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# **BMJ Open**

#### Association between cardio-metabolic risk factors and body mass index, waist circumferences and body fat in a Zanzibari cross-sectional study

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## 26 Abstract

Objectives: To determine the prevalence of obesity indices (body mass index (BMI), waist circumference (WC), body fat percent (BF%)) and cardio-metabolic risk factors. To investigate the association between obesity indices and cardio-metabolic risk factors in a Zanzibari population.

**Designs:** Cross-sectional study.

Settings: Participants randomly selected from 80 Shehias (wards) in Unguja, Zanzibar in
2013.

Participants: A total of 470 participants between 5-95 years were examined. Data on socioeconomic status, area of residence, anthropometry and venous blood were collected.
Associations between obesity indices and cardio-metabolic risk factors were investigated
using multilevel logistic regression analyses.

**Results:** The proportion of overweight/obese individuals was 26.4%, high WC (24.9%) and high BF% (31.1%). Cardio-metabolic risk factors with highest prevalence of abnormal values included hypertension (24.5%), low HDL-C (29.4%), high HDL-C (21.3%) and high HbA1c (19.1%). Obesity and hypertension increased with age, most prevalent in participants above 45 years of age. Low-HDL-C was most prevalent among participants  $\geq 18$  to < 45 years old, while high LDL-C was more prevalent above 45 years. BMI, WC and BF% were associated with hypertension (OR=2.41 (1.33, 4.47); OR=3.68 (1.81, 7.52); OR=2.51 (1.40, 4.51), respectively). High WC or high BF% was associated with higher chances of high levels of LDL-C (OR=2.52 (1.24, 5.13), OR=1.91 (1.02, 3.58), respectively). Additionally, BMI and WC were associated with levels of HbA1c (OR=2.08 (1.15, 3.79), OR=3.01 (1.51, 6.03), respectively). Considering obesity indices within one regression model, only high WC was associated with higher chances for hypertension (OR=2.62 (1.14, 6.06)) and for high levels of HbA1c (OR=2.62 (1.12, 6.15)). Conclusion: High BMI, WC and BF% were strongly 

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2 3	51	associated with hypertension, individuals with high WC were twice more likely to have
4 5	52	hypertension. Overweight/obesity and cardio-metabolic risk factors were highly prevalent in
6 7 8	53	the present study population which calls for early and effective screening strategies for this
9 10	54	population.
11 12	55	
13 14	56	Key words: hypertension, diabetes, children, adolescents, adults, sub-Saharan Africa
15 16 17 18	57	
19 20	58	Strengths and limitations of this study
21 22		
23 24	59	• This is the first study to report the associations between obesity indices with cardio-
25 26	60	metabolic risk factors in Zanzibar.
27 28	61	• The household-based approach, which involved visiting the families in the home setting,
29 30	62	resulted in a high individual response rate, thus minimise risk of selection bias
31 32	63	• The cross-sectional design hindered us from concluding the impact of changes in obesity
33 34 35	64	indices on risk factors
36 37	65	• Bioelectrical Impedance Analysis (BIA) was used to estimate body fat percentage which
38 39	66	might have underestimated adiposity in children.
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## 68 Introduction

Worldwide, cardiovascular diseases (CVDs) are the leading cause of death in individuals above 45 years of age<sup>1</sup> at least three quarters of the world's deaths from CVDs occur in low-and-middle-income countries (LMIC)<sup>2</sup> and CVDs are emerging as notable public health problem in sub-Saharan Africa<sup>3</sup>. These countries are undergoing epidemiological transition from communicable to non-communiable diseases (NCDs), which has been closely linked to increased urbanization and rural-urban migration which leads to unhealthy behaviours including poor dietary habits and sedentary lifestyles <sup>3 4</sup>. Most LMIC are dealing with a double burden of coexistance of underweight children and overweight/obese adults<sup>5</sup>, thus making it particulary difficult for policy makers to address the diverse population needs. Obesity is one of the global public health problems that is associated with CVDs <sup>6</sup>. Data from mainland Tanzania showed increasing prevalence of overweight and obesity in urban, peri-urban and rural areas <sup>7</sup>. According to the International Diabetes Federation (IDF) about 12 million people are estimated to have type 2 diabetes mellitus in Africa<sup>8</sup>, where the prevalence ranged from 1% in rural Uganda to 12 % in urban Kenya <sup>9 10</sup>. Overweight and obesity have been identified to be modifiable risk factors for cardio-metabolic and other chronic diseases <sup>11</sup> including hypertension <sup>12</sup>, diabetes <sup>13</sup> and dyslipidemia <sup>14</sup>. Previous research <sup>15 16</sup> reported that both total body fat and adipose tissue distribution were associated with cardio-metabolic risk. Previous studies from sub-Saharan African countries described high prevalences of obesity and cardio-metabolic risk factors in adults in rural and urban areas <sup>11</sup>. Also associations between cardio-metabolic risk factors and socio-economic status (SES), urbanisation and lifestyle patterns in adults were found to be low  $^{3}$ . However, there is still a dearth of pupulation-based studies in sub-Saharan Africa investigating these associations with multiple cardio-metabolic risk factors and different obesity indices including body fat percent, e.g. in both Tanzania mainland and Zanzibar Island.

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Thus, based on cross-sectional data of 470 individuals between 5-95 years recruited in 2013 in Unguja Island, Zanzibar, this study first describes the prevalence of overweight/obesity and cardio-metabolic risk factors in three age groups ( $\geq 5$  to <18 years,  $\geq 18$  to <45 years and above 45 years), and secondly investigates the association of BMI, WC and BF% with cardio-metabolic risk factors (hypertension, total cholesterol, triglycerides, high-density-lipoprotein, low-density-lipoprotein, Glycated HbA1c, fasting plasma glucose and HOMA-IR) considering either three obesity indices independently as well as BMI, WC, and BF% combined reflecting different aspects of body composition. Toeer terier only

## Subjects and Methods

#### 103 <u>Study population and design</u>

We conducted a cross-sectional survey from September to December 2013 in a representative population sample in Unguja Island, Zanzibar. A total of 239 households were randomly selecetd and all household members were invited for the examination. 1,443 family members were willing to participate and completed anthropometric and blood pressure measurements, interviewer-administered questionnaires, collection of morning spot urine and venous blood; detailed subgroup examinations were described below. The complete description of the study design and methods has been described in detail elsewhere <sup>17</sup>. The study was performed according to the Helsinki Declaration and the study protocol was evaluated and approved by the Ethics Committees of the University of Bremen and of the Zanzibar Ministry of Health and the Zanzibar Medical Research and Ethics Committee. All participants gave a written consent and parents/guardians gave a written consent on behalf of their children.

#### 116 Patient and Public Involvement

117 Patients were not involved in this study.

#### 119 Questionnaires and anthropometric measurements

Questionnaires were developed in English, translated into Swahili, and then back-translated to controll for translation errors. Parents reported age and sex of their children and of themselves. Age was grouped into three categories  $\geq 5$  to <18 years,  $\geq 18$  to <45 years and 45 years and above. In addition, their highest educational level according to the International Standard Classification of Education (ISCED)<sup>18</sup> was used as a proxy indicator for socioPage 7 of 26

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economic status (SES) of the family and categorized into low education (no education and primary school) and high education (secondary school and above). For assessing area of residence of the participants, information on region, district and Shehia (the smallest administrative unit in Zanzibar) were recorded and two categories for area of residence were developed (urban and rural). For quality data collection, this study used proven examination methods and laboratory standards <sup>19 20</sup>. All anthropometric measurements and physical examinations were adopted from the IDEFICS Study and conducted following standardized procedures <sup>21 22</sup>. Measurement of body weight was carried out to the nearest 0.1kg and body fat percent was determined using bioelectrical impedance analysis (BIA) method using an electronic scale (TANITA BC-420 SMA, Germany). Height was measured using (SECA 213 stadiometer. UK) and waist circumference (WC) was measured using an inelastic measuring tape (SECA 201) midway between the lowest rib and the iliac creast, all measurements were taken over light clothing and on standing position and were recorded to the nearest 0.1cm. The complete description of the anthropometric measurements of the study have been described elsewhere <sup>17</sup>. 

For children and adolescents, Body Mass Index (BMI) was calculated as kg/m<sup>2</sup> and then transformed to age-and sex-specific z-score and percentiles as well as categories for overweight (BMI between >75<sup>th</sup> and <95<sup>th</sup> percentile) and obesity (BMI >95th percentile) according to the WHO centile curves <sup>23 24</sup>. For adults, overweight/obesity was defined as BMI  $\geq$ 25kg/m<sup>2</sup> as recommended by WHO <sup>25</sup>. Considering waist circumference (WC), high abdominal obesity was defined as (WC  $\ge 90^{\text{th}}$  percentile) for children below 10 years <sup>26</sup>, WC  $>90^{\text{th}}$  percentile for adolescents below 16 years and WC >94 cm for men and > 80 cm for women for participants above 16 years as recommended by IDF<sup>27</sup>. Body fat percentage (BF%) was categorized as high according to the  $\geq$ 85th percentile with regard to boys and girls below 18 years as recommended by McCarthy et al.<sup>28</sup>. For adults above 18 years, high 

BF% was categorised as ≥20 for men and ≥32 for women <sup>29</sup>. The cut-offs and references are
listed in Table 1 below.

#### 153 <u>Cardio-metabolic risk factors</u>

Fasting blood samples were collected from all eligible participants over 5 years of age by venepuncture <sup>30</sup>, detailed procedures about the collection, processing and storage of blood samples are described elsewhere <sup>17</sup>. Anthropometric measurements and collection of venous blood was carried out in fasting status and processed according to international standards<sup>20</sup>. Not being in fasting status was recorded using anthropometry documentation sheet. Metabolic parameters were categorized for investigating the prevalence of cardio-metabolic disorders in the study population. Due to the wide range of age groups in this study population, different cardio-metabolic risk definitions and cut-offs were used (Table 1). Cardio-metabolic risk for children between 5-10 years was defined according to age-sex-specific cut-offs including hypertension (Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP)), blood lipids (high Total Cholesterol (TC), high Trigylcerides (TG), Low-Density-Lipoprotein Cholesterol (LDL-C) and High-Density-Lipoprotein Cholesterol (HDL-C)) and blood glucose/insulin (Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) and elevated Fasting Plasma Glucose (FPG) were defined according to the IDEFICS Study <sup>26 31</sup> and Glycated hemoglobin (HbA1c) was defined according to Rodoo et al. <sup>32</sup> for children under 17 years. For children, adolescence and adults from 10 years and above, hypertension was defined according to age-sex-specific cut-offs as recommended <sup>33</sup> we used this cut-off for children between 10 and 18 years only and for adult above 18 years hypertension was defined as recommended <sup>34</sup>. Blood lipids (TC and LDL-C) were defined according to National Cholesterol Education Program (NCEP)<sup>35</sup> and TG, HDL-C and FPG 

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were defined according to International Diabetes Federation (IDF) <sup>27</sup>. HbA1c for adults above 17 years was defined according to Stern et al. <sup>36</sup> and insulin resistance was estimated as HOMA-IR according to reference value of HOMA-IR as recommended by Shashaj et al. <sup>37</sup>. In the present study, 75<sup>th</sup> percentile cut-off was used for children and adolescents from 10 till 178 17 years and for participants above 17 years, HOMA-IR was defined according to von Eyben et al <sup>38</sup>. HOMA-IR was calculated from glucose (mmol/l)) and insulin ( $\mu$ U/ml) concentrations using the formula: HOMA-IR=(fasting insulin×fasting glucose/22.5)<sup>39</sup>.

