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#### RESEARCH ARTICLE

**REVISED** Bioelectrical impedance vector analysis as an indicator

of malnutrition in children under five years with and without

pneumonia in Mchinji District, Malawi: An exploratory mixed-

methods analysis [version 3; peer review: 1 approved, 1

# approved with reservations]

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#### Abstract

#### Background

Bioelectrical impedance vector analysis (BIVA) is a non-invasive approach to assessing body composition and cellular health, which may improve the assessment of nutritional status in sick children. We explored the reliability, clinical utility, and acceptability of BIVA, as an indicator of nutritional status for children under five years with and without pneumonia, in Malawi.

#### Methods

We conducted a parallel convergent mixed-methods exploratory study in Mchinji District Hospital, Malawi, in 2017. We recruited a convenience sample of children aged 0–59 months with clinical

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pneumonia, and without an acute illness. Children had duplicate anthropometric and BIVA measurements taken. BIVA measurements of phase angle were taken of the whole body, and trunk and arm segments. Reliability was assessed by comparing the variability in the two measures, and clinical utility by estimating the association between anthropometry and phase angle using linear regression. Focus group discussions with healthcare workers who had not previously used BIVA instrumentation were conducted to explore acceptability.

#### Results

A total of 52 children (24 with pneumonia and 28 healthy) were analysed. The reliability of sequential phase angle measurements was lower than anthropometric measurements, but trunk and arm segments performed better. The largest associations with phase angle were a negative relationship with weight-for-age z-score (WAZ) in children with pneumonia in the trunk segment, and a positive association with WAZ in the full body measurement in healthy children. Healthcare workers in focus group discussions expressed trust in BIVA technology and that it would enable more accurate diagnosis of malnutrition; however, they raised concerns about the sustainability and necessary resources to implement BIVA.

#### Conclusions

While healthcare workers were positive towards BIVA as a novel technology, implementation challenges should be expected. The differential direction of association between anthropometry and phase angle for children with pneumonia warrants further investigation.

#### **Keywords**

Bio-electrical impedance vector analysis, malnutrition, pneumonia, child

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Any reports and responses or comments on the article can be found at the end of the article.

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#### **REVISED** Amendments from Version 2

Minor edits to remove an acronym, reword a sentence in the introduction and methods, and added 2 sentences to the discussion on the use of 3cm inter-electrode distance.

Any further responses from the reviewers can be found at the end of the article

#### Introduction

In 2017, pneumonia was reported as the leading cause of infectious death for children under five years<sup>1</sup>. Despite a 30% reduction in global incidence and a 51% reduction of mortality from pneumonia from 2000 to 2015, the implementation of targeted actions to reduce the risk-factors associated with pneumonia mortality is needed to reach Sustainable Development Goals 3.2 by 2030<sup>2</sup>. Paediatric pneumonia fatality rates remain high for children under one year of age, malnourished children and hypoxemic children<sup>3,4</sup>.

Malnutrition is a key cause of morbidity across the life-course and contributes to a high proportion of under-five deaths<sup>5–7</sup>. Currently, malnutrition in children is assessed through anthropometric measurements of weight, height and middle-upper arm circumference (MUAC), and classified by the World Health Organisation (WHO) into the conditions of underweight (weight-for-age z-score (WAZ) of <-2), stunting (height-for-age z-score of <-2) and wasting (weight-for-height z-score of <-2 and/or a MUAC <125mm)<sup>8</sup>. Severe malnutrition, including the presence of bilateral pitting oedema, is considered a danger sign which triggers referral for hospital care amongst sick children<sup>9</sup>.

However, these traditional anthropometric approaches are not sensitive to cellular health or dehydration, and the presence of oedema will increase a child's weight and potentially bias malnutrition classification<sup>10</sup>. As an alternative approach to assessing nutritional status, there is a growing interest in body composition measurements to diagnose and treat malnutrition<sup>11,12</sup>. Bioelectrical impedance vector analysis (BIVA) is a technique used to analyse bioelectrical impedance data in a vector format. Bioelectrical impedance involves the measurement of the opposition to the flow of an electric current through the body's tissues. BIVA specifically focuses on the vector representation of impedance measurements to assess body composition e.g. measuring cellular health<sup>13</sup>.

Specifically one output of bioelectrical impedance measurements, phase angle, has been found to be correlated with severe acute malnutrition in children<sup>12</sup>, and with an increased risk of mortality among hospitalized patients<sup>14</sup>. In longitudinal studies of children with severe malnutrition, BIVA has shown the ability to discriminate children with or without oedema, and to identify loss of excess fluid over time in oedematous children and accretion of lean tissue in non-oedematous children<sup>15,16</sup>. In one study, children who died had extreme high or low BIVA values at baseline<sup>16</sup>. However, the extent to which BIVA adds information of clinical value beyond anthropometric measurements remains unclear, and may depend on complications of malnutrition, such as oedematous status.

Given the high morbidity and mortality burden of malnutrition and pneumonia co-presentation, more sensitive approaches to assessing a child's physiological state could improve outcomes in this group and the use of BIVA in this context is promising. Therefore, we aimed to assess the reliability, clinical utility, and acceptability of BIVA among healthcare workers as an indicator of malnutrition for children under five years of age, with and without pneumonia in Malawi.

#### Methods

We conducted a convergent parallel mixed-methods study, between April and July 2017, in Mchinji District, Malawi. Clinical assessments, anthropometry and bioelectrical impedance measurements amongst children aged 0-59 months, with and without pneumonia, were collected to explore reliability and clinical utility. Focus group discussions (FGDs) with healthcare workers were conducted to assess acceptability. Synthesis of the mixed-methods was done through Venkatesh and Davis' Extended Technology Acceptance Model<sup>17</sup>, which explores a range of attributes of novel technology, including: job relevance, output quality, result demonstrability, perceived usefulness, perceived ease of use, and intention to use. While BIVA is the approach to analysing measurements from a bioelectrical impedance (BIA) machine, we use the term 'BIVA' throughout to refer to both the device and interpretation. This was done to help simplify the presentation of this novel technology in this context.

#### Ethics statement

Ethical approval for the data collection was granted by the University College London Research Ethics Committee (reference: 8075/001) and Malawi National Health Sciences Research Committee (reference: 16/4/1568). The child's caregiver (including parents, grandparents or older siblings) who was present with them at the hospital provided informed verbal consent for the clinical assessments, anthropometric and BIVA measurements. The verbal consent process was approved by the research ethics committees and was explicitly recorded within the study's electronic data collection tool; verbal information and consent was used due to literacy levels of caregivers. FGD participants provided informed written consent. The information given to all participants before consenting included the process for data anonymization prior to sharing.

