	Ref. 0.177 0.574 0.783	Ref. –1.509, 8.157 –6.743, 3.739 –2.893, 3.814
Variance component				
SD of intercept		8.455		
SD of time		0.115		
Residual SD		3.004		

Note: Others=Daily worker, Drivers, Merchant. Bold indicates that variables are significantly associated with the outcome.

Abbreviations: Ref, reference category; SD, standard deviation; RVI, retroviral infection.

Discussion

This longitudinal study examined weight change and its predictors among PLWH. The expected weight for all patients at baseline is 8.455 but shows variation from one patient to another with a standard deviation of 0.115. The study found that sex, educational status, age, time

since ART initiation, functional status and baseline CD4 count were significantly associated with weight change.

Time since the start of ART is one of the factors that is significantly associated with weight change. For a unit increase in time spent on ART, the expected weight of PLWH is increased by 0.089. This finding is consistent

with the study in Ethiopia⁸ and may be due to the effect of combined antiretroviral therapy which may result in changes in body fat composition overtime.⁹

In our study female sex is an independent predictor of weight change. People Living with HIV who are female are expected to have 5.514 lower mean weight as compared to male patients. This finding is supported by a low-resource setting study which reported that after initiation of ART, the mean adjusted body weight change was higher in males than in females.¹⁰ This could be due to females have less ability to bear traumatic life stressors like HIV/AIDS and in addition biological (hormonal) difference of female with their counterparts make them more likely to experience psychological problems like anxiety and depression which is negatively related to weight.

Age is another significant predictor of weight change. Expected weight of PLWH is increased by 13.6% for a unit increase in age of the patient in years. This finding is in line with previous study in USA which indicated as age of patient increases PLWH gain weight due to increment in lean body mass related to effect of combined ART.

Educational status is another variable that has shown significant association with weight change. Patients with primary, secondary and tertiary and above educational status are expected to have 2.403, 4.305 and 3.444 times higher mean weights compared to uneducated patients, respectively. The possible explanation for this could be that literate patients have a better awareness on the importance of continuous intake of drugs in order to have better adherence, and that literate persons may have a better socio-economic status and be able to eat balanced and adequate food.

In the current study, the mean weight of patients with ambulatory baseline functional status is expected to be 3.419 lower compared to those with working baseline functional status and this might be due to patients with ambulatory baseline functional status may be more susceptible and likely to have to opportunistic infection and complications which, in turn, have a negative effect on weight.

This study found that PLWH with baseline CD4 counts greater than 200 are expected to have 2.205 higher mean weights than those with baseline CD4 counts less than or equal to 200. This finding is in line with previous studies^{8,11} which reported a significant positive association between weight change and CD4 count. This can be explained by the fact that patients with baseline CD4 counts above 200 have a lower risk of developing

opportunistic infections and malignancies, which could contribute to higher mean weight.

The limitation of this study was that it was based on secondary data from patient records that could not be obtained for some important variables such as nutritional status and substance use. In the conclusion, we observed an increment in weight among PLWH who were on ART in Ethiopia. Educational status, time since the beginning of ART, age and having CD4 count above 200 have contributed positively to the change in weight, while ambulatory functional status and being female are negatively associated with longitudinal change in weight. Close monitoring is recommended for patients with ambulatory baseline functional status and for patients with baseline CD4 count ≤ 200 .

Abbreviations

AIC, Akaike Information Criteria; AIDS, acquired immunodeficiency syndrome; ART, anti-retroviral therapy; CI, confidence interval; HIV, human immunodeficiency virus; LMM, linear mixed model; OIP, opportunistic infection prophylaxis; PLWH, people living with HIV; RVI, retroviral infection; SD, standard deviation; SE, standard error; TB, tuberculosis; WHO, World Health Organization.

Data Sharing Statement

The datasets supporting the conclusions of this article are available upon request to the corresponding author.

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Author Contributions

ABW conceptualized the study, participated in proposal writing, data collection, formal analysis, investigation, interpretation, and critical revision of the manuscript. TAA, MMS, BST, SAK participated in formal analysis, investigation, interpretation and critical revision of the manuscript. All authors have agreed on the journal to which the article will be submitted, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests.

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