181 Table 1. Cardio-metabolic risk definitions and references

Age group	Obesity Indices and Blood Pressure	Blood lipids	Blood Glucose/Insulin
Children:	BMI $\geq 75^{\text{th}}$ percentile <sup>1</sup>	TC $\ge 90^{\text{th}}$ percentile <sup>2</sup>	HbA1c $\ge$ 97.5 <sup>th</sup> percentile <sup>10</sup>
≤10y	WC $\ge 90^{\text{th}}$ percentile <sup>2</sup>	TG $\ge 90^{\text{th}}$ percentile <sup>2</sup>	HOMA-IR $\ge 95^{\text{th}}$ percentile <sup>2</sup>
	BF $\% \ge 85^{\text{th}}$ percentile <sup>3</sup>	HDL-C $\leq 10^{\text{th}}$ percentile <sup>2</sup>	$FPG \ge 95^{th}$ percentile <sup>2</sup>
	SBP $\ge 90^{\text{th}}$ centile or DBP $\ge 90^{\text{th}}$ centile <sup>2</sup>	$LDL \ge 90^{\text{th}}$ percentile <sup>2</sup>	
Adolescents:	BMI $\geq 75^{\text{th}}$ percentile <sup>1</sup>	TC $\geq$ 5.2 mmol/L <sup>6</sup>	HbA1c $\ge$ 97.5 <sup>th</sup> percentile <sup>10</sup>
>10 to	WC $\ge 90^{\text{th}}$ percentile <sup>4</sup>	$TG \ge 1.7 \text{mmol/L}^4$	HOMA-IR $\geq$ 75 <sup>th</sup> percentile <sup>9</sup>
<16 y	BF $\% \ge 85^{\text{th}}$ percentile <sup>3</sup>	HDL-C < 1.03 <sup>4</sup>	$FPG \ge 5.6 \text{mmol/L}^4$
	SBP≥140mmHg or DBP≥90mmHg <sup>11</sup>	$LDL \ge 3.4 \text{mmol/L}^{6}$	
Adults:	$BMI \ge 25 \text{ kg/m}^1$	TC $\geq$ 5.2 mmol/l <sup>6</sup>	$HbA1c \ge 6.1\%^{5}$
≥16y	WC $\ge$ 94 cm male, $\ge$ 80cm female <sup>4</sup>	$TG \ge 1.7 \text{mmol/L},^4$	HOMA-IR >4.65 or HOMA IR >3.60 and BMI >27.5 kg/m <sup>27</sup>
	BF % $\geq$ 20 male and $\geq$ 32 female <sup>8</sup>	HDL-C < 1.03 male,< 1.29 female <sup>4</sup>	$FPG \ge 5.6 mmol/L^4$
	SBP≥140mmHg or DBP≥90mmHg <sup>12</sup>	$LDL \ge 3.4 \text{mmol/L}^{6}$	

182 183 1 WHO

184 2 IDEFICS Study

185 3 McCarthy, H.D., et al. (2006)

18	5 4 IDF
18	5 Stern, S.E., et al (2003) for adults above 17 years
18	8 6 NCEP
18	9 7 von Eyben, F.E., et al (2005)
19	0 8 Gallagher, D., et al (200)
19	9 Shashaj et al. (2015) for children and adolescence under 17 years
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19	11, 12 National Institute of Health 3 <sup>rd</sup> and 7 <sup>th</sup> report respectively
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19	5 <u>Inclusion criteria for study sample</u>
10	<u>inclusion enterna for study sumpte</u>
19	6 Out of 1,443 individuals who participated in this study, 1,314 fullfilled the inclusion criteria
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19	7 (age, sex, weight, height) for the oeverall study analysis. Of the 1,314 participants, 1,234
19	8 provided complete waist circumference and body fat percent measurements. Among those,
19	557 provided complete blood samples for the cardio-metabolic risk analysis and out of those
20	only 505 were on fasting status. Top 1% was excluded for cardio-metabolic risk and obesity
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20	1 indices variables with high extreme values, thus remaining with a complete sample size of
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20	2 470 participants included in the analysis.
20	2 470 participants included in the analysis.
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#### Statistical analysis

Descriptive analyses were conducted to calcuate mean standard deviation (SD) and range (minimum, maximum) for continuous variables as well as distribution of the categorical data in N and percentages (%). Mixed logistic regression models were used to analyse the association between obesity indices and cardio-metabolic risk factors. In addition, potential clustering within households was considered in terms of a random intercept. Following the hierarchy of the municipal structure in Zanzibar, we conducted sensitivity analysis modeling either shehias or households within shehias as a random intercept in the models. Since results of the models showed only marginal differences, we only considered household as a random intercept in our analyses. First, logistic regression models were calculated separately for each obesity indicator (BMI, WC and BF%) as exposure variables against each of the risk factors

(hypertension, TC, TG, HDL-C, LDL-C, HbA1C, FPG and HOMA-IR) as dependent variables. Since BMI, WC and BF% are interrelated, their predictive power on cardio-metabolic risk factors was investigated in a regression model considering all obesity indices against each of the risk factors. All models were adjusted for potential confounders such as gender, age, education level (ISCED) and area of residence, while with regard to hypertension, utilization of medication was also included in the analysis. Statistical analyses were performed using SAS 9.3 (SAS Institute. Cary. NC. U SA) and particularly mixed logistic regression models were conducted based on the GLIMMIX procedure. Tore to the only

## **Results**

#### 225 <u>Characteristics of study population</u>

General characteristics of the study sample (N=470) are described in Table 2. Mean age was 29 ( $\pm$ 18) years with the highest proportion of participants from the age group ( $\geq$ 18 to <45 years). The overall mean BMI was 22 ( $\pm$  5.2)kg/m<sup>2</sup>, WC was 75 ( $\pm$  16) cm and BF% was 22  $(\pm 11)$  %, the mean BMI 26  $(\pm 5.7)$ kg/m<sup>2</sup> for participants above 45 years was slightly higher than normal indicating overweight. Mean diastolic blood pressure was on normal range for all the age groups, a higher mean value of systolic blood pressure 150 ( $\pm$  280)mmHg was observed among participants above 45 years. The mean values of most of the variables showed an increase with age group except for HDL-C and diabetes markers (HbA1c, serum insulin, plasma glucose and HOMA-IR) which showed no specific trend.

#### Table 2: characteristics of study population (n=470) in terms of means and standard deviation

	$\geq 5$ to $<18$	5	$\geq 18$ to <4			years	Tot	
	(n=16		(n=1			110)	(n=4	/
	Mean	Range	Mean	Range	Mean	Range	Mean	Range
	(SD)		(SD)		(SD)		(SD)	
Age (years)	12 (3.4)	4.9 -18	28 (8.1)	18-44	57 (9.8)	45-95	29 (18)	4.9-95
BMI (kg/m)	17 (3.4)	11-34	23 (4.5)	16-37	26 (5.7)	15-49	22 (5.7)	11-49
WC (cm)	61 (11)	12-103	79 (12)	37-111	88 (0.2)	35-126	75 (16)	12-126
BF (%)	15 (7.0)	1.6-45	23 (11)	3.0-53	28 (10)	6.2-53	22 (11)	1.6-53
DBP (mmHg)	67 (9.8)	44-97	76 (10)	53-126	88 (15)	62-140	75 (14)	44-140
SBP (mmHg)	110 (13)	69-152	123 (16)	72-197	150 (28)	100-229	125 (24)	69-229
TC (mmol/l)	3.7 (0.7)	1.8-5.9	3.9 (0.8)	2.1-6.0	4.2 (0.8)	0.2-5.9	3.9 (0.8)	0.2-6.0
TG (mmol/l)	0.8 (0.3)	0.3-2.5	0.9 (0.4)	0.0-2.6	1.0 (0.4)	0.4-2.7	0.9 (0.4)	0.0-2.7
HDL-C (mmol/l)	1.4 (0.5)	0.7-3.3	1.5 (0.5)	0.6-3.7	1.4 (0.4)	0.6-3.6	1.4 (0.5)	0.6-3.7
LDL-C (mmol/l)	2.3 (0.9)	0.0-5.0	2.5 (0.9)	0.7-5.1	3.0 (1.0)	0.6-5.1	2.5 (1.0)	0.0-5.1
HbA1c (%)	5.7 (0.5)	4.2-8.5	5.6 (0.6)	3.9-9.4	6.0 (0.8)	4.4-10	5.8 (0.6)	3.9-10
Serum Insulin (mmol/l)	4.3 (3.1)	0.4-18	4.8 (2.8)	0.8-17	3.6 (2.3)	0.4-17	4.4 (2.8)	0.4-18
FPG (mmol/l)	4.9 (0.8)	2.0-7.7	4.8 (0.9)	0.5-9.4	5.1 (1.3)	0.2-13	4.9 (1.0)	0.2-13
HOMA-IR	1.0 (0.7)	0.1-4.6	1.1 (0.7)	0.0-4.3	0.9 (0.6)	0.0-4.0	1.0 (0.7)	0.0-4.6

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236 (SD) and range.

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#### 238 <u>Distribution of obesity and cardio-metabolic risk in the study population by age groups</u>

Table 3 shows the distribution of obesity markers and cardio-metabolic risks by age-group. Of the 470 participants, more than half were women 52.6% (n=247). The overall proportion of overweight/obesity with regard to BMI, WC and BF % was 26.4%, 24.9% and 31.1% respectively and increased with age, where the highest proportions were observed in participants above 45 years. We observed different trends in the prevalence of metabolic parameters and hypertension across age groups: the prevelance of hypertension, total cholesterol, LDL-C and HbA1c increased with age except for trigylcerides and HOMA-IR which decreased with age. The most prevalent factors were reduced HDL-C (29.4%), hypertension (24.5%), raised LDL-C (21.3%) and HbA1c levels (19.1%). Hypertension, LDL-C and HbA1c were more prevalent in participants above 45 years, and low HDL-C was most prevalent among  $\geq 18$  to <45 year olds. 

Table 3: Distribution of obesity and cardio-metabolic risk in the study population by agegroup, n=470.

			≥18 to years	<45	45+ y	ears	Total	
	n	(%)	n	(%)	n	(%)	n	(%)
All	165	(100)	195	(100)	110	(100)	470	(100)
Gender								
Male	85	(51.5)	86	(44.1)	52	(47.3)	223	(47.4)
Female	80	(48.5)	109	(55.9)	58	(52.7)	247	(52.6)
<b>Obesity Indices</b>								
BMI								
Underweight	83	(50.3)	29	(14.9)	9	(8.18)	121	(25.7)
Normal weight	73	(44.2)	106	(54.4)	46	(41.8)	225	(47.9)
Overweight/obese	9	(5.45)	60	(30.8)	55	(50.0)	124	(26.4)
Waist circumference								
Normal	165	(100)	141	(72.2)	47	(42.7)	353	(75.1)

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	≥5 to years		≥18 to years	≥18 to <45 years		ears	Total	
	n	(%)	n	(%)	n	(%)	n	(%)
High <sup>a</sup>	0	(0)	54	(27.7)	63	(57.3)	117	(24.9
Body fat %								
Normal	157	(95.2)	121	(62.1)	46	(41.8)	324	(69.0
High <sup>b</sup>	8	(4.86)	74	(37.9)	64	(58.2)	146	(31.1
Hypertension								
Normal	123	(74.5)	76	(39.0)	10	(9.09)	209	(44.5
Pre-hypertension	25	(15.8)	89	(45.6)	31	(28.2)	146	(31.1
Hypertension	16	(9.70)	30	(15.4)	69	(62.7)	115	(24.5
Dyslipidaemia <sup>c</sup>								
Total cholesterol								
Normal	161	(97.6)	183	(93.8)	102	(92.7)	446	(94.9
High	4	(2.42)	12	(6.15)	8	(7.27)	24	(5.11
Triglycerides								
Normal	157	(95.2)	186	(95.4)	105	(95.5)	448	(95.3
High	8	(4.85)	9	(4.62)	5	(4.55)	22	(4.68
HDL-cholesterol								
Normal	126	(76.4)	128	(65.6)	78	(70.9)	332	(70.5
Low	39	(23.6)	67	(34.4)	32	(29.1)	138	(29.4
LDL-cholesterol					•			
Normal	141	(85.5)	163	(83.6)	66	(60.0)	370	(78.7
High	24	(14.5)	32	(16.4)	44	(40.0)	100	(21.3
Diabetes Markers <sup>d</sup>								
HbA1C								
Normal	142	(86.1)	166	(85.1)	72	(65.5)	380	(80.9
High	23	(13.9)	29	(14.9)	38	(34.5)	90	(19.1
Plasma glucose								
Normal	136	(82.4)	167	(85.6)	88	(80.0)	391	(83.2
High	29	(17.6)	28	(14.4)	22	(20.0)	79	(16.8
HOMA-IR								
Normal	162	(98.2)	193	(99.0)	109	(99.1)	464	(98.7
High	3	(1.82)	2	(1.03)	1	(0.91)	6	(1.28

<sup>a</sup> High WC was defined as WC  $\ge 90^{\text{th}}$  percentile for children under 10y <sup>26</sup>. Adolescents 

between 10-16 years and adults above 16 years WC > 94 cm for men and > 80 cm for women according to IDF cut-off <sup>27</sup> 

<sup>b</sup> High BF% for adults (overweight/obese) $\geq$  20 for men and  $\geq$ 32 for women according to (NIH/WHO) BMI guidelines <sup>29</sup> and  $\geq$ 85<sup>th</sup> percentile for children <sup>28</sup> <sup>c</sup> High dyslipidemia for adults; was defined as total serum cholesterol ( $\geq$ 6.2mmol/l) and LDL-cholesterol ( $\geq$ 3.4mmol/l) <sup>35</sup> low HDL-C:<1.03 mmol/l in men or <1.29 mmol/l in 

Page 15 of 26

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26 26 26 26 26 26 26	1DEFICS study <sup>26</sup> <sup>d</sup> High diabetes risk markers; high HbA1C (>6.1%) <sup>38</sup> , high fasting plasma glucose ( $\geq$ 5.6 mmol/l) <sup>27</sup> and HOMA-insulin resistance was defined as HOMA-IR >4.65. or HOMA-IR >3.60 and BMI >27.5 kg/m <sup>2 36</sup> and for children high HbA1c ( $\geq$ 97.5 <sup>th</sup> percentile), high fasting plasma glucose $\geq$ 95 <sup>th</sup> percentile and HOMA-IR $\geq$ 95 <sup>th</sup> percentile.
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27	Association between obesity indices and cardio-metabolic risk factors
27	Results of the mixed logistic regression models are presented in Table 4. Obesity indices
27	(BMI, WC and BF %) were found to be associated with one or more risk factors. Participants
27	having high BMI (OR=2.41 (1.33, 4.47)), high WC (OR=3.68 (1.81, 7.52)) or high BF%
27	(OR=2.51 (1.40, 4.51)) were more likely to be hypertensive. Having high WC (OR=2.52
27	(1.24, 5.13)) or high BF% (OR=1.91 (1.02, 3.58)) were associated with higher chances of
27	having high LDL-C. Furthermore, BMI (OR=2.08 (1.15-3.79)) and WC (OR=3.01 (1.51-
27	6.03)) were associated with HbA1c levels. We further observed increased OR for obesity
27	indices with regard to high total cholesterol, high triglycerides, low HDL-C, elevated glucose
27	and HOMA-IR. Due to a very small sample in HOMA-IR, the results were omitted. Looking
28	at goodness of fit of the the models, the AIC values showed that models including WC as an
28	obesity index tend to have a slightly stronger predictive power compared to models including
28	BMI and BF%.