#### Setting

The study was conducted at Mchinji District Hospital, in the central region of Malawi. The hospital provides a secondary level of care, with paediatric and neonatal inpatient wards but limited intensive care capacity. It acts as the main referral facility for the district, which has a population of approximately 600,000, and is mostly rural with a subsistence farming economy. The 2016 Demographic Health Survey reported 10.7% of children under five years were underweight and 32.6% were stunted in Malawi<sup>18</sup>.

#### Quantitative methods

Sampling. Children were recruited using a purposive convenience sampling approach, with the aim to have variation in age, nutritional and HIV status, and equal numbers of those with pneumonia and without pneumonia or another acute infection. We did not conduct a sample size calculation given the exploratory design, but set a pragmatic target of recruiting 50 children with and without pneumonia. Inclusion criteria were being 0-59 months of age and having no previous participation in the study. Children were recruited from the paediatric inpatient ward and outpatient clinic at the hospital (which includes growth monitoring and routine vaccinations). Healthcare workers alerted study staff when children with suspected pneumonia presented and study staff reviewed ward admission notes daily. All children were then screened by study staff for pneumonia using WHO's Integrated Management of Childhood Illnesses (IMCI) guidelines, enhanced with pulse oximetry9. Healthy children were defined as those who did not have any signs of pneumonia or another acute illness, and were not admitted to the paediatric ward (e.g. children presenting for routine vaccination).

*Data collection*. Socio-demographic, clinical, anthropometric, and BIVA data were collected by two clinical study staff (BZ and EK), supported by a clinical officer working in the paediatric ward. Staff underwent one-week of training, including: BIVA measurements, refresher anthropometry training, supervised field testing and piloting. All children underwent a clinical pneumonia examination, followed by the anthropometric and BIVA measurements. Other clinical data was

extracted from the child's routine medical records (e.g. malaria and HIV status). Each of the following anthropometric measurements were taken twice, in immediate succession: weight, length (for children <2 years) or height (for children aged 2–5 years) and mid-upper arm circumference (MUAC). Weight was measured using a Salter scale or standing scale, depending on the child's ability to stand unaided.

BIVA measurements were taken using the BodyStat 1500MDD (BodyStat Ltd, 2016 Body Composition/Wellness Monitoring Unit, Isle of Man, UK) battery operated machine, with the same machine used for all measurements in a single child. The child was positioned on their back, with their arms and legs placed at an angle away the body. Measurements were done on the left side of the body where possible, with sensor pads placed at the testing locations as shown in Figure 1, with the red electrode sensor pad placed first, and then the black electrode sensor pad placed a minimum of 3cm away (Figure 1, Table 1). The following BIVA measurements were taken twice in immediate succession: full body, trunk, and arm. To reduce the movement of children during the measurement, children who were not able to lie calmly were held in place using either a "hugger" (a paediatric immobilizer commonly used for x-rays and scans), or the caregiver held them in position with a folded cotton cloth used as a barrier to the electric current. This pragmatic testing protocol was developed during a piloting period conducted before recruitment for this study, where the influence of movement, electrode position and restraint on measurement results was explored. This resulted in some non-standardised approaches, such as: allowing 3cm between electrodes instead of



1. Full body2. Reduced trunk3. Reduced upper armFigure 1. Bioelectrical impedance vector analysis (BIVA) measurements and electrode placement sites.

	Right cable lead		Left cable lead		
Measurement	Red	Black	Red	Black	Body segment
1	Top of foot (dorsum)	Ankle	Back of hand (dorsal)	Wrist	Whole-body
2	Hip (anterior superior iliac spine)	Hip	Shoulder (acromion)	Shoulder	<b>Reduced trunk</b>
3	Shoulder (acromion)	Shoulder	Elbow (cubital fossa)	Elbow	Reduced upper arm

#### Table 1. Description of electrode placement.

5cm, conducting measurements in a non-temperature-controlled environment, and restricting to two measurements per site (rather than repeating until stable)<sup>19</sup>. All equipment was calibrated at the start of the day, and all assessments were conducted within a private side-room in the paediatric ward of Mchinji District Hospital, equipped with a padded hospital bed. We did not record time of last feeding, and did not require participants to fast, urinate, or have a prolonged period of rest before measurements, given the logistical constraints of the setting and patient population.

The following outputs for BIVA were recorded for each measurement site: phase angle at 50kHz, resistance at 50kHz and reactance at 50kHz. The phase angle was calculated as (reactance/resistance)×(180°/ $\pi$ ); it represents cell mass and cellular health, with higher values hypothesized to reflect higher lean mass and better cell function, hydration, and higher cell membrane integrity<sup>11,14,20</sup>.

*Analysis*. Reliability of BIVA and anthropometric measurements was calculated as the difference between the first and second measurements. All differences between the first and second measurements were converted into positive numbers, and the mean, standard deviation and 95% confidence intervals of the mean for each measure calculated. To investigate the relationship between WAZ, WHZ and MUAC (exposures), and phase angle for the full body, trunk, and arm segments (outcomes) we conducted linear regression adjusted for age and sex<sup>21,22</sup>, and stratified by pneumonia status. We also made a BIVA plot for the full body measurement, using software from Piccoli & Pstori (2002). Children with missing data for any variable were excluded from analyses, as a complete case analysis. Analysis was done using Stata 15.1.

#### Qualitative methods

*Sampling*. The healthcare workers were purposively sampled for the FGDs, with two FGDs planned. The first included community healthcare workers, locally know as Health Surveillance Assistants (HSAs), who had not participated in any other recently on-going pneumonia studies in the district<sup>23</sup>. The second FGD included healthcare workers working at Mchinji District Hospital, but who had not previously participated in the BIVA study. Participants were invited to take part by phone, following approval to leave their posts from the District Health Officer.

*Data collection*. The FGDs were facilitated by a local female nurse (EK, ENM qualification) experienced in qualitative research. FGDs were also attended by the project coordinator, a

male clinical officer (BZ, Diploma qualification), to introduce the project and answer specific questions relating to the BIVA technology. Both EK and BZ had worked on community and facility-based research in Mchinji District and were present in the hospital for the quantitative data collection, they may therefore have had prior interactions with FGD participants in a research capacity. Prior to the discussions, the participants were given a demonstration on how to use the BIVA machine, an explanation of its function and purpose, and the overall purpose of the study.

The discussion followed a structured guide, with the following topics: current malnutrition assessment methods, burden of malnutrition, initial impressions of the device, improvability, and proposed modifications (see *Extended data*<sup>24</sup>). The FGDs were conducted in a mixture of English and Chichewa, based on participant preference and lasted between 25–45 minutes. Discussions were audio recorded following participant consent and then transcribed and translated as a team by BZ and EK (see *Underlying data*. Field notes were not used, and the transcripts were not returned to participants for checking.