Table 4: Associations between obesity indices (independent) and cardio-metabolic risk
factors (dependent), adjusted for gender, age, education level, area of residence, and
medication (for hypertension only) (n=470)

	<b>Obesity indices</b>	High BMI				High WC		High BF%		
R	Risk factors		(95% CI)	AIC	OR	(95% CI)	AIC	OR	(95% CI)	AIC

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Hypertension	2.41	1.33	4.47	504.86	3.68	1.81	7.52	499.79	2.51	1.40	4.51	503.46
High Total cholesterol	1.13	0.40	3.19	192.74	0.84	0.27	2.66	192.71	1.05	0.37	2.95	192.79
High Trigycerides	1.79	0.55	5.77	189.88	2.23	0.58	8.66	189.38	1.64	0.52	5.14	190.11
Low HDL cholesterol	1.21	0.62	2.37	516.08	1.15	0.55	2.42	516.25	1.06	0.54	2.05	516.37
High LDL cholesterol	1.45	0.78	2.69	457.62	2.52	1.24	5.13	452.23	1.91	1.02	3.58	454.77
High HbA1c	2.08	1.15	3.79	442.70	3.01	1.51	6.03	438.53	1.75	0.96	3.18	445.23
High Glucose	2.04	0.93	4.50	397.36	2.07	0.84	5.07	397.98	1.76	0.80	3.87	398.56

Table 5 presents results of mixed logistic regression models including all three obesity indices to investigate the association with single cardio-metabolic risk factors. Compared to the separate regression models, the ORs for most of the associations were attenuated. However, having high WC again was associated with a higher chance of hypertension (OR=2.62 (1.14, 6.06)) and having high HbA1c levels (OR=2.62 (1.12, 6.15)).

Table 5: Associations between obesity indices (independent) and cardio-metabolic risk
factors (outcome) adjusted by gender, age, education level and area of residence (n=470)

Q.

			Con	nbined	Obesi	ty Indi	ces			AIC
Obesity indices		BMI			WC			BF%		
<b>Risk Factors</b>	OR	(95%	CI)	OR	(95%	6 CI)	OR	(95%	CI)	
Hypertension	1.19	0.48	2.95	2.62	1.1	6.06	1.48	0.63	3.51	501.3
High Total	1.31	0.25	6.79	0.71	0.1	2.92	1.01	0.19	5.32	196.5
High Triglycerides	1.34	0.25	7.16	1.90	0.3	9.52	1.02	0.19	5.52	193.2
Low HDL	1.35	0.48	3.76	1.09	0.4	2.67	0.82	0.98	2.25	519.9
High LDL	0.63	0.24	1.65	2.34	0.9	5.50	1.81	0.70	4.70	454.6
High HbA1c	1.53	0.61	3.81	2.62	1.1	6.15	0.82	0.32	2.10	441.6
Elevated Glucose	1.67	0.55	5.06	1.54	0.5	4.44	1.03	0.33	3.17	400.6

## **Discussion**

This study is the first population-based survey in Unguja Island that investigated the association between multiple obesity indices (BMI, WC and BF%) with multiple cardio-metabolic risk factors in a representative Zanzibari population, aged between 5-95 years. This study population, like in many other LMICs is undergoing a coessistance of a double burden of underweight children and overweight/obese adults. Generally, about a quarter of the study population were overweight/obese, and obesity increased with age, this has also been reported in demographic health surveys from seven sub-Saharan African countries <sup>40</sup>. In the adult population, the prevalence of overweight/obesity was lower than the prevalence reported for example in Ghana<sup>11</sup> but higher than that reported in Nigeria<sup>3</sup> and Benin<sup>41</sup>. In paralel, more than 50% of the children in this study were underweight, which is higher than the reported prevalence in other sub-Sharan African countries (Kenya, Nigeria, South Africa, Equatorial Guinea and Cameroon)<sup>42</sup>. 

Dyslipidemia is a risk for variety of cardiovascular diseases and is becoming more prevalent in sub-Saharan Africa, particulary in terms of low HDL-C<sup>43 44</sup>. Despite the relatively normal levels of total cholesterol and trigylcerides, low HDL-C affected about 29% of the overall population, an indication that low HDL-C afffects a large proportion of adults above 18 years, this is in line with a recent study in sub-Saharan Africa and Middle East with 30% of the participant having low HDL-C<sup>45</sup>; other studies in sub-Saharan Africa reported even a higher prevalence of 43.1% in Nigeria<sup>3</sup> and 80% in Botswana<sup>46</sup>, mostly affecting individuals between 35-54 years. 

In the present study, high proportion of participants with high HbA1c (14.1%) and elevated fasting glucose (18%) are children below 18 years; since diabetes in children in LMICs has not been given much attention, there is a high chance of having more children with sub-

clinical complications due to delayed or missed diagnosis and lack of frequent monitoring. The high proportions in this study could be due to the fact that majority of the diabetic participants are not aware of their status and are not monitored or treated. However, when using WHO diabetes diagnostic criteria  $^{47}$ , i.e. HbA1c cut-off  $\geq 6.5\%$  and FPG  $\geq 7.0$ mmol/l, the prevalence of diabetes in participants above 18 years reduced to 8.14% and 3.05%, respectively (data not shown). The most intriguing result is the risk for diabetes and/or diabetic in children below 18 years when screened by elevated fasting glucose levels  $\geq$ 5.6mmol/l, as recommended by IDF<sup>27</sup>. In this study, the prevalence is higher than that of adults above 18 years but less than adults above 45 years. This could be due to both a) misreporting (children did not report having eaten prior to the blood drawing) and b) a true high risk within this age group. However, when using WHO <sup>47</sup> diabetes diagnostic criteria (FPG  $\geq$ 7mmol/l) for the same age group, the prevalence reduced to 0.61% (data not shown). This indicates, that majority of the children are at risk for diabetes and that the cut-off for HbA1c  $\geq 6.1\%$  as well as elevated FPG $\geq 5.6$  mmol/l seem to be better screening tools in identyfing those at risk earlier. 

Our study showed that there is an association between BMI, WC and BF% with major cardio-metabolic risk factors in the study population. These findings are in agreement with other studies who also reported the association between hypertension/pre-hypertension, BMI and WC<sup>48</sup> as well as BF%<sup>11</sup>. This study also observed a strong association between WC and LDL-C levels, similar association has also beenreported in a comperative cross-sectional study in Ghana by Obirikorang<sup>11</sup>. In the separate models, strong associations were observed between BMI and WC with HbA1c levels, which could be explained by the interrelation of the two indices, since abdominal fat accumulation is increased in proportion to BMI<sup>49</sup> and BMI is one of the main risk factors for diabetes and pre-diabetes <sup>50 51</sup>. However, considering 

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the association of all three obesity indices, only the strong associations of WC with HbA1clevels and hypertension remained.

This study has some limititations that should be considered. First, we were only able to investigate the association between obesity indices and risk factors using cross-sectional data, thus the impact of changes in obesity indices on risk factors could not be considered. Second, we used Bioelectrical Impedance Analysis (BIA) to estimate body fat percentage as many epidemiological studies and clinical trials. Still, BIA measurements compared to skinfold measurements may underestimate adiposity in children <sup>52</sup> Third, even though participants who reported food or beverage intake prior to blood drawing were excluded during the data cleaning process, we can not entirely exclude misreporting of "fasting status". 

The main strengths of the present study are; the random selection of the study participants, and the standardised assessment of anthropometrical and laboratory measurements. Moreover, we consequently applied age- and sex-specific cut-offs that take into account the physiological development characteristic of the young age group rather than applying the fixed cut-offs used in the adult population. There is little information on the association of multiple obesity indices with multiple cardio-metabolic risk factors in this population, hence this study to our knowledge is the first to report such associations in the Island of Unguja in Zanzibar.

#### Conclusion

This study adds up to the literature that obesity is associated with higher risks for having hypertension, dyslipidemia and type 2 diabetes mellitus, but for the first time in a Zanzibari population. For similar epidemiological studies incuding children, adolescents, adults and elderly, we suggest to set diabetes and/or pre-diabetes cut-offs of HbA1c at  $\geq 6.1\%$  and/or elevated fasting glucose at  $\geq$ 5.6mmol/l. The study also suggests, when feasible, using BF% and WC besides BMI in screening and health monitoring for dyslipedemia and hypertension. We further conclude, there is a need for effective interventions to create awareness and a need for primary prevention strategies for cardio-metabolic risks and its complications in Unguja Island using local multidiscipinary approaches in the local language, Swahili. Additionally, health surveillance initiatives, targeting in particular the age group  $\geq 18$  to <45years will help to monitor prevention activities in future. 

#### **List of Abbreviations**

BIA	Bioelectrical Impedance Analysis
BMI	Body Mass Index
HbA1c	Glycated Haemoglobin
HDL-C	High Density-Lipoprotein Cholesterol
HOMA-IR	homeostasis model assessment of insulin resistance
IDEFICS	Identification and prevention of Dietary-and lifestyle-induced health EFects
	Children and infantS
IDF	International Diabetes Federation
ISCED	International Standard Classification of Education
LDL-C	Low Density-Lipoprotein Cholesterol
LMICs	Low-middle-Income Countries
NCDs	Non-Communicable Diseases
WC	Waist Circumference
WHO	World Health Organization
	2

## **Declarations**

#### 382 Ethics Approval and Consent to participate

Ethical approval was obtained from the Ethics Committees of the University of Bremen in Germany with a reference number 06-3 and of the Zanzibar Ministry of Health and the Zanzibar Medical Research and Ethics Committee in Zanzibar, Tanzania with a reference number ZAMREC/0001/AUGUST/013. Written informed consents were taken from all participants and parents/guardians gave a written informed consent for their children. The consent forms were approved by the Institutional Ethics Committee.

**Competing interests** 

391 The authors declare that they have no competing interests.

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#### Author Contributions

The authors' responsibilities were as follows: AH and SK were responsible for study design. AH and MAN conducted data collection and developed study hypothesis. MAN and CB conducted statistical analyses and KB assisted in the statistical data cleaning. MAN wrote the manuscript and had primary responsibility for final content. MN,CB,SK,MS,KB and AH critically revised the manuscript and gave final consent.

#### 403 Availability of data and materials

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2 3	404	The datasets generated and/or analysed during the current study are not publicly available
4 5	405	since a follow-up study is planned.
6		Since a fonon ap staal to plained.
7 8	406	
9 10	407	Consent for publication
11 12	408	All participants agreed and signed that; the data collected during the survey can be stored and
13 14	409	used for future analysis.
15 16 17	410	
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#### Association between cardio-metabolic risk factors and body mass index, waist circumferences and body fat in a Zanzibari cross-sectional study

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4	1	Association between cardio-metabolic risk factors and body mass index, waist
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## 26 Abstract

Objectives: To determine the prevalence of obesity indices (body mass index (BMI), waist
circumference (WC), body fat percent (BF%)) and cardio-metabolic risk factors. To
investigate the association between obesity indices and cardio-metabolic risk factors in a
Zanzibari population.

**Designs:** Cross-sectional study.

Settings: Participants randomly selected from 80 Shehias (wards) in Unguja, Zanzibar in
2013.

Participants: A total of 470 participants between 5-95 years were examined. Data on socioeconomic status, area of residence, anthropometry and venous blood were collected. Associations between obesity indices and cardio-metabolic risk factors were investigated using multilevel logistic regression analyses in two steps: first, each obesity indicator was tested independently; second, all indicators combined in one model were tested for their association with cardio-metabolic risk factors.

**Results:** The proportion of overweight/obese individuals was 26.4%, high WC (24.9%) and high BF% (31.1%). Cardio-metabolic risk factors with highest prevalence of abnormal values included hypertension (24.5%), low HDL-C (29.4%), high LDL-C (21.3%) and high HbA1c (19.1%). Obesity and hypertension increased with age, and were most prevalent in participants aged 45 years and above. Low HDL-C was most prevalent among participants  $\geq$ 18 to < 45 years old, while high LDL-C was more prevalent in those above 45 years. High WC and high BF% were associated with high levels of LDL-C (OR=2.52 (1.24, 5.13), OR=1.91 (1.02, 3.58), respectively). Additionally, BMI and WC were associated with high levels of HbA1c (OR=2.08 (1.15, 3.79), OR=3.01 (1.51, 6.03), respectively). In the combined regression model WC was associated with higher chances for hypertension (OR=2.62 (1.14, 6.06)) and for high levels of HbA1c (OR=2.62 (1.12, 6.15)). Conclusion: High BMI, WC 

3 4	51	and BF% were strongly associated with hypertension, with individuals with high WC being
5 6 7	52	twice more likely to have hypertension; this calls for early and effective screening strategies
7 8 9	53	for this study population.
10 11	54	
12 13 14	55	Key words: hypertension, diabetes, children, adolescents, adults, sub-Saharan Africa
15 16 17	56	
17 18 19		Stuar aths and limitations of this study
20 21	57	Strengths and limitations of this study
22 23	58	• This is the first study to report the associations between obesity indices and cardio-
24 25 26	59	metabolic risk factors in Zanzibar.
20 27 28	60	• The household-based approach, which involved visiting the families in the home setting,
29 30 31	61	resulted in a high individual response rate, thus minimising risk of selection bias.
31 32 33	62	• The cross-sectional design prevents us from drawing conclusions regarding the impact of
34 35	63	changes in obesity indices on risk factors.
36 37 38	64	• Bioelectrical Impedance Analysis (BIA) was used to estimate body fat percentage, which
39 40	65	might have underestimated adiposity in children.
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## Introduction

Worldwide, cardiovascular diseases (CVDs) are not only the leading cause of death<sup>1</sup>, they are also emerging as a notable public health problem in sub-Saharan African countries <sup>2</sup>. These countries are undergoing epidemiological transitions from communicable to non-communicable diseases (NCDs) that have been closely linked to increased urbanization and rural-urban migration, which has led to unhealthy behaviours, including poor dietary habits and sedentary lifestyles <sup>23</sup>. According to the International Diabetes Federation (IDF), about 12 million people in Africa are estimated to have type 2 diabetes mellitus <sup>4</sup>, with the prevalence ranging from 1% in rural Uganda to 12 % in urban Kenya <sup>56</sup>. Overweight and obesity have been found to be modifiable risk factors for cardio-metabolic and other chronic diseases <sup>7</sup> including hypertension <sup>8</sup>, diabetes <sup>9</sup> and dyslipidemia <sup>10</sup>. The third report of the National Cholesterol Education Program-Adult treatment Panel (NCEP-ATP III) also identified central obesity, dyslipidemia (hypertriglyceridemia and low levels of high-density lipoprotein cholesterol [HDL-C]), impaired glucose tolerance, and elevated blood pressure as cardio-metabolic risk factors<sup>11</sup>. 

Multiple obesity indices such as BMI, Waist Circumference (WC), Body fat percent (BF%) and Waist to Hip Ratio (WtHR) have been widely used to screen individuals for cardiometabolic risk in clinical and research settings<sup>12-14</sup> due to their low-cost and ease of administration. The performance of anthropometric indices may however vary according to different factors, including ethnicity, age, geographical area and population<sup>13</sup><sup>15</sup>. BMI, which is based on weight and height, is the most widely used marker to assess body mass. In children and adolescents, the z-scores are used to classify obesity status <sup>16</sup>, which is linked to metabolic risk, e.g. in South African youth<sup>17</sup>. However, BMI does not distinguish well between lean mass and fat mass<sup>18</sup>. In contrast, WC is a measure of total body and abdominal fat accumulation and is better correlated with visceral adipose tissues than BMI. The 

Page 5 of 34

#### **BMJ** Open

correlation on the other hand varies significantly across ethnicities <sup>19 20</sup>. Another approach for measuring body fat is through bioelectrical impedance analysis, which has also been done in several epidemiological studies<sup>21</sup>. The use of different anthropometric measurements might also provide complementary information which can be used to aid screening for cardio-metabolic risk in different population settings <sup>22</sup> <sup>23</sup>. 

Few studies have investigated the performance of different obesity indices in association with cardio-metabolic risk factors in sub Saharan African populations <sup>2 7 18</sup>. Data from mainland Tanzania have shown an increasing prevalence of overweight and obesity in urban, peri-urban and rural areas <sup>24</sup>. However, there is still a dearth of population-based studies investigating the associations of cardio-metabolic risk factors with obesity indices in Tanzania mainland and Zanzibar. To help fill this gap, this study uses cross-sectional data of 470 individuals between 5-95 years who were examined in 2013 in Unguja Island, Zanzibar, to describe the prevalence of overweight/obesity and cardio-metabolic risk factors in three age groups ( $\geq 5$  to <18 years,  $\geq 18$  to <45 years and above 45 years). The aim of the study was to identify vulnerable groups in the Zanzibari population with respect to cardio-metabolic risk. Consequently, we investigated the association of BMI, WC and BF% with cardio-metabolic risk factors (hypertension, total cholesterol, triglycerides, high-density-lipoprotein, low-density-lipoprotein, glycated HbA1c, fasting plasma glucose and HOMA-IR). We considered the three obesity indices independently as well as combined, thereby reflecting different aspects of body composition.

## Subjects and Methods

#### 114 <u>Study population and design</u>

We conducted a cross-sectional survey from September to December 2013 in a representative population sample in Unguja Island, Zanzibar. A total of 239 households were randomly selected and all household members were invited for the examination. As we also aimed to identify vulnerable groups within the families, we included young children and the elderly, who both normally depend on the family food environment. A two-staged sampling approach was used: (1) from a list of all 213 Shehias (wards), 80 Shehias were randomly selected; (2) households were randomly selected based on the Shehia's registration records. Participation agreement was requested from all members of a household. A total of 1,443 family members agreed to participate and completed anthropometric and blood pressure measurements, as well as interviewer-administered questionnaires. Venous blood was also collected. The subgroup examinations are described in detail below. The complete description of the study design and methods has been described in detail elsewhere <sup>25</sup>. The study was performed according to the Helsinki Declaration and the study protocol was evaluated and approved by the Ethics Committees of the University of Bremen and of the Zanzibar Ministry of Health and the Zanzibar Medical Research and Ethics Committee. All participants gave written informed consent and parents/guardians consented on behalf of minors in writing. 

#### 131 <u>Patient and Public Involvement</u>

During the development of the survey tools, measurements and the study protocol, a meeting was held with the local partners, government officials and researchers in Zanzibar to discuss the needs and gaps of the nutrition and health survey planned in Zanzibar. The documents and instruments were then modified according to the needs of the Zanzibari population as recommended in the meeting. 

Page 7 of 34

#### **BMJ** Open

A year after the survey, preliminary results on the major health outcomes and related risk factors were presented and discussed during a two days feedback workshop with the administrative leaders (e.g. Shehas, district commissioners), stakeholders (from health services, government officials, food safety) and our local partners in Zanzibar (academics and research). Each Sheha was handed a poster of the preliminary results, which was then displayed at their local offices for all Shehia members to see. District commissioners received a summary report on all Shehias of their districts. The preliminary results were further publicised on TV and print media. The same group of workshop participants was invited to a further workshop in 2018, whose aim was to identify target populations and channels for future nutrition education to address the aetiology and prevention of NCDs in the Zanzibari population, taking into consideration the survey results presented also in this study. 

148 This observational epidemiological study examined participants in their home environment149 and did not enrol clinical patients.

#### 150 <u>Questionnaires and anthropometric measurements</u>

Questionnaires were developed in English, translated into Swahili, and then back-translated to control for translation errors. Information was collected during an interviewer administered personal interview conducted by trained survey staff. Parents reported their age and sex, as well as of their children. Age was grouped into three categories  $\geq 5$  to  $\leq 18$  years,  $\geq 18$  to  $\leq 45$ years, and 45 years and above. In addition, parental highest educational level according to the International Standard Classification of Education (ISCED) <sup>26</sup> was used as a proxy indicator for socio-economic status (SES) of the family. It was categorized into low education (no education and primary school) and high education (secondary school and above). To determine participants' area of residence, information on region, district and Shehia (the smallest administrative unit in Zanzibar) was recorded and two categories for area of residence were developed (urban and rural). Utilization of medication was also documented

#### **BMJ** Open

in the questionnaire. Regarding medication for obesity-related conditions, participants reported use of hypertension medication but not of diabetes or dyslipoprotenemia medication. Hence, the variable was later categorized as "hypertension medication" and "other medication" (e.g. anti-Malaria therapy or antipyretic products). To ensure a high quality of data collection, this study used proven examination methods and laboratory standards <sup>27 28</sup>. All anthropometric measurements and physical examinations were adopted from the IDEFICS Study and conducted following standardized procedures <sup>29 30</sup>. Measurement of body weight was carried out to the nearest 0.1kg and body fat percent was determined using the bioelectrical impedance analysis (BIA) method using an electronic scale (TANITA BC-420 SMA, Germany). Height was measured using a SECA 213 stadiometer, UK, and waist circumference (WC) was measured midway between the lowest rib and the iliac crest, using an inelastic measuring tape (SECA 201). For all measurements, participants wore light clothing and were standing. The measures were recorded to the nearest 0.1cm. The complete description of the anthropometric measurements of the study is described elsewhere <sup>25</sup>. 

For children and adolescents, Body Mass Index (BMI) was calculated as kg/m<sup>2</sup> and then transformed to age-and sex-specific z-score and percentiles. Thereafter, categories for overweight (BMI between >75<sup>th</sup> and <95<sup>th</sup> percentile) and obesity (BMI >95<sup>th</sup> percentile) were built according to the WHO centile curves <sup>31 32</sup>. For adults, overweight/obesity was defined as BMI  $\geq 25 \text{kg/m}^2$  as recommended by WHO <sup>33</sup>. For statistical analysis, the BMI categories were merged into two 1) under-weight/ normal weight ( $\leq 75^{\text{th}}$  percentile for children and adolescents and  $< 25 \text{kg/m}^2$  for adults) and 2) overweight/obesity (>75<sup>th</sup> percentile and  $\geq 25 \text{kg/m}^2$ ). Regarding waist circumference (WC), high abdominal obesity was defined as WC  $\geq$ 90<sup>th</sup> percentile for children below 10 years <sup>34</sup>;WC  $\geq$ 90<sup>th</sup> percentile for adolescents aged 10 - <16 years; and WC >94 cm for men and > 80 cm for women for participants 16 years and older, as recommended by the IDF <sup>35</sup>. As recommended by 

Page 9 of 34

#### **BMJ** Open

187 McCarthy et al. <sup>36</sup>, for boys and girls below 18 years, high body fat percentage (BF%) was set 188 at  $\geq$ 85th percentile. For adults above 18 years, high BF% was defined as  $\geq$ 20 % for men and 189  $\geq$ 32 % for women <sup>37</sup>. The cut-offs and references are listed in Table 1.

#### 190 <u>Cardio-metabolic risk factors</u>

All blood samples were drawn after overnight fasting and were collected from all eligible participants over 5 years of age by venepuncture <sup>38</sup>. To reduce pain, children below 10 years of age were given a local anaesthetic plaster before blood drawing, which motivated the children to participate. Before blood drawing, the procedure was once again explained to all participants in easy language and they were informed that they still could refuse to participate. For children weighing 10kg, the blood collection was restricted to 1%, corresponding to approximately 8 mL. For healthy, non-pregnant adults weighing at least 50 kg, a maximum of 20.5 mL venous blood was drawn. All blood samples collected at the field were kept at 4°C and the processing was performed immediately at the laboratory in Zanzibar, according to international standards<sup>28</sup>. EDTA Blood was centrifuged for 10 minutes at 2500g and then separated into 3 aliquots; plasma, red blood cells (RBC) and white blood cells (WBC), which were then stored at -80 °C. Detailed procedures about the collection, processing and storage of blood samples are described elsewhere <sup>25</sup>. 