Analysis. The data was analysed thematically using framework analysis by HD25. Framework analysis was selected due to its systematic matrix approach to allow comparison between participants' viewpoints. After reading through the transcripts multiple times for familiarization, the transcripts were single coded by HD in their entirety using the freely available OpenCode 4.03 software with supervision from CK. The descriptive codes were summarized into categories, and then into inductive themes relevant for addressing the research aim. The transcripts were then re-read to verify that the analytic framework was still reflective of the transcripts. Transcripts were then indexed, and quotes from the FGD participants were charted into the framework. To cross-validate and triangulate the findings, the final interpretation was discussed and agreed between HD, BZ and CK; we did not seek feedback on our interpretations from participants.

#### Results

#### Quantitative results

Overall, we recruited 52 children (Table 2)<sup>26</sup>. Although the children with and without pneumonia were comparable by sex distribution, the children with pneumonia were younger than the healthy children (mean age in months: 13.53 vs. 28.57, p-value <0.001). The mean phase angle of the children with pneumonia was lower in all three BIVA measurements compared to the children without pneumonia.

	Total (n=52)	Pneumonia cases (n=24)	Healthy children (n=28)
Age in months			
Mean (SD)	21.63 (17.37)	13.53 (11.19)	28.57 (18.84)
<12 months (%)	20 (39)	12 (50)	8 (29)
12–24 months (%)	9 (17)	7 (29)	2 (7)
24–59 months (%)	23 (44)	5 (21)	18 (64)
Gender			
Male (%)	25 (48)	12 (50)	13 (46)
Female (%)	27 (52)	12 (50)	15 (54)
Nutritional Status			
Height-for-age z-score	-0.84 (1.30)	-0.87 (1.19)	-0.81 (1.39)
Weight-for-age z-score	-0.32 (1.26)	-0.44 (1.43)	-0.22 (1.11)
Weight-for-height z-score	0.23 (1.24)	0.07 (1.54)	0.36 (0.92)
Body Mass Index (SD)	16.53 (2.08)	16.51 (2.61)	16.54 (1.55)
Underweight (%)	2 (4)	2 (8)	0 (0)
Wasted (%)	2 (4)	1 (4)	1 (4)
Stunted (%)	8 (15)	3 (13)	5 (18)
Disease Status			
Malaria RDT positive (%)	5 (10)	5 (21)	0 (0)
HIV positive (%)	0 (0)	0 (0)	0(0)
HIV exposed (%)	2 (4)	0 (0)	2 (7)
HIV unknown (%)	3 (6)	3 (13)	0(0)
BIVA*			
Body Phase Angle (°) (SD)	3.65 (0.62)	3.43 (0.48)	3.84 (0.67)
Trunk Phase Angle (°) (SD)	4.96 (1.07)	4.69 (0.87)	5.19 (1.18)
Arm Phase Angle (°) (SD)	4.19 (0.80)	3.99 (0.72)	4.37 (0.83)

#### Table 2. Description of the children measured in the BIVA pilot study.

\*One healthy child was missing the BIVA measurement. SD = Standard Deviation; RDT = rapid diagnostic test.

Table 3 describes the reliability of measurements. Overall, the variation was larger for the children with pneumonia than healthy children for all measures, except weight. For the BIVA measures, the mean difference in the phase angle was similar across the three sites, with a mean difference of  $0.20^{\circ}$  (95% CI: 0.06, 0.34) for full body,  $0.25^{\circ}$  (95% CI: 0.17, 0.34) for the trunk and  $0.29^{\circ}$  (95% CI: 0.18, 0.39) for the arm. Resistance values varied considerably between measurements.

Table 4 shows the adjusted association between WAZ, WHZ and MUAC with the BIVA phase angle, for each of the three BIVA measurements, and Figure 2 presents the full body BIVA plot. The direction of associations between WAZ, WHZ and MUAC exposures and phase angle were negative for all measures in pneumonia cases, with the strongest associations for trunk measurements (WAZ: aCoeff: -0.261; 95%CI: -0.523, 0.001; WHZ: aCoeff: -0.187; 95%CI: -0.452, 0.078; MUAC: aCoeff: -0.044; 95%CI: -0.065, -0.024). With the exception of three analyses (two arm and one trunk), the direction of association was positive for healthy children, but none were statistically significant.

#### Qualitative results

A total of 11 healthcare workers participated in the two FGDs (five in the hospital discussion and 8 in the community

		All Children		Pneumonia cases		Healthy children	
Variable	Range in values	Mean difference (SD)	95% CI	Mean difference (SD)	95% CI	Mean difference (SD)	95% CI
Anthropometry							
Weight (kg)	3.6 - 18.2	0.07 (0.11)	0.04 0.10	0.07 (0.09)	0.03 0.11	0.06 (0.13)	0.02 0.11
Height (cm)	51.3 - 101.6	0.30 (0.82)	0.07 0.53	0.22 (0.19)	0.14 0.29	0.37 (1.11)	-0.63 0.79
MUAC (cm)	103 - 175	1.62 (1.71)	0.84 2.57	1.71 (2.05)	0.84 2.58	1.54 (1.37)	1.00 2.07
BIVA – full body							
Phase angle (°)	2.4 - 6.8	0.20 (0.50)	0.06 0.34	0.20 (0.38)	0.04 0.36	0.21 (0.59)	-0.03 0.44
Resistance (ohm)	549 - 993	19.86 (37.69)	9.26 30.46	23.25 (47.48)	3.20 43.30	16.85 (26.76)	6.26 27.44
Reactance (ohm)	32.6 - 95.5	2.36 (6.28)	0.60 4.12	2.82 (7.18)	-0.22 5.85	1.95 (5.47)	-0.22 4.11
BIVA – trunk segment							
Phase angle (°)	2.5 - 8.2	0.25 (0.29)	0.17 0.34	0.32 (0.29)	0.20 0.44	0.20 (0.28)	0.09 0.31
Resistance (ohm)	72 - 131	1.88 (2.27)	1.24 2.52	2.33 (2.70)	1.19 3.47	1.48 (1.76)	0.78 2.18
Reactance (ohm)	3.8 - 13.1	0.47 (0.50)	0.33 0.61	0.60 (0.47)	0.40 0.79	0.35 (0.51)	0.15 0.55
BIVA – arm segment							
Phase angle (°)	2.3 - 6.1	0.29 (0.37)	0.18 0.39	0.40 (0.47)	0.21 0.60	0.19 (0.23)	0.09 0.28
Resistance (ohm)	103 - 233	6.18 (9.81)	3.42 8.94	10.46 (12.72)	5.08 15.83	2.37 (3.14)	1.13 3.61
Reactance (ohm)	4.6 - 93	1.01 (1.42)	0.61 1.41	1.55 (1.87)	0.76 2.33	0.54 (0.56)	0.31 0.76