Metabolic parameters were categorized for investigating the prevalence of cardio-metabolic disorders in the study population. Due to the wide range of age groups in this study population, different cardio-metabolic risk definitions and cut-offs were used (Table 1). Cardio-metabolic risk for children between 5-10 years was defined according to age-sex-specific cut-offs. The parameters, including hypertension (Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP)), blood lipids (high Total Cholesterol (TC), high Triglycerides (TG), Low-Density-Lipoprotein Cholesterol (LDL-C) and High-Density-Lipoprotein Cholesterol (HDL-C)), blood glucose/insulin (Homeostasis Model Assessment of 

#### **BMJ** Open

Insulin Resistance (HOMA-IR) and elevated Fasting Plasma Glucose (FPG), were defined according to the IDEFICS Study <sup>34 39</sup>. Glycated haemoglobin (HbA1c) was defined according to Rodoo et al. <sup>40</sup> for children under 17 years. For children and adolescents between 10 years and 16 years, hypertension was defined according to age-sex-specific cut-offs as recommended <sup>41</sup>; for adolescents and adults above 16 years hypertension was defined as recommended <sup>42</sup>. Blood lipids (TC and LDL-C) were defined according to the National Cholesterol Education Program (NCEP)<sup>11</sup> and TG, HDL-C and FPG according to the International Diabetes Federation (IDF) <sup>35</sup>. HbA1c for participants above 17 years was defined according to Stern et al. 43 and insulin resistance was estimated as HOMA-IR according to the reference value of HOMA-IR as recommended by Shashaj et al. <sup>44</sup>. In the present study, the 75<sup>th</sup> percentile cut-off was used for children and adolescents from 10 to 17 years. For participants above 17 years, HOMA-IR was defined according to von Eyben et al <sup>45</sup>. HOMA-IR was calculated from glucose (mmol/l)) and insulin ( $\mu$ U/ml) concentrations using the formula: HOMA-IR=(fasting insulin×fasting glucose/22.5)<sup>46</sup>. 

#### 227 Table 1. Cardio-metabolic risk definitions and references

Age group	Obesity Indices and Blood Pressure	Blood lipids	Blood Glucose/Insulin
Children:	BMI $\geq$ 75 <sup>th</sup> percentile <sup>1</sup>	TC $\geq$ 90 <sup>th</sup> percentile <sup>2</sup>	HbA1c $\geq$ 97.5 <sup>th</sup> percentile <sup>10</sup>
≤10y	WC $\geq$ 90 <sup>th</sup> percentile <sup>2</sup>	TG $\geq$ 90 <sup>th</sup> percentile <sup>2</sup>	HOMA-IR $\geq$ 95 <sup>th</sup> percentile <sup>2</sup>
	BF %≥85 <sup>th</sup> percentile <sup>3</sup>	HDL-C $\leq 10^{\text{th}}$ percentile <sup>2</sup>	$FPG \ge 95^{th}$ percentile <sup>2</sup>
	$\frac{\text{SBP} \ge 90^{\text{th}} \text{ centile or}}{\text{DBP} \ge 90^{\text{th}} \text{ centile }^2}$	LDL $\geq 90^{\text{th}}$ percentile <sup>2</sup>	
Adolescents:	BMI $\geq$ 75 <sup>th</sup> percentile <sup>1</sup>	TC ≥5.2 mmol/L <sup>6</sup>	$HbA1c \ge 97.5^{th} percentile^{10}$
>10 to	WC $\geq$ 90 <sup>th</sup> percentile <sup>4</sup>	TG $\geq$ 1.7mmol/L <sup>4</sup>	HOMA-IR $\geq$ 75 <sup>th</sup> percentile <sup>9</sup>
<16 y	BF %≥85 <sup>th</sup> percentile <sup>3</sup>	HDL-C < 1.03 <sup>4</sup>	$FPG \ge 5.6 mmol/L^4$
	SBP≥140mmHg or	LDL $\geq$ 3.4mmol/L <sup>6</sup>	

		DBP≥90mmHg <sup>11</sup>		
			TO \$ 5.0 1/16	
	Adults:	$BMI \ge 25 \text{ kg/m}^1$	TC $\geq$ 5.2 mmol/l <sup>6</sup>	HbA1c $\ge$ 6.1% <sup>5</sup>
	≥16y	WC $\geq$ 94 cm male, $\geq$ 80cm female <sup>4</sup>	TG≥1.7mmol/L, <sup>4</sup>	HOMA-IR >4.65 or HOMA- IR >3.60 and BMI >27.5 kg/m <sup>2 7</sup>
		BF % $\geq$ 20 % male and $\geq$ 32 % female <sup>8</sup>	HDL-C < 1.03 male,< 1.29 female <sup>4</sup>	$FPG \ge 5.6 mmol/L^4$
		SBP≥140mmHg or DBP≥90mmHg <sup>12</sup>	LDL ≥3.4mmol/L <sup>6</sup>	
228	L			
229	1 WHO	4		
230 231	2 IDEFICS S 3 McCarthy	H.D., et al. (2006)		
232	4 IDF			
233		et al (2003) for adults above	17 years	
234 235	6 NCEP 7 von Evben	F.E., et al (2005)		
236	8 Gallagher, 1			
237		al. (2015) for children and add	plescents under 17 years	
238 239	10 Rodoo P e	at al. (2013) al Institute of Health 3 <sup>rd</sup> and '	7 <sup>th</sup> report respectively	
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241	Inclusion cri	iteria for study sample		
242	061442	1		· · · · · · · · · · · · · · · · · · ·
242	Of 1,443 inc	inviduals who participated	in this study, 1,314 fulfilled th	te inclusion criteria (age,
243	sex, weight,	height) for the overall st	udy analysis. Of the 1,314, 1	,234 provided complete
244	waist circu	mference and body fat p	percent measurements. Amor	ng these, 557 provided
245	complete bl	ood samples for the cardio	-metabolic risk analysis and o	nly 505 were on fasting
245	complete on	ood samples for the cardio	-metabolie fisk analysis and C	July 505 were on fasting
246	status. To re	duce bias when estimating	mean and SD in the regression	on analysis, we excluded
	41 4 10/		1 1 1 1 0 1	, <b>1</b> 1 <sup>.</sup> · <b>1</b> 1 1 · <i>i</i>
247	the top 1%	of individuals with extrem	hely high values for cardio-me	etabolic risk and obesity
248	indices, leav	ring us with a complete sam	pple of 470 participants for the	analysis.
	,	<b>c</b> 1		
249				
250	Statistical ar	alveie		
230	<u>Statistical al</u>	1419515		
251	Descriptive	analysis was conducted to	calculate the mean standard c	leviation (SD) and range
252		maximum) for continuous		

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data in N and percentages (%). As part of the regression analysis, we tested the necessary assumptions in terms of symmetry and normality using residual-plots and Q-Q-Plots. Mixed logistic regression models were used to analyse the association between obesity indices and cardio-metabolic risk factors. In addition, potential clustering within households was considered in terms of a random intercept. Following the hierarchy of the municipal structure in Zanzibar, we conducted sensitivity analysis modelling either Shehias or households within Shehias as a random intercept in the models. Since the results of the models only showed marginal differences, we only considered the household as a random intercept in our analyses. First, mixed logistic regression models were conducted to estimate the association between each of the three obesity indicators (BMI, WC and BF%) as exposure variables and each of the eight risk factors (hypertension, TC, TG, HDL-C, LDL-C, HbA1c, FPG and HOMA-IR) as dependent variables, in terms of odds ratios (OR) and 95% confidence limits (CI). Since BMI, WC and BF% are interrelated, their predictive power on cardio-metabolic risk factors was investigated by conducting mixed logistic regression models. This was done by estimating the association (ORs and 95% CIs) between all three obesity indices as dependent variables in one model and each of the eight risk factors as outcome variables. All models were adjusted for potential confounders and covariates such as gender, age, education level (ISCED), area of residence and utilization of hypertension medication. Statistical analysis was performed using SAS 9.3 (SAS Institute. Cary. NC. U SA); mixed logistic regression models were conducted based on the GLIMMIX procedure; statistical significance was set at  $\alpha = 0.05$ . 

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## **Results**

# 275 <u>Distribution of obesity and cardio-metabolic risk and characteristics of the study population</u> 276 <u>by age groups (n=470)</u>

The mean age was 29 ( $\pm 18$ ) years, with the highest proportion being in the age group ( $\geq 18$  to <45 years) (Table 2). The overall mean values for BMI, WC and BF% were as follows: BMI 22 (± 5.2) kg/m<sup>2</sup>, WC 75 (± 16) cm and BF% 22 (± 11) %. The mean BMI of 26 (± 5.7) kg/m<sup>2</sup> for participants above 45 years was slightly higher than normal, indicating overweight. Mean diastolic blood pressure was in the normal range for all the age groups, but a higher mean value of systolic blood pressure,  $150 (\pm 280)$  mmHg, was observed among participants above 45 years. The mean values of most of the variables showed an increase with age group, except for HDL-C and diabetes markers (HbA1c, serum insulin, plasma glucose and HOMA-IR), which showed no specific trend. 

Of the 470 participants, more than half were women 52.6% (n=247), 51.9% (244) had a higher education level and 73.4% (345) resided in urban area. Regarding education level, the majority of those with a higher education level were aged  $\geq 18$ -<45 years (150/244 = 61%) (Table 3).

 Table 2: Distribution of obesity and cardio-metabolic risk in the study population (n=470) by
age group (means and standard deviation (SD))

	$\geq 5 \text{ to } < 18$ (n=16)	-	$\geq 18$ to $< 2$ (n=1)	2	-	years 110)	Tot (n=4	
	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range	Mean (SD)	Range
Age (years)	12 (3.4)	4.9 -18	28 (8.1)	18-44	57 (9.8)	45-95	29 (18)	4.9-95
BMI (kg/m)	17 (3.4)	11-34	23 (4.5)	16-37	26 (5.7)	15-49	22 (5.7)	11-49
WC (cm)	61 (11)	12-103	79 (12)	37-111	88 (0.2)	35-126	75 (16)	12-126
BF (%)	15 (7.0)	1.6-45	23 (11)	3.0-53	28 (10)	6.2-53	22 (11)	1.6-53

DBP (mmHg)	67 (9.8)	44-97	76 (10)	53-126	88 (15)	62-140	75 (14)	44-140
SBP (mmHg)	110 (13)	69-152	123 (16)	72-197	150 (28)	100-229	125 (24)	69-229
TC (mmol/l)	3.7 (0.7)	1.8-5.9	3.9 (0.8)	2.1-6.0	4.2 (0.8)	0.2-5.9	3.9 (0.8)	0.2-6.0
TG (mmol/l)	0.8 (0.3)	0.3-2.5	0.9 (0.4)	0.0-2.6	1.0 (0.4)	0.4-2.7	0.9 (0.4)	0.0-2.7
HDL-C (mmol/l)	1.4 (0.5)	0.7-3.3	1.5 (0.5)	0.6-3.7	1.4 (0.4)	0.6-3.6	1.4 (0.5)	0.6-3.7
LDL-C (mmol/l)	2.3 (0.9)	0.0-5.0	2.5 (0.9)	0.7-5.1	3.0 (1.0)	0.6-5.1	2.5 (1.0)	0.0-5.1
HbA1c (%)	5.7 (0.5)	4.2-8.5	5.6 (0.6)	3.9-9.4	6.0 (0.8)	4.4-10	5.8 (0.6)	3.9-10
Serum Insulin (mmol/l)	4.3 (3.1)	0.4-18	4.8 (2.8)	0.8-17	3.6 (2.3)	0.4-17	4.4 (2.8)	0.4-18
FPG (mmol/l)	4.9 (0.8)	2.0-7.7	4.8 (0.9)	0.5-9.4	5.1 (1.3)	0.2-13	4.9 (1.0)	0.2-13
HOMA-IR	1.0 (0.7)	0.1-4.6	1.1 (0.7)	0.0-4.3	0.9 (0.6)	0.0-4.0	1.0 (0.7)	0.0-4.6

> The overall proportion of overweight/obesity with regard to BMI, WC and BF % was 26.4%, 24.9% and 31.1% respectively, and increased with age (Table 2). The highest proportion was observed among participants above 45 years. We observed different trends in the prevalence of metabolic parameters and hypertension across age groups. The prevalence of hypertension, high total cholesterol, LDL-C and HbA1c increased with age, while that for triglycerides and HOMA-IR decreased with age. The most prevalent factors were reduced HDL-C (29.4%), hypertension (24.5%) as well as raised LDL-C (21.3%) and HbA1c levels (19.1%). Although hypertension was more prevalent among participants above 45 years, only 9.4% (10) of the participants in this age group were on hypertension medication. Further, high LDL-C and HbA1c were more prevalent among participants above 45 years, and low HDL-C was most prevalent among  $\geq 18$  to <45 year olds.