#### Table 3. The variation between the first and second measurements of anthropometrics and BIVA measurements.

SD = standard deviation; MUAC = mid-upper arm circumference; CI = confidence interval; BIVA = bio-electrical impedance vector analysis

#### Table 4. Adjusted multivariable linear regression of weightfor-age z-scores and MUAC with BIVA phase angle.

	Pneu	imonia cases	Healt	hy children:		
	Coeff.	95% CI	Coeff.	95% CI		
Weight for age z-score (exposure)						
Full body	-0.039	-0.193, 0.115	0.309	-0.039, 0.658		
Trunk	-0.261	-0.523, 0.001	0.219	-0.170, 0.609		
Arm	-0.047	-0.256, 0.163	-0.023	-0.320, 0.274		
Weight for height z-score (exposure)						
Full body	-0.032	-0.192, 0.128	0.017	-0.342, 0.378		
Trunk	-0.187	-0.452, 0.078	-0.100	-0.533, 0.333		
Arm	-0.029	-0.227, 0.169	0.053	-0.213, 0.319		
Mid-upper arm circumference (exposure)						
Full body	-0.013	-0.028, 0.001	0.004	-0.026, 0.033		
Trunk	-0.044	-0.065, -0.024	0.001	-0.030, 0.033		
Arm	-0.009	-0.030, 0.012	-0.001	-0.025, 0.022		



**Figure 2. Full body BIVA plot.** Plotted using: Piccoli A, Pastori G. BIVA software, Department of Medical and Surgical Sciences, University of Padova, Padova, Italy, 2002.

All models were adjusted for child age and sex

healthcare worker discussion), with all those invited taking part. Through the framework four inductive themes emerged, which are summarized in Box 1: trust in technology, capacity, sustainability, and device usability.

Box 1. Themes and sub-themes from the healthcare worker focus group discussions				
Theme 1: Trust in technology	Theme 2: Capacity			
<ul> <li>HCP Trust <ul> <li>Accurate results</li> <li>BIVA's Reliability</li> <li>Can help more children</li> <li>Potential side-effect</li> </ul> </li> <li>Caregiver Trust <ul> <li>Barriers to trust</li> <li>Increases trust</li> <li>Terminology is key</li> </ul> </li> </ul>	Training - HCP need training - Community Education Resources - Lack of resources Self-Determination - Lacking capacity			
Theme 3: Sustainability	Theme 4: Usability			
Sustained Practice - Distribution of machines - Two measurements instead of three	<i>Easy and Simple</i> Time saving - Simpler than anthropometrics			
Sustained supplies - Maintenance - Running out of batteries/ stickers	Ideas for Improvement - Solar Powered - No electrode stickers			

*Trust in technology*. This theme encompasses the healthcare workers trust and mistrust of the BIVA technology, as well as how they perceived caregivers would accept and trust that appropriate care was being provided.

Based on the demonstration of the BIVA machine, many participants expressed that BIVA would provide an accurate and time saving method to assess the nutritional status of children. There was also trust that with BIVA, malnourished children who are not identified by the current measurements, would be identified given the perception of the device being inherently more accurate.

To the current way of assessing malnutrition sometimes we can measure wrongly and come up with false results and we were telling the child to go home without any help as if the child is ok when in reality the child has a problem, but with this we shall find the real problem (Senior HSA, participant 1)

However, this view was not universal, with some participants expressing hesitation around BIVA due to their lack of knowledge on how is works, and therefore the potential for side effects during measurements. They indicated the need for monitoring and evaluation of the technology to be sure it is trustworthy and safe. Similar to their own concerns, the healthcare workers raised the issue of caregivers being worried the device could cause harm, discussing that if a negative perception or myth around BIVA arose it would then be hard to gain their trust. However, other participants said that it would not only be accepted, but it would increase trust in the health system.

BIVA will give them trust that the health workers are really doing science. Unlike the past they could not trust measuring a child using height board (Senior HSA, participant 2)

The communication and terminology used with caregivers was discussed as a key determining factor of whether they would accept BIVA.

*Capacity*. Capacity emerged in the context of both a barrier and opportunity of BIVA, with the following sub-themes: capacity building through training, increasing capacity through adequate resourcing and self-determination.

Participants in both FGDs voiced the need for education and training on how to use BIVA before they would feel confident. Specifically, the issue of where and how to place the electrodes on the child was addressed by many participants as a something they would need training on. They also voiced the need for community education on BIVA prior to implementation to increase the knowledge of caregivers.

Before we start using it, we need to tell the community, so that when we start using it they will not be surprised, because we informed them, but if we just start without informing them, they will have some fears. (Senior HSA, participant 2)

A reported barrier to current malnutrition assessments was a lack of capacity due to limited resources. This opinion was shared by all participants in the FGD with hospital-based healthcare workers, but wasn't reflected by the HSAs. Many resources were mentioned as being insufficient – time, tools such as a height board or scale, and knowledge. Some participants stated that BIVA has the potential to solve those problems and increase their capacity to assess malnutrition since currently nutritional status is only being measured by one department in the hospital. However, this was based on the participants' assumption that BIVA would be made available in multiple departments.

Where I am it happened that it took three days, no seven days for the child to be assessed, just because you have to delegate to another colleague who is also busy, and they said that it was closed and knocked off, if the resources were available in that department that child could have been assessed and treated carefully. (Nurse Midwife Technician, participant 2)

Related to this was a lack of self-determination, with healthcare workers in the hospital FGD expressing concern that due to the overwhelming workload and lack of resources, other healthcare workers don't make efforts to properly identify and treat malnutrition.

*Sustainability*. The theme of sustainability includes the sustained practice of implementing BIVA as an indicator of malnutrition, and the physical sustainability of the tool itself. For sustained practice, concerns were raised over how many BIVA machines would be available and who would use them. One participant explained that for BIVA to be successful there would need to be a broad distribution of machines in different wards of the hospital.

The overall concern voiced by almost every participant was that necessary resourcing would need to be secured, otherwise the implementation of BIVA would be unsustainable.

My concern will be the life span of BIVA. How long can we use BIVA because sometimes it can come for the program when it comes to an end you find no more supplies which is also a challenge to go back to old ways of assessing malnutrition. I think it has its expiry date as a machine, unlike the [height] board and MUAC. (Senior HSA, participant 4)

The sustainability of the device was reflected by participants raising questions regarding maintenance and fragility. Most participants also pointed out that the BIVA machine needs constant supplies such as batteries and stickers for the electrodes and running out of either would mean the end of implementation. Despite these barriers, participants overall remained positive that if sufficient resources are available, successful implementation would be possible.

**Device usability**. The theme of usability includes healthcare workers' initial reaction to the demonstration, and their ideas to improve the device to make it more user friendly. Almost all participants were positive that the BIVA tool would decrease their workload and be simple to use. For some it wasn't intuitive, but they felt more confident that it would be a useful tool after seeing the demonstration.

Many participants in both FGDs stated that the BIVA tool would be more user friendly than determining malnutrition using z-scores as obtaining the date of birth and interpreting age-specific results is a key implementation barrier.

Instead of using many tools, for example MUAC, height board, you just use one instead of using more, so I put that BIVA is very easy to use it and we can use it effectively (HSA, participant 3)

Several ideas of how the device could be improved were proposed, the main one being to make the device solar powered instead of using batteries. Participants also expressed a preference for re-usable alternative to the sensor stickers, instead of needing to replace the disposable ones. The facilitators had introduced in their demonstration that the manufacturers were considering alternative ways of attaching electrodes, such as bracelets or cuffs, and many participants were supportive. One participant proposed that the BIVA machine could be improved with the addition of audio outputs. Another proposed that the measurements would be simplified if children could remain dressed for measurements, which was put forward as time-saving and would make the procedure more acceptable to caregivers of sick children.

#### Discussion

The aim of this exploratory study was to describe the reliability, clinical utility, and healthcare workers' acceptance of BIVA as a malnutrition measure for children with and without pneumonia. We observed that children with pneumonia had lower phase angle across all three body segment measurements than healthy children, despite other measures of nutrition being relatively similar between the groups. An interesting finding was the negative relationships with BIVA phase angle for trunk measurements in children with pneumonia, which differed from healthy children when adjusted for age and sex. However, traditional anthropometry had less variation between immediately sequential measurements than BIVA, suggesting usability and practical applications within a clinical context may pose challenges.

Healthcare workers expressed trust in this new technology, and thought that BIVA would enable them to diagnose malnutrition more accurately in a time-saving way. This appeared to rest on several assumptions, that the machine's outputs would be easily interpreted, reliable, and would replace other existing assessments. This was not necessarily triangulated in the quantitative data, with more variability than the traditional anthropometric measurements when two measurements were taken sequentially. We also observed higher variation in the group with pneumonia; it's likely this was due to the children being younger overall and so less compliant to lying still without restraint, and possibly increased chest movement from effort of breathing. We also allowed for a 3cm inter-electrode distance, compared to the standard 5cm, to accommodate these smaller children. This concern was noted by study staff that placing the sensor pads in smaller children and those with cannulas in place was challenging and would differentially affect reliability in sicker children. While our piloting suggested the reduction of the inter-electrode difference would not be an issue, given the burden of severe pneumonia is in younger children<sup>3</sup>, a more rigorous evaluation of this deviation from standard testing protocols is needed.

While we saw this variation between measurements, using an average of two sequential measures is common in some clinical practice. A clear protocol would be needed however, for when a third measure might be needed, or a threshold of difference that would be deemed too unreliable for clinical use. For BIVA outputs to be easily interpreted, a population specific reference needs to be created<sup>11</sup>. European studies have collected data on large samples of children to make a theoretical model for "healthy" and "unhealthy" phase angle, and the scalability and generalizability of BIVA's population reference standards varies in literature based on the setting<sup>21,22,27</sup>. Given the epidemiology of child health is dependent on several context-specific factors (e.g. HIV, malaria, anaemia and nutrition),

there would be a need to set not only regional reference standards, but also explore how to differentiate specialized sub-groups, like pneumonia. The fact that BIVA's outputs would need to be interpreted against population specific references was not presented to FGD participants, and this knowledge may have shaped a more negative perception given the issues raised with interpreting weight in relation to age for current malnutrition assessment.

Results from a study investigating severe acute malnutrition in Ethiopian children supports our finding that sick children have a lower phase angle than healthy children; however, this study reported a significantly positive correlation between MUAC and phase angle in severely malnourished children<sup>12</sup>. We found the direction of association differed between those with and without pneumonia for full body and trunk phase angle - where a large part of the tissue volume is the lungs. The pulmonary parenchymal inflammation from pneumonia can result in fluid accumulation in the alveoli and swelling of surrounding lung tissue. Depending upon the underlying pathogen(s) airway inflammation and oedema are also typical. We therefore hypothesize that given electrical current faces less resistance in fluid than other denser tissues, a lower phase angle value of the trunk would be expected in children who have pneumonia. Historically chest radiographs have been considered "the gold standard" for the diagnosis of pneumonia in children, with the aim to identify consolidation. However chest radiography lacks sensitivity in differentiating between bacterial and viral pneumonia, are rarely available in low-resource outpatient settings where the majority of pneumonia burden is seen, and require specialized clinical capacity<sup>28,29</sup>. Therefore, if BIVA can serve a similar function, i.e. indicating fluid in the lungs of sick children, it could provide an alternative differential pneumonia diagnostic that is intended for use at the bedside.

The main concern raised by healthcare workers was in the sustainability of BIVA, and issues with a renewable power supply, maintenance and continued professional development echo those raised around other technologies in this context<sup>23</sup>. Several suggestions for improvement and adaption to this context were proposed and provide a good starting point for further development. However, while healthcare workers were unanimous in their desire for improvements in how they assess malnutrition among children, it is still not clear if their endorsement of BIVA was unbiased. The trust that health care professionals had in the new technology after a description and demonstration was high. A study with high-income health care reported that providers can be hesitant to use new technology however<sup>30</sup>, and the differing perception on welcoming new technology amongst our study participants could stem from the practice of medical device donation. WHO estimate that up to 80% of medical equipment in low-income countries is donated<sup>31</sup>. Recipients of donations may not feel they have an opportunity or may be hesitant to give feedback to donors on their needs, for fear of losing donations or ruining the relationship with the donor<sup>32</sup>. The Malawian health care system is heavily reliant on international donations, and therefore this could create a social desirability bias among the respondents who want to maintain the positive relationship with potential

donors of BIVA machines and research partners. This likely poses a key limitation in our evaluation of acceptability.

This study had two further key limitations, firstly that we recruited fewer children than initially planned and may have led to under-powered analyses. Our original recruitment plan was aiming for age and sex balance between children with and without pneumonia, however, we struggled to recruit older children admitted to the paediatric ward with pneumonia. Despite adjusting for age in the regression models, this may still account for some of the differences observed. Secondly, we were unable to conduct confirmation chest radiographs and other laboratory measures of cellular health, and therefore it's possible that some of the children classified with pneumonia did not have lung consolidation.

In this exploratory project, we found a potentially interesting finding around BIVA's potential clinical utility among children with pneumonia, which warrants further investigation and the creation of population reference standards. The potential for BIVA to be deployed in clinical contexts as a quick and non-invasive indicator of fluid or differential cellular health in the trunk segment of sick children is worth pursuing, given the challenges in accurate pneumonia diagnosis. However, in its current form, the BIVA device is likely to encounter implementation challenges in a low-resource and high-burden setting. Future research is needed to determine real-world prognostic and therefore impact potential of this technology at the bedside.