Table 3: Characteristics of the study population (n=470) by age group (n/%)

			≥18 to years	<45	45+ y	rears	Total		
	n	(%)	n	(%)	n	(%)	n	(%)	
All	165	(100)	195	(100)	110	(100)	470	(100)	
Gender									
Male	85	(51.5)	86	(44.1)	52	(47.3)	223	(47.4)	

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Page 15 of 34

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	≥5 to years		≥18 to years	<45	45+ y	ears	Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Female	80	(48.5)	109	(55.9)	58	(52.7)	247	(52.6)
Education level								
Low	122	(73.9)	45	(23.1)	59	(53.6)	226	(48.1)
High	43	(26.1)	150	(76.9)	51	(46.4)	244	(51.9)
Area of residence								
Rural	43	(26.1)	49	(25.1)	33	(30.0)	125	(26.6)
Urban	122	(73.9)	146	(74.9)	77	(70.0)	345	(73.4)
Obesity Indices								
BMI								
Underweight	83	(50.3)	29	(14.9)	9	(8.18)	121	(25.7)
Normal weight	73	(44.2)	106	(54.4)	46	(41.8)	225	(47.9)
Overweight/obese	9	(5.45)	60	(30.8)	55	(50.0)	124	(26.4)
Waist circumference		6						
Normal	165	(100)	141	(72.2)	47	(42.7)	353	(75.1)
High <sup>a</sup>	0	(0)	54	(27.7)	63	(57.3)	117	(24.9)
Body fat %								
Normal	157	(95.2)	121	(62.1)	46	(41.8)	324	(69.0)
High <sup>b</sup>	8	(4.86)	74	(37.9)	64	(58.2)	146	(31.1)
Hypertension					•			
Normal	123	(74.5)	76	(39.0)	10	(9.09)	209	(44.5)
Pre-hypertension	25	(15.8)	89	(45.6)	31	(28.2)	146	(31.1)
Hypertension	16	(9.70)	30	(15.4)	69	(62.7)	115	(24.5)
Hypertension medication <sup>c</sup>								
Yes	1	(0.61)	12	(6.38)	10	(9.43)	23	(5.02)
No	163	(99.4)	176	(93.6)	96	(90.6)	435	(95.0)
Dyslipidaemia <sup>d</sup>								
Total cholesterol								
Normal	161	(97.6)	183	(93.8)	102	(92.7)	446	(94.9)
High	4	(2.42)	12	(6.15)	8	(7.27)	24	
Triglycerides		()		(0.00)		(,,_,)		(
Normal	157	(95.2)	186	(95.4)	105	(95.5)	448	(95.3)
High	8	(4.85)	9	(4.62)	5	(4.55)	22	(4.68)
HDL-cholesterol		(1.05)	,	(1.02)	5	(1.55)		(1.00
Normal	126	(76.4)	128	(65.6)	78	(70.9)	332	(70.5)
Low	39	(23.6)	67	(34.4)	32	(29.1)	138	(29.4
LDL-cholesterol		(23.0)		(JT.T)	52	(27.1)	150	<u>(</u> 27.+
Normal	141	(85.5)	163	(83.6)	66	(60.0)	370	(78.7)
High						, í		
nıgli	24	(14.5)	32	(16.4)	44	(40.0)	100	(21.3)

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	≥5 to <18 years		≥18 to years	<45	45+ y	ears	Total		
	n	(%)	n	(%)	n	(%)	n	(%)	
Diabetes Markers <sup>e</sup>									
HbA1c									
Normal	142	(86.1)	166	(85.1)	72	(65.5)	380	(80.9)	
High	23	(13.9)	29	(14.9)	38	(34.5)	90	(19.1)	
Plasma glucose									
Normal	136	(82.4)	167	(85.6)	88	(80.0)	391	(83.2)	
High	29	(17.6)	28	(14.4)	22	(20.0)	79	(16.8)	
HOMA-IR									
Normal	162	(98.2)	193	(99.0)	109	(99.1)	464	(98.7)	
High	3	(1.82)	2	(1.03)	1	(0.91)	6	(1.28)	

<sup>a</sup> High WC was defined as WC  $\geq$  90<sup>th</sup> percentile for children under 10y <sup>34</sup>. Adolescents

between 10-16 years and adults above 16 years WC > 94 cm for men and > 80 cm for women according to IDF cut-off  $^{35}$ 

<sup>311</sup> <sup>b</sup>High BF% for adults (overweight/obese)  $\geq 20$  for men and  $\geq 32$  for women according to (NIH/WHO) BMI guidelines <sup>37</sup> and  $\geq 85^{\text{th}}$  percentile for children <sup>36</sup>

9 313 <sup>c</sup> Missing information from 12 participants (n=458)

<sup>30</sup> 314 <sup>d</sup> High dyslipidemia for adults; was defined as total serum cholesterol ( $\geq 6.2$ mmol/l) and

1 315 LDL-cholesterol ( $\geq$ 3.4mmol/l) <sup>11</sup> low HDL-C:<1.03 mmol/l in men or <1.29 mmol/l in 316 women high and hypertriglyceridemia ( $\geq$ 1.7 mmol/l) <sup>35</sup> and for children according to 317 IDEFICS study <sup>34</sup>

<sup>34</sup> 317 IDEFICS study <sup>45</sup>
<sup>35</sup> 318 <sup>e</sup> High diabetes risk markers; high HbA1c (>6.1%) <sup>45</sup>, high fasting plasma glucose (≥5.6 mmol/l) <sup>35</sup> and HOMA-insulin resistance was defined as HOMA-IR >4.65. or HOMA-IR

320 >3.60 and BMI >27.5 kg/m<sup>2 43</sup> and for children high HbA1c ( $\geq 97.5$ <sup>th</sup> percentile), high fasting

<sup>8</sup> 321 plasma glucose  $\geq$ 95<sup>th</sup> percentile and HOMA-IR  $\geq$ 95<sup>th</sup> percentile.

323 Association between obesity indices and cardio-metabolic risk factors

324 Obesity indices (BMI, WC and BF %) were observed to be associated with one or more risk

5 325 factors. Participants with high BMI (OR=2.41 (1.33, 4.47)), high WC (OR=3.68 (1.81, 7.52))

<sup>3</sup> 326 or high BF% (OR=2.51 (1.40, 4.51)) were more likely to be hypertensive (Table 4). Having

327 high WC (OR=2.52 (1.24, 5.13)) or high BF% (OR=1.91 (1.02, 3.58)) was associated with

3 328 higher chances of having high LDL-C. Furthermore, BMI (OR=2.08 (1.15-3.79)) and WC

<sup>5</sup> 329 (OR=3.01 (1.51-6.03)) were associated with HbA1c levels. We further observed increased

 $_{58}^{57}$  330 OR for obesity indices with regard to high total cholesterol, high triglycerides, low HDL-C,

<sup>59</sup> 60 331 elevated glucose and HOMA-IR. As the proportion of individuals with high HOMA-IR was

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very small in our sample (1,28%/n=6), the results was not considered in the final regression
analysis. Regarding goodness of fit of the models, values of the Akaike Information Criterion
(AIC), which estimates the quality of each model relative to that of each of the other models,
showed that models including WC as an obesity index tended to have a slightly stronger
predictive power compared to those including BMI and BF%.

Table 4: Associations between obesity indices (independent) and cardio-metabolic risk factors (dependent), adjusted for gender, age, education level, area of residence, and hypertension medication (n=470)

Obesity indices		High BMI				Hig	h WC		High BF%			
Risk factors	OR	(95%	CI)	AIC	OR	(95%	CI)	AIC	OR	(95%	CI)	AIC
Hypertension	2.41	1.33	4.47	504.86	3.68	1.81	7.52	499.79	2.51	1.40	4.51	503.46
High Total cholesterol	1.13	0.40	3.19	192.74	0.84	0.27	2.66	192.71	1.05	0.37	2.95	192.79
High Triglycerides	1.79	0.55	5.77	189.88	2.23	0.58	8.66	189.38	1.64	0.52	5.14	190.11
Low HDL cholesterol	1.21	0.62	2.37	516.08	1.15	0.55	2.42	516.25	1.06	0.54	2.05	516.37
High LDL cholesterol	1.45	0.78	2.69	457.62	2.52	1.24	5.13	452.23	1.91	1.02	3.58	454.77
High HbA1c	2.08	1.15	3.79	442.70	3.01	1.51	6.03	438.53	1.75	0.96	3.18	445.23
High Glucose	2.04	0.93	4.50	397.36	2.07	0.84	5.07	397.98	1.76	0.80	3.87	398.56

Table 5 presents results of mixed logistic regression models including all three obesity indices to investigate the association with single cardio-metabolic risk factors. Compared to the separate regression models, the ORs for most of the associations were attenuated. However, having high WC was again associated with a higher chance of having hypertension (OR=2.62 (1.14, 6.06)) and having high HbA1c levels (OR=2.62 (1.12, 6.15)). Again, as the proportion of individuals with high HOMA-IR (1,28%/n=6), the results are not shown was very small, it was not considered in the final regression analysis. in our sample.

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> Table 5: Associations between obesity indices (independent) and cardio-metabolic risk factors (outcome) adjusted by gender, age, education level and area of residence (n=470)

				nbined		ty Indi	ces			AIC
Obesity indices		BMI			WC			BF%		total
Risk Factors	OR	(95%	CI)	OR	(95%	6 CI)	OR	(95%	CI)	
Hypertension	1.19	0.48	2.95	2.62	1.1	6.06	1.48	0.63	3.51	501.3
High Total	1.31	0.25	6.79	0.71	0.1	2.92	1.01	0.19	5.32	196.5
High Triglycerides	1.34	0.25	7.16	1.90	0.3	9.52	1.02	0.19	5.52	193.2
Low HDL	1.35	0.48	3.76	1.09	0.4	2.67	0.82	0.98	2.25	519.9
High LDL	0.63	0.24	1.65	2.34	0.9	5.50	1.81	0.70	4.70	454.6
High HbA1c		0.61	3.81	2.62	1.1		0.82	0.32	2.10	441.6
Elevated Glucose	1.67	0.55	5.06	1.54	0.5	4.44	1.03	0.33	3.17	400.6
			3.81 5.06							

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## **Discussion**

This study is the first population-based survey in Unguja Island that investigated the association between multiple obesity indices (BMI, WC and BF%) and multiple cardio-metabolic risk factors in a representative Zanzibari population, aged 5-95 years. This study population, as in many other LMICs, is undergoing a coexistence of the double burden of underweight children and overweight/obese adults. Generally, about a quarter of the study population was overweight/obese, and obesity increased with age. This observation has also been reported in demographic health surveys from seven sub-Saharan African countries <sup>47</sup>. In the adult population, the prevalence of overweight/obesity was lower than that in Ghana<sup>7</sup>, but higher than in Nigeria<sup>2</sup> and Benin<sup>48</sup>. On the other hand, more than 50% of the children in this study were underweight, a proportion higher than that in other sub-Saharan African countries (Kenya, Nigeria, South Africa, Equatorial Guinea and Cameroon)<sup>49</sup>.

Dyslipidemia is a risk factor for a variety of cardiovascular diseases and is becoming more prevalent in sub-Saharan Africa, particularly the form of low HDL-C <sup>50 51</sup>. Despite the relatively normal levels of total cholesterol and triglycerides, low HDL-C affected about 29% of the overall population, an indication that low HDL-C affects a large proportion of adults above 18 years. As HDL-C plays a key role in reverse cholesterol transport, has anti-thrombotic, anti-inflammatory and anti-oxidant properties, as well as the ability to improve diabetic control and promote angiogenesis, it is referred to as cardioprotective<sup>52</sup>. The low HDL-C levels observed in our study population might therefore be indicative of a notable and evolving cardiovascular risk in the study region. Our results are in line with a recent study in sub-Saharan Africa and Middle East with 30% of the participant having low HDL-C <sup>53</sup>. Other studies in sub-Saharan Africa reported even higher prevalence of low HDL-C, 43.1% in Nigeria<sup>2</sup> and 80% in Botswana<sup>54</sup>, mostly affecting individuals between 35-54 years. 

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In the present study, a high proportion of participants with high HbA1c (14%) and elevated fasting glucose (18%) are children below 18 years. Since diabetes in children in LMICs has not received much attention, it is likely that there is a high number of children with sub-clinical complications due to delayed or missed diagnosis as well as a lack of regular monitoring. The high proportions observed in this study are a possible indication that a large proportion of diabetic participants are not aware of their status and are hence not monitored or treated. The fact that diabetes medication was not reported in this sample supports this assumption. However, when using WHO diabetes diagnostic criteria <sup>55</sup>, i.e. HbA1c cut-off  $\geq 6.5\%$  and FPG  $\geq 7.0$  mmol/l, the prevalence of diabetes in participants above 18 years decreased to 8.14% and 3.05%, respectively (data not shown). The most intriguing result however is the high proportion of children between 5 and <18 years being at high risk for diabetes with elevated FPG levels when using cut-off of  $\geq$ 5.6mmol/l, as recommended by IDF <sup>35</sup>. Our results showed that the prevalence of FPG and HOMA-IR in children and adolescents below 18 years was in general higher than that of adults above 18 years, but less than that of adults above 45 years. Results from previous cross-sectional studies have shown that physiological transient insulin resistance develops in children during puberty<sup>56</sup> and decreases again by the end of puberty, regardless of obesity. The decrease in insulin sensitivity in the pubertal period is said to lead to an increase in glucose-stimulated insulin secretion<sup>57</sup>. The high prevalence of FPG and HOMA-IR observed in children and adolescents in our study could hence be due to physiological changes in children and adolescents during pre-pubertal period and puberty. They could however also be due to misreporting (children did not report having eaten prior to the blood drawing), or to a true high risk within this age group. Taking this into account, we adjusted for age in the regression models in order to control for possible confounding effects of physiological changes through maturation and aging. Interestingly, the prevalence of high FPG decreased from approximately 18% to 

Page 21 of 34

#### **BMJ** Open

402 0.61% when we used the WHO <sup>55</sup> diabetes diagnostic criteria (FPG  $\ge$ 7mmol/l) for the same 403 age group (data not shown). This, in our opinion, indicates that the majority of the children 404 are at risk for diabetes, and that the cut-off for HbA1c  $\ge$ 6.1% as well as elevated FPG $\ge$ 5.6 405 mmol/l seem to be better screening tools for identifying those at risk, earlier.