## Data availability

Underlying data Figshare: BIVA Malawi Project. https://doi.org/10.6084/ m9.figshare.c.6052871<sup>26</sup>.

This project contains the following underlying data:

- BIVA\_anonymous\_analysis.csv (raw data used to conduct the quantitative analysis comparing BIVA and anthropometry measurements).
- BIVA\_DataDictionary.csv (data dictionary for the dataset used to conduct the quantitative analysis comparing BIVA and anthropometry measurements)
- Focus Group Discussion transcripts BIVA Malawi project.pdf (English translated verbatim transcripts used for qualitative analysis)

#### Extended data

Figshare: Bioelectrical impedance vector analysis in Malawi – Supplementary Appendix 1 (FGD topic guide). https://doi.org/ 10.6084/m9.figshare.19801756<sup>24</sup>.

This project contains the following extended data:

• Supplementary Appendix 1.pdf (focus group discussion topic guides).

Data are available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

#### Acknowledgements

We would like to thank the children and caregivers who took part in the study and gave us their time and information. We would also like to thank the District Health Management Team and clinical staff at Mchinji District Hospital, who supported the conduct of the study - in particular the Clinical Officer in charge of the paediatric ward who contributed to patient recruitment and assessment.

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# **Open Peer Review**

# Current Peer Review Status: 🥇 🗸

Version 3

Reviewer Report 05 March 2024

https://doi.org/10.21956/gatesopenres.16780.r36002

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## Steven Brantlov 🔟

Department of Procurement and Clinical Engineering, Central Denmark Region, Aarhus University Hospital,, Olof Palmes Allé 15, 8200, Aarhus, Denmark

No more comments.

Competing Interests: No competing interests were disclosed.

*Reviewer Expertise:* My area of research is within body composition, with special focus on the BIA-technique in clinical practice.

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.

## Version 2

Reviewer Report 23 February 2024

https://doi.org/10.21956/gatesopenres.16532.r35731

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## ? 🛛 Steven Brantlov 🛈

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Please change from PA to PhA throughout the paper. Why use the abbreviation of PhA in the abstract but not in the main text?

#### Introduction:

"BIVA is based on passing small electrical currents through the body, giving an indication of the composition of tissues, which can be interpreted to understand the balance between lean mass and fluid". *This is not correct. Try to adapt following sentence in the introduction section: "Bioelectrical Impedance Vector Analysis (BIVA) is a technique used to analyze bioelectrical impedance data in a vector format. Bioelectrical impedance involves the measurement of the opposition to the flow of an electric current through the body's tissues. BIVA specifically focuses on the vector representation of impedance measurements to assess body composition, e.g., measuring cellular health".* 

#### Methods

Please specify following: BodyStat 1500MDD (BodyStat Ltd, [model name]m [location], [country]).

#### Discussion

Maybe you should discuss the consequences of having an inter-electrode distance of 3cm instead of the recommended distance of 5cm?

Competing Interests: No competing interests were disclosed.

*Reviewer Expertise:* My area of research is within body composition, with special focus on the BIA-technique in clinical practice.

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.

Author Response 26 Feb 2024

**Carina King** 

#### General:

Please change from PA to PhA throughout the paper. Why use the abbreviation of PhA in the abstract but not in the main text?

**Response:** We have removed this abbreviation in the abstract, and checked for any other instances of PA and didn't find any.

## Introduction:

"BIVA is based on passing small electrical currents through the body, giving an indication of the composition of tissues, which can be interpreted to understand the balance between lean mass and fluid". This is not correct. Try to adapt following sentence in the introduction section: "Bioelectrical Impedance Vector Analysis (BIVA) is a technique used to analyze bioelectrical impedance data in a vector format. Bioelectrical impedance involves the measurement of the opposition to the flow of an electric current through the body's tissues. BIVA specifically focuses on the vector representation of impedance measurements to assess body composition, e.g., measuring cellular health".

**Response:** Updated the statement to reflect the suggestion.

## Methods

Please specify following: BodyStat 1500MDD (BodyStat Ltd, [model name]m [location], [country]).

Response: Added

## Discussion

Maybe you should discuss the consequences of having an inter-electrode distance of 3cm instead of the recommended distance of 5cm? **Response:** We have added a more on this to the 2<sup>nd</sup> paragraph of the discussion.

Competing Interests: No competing interests were disclosed.

## Version 1

Reviewer Report 26 October 2023

## https://doi.org/10.21956/gatesopenres.14937.r34818

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## ?

## Steven Brantlov 问

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I would like to express my gratitude for the opportunity to review the manuscript titled "Bioelectrical impedance vector analysis as an indicator of malnutrition in children under five years with and without pneumonia in Mchinji District, Malawi: An exploratory mixed-methods analysis" by Dunning H, Zadutsa B, Kainja E, Colbourn T, McCollum ED, Makwenda C, Wells J, Grijalva-Eternod CS et al.

The study addresses an important topic in malnutrition and the use of BIVA, and I commend the authors for their efforts in conducting this research.

## Summary

The paper explores the use of Bioelectrical Impedance Vector Analysis (BIVA) as a non-invasive method to assess nutritional status in children under five years old, both with and without pneumonia, in Malawi. It investigates the reliability and clinical utility of BIVA measurements, particularly phase angle (PA), and explores the acceptability of this technology among healthcare workers. Results show varying associations between PA and anthropometric measurements, and while healthcare workers are positive about BIVA, implementation challenges are expected.

## General

- Change abbreviation of phase angle from PA to PhA.
- Phase angle is in degrees.
- Resistance and reactance are in ohm.
- BIVA is a tool to analyze impedance data measured with a BIA device, and not a piece of equipment.

## Strengths

- Rigorous study design.
- Clear and comprehensive presentation of data through tables and figures.
- Valuable insights into the use of BIVA in children.

## **Areas for Improvement:**

- Why was a inter electrode distance of 3 cm chosen? In general, there is consensus on an interelectrode distance of min. 5 cm to help reduce interference and improve the accuracy of BIA measurements.
- I miss some specific information about where on the body the electrodes were placed. Figure 1 is good and informative but miss exact location sites of the electrodes.
- Could you provide some more information about how the measurement setup was standardized since this is important for valid and reproducible measurements. Following source are worth studying.

ESPEN GUIDELINES Bioelectrical impedance analysis—part II: utilization in clinical practice, Kyle et al.<sup>1</sup>

Critical factors and their impact on bioelectrical impedance analysis in children: a review, Brantlov et al.<sup>2</sup>

Standardisation of bioelectrical impedance analysis for the estimation of body composition in healthy paediatric populations: a systematic review, Brantlov et al.<sup>3</sup>

• Please provide this information about how you made the BIVA plots.

- The Tables are very informative, but why not provide the reader with a BIVA plot as well. This gives a visual understanding of BIVA plots and strength of presenting impedance data graphically.
- What is meant with "... some participants expressed hesitation around BIVA due to the lack of knowledge on potential side effects or functionality". Please elaborate on this.
- Please elaborate on what is meant by "... life span of BIVA". BIVA is way of presenting impedance data graphically, and not a device. BIVA plots only need in information about resistance and reactance. This can be achieved by several suppliers of BIA devices. Delivery problems should not be a problem.

## Recommendation

Accept if above mentioned is explained and implemented in the paper.

## References

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3. Brantlov S, Jødal L, Lange A, Rittig S, et al.: Standardisation of bioelectrical impedance analysis for the estimation of body composition in healthy paediatric populations: a systematic review.*J Med Eng Technol*. 2017; **41** (6): 460-479 PubMed Abstract | Publisher Full Text

Is the work clearly and accurately presented and does it cite the current literature?  $\ensuremath{\mathsf{Yes}}$ 

## 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?  $\ensuremath{\mathsf{Yes}}$ 

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

Yes

*Competing Interests:* No competing interests were disclosed.

*Reviewer Expertise:* My area of research is within body composition, with special focus on the BIA-technique in clinical practice.

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.

Author Response 11 Dec 2023

## **Carina King**

We would like to thank both reviewers for their constructive and supportive comments. Please find the specific responses and edits detailed below.

#### **Reviewer 1 (APPROVED WITH RESERVATIONS)**

The paper by Dunning and colleagues adds new and interesting data on bio-impedance measurements in acute malnutrition. The authors describe how the associations in phase angle and weight-for-age are affected by pneumonia. However, results are still far away from adding clinical diagnosis in clinical settings.

Thank you for providing this review – we agree that while our results are interesting, more work is needed before determining if this would be a useful clinical application for this technology.

Overall:

What surprised me in the paper, however, is that the authors have chosen to only show associations between PA and WAZ and MUAC, and not with WHZ or BMI for age. Malnutrition in children <5 yrs is still being diagnosed through WHZ and/or MUAC, so it would seem more logical to compare PA with WHZ than with WAZ. Indeed, WAZ is a mixed indicator of both stunting and wasting. Therefore, I would strongly recommended to add these anthropometric indicators to Table 3 (and WHZ to Table 1).

We have now included WHZ score in table 2 and table 4 (note, table numbers have been updated during the revision). Initially we did not use this, as in this particular setting, we felt that healthcare workers were most familiar with MUAC and WAZ as measures of malnutrition.

Abstract:

We planned to recruit: change to "We recruited.."

Done

## Introduction:

Please give the correct definition of wasting :

Wasting is a weight-for-height Z score < -2 AND/OR a mid upper arm circumference <125 mm, with severe wasting present with WHZ<-3 Z score and/or MUAC<115 mm OR nutritional oedema regardless of anthropometry.

• Updated the text.

Discussion:

• It might be good to add a few sentences on the fact that BIVA is to be used in a clinical setting, and not for the early detection of wasting in communities.

- We have edited several sentences in the discussion to try and make this point clearer.
- Also, please add that future research should aim to look at prognostic features of BIVA, that is, whether it can predict negative health outcomes.
  - This is a good point we have added this to the conclusion.

## Reviewer 2 (APPROVED WITH RESERVATIONS)

I would like to express my gratitude for the opportunity to review the manuscript titled "Bioelectrical impedance vector analysis as an indicator of malnutrition in children under five years with and without pneumonia in Mchinji District, Malawi: An exploratory mixed-methods analysis" by Dunning H, Zadutsa B, Kainja E, Colbourn T, McCollum ED, Makwenda C, Wells J, Grijalva-Eternod CS et al. The study addresses an important topic in malnutrition and the use of BIVA, and I commend the authors for their efforts in conducting this research.

The paper explores the use of Bioelectrical Impedance Vector Analysis (BIVA) as a noninvasive method to assess nutritional status in children under five years old, both with and without pneumonia, in Malawi. It investigates the reliability and clinical utility of BIVA measurements, particularly phase angle (PA), and explores the acceptability of this technology among healthcare workers. Results show varying associations between PA and anthropometric measurements, and while healthcare workers are positive about BIVA, implementation challenges are expected.

# Thank you for the considered review, and suggestions for improvement. We have edited the paper throughout to reflect these comments.

#### General

- $\circ~$  Change abbreviation of phase angle from PA to PhA.
  - Done
- Phase angle is in degrees.
  - Clarified in the text
- Resistance and reactance are in ohm.
  - Clarified in the text
- BIVA is a tool to analyze impedance data measured with a BIA device, and not a piece of equipment.
  - Thank you for making this clarification we defaulted to calling the device the "BIVA machine" in the project for simplicity around communication, and this therefore got reflected here. Given this is the way we presented the machine to FGD participants, and its therefore referred to as BIVA in the quotes, we have clarified this distinction in the text.

#### Strengths

- Rigorous study design.
- Clear and comprehensive presentation of data through tables and figures.
- Valuable insights into the use of BIVA in children.
  - Thank you for recognising these strengths!

Areas for Improvement:

- Why was a inter electrode distance of 3 cm chosen? In general, there is consensus on an interelectrode distance of min. 5 cm to help reduce interference and improve the accuracy of BIA measurements.
  - We did a pilot testing phase before this recruitment, to adapt BIA protocols to the setting and patient group. Part of this project's aim was to see how to make a testing protocol as pragmatic as possible, and we tested several assumptions around movement, methods for restricting movement, and electrode placement. These results have not been published. During this testing, we found that 5cm sometimes would not fit all the electrodes for the arm measure in the youngest children, that 3cm was approximately 2 fingers width (acting as a pragmatic marker versus using measuring tape in an agitated and moving infant) and crucially did not materially change results during piloting. I've added a clarification in the text around this.
- I miss some specific information about where on the body the electrodes were placed. Figure 1 is good and informative but miss exact location sites of the electrodes.
  - We've added a new Table 1, taken from our Standard Operating Procedure, which has the physiological feature that was used to place the red sensor pads.
- Could you provide some more information about how the measurement setup was standardized since this is important for valid and reproducible measurements.
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  - ESPEN GUIDELINES Bioelectrical impedance analysis—part II: utilization in clinical practice, Kyle et al.<sup>1</sup>
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  - Standardisation of bioelectrical impedance analysis for the estimation of body composition in healthy paediatric populations: a systematic review, Brantlov et al.<sup>3</sup>
  - Thank you for sharing these references we have gone through the items recommended for reporting in reference 3, and added missing information in the paper.
- Please provide this information about how you made the BIVA plots. The Tables are very informative, but why not provide the reader with a BIVA plot as well. This gives a visual understanding of BIVA plots and strength of presenting impedance data graphically.
  - We have now added a BIVA plot for the full body measurement, and referenced the software used.
- What is meant with "... some participants expressed hesitation around BIVA due to the lack of knowledge on potential side effects or functionality". Please elaborate on this.
  - This reflected the fact that when presenting BIVA, we explained that it involved electrical currents. Given the novelty of this technology in this setting, healthcare workers were understandably concerned that this might be dangerous, misunderstood, or have side effects, and lacked a full

appreciation for how this technology could lead to a measure of cellular health and nutrition. We edited this sentence to make this clearer.