Our study showed a strong association between BMI, WC and BF% and hypertension in the study population. These findings are in agreement with other studies that also reported an association between hypertension/pre-hypertension, BMI and WC <sup>58</sup> as well as BF% <sup>7</sup>. Moreover, the association between hypertension and high WC was twice as strong as that with high BMI and high %BF. This result suggests that central obesity may be a better predictor for the risk of hypertension and other cardiovascular diseases in our study population. Thus, optimal body weight control and reduced central obesity risk may have beneficial effects on hypertension control in this population. This study also observed a strong association between WC and LDL-C levels. Obirikorang also reported similar associations in a comparative cross-sectional study conducted in Ghana<sup>7</sup>. 

In the separate models, strong associations were observed between BMI, WC and HbA1c levels, which can be explained by the interrelation of the two indices, since abdominal fat accumulation increases in proportion to BMI <sup>59</sup> and BMI is one of the main risk factors for diabetes and pre-diabetes <sup>60</sup>. However, when all three obesity indices were considered combined, it is only the association between WC and HbA1c levels and hypertension that remained strong. Excessive visceral fat in abdominal obesity is the main source of free fatty acids and inflammatory cytokines, which, according to the literature, might lead to insulin resistance and type 2 diabetes mellitus<sup>61</sup>. This probably explains why WC was strongly associated with diabetes and hypertension in our study population. Therefore, measuring WC using optimal WC cut-off values as was done in this study would be a feasible, less time 

426 consuming and cost-effective screening tool to identify at-risk individuals in the Zanzibari427 population.

This study has some limitations that should be considered. First, we were only able to investigate the association between obesity indices and risk factors using cross-sectional data, thus the impact of changes in obesity indices on risk factors could not be considered. Second, as is done in many epidemiological studies and clinical trials, we used Bioelectrical Impedance Analysis (BIA) to estimate body fat percentage. However, compared to skinfold measurements, BIA measurements may underestimate adiposity in children <sup>62</sup>. Third, even though participants who reported food or beverage intake prior to blood drawing were excluded during the data cleaning process, we cannot entirely rule out misreporting of the "fasting status". According to our power calculation, our sample size of 1,314 individuals would have been enough to reach a statistical power. However, our study sample decreased to 470 due to the individual opt-out option for particular examinations as well as the exclusion of outliers and the requirement of completeness of variables of interest. We nevertheless believe that our findings provide important information for public health stakeholders, policy makers and researchers, despite the fact that some of the detected associations did not reach the significance threshold due to the small sample size. 

The results of this research, the first study providing information on the prevalence and risk of NCDs with particular focus on identifying vulnerable age groups in Zanzibar, can be used for the development of interventions or policies by researchers, stakeholders and government officials. The random selection of the study participants and the standardised assessment of anthropometrical and laboratory measurements are main strengths of the present study. Moreover, we consequently applied age- and sex-specific cut-offs that take into account the physiological development characteristic of the young age group, rather than applying the fixed cut-offs used in the adult population. There is little information on the association of

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451 multiple obesity indices with multiple cardio-metabolic risk factors in this population; hence,452 our study provides an important contribution towards filling this gap.

## 453 Conclusion

This study adds to the literature on the association of obesity with higher risks for hypertension, dyslipidemia and type 2 diabetes mellitus, but for the first time in a Zanzibari population. Based on our findings, we recommend that similar epidemiological studies including children, adolescents, adults and elderly set diabetes and/or pre-diabetes cut-offs of HbA1c at  $\geq 6.1\%$  and/or elevated fasting glucose at  $\geq 5.6$ mmol/l. Where feasible, BF% and WC should be used in addition to BMI for screening and monitoring for dyslipidemia and hypertension. We further conclude that there is a need for effective interventions to create awareness as well as for primary prevention strategies for cardio-metabolic risks and its complications in Unguja Island, using local multidisciplinary approaches in the local language, Swahili. Additionally, there is a need for health surveillance initiatives that particularly target the age group  $\geq 18$  to < 45 years. These can also be used to help monitor prevention activities. 

#### List of Abbreviations

#### 

BIA	Bioelectrical Impedance Analysis
BMI	Body Mass Index
HbA1c	Glycated Haemoglobin
HDL-C	High Density-Lipoprotein Cholesterol
HOMA-IR	homeostasis model assessment of insulin resistance
IDEFICS	Identification and prevention of Dietary-and lifestyle-induced health EFects In         Children and infantS
IDF	International Diabetes Federation
ISCED	International Standard Classification of Education
LDL-C	Low Density-Lipoprotein Cholesterol
LMICs	Low-middle-Income Countries
NCDs	Non-Communicable Diseases
WC	Waist Circumference
WHO	World Health Organization

Objectives

2 3 4	470	Declarations							
5 6 7	471	Funding							
8 9 10	472	The Leibniz-Gemeinsch	naft gran	t number SAW-2012-ZMT-4 supported this work					
10 11 12	473								
13 14	474	Competing interests							
15 16 17	475	The authors declare that	t they ha	ve no competing interests.					
18 19	476								
20 21	477	Author's Contribution							
22 23 24	478	The authors' responsibilities were as follows: AH and MN were responsible for study							
24 25 26	479	design. AH , MN and SK conducted data collection and developed study hypothesis. MAN							
27 28	480	and CB conducted statistical analyses and KB assisted in the statistical data cleaning. MAN							
29 30	481	wrote the manuscript and had primary responsibility for final content. MN, CB, SK, MS ,KB							
31 32 33	482	and AH critically revised the manuscript and gave final consent.							
34 35	483								
36 37	484	STROBE checklist							
38 39 40 41	485 486 487	86 studies							
42 43 44			Item No	Recommendation					
45 46		Title and abstract	1	( <i>a</i> ) Indicate the study's design with a commonly used term					
47				in the title or the abstract					
48 49				Cross-sectional study					
50		(b) Provide in the abstract an informative and balanced							
51		summary of what was done and what was found							
52 53		Completed in the abstract, please refer to <i>line 27-53</i>							
54		Introduction							
55 56									
56 57		investigation being reported							
This has been explained in the Introduction section									
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State specific objectives, including any prespecified

		<ul> <li>hypotheses</li> <li>-To determine the prevalence of obesity indices (body mass index (BMI), waist circumference (WC), body fat percent (BF%)) and cardio-metabolic risk factors.</li> <li>-To investigate the association between obesity indices and cardio-metabolic risk factors in a Zanzibari population.</li> </ul>
Methods		
Study design	4	Present key elements of study design early in the paper This has been presented in the abstract, please refer to <i>lin</i> <i>31-34</i> .
	10	Key elements of study design : cross-sectional survey, in representative population sample in Unguja Island Zanzibar, households were randomly selected and al household members were invited for the examination.
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection This has been described in the method section, please refer to <i>line 115-125</i>
Participants	6	<ul> <li>(a) Give the eligibility criteria, and the sources and methods of selection of participants</li> <li>This has been described in the method section, refer to <i>line</i> 116-124</li> </ul>
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable This has been defined in the method section, refer to <i>line</i> 150-225 including <b>Table 1</b> <i>line</i> 225-237 Since clinical patients were not included, diagnostic criteric is not applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). -Please refer to method section <i>line 161-225</i> Describe comparability of assessment methods if there is more than one group - <i>Not applicable</i>

### 489 Data sharing statement

490 The datasets generated and/or analysed during the current study are not publicly available

491 since a follow-up study is planned.

#### 492 Acknowledgement

This work was done as part of the Leibniz Graduate School SUTAS (Sustainable Use of Tropical Aquatic Systems; <u>http://www.zmt-bremen.de/SUTAS.html</u>). This study would not have been possible without the voluntary collaboration of the Zanzibari families who participated in the extensive examinations. We are grateful for the support from regional and local community leaders and municipalities. The authors gratefully acknowledge the assistance from all fieldworkers and the laboratory technicians.

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	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract
		Cross-sectional study
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found
		Completed in the abstract, please refer to line 27-53
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
		This has been explained in the Introducion section.
Objectives	3	State specific objectives, including any prespecified hypotheses
		-To determine the prevalence of obesity indices (body mass index (BMI), waist circumference (WC), body fat percent (BF%)) and cardio-metabolic risk factors. -To investigate the association between obesity indices and cardio-metabolic risk factors in a Zanzibari population.
Methods		
Study design	4	Present key elements of study design early in the paper
		This has been presented in the abstract, please refer to line 31-34.
		<b>Key elements of study design</b> : cross-sectional survey , in a representative population sample in Unguja Island, Zanzibar, households were randomly selected and all household members were invited for the examination.
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment,
		exposure, follow-up, and data collection
		This has been described in the method section, please refer to <i>line 115-125</i>
Participants	6	( <i>a</i> ) Give the eligibility criteria, and the sources and methods of selection of participants
		This has been described in the method section, refere to <i>line 116-124</i>
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
		This has been defined in the method section, refer to <i>line 150-225</i> including <b>Table 1</b> <i>line 225-237</i>
		Since clinical patients were not included, diagnostic criteris is not applicable
Data sources/	8*	For each variable of interest, give sources of data and details of methods of
measurement		assessment (measurement).
		-Please refer to method section <i>line 161-225</i>

		-Not applicable
Bias	9	Describe any efforts to address potential sources of bias
		This was described in the inclusion criteria were outliers were deleted from the
		sample in order to reduce bias. Refer to line 246
Study size	10	Explain how the study size was arrived at
		This has been described in <i>line 119-122</i>
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable,
		describe which groupings were chosen and why
		-Quantitative variables were grouped into categories according to the given cut-off
		please refer to method sections anthropometric measurements and cardiometabolic
		risk factors
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding
		(b) Describe any methods used to examine subgroups and interactions
		(c) Explain how missing data were addressed
		( <i>d</i> ) If applicable, describe analytical methods taking account of sampling strategy
		(e) Describe any sensitivity analyses
		-all the above points have been discussed in the statistical analysis, refer to <i>line 25</i>
		272
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially
1		eligible, examined for eligibility, confirmed eligible, included in the study,
		completing follow-up, and analysed
		This has been described in <i>line 242-246</i>
		(b) Give reasons for non-participation at each stage
		This has been described in <i>line 242-246</i>
		(c) Consider use of a flow diagram
		Not fossible because of different and means
Description 1-1	114	-Not feasible because of differet age groups
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and
		information on exposures and potential confounders
		Please refer to <i>line 277-304</i> and <i>Tables 2 and 3</i>
		(b) Indicate number of participants with missing data for each variable of interest
		-This was not described in the manuscript, the missing data for each variable of
		interest were deleted during data cleaning and before running the statistical analysi
		Please refer to the inclusion criteria section for general overview, line 242-248
Outcome data	15*	Report numbers of outcome events or summary measures
		-Please refer to result sections table 3
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and

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		adjusted for and why they were included
		(b) Report category boundaries when continuous variables were categorized
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a
		meaningful time period . Not relevant
		-Please refer to result section tables 4 and 5
Other analyses	17	Report other analyses done-eg analyses of subgroups and interactions, and
		sensitivity analyses
		-This is was not applied to this manuscript.
Discussion		
Key results	18	Summarise key results with reference to study objectives
		-This has been decribed in the discussion section, please refer to line 348 onwards
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or
		imprecision. Discuss both direction and magnitude of any potential bias
		-Limitations of the study have been described in line 427-441
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations,
		multiplicity of analyses, results from similar studies, and other relevant evidence
		-Please refer to the conclusion section from line 353 onwards
Generalisability	21	Discuss the generalisability (external validity) of the study results
		-Based on the findings of the study, similar epidemiological surveys could be
		conducted in the rest of the Island. Please refer to the conclusion section.
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if
		applicable, for the original study on which the present article is based
		-This work was supported by the Leibniz-Gemeinschaft grant number SAW-2012-
		ZMT-4. See line 483
		-The present article is based on the "Access to Food and Nutritional Status of the
		Zanzibari population" study, please refer to reference no.25

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

**BMJ** Open

## **BMJ Open**

#### Association between cardio-metabolic risk factors and body mass index, waist circumferences and body fat in a Zanzibari cross-sectional study

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Complete List of Authors:	Nyangasa, Maria Adam; Leibniz-Institut fur Praventionsforschung und Epidemiologie - BIPS GmbH, Buck, Christoph; Leibniz-Institut fur Praventionsforschung und Epidemiologie - BIPS GmbH Kelm, Soerge; Bremen University Sheikh, Mohammed Ali; State University of Zanzibar Brackmann, Kim Laura; Leibniz-Institut fur Praventionsforschung und Epidemiologie - BIPS GmbH Hebestreit, Antje; Leibniz-Institut fur Praventionsforschung und Epidemiologie - BIPS GmbH
<b>Primary Subject Heading</b> :	Epidemiology
Secondary Subject Heading:	Epidemiology, Diabetes and endocrinology
Keywords:	Hypertension < CARDIOLOGY, children, DIABETES & ENDOCRINOLOGY, adolescents, adults, sub-Saharan Africa

SCHOLARONE<sup>™</sup> Manuscripts

1		
2 3	1	Association between cardio-metabolic risk factors and body mass index, waist
4 5 6	2	circumferences and body fat in a Zanzibari cross-sectional study
6 7 8	3	
9 10		
11 12	4	
13 14	5	Maria Adam Nyangasa <sup>1</sup> , Christoph Buck <sup>1</sup> , Soerge Kelm <sup>2</sup> , Mohammed Ali Sheikh <sup>3</sup> , Kim
15 16	6	Brackmann <sup>1</sup> , Antje Hebestreit <sup>1*</sup>
17 18	7	
19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34	8	
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## 26 Abstract

Objectives: To determine the prevalence of obesity indices (body mass index (BMI), waist
circumference (WC), body fat percent (BF%)) and cardio-metabolic risk factors. To
investigate the association between obesity indices and cardio-metabolic risk factors in a
Zanzibari population.