- Please elaborate on what is meant by "... life span of BIVA". BIVA is way of presenting impedance data graphically, and not a device. BIVA plots only need in information about resistance and reactance. This can be achieved by several suppliers of BIA devices. Delivery problems should not be a problem.
  - As elaborated above, we used the term BIVA in this context to the refer to the machine, and have clarified this in the text. In this case, the healthcare workers were referring to the durability of the device.

*Competing Interests:* No competing interests were disclosed.

Reviewer Report 22 September 2022

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## ?

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The paper by Dunning and colleagues adds new and interesting data on bio-impedance measurements in acute malnutrition. The authors describe how the associations in phase angle and weight-for-age are affected by pneumonia. However, results are still far away from adding clinical diagnosis in clinical settings.

What surprised me in the paper, however, is that the authors have chosen to only show associations between PA and WAZ and MUAC, and not with WHZ or BMI for age. Malnutrition in children <5 yrs is still being diagnosed through WHZ and/or MUAC, so it would seem more logical to compare PA with WHZ than with WAZ. Indeed, WAZ is a mixed indicator of both stunting and wasting. Therefore, I would strongly recommended to add these anthropometric indicators to Table 3 (and WHZ to Table 1).

Some minor comments:

## Abstract:

• We planned to recruit: change to "We recruited.."

Introduction:

• Please give the correct definition of wasting :

Wasting is a weight-for-height Z score < -2 AND/OR a mid upper arm circumference <125 mm, with severe wasting present with WHZ<-3 Z score and/or MUAC<115 mm OR nutritional oedema regardless of anthropometry.

Discussion:

- It might be good to add a few sentences on the fact that BIVA is to be used in a clinical setting, and not for the early detection of wasting in communities.
- Also, please add that future research should aim to look at prognostic features of BIVA, that is, whether it can predict negative health outcomes.

Is the work clearly and accurately presented and does it cite the current literature?  $\ensuremath{\mathsf{Yes}}$ 

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?  $\ensuremath{\mathsf{Yes}}$ 

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

Are all the source data underlying the results available to ensure full reproducibility?  $\ensuremath{\mathsf{Yes}}$ 

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

**Reviewer Expertise:** malnutrition ; stunting ; child health ; low- and middle income countries ; local produced ready to use foods ; micronutrient deficiencies

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.

Author Response 11 Dec 2023

#### **Carina King**

We would like to thank both reviewers for their constructive and supportive comments. Please find the specific responses and edits detailed below.

## Reviewer 1 (APPROVED WITH RESERVATIONS)

The paper by Dunning and colleagues adds new and interesting data on bio-impedance measurements in acute malnutrition. The authors describe how the associations in phase angle and weight-for-age are affected by pneumonia. However, results are still far away from adding clinical diagnosis in clinical settings.

Thank you for providing this review – we agree that while our results are interesting, more work is needed before determining if this would be a useful clinical application for this technology.

## Overall:

What surprised me in the paper, however, is that the authors have chosen to only show associations between PA and WAZ and MUAC, and not with WHZ or BMI for age. Malnutrition in children <5 yrs is still being diagnosed through WHZ and/or MUAC, so it would seem more logical to compare PA with WHZ than with WAZ. Indeed, WAZ is a mixed indicator of both stunting and wasting. Therefore, I would strongly recommended to add these anthropometric indicators to Table 3 (and WHZ to Table 1).

We have now included WHZ score in table 2 and table 4 (note, table numbers have been updated during the revision). Initially we did not use this, as in this particular setting, we felt that healthcare workers were most familiar with MUAC and WAZ as measures of malnutrition.

Abstract:

- We planned to recruit: change to "We recruited.."
  - Done

Introduction:

• Please give the correct definition of wasting :

Wasting is a weight-for-height Z score < -2 AND/OR a mid upper arm circumference <125 mm, with severe wasting present with WHZ<-3 Z score and/or MUAC<115 mm OR nutritional oedema regardless of anthropometry.

• Updated the text.

Discussion:

- It might be good to add a few sentences on the fact that BIVA is to be used in a clinical setting, and not for the early detection of wasting in communities.
  - We have edited several sentences in the discussion to try and make this point clearer.
- Also, please add that future research should aim to look at prognostic features of BIVA, that is, whether it can predict negative health outcomes.
  - This is a good point we have added this to the conclusion.

## Reviewer 2 (APPROVED WITH RESERVATIONS)

I would like to express my gratitude for the opportunity to review the manuscript titled "Bioelectrical impedance vector analysis as an indicator of malnutrition in children under five years with and without pneumonia in Mchinji District, Malawi: An exploratory mixedmethods analysis" by Dunning H, Zadutsa B, Kainja E, Colbourn T, McCollum ED, Makwenda C, Wells J, Grijalva-Eternod CS et al. The study addresses an important topic in malnutrition and the use of BIVA, and I commend the authors for their efforts in conducting this research.

The paper explores the use of Bioelectrical Impedance Vector Analysis (BIVA) as a noninvasive method to assess nutritional status in children under five years old, both with and without pneumonia, in Malawi. It investigates the reliability and clinical utility of BIVA measurements, particularly phase angle (PA), and explores the acceptability of this technology among healthcare workers. Results show varying associations between PA and anthropometric measurements, and while healthcare workers are positive about BIVA, implementation challenges are expected.

Thank you for the considered review, and suggestions for improvement. We have edited the paper throughout to reflect these comments.

General

- Change abbreviation of phase angle from PA to PhA.
  - Done
- Phase angle is in degrees.

• Clarified in the text

- Resistance and reactance are in ohm.
   Clarified in the text
- BIVA is a tool to analyze impedance data measured with a BIA device, and not a piece of equipment.
  - Thank you for making this clarification we defaulted to calling the device the "BIVA machine" in the project for simplicity around communication, and this therefore got reflected here. Given this is the way we presented the machine to FGD participants, and its therefore referred to as BIVA in the quotes, we have clarified this distinction in the text.

## Strengths

- Rigorous study design.
- Clear and comprehensive presentation of data through tables and figures.
- Valuable insights into the use of BIVA in children.
  - Thank you for recognising these strengths!

Areas for Improvement:

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