**Designs:** Cross-sectional study.

Settings: Participants randomly selected from 80 Shehias (wards) in Unguja, Zanzibar in
2013.

Participants: A total of 470 participants between 5-95 years were examined. Data on socioeconomic status, area of residence, anthropometry and venous blood were collected. Associations between obesity indices and cardio-metabolic risk factors were investigated using multilevel logistic regression analyses in two steps: first, each obesity indicator was tested independently; second, all indicators combined in one model were tested for their association with cardio-metabolic risk factors.

**Results:** The proportion of overweight/obese individuals was 26.4%, high WC (24.9%) and high BF% (31.1%). Cardio-metabolic risk factors with highest prevalence of abnormal values included hypertension (24.5%), low HDL-C (29.4%), high LDL-C (21.3%) and high HbA1c (19.1%). Obesity and hypertension increased with age, and were most prevalent in participants aged 45 years and above. Low HDL-C was most prevalent among participants  $\geq$ 18 to < 45 years old, while high LDL-C was more prevalent in those above 45 years. High WC and high BF% were associated with high levels of LDL-C (OR=2.52 (1.24, 5.13), OR=1.91 (1.02, 3.58), respectively). Additionally, BMI and WC were associated with high levels of HbA1c (OR=2.08 (1.15, 3.79), OR=3.01 (1.51, 6.03), respectively). In the combined regression model WC was associated with higher chances for hypertension (OR=2.62 (1.14, 6.06)) and for high levels of HbA1c (OR=2.62 (1.12, 6.15)). Conclusion: High BMI, WC 

3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19	51	and BF% were strongly associated with hypertension, with individuals with high WC being
	52	twice more likely to have hypertension; this calls for early and effective screening strategies
	53	for this study population.
	54	
	55	Key words: hypertension, diabetes, children, adolescents, adults, sub-Saharan Africa
	56	
	57	Strengths and limitations of this study
20 21	57	Strengths and minitations of this study
22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42	58	• This is the first study to report the associations between obesity indices and cardio-
	59	metabolic risk factors in Zanzibar.
	60	• The household-based approach, which involved visiting the families in the home setting,
	61	resulted in a high individual response rate, thus minimising risk of selection bias.
	62	• The cross-sectional design prevents us from drawing conclusions regarding the impact of
	63	changes in obesity indices on risk factors.
	64	• Bioelectrical Impedance Analysis (BIA) was used to estimate body fat percentage, which
	65	might have underestimated adiposity in children.
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## Introduction

Worldwide, cardiovascular diseases (CVDs) are not only the leading cause of death<sup>1</sup>, they are also emerging as a notable public health problem in sub-Saharan African countries <sup>2</sup>. These countries are undergoing epidemiological transitions from communicable to non-communicable diseases (NCDs) that have been closely linked to increased urbanization and rural-urban migration, which has led to unhealthy behaviours, including poor dietary habits and sedentary lifestyles <sup>23</sup>. According to the International Diabetes Federation (IDF), about 12 million people in Africa are estimated to have type 2 diabetes mellitus <sup>4</sup>, with the prevalence ranging from 1% in rural Uganda to 12 % in urban Kenya <sup>56</sup>. Overweight and obesity have been found to be modifiable risk factors for cardio-metabolic and other chronic diseases <sup>7</sup> including hypertension <sup>8</sup>, diabetes <sup>9</sup> and dyslipidemia <sup>10</sup>. The third report of the National Cholesterol Education Program-Adult treatment Panel (NCEP-ATP III) also identified central obesity, dyslipidemia (hypertriglyceridemia and low levels of high-density lipoprotein cholesterol [HDL-C]), impaired glucose tolerance, and elevated blood pressure as cardio-metabolic risk factors<sup>11</sup>. 

Multiple obesity indices such as BMI, Waist Circumference (WC), Body fat percent (BF%) and Waist to Hip Ratio (WtHR) have been widely used to screen individuals for cardiometabolic risk in clinical and research settings<sup>12-14</sup> due to their low-cost and ease of administration. The performance of anthropometric indices may however vary according to different factors, including ethnicity, age, geographical area and population<sup>13</sup><sup>15</sup>. BMI, which is based on weight and height, is the most widely used marker to assess body mass. In children and adolescents, the z-scores are used to classify obesity status <sup>16</sup>, which is linked to metabolic risk, e.g. in South African youth<sup>17</sup>. However, BMI does not distinguish well between lean mass and fat mass<sup>18</sup>. In contrast, WC is a measure of total body and abdominal fat accumulation and is better correlated with visceral adipose tissues than BMI. The 

Page 5 of 31

#### **BMJ** Open

correlation on the other hand varies significantly across ethnicities <sup>19 20</sup>. Another approach for measuring body fat is through bioelectrical impedance analysis, which has also been done in several epidemiological studies<sup>21</sup>. The use of different anthropometric measurements might also provide complementary information which can be used to aid screening for cardio-metabolic risk in different population settings <sup>22</sup> <sup>23</sup>. 

Few studies have investigated the performance of different obesity indices in association with cardio-metabolic risk factors in sub Saharan African populations <sup>2 7 18</sup>. Data from mainland Tanzania have shown an increasing prevalence of overweight and obesity in urban, peri-urban and rural areas <sup>24</sup>. However, there is still a dearth of population-based studies investigating the associations of cardio-metabolic risk factors with obesity indices in Tanzania mainland and Zanzibar. To help fill this gap, this study uses cross-sectional data of 470 individuals between 5-95 years who were examined in 2013 in Unguja Island, Zanzibar, to describe the prevalence of overweight/obesity and cardio-metabolic risk factors in three age groups ( $\geq 5$  to <18 years,  $\geq 18$  to <45 years and above 45 years). The aim of the study was to identify vulnerable groups in the Zanzibari population with respect to cardio-metabolic risk. Consequently, we investigated the association of BMI, WC and BF% with cardio-metabolic risk factors (hypertension, total cholesterol, triglycerides, high-density-lipoprotein, low-density-lipoprotein, glycated HbA1c, fasting plasma glucose and HOMA-IR). We considered the three obesity indices independently as well as combined, thereby reflecting different aspects of body composition.

## Subjects and Methods

#### 114 <u>Study population and design</u>

We conducted a cross-sectional survey from September to December 2013 in a representative population sample in Unguja Island, Zanzibar. A total of 239 households were randomly selected and all household members were invited for the examination. As we also aimed to identify vulnerable groups within the families, we included young children and the elderly, who both normally depend on the family food environment. A two-staged sampling approach was used: (1) from a list of all 213 Shehias (wards), 80 Shehias were randomly selected; (2) households were randomly selected based on the Shehia's registration records. Participation agreement was requested from all members of a household. A total of 1,443 family members agreed to participate and completed anthropometric and blood pressure measurements, as well as interviewer-administered questionnaires. Venous blood was also collected. The subgroup examinations are described in detail below. The complete description of the study design and methods has been described in detail elsewhere <sup>25</sup>. The study was performed according to the Helsinki Declaration and the study protocol was evaluated and approved by the Ethics Committees of the University of Bremen and of the Zanzibar Ministry of Health and the Zanzibar Medical Research and Ethics Committee. All participants gave written informed consent and parents/guardians consented on behalf of their children in writing. 

#### 131 <u>Patient and Public Involvement</u>

During the development of the survey tools, measurements and the study protocol, a meeting was held with the local partners, government officials and researchers in Zanzibar to discuss the needs and gaps of the nutrition and health survey planned in Zanzibar. The documents and instruments were then modified according to the needs of the Zanzibari population as recommended in the meeting. 

Page 7 of 31

#### **BMJ** Open

A year after the survey, preliminary results on the major health outcomes and related risk factors were presented and discussed during a two days feedback workshop with the administrative leaders (e.g. Shehas, district commissioners), stakeholders (from health services, government officials, food safety) and our local partners in Zanzibar (academics and research). Each Sheha was handed a poster of the preliminary results, which was then displayed at their local offices for all Shehia members to see. District commissioners received a summary report on all Shehias of their districts. The preliminary results were further publicised on TV and print media. The same group of workshop participants was invited to a further workshop in 2018, whose aim was to identify target populations and channels for future nutrition education to address the aetiology and prevention of NCDs in the Zanzibari population, taking into consideration the survey results presented also in this study. 

148 This observational epidemiological study examined participants in their home environment149 and did not enrol clinical patients.

#### 150 <u>Questionnaires and anthropometric measurements</u>

Questionnaires were developed in English, translated into Swahili, and then back translated to control for translation errors. Trained field staff collected the survey information. Parents reported their age and sex, as well as that of their children. Age was grouped into three categories  $\geq 5$  to <18 years,  $\geq 18$  to <45 years, and 45 years and above. In addition, parental highest educational level according to the International Standard Classification of Education (ISCED) <sup>26</sup> was used as a proxy indicator for socio-economic status (SES) of the family. Education was categorized into low education (no education and primary school) and high education (secondary school and above). To determine participants' area of residence, information on region, district and Shehia (the smallest administrative unit in Zanzibar) was recorded and two categories for area of residence were developed (urban and rural). Utilization of medication was also documented in the questionnaire. Regarding medication

#### **BMJ** Open

for obesity-related conditions, participants reported use of hypertension medication but not of diabetes or dyslipoproteinemia medication. Hence, the variable was later categorized as "hypertension medication" and "other medication" (e.g. anti-Malaria therapy or antipyretic products). To ensure a high quality of data collection, this study used proven examination methods and laboratory standards <sup>27</sup> <sup>28</sup>. All anthropometric measurements and physical examinations were adopted from the IDEFICS Study and conducted following standardized procedures <sup>29 30</sup>. Measurement of body weight was carried out to the nearest 0.1kg and body fat percent was determined using the bioelectrical impedance analysis (BIA) method using an electronic scale (TANITA BC-420 SMA, Germany). Height was measured using a SECA 213 stadiometer, UK, and waist circumference (WC) was measured midway between the lowest rib and the iliac crest, using an inelastic measuring tape (SECA 201). For all measurements, participants wore light clothing. The measures were recorded to the nearest 0.1cm. The complete description of the anthropometric measurements of the study is described elsewhere <sup>25</sup>. 

For children and adolescents, Body Mass Index (BMI) was calculated as kg/m<sup>2</sup> and then transformed to age-and sex-specific z-score and percentiles. Thereafter, categories for overweight (BMI between >75<sup>th</sup> and <95<sup>th</sup> percentile) and obesity (BMI >95<sup>th</sup> percentile) were built according to the WHO centile curves <sup>31 32</sup>. For adults, overweight/obesity was defined as BMI  $\geq 25 \text{kg/m}^2$  as recommended by WHO <sup>33</sup>. For statistical analysis, the BMI categories were merged into two 1) under-weight/ normal weight ( $\leq 75^{\text{th}}$  percentile for children and adolescents and  $< 25 \text{kg/m}^2$  for adults) and 2) overweight/obesity (>75<sup>th</sup> percentile and  $\geq 25 \text{kg/m}^2$ ). Regarding waist circumference (WC), high abdominal obesity was defined as WC  $\geq$ 90<sup>th</sup> percentile for children below 10 years <sup>34</sup>;WC  $\geq$ 90<sup>th</sup> percentile for adolescents aged 10 - <16 years; and WC >94 cm for men and > 80 cm for women for participants 16 years and older, as recommended by the IDF <sup>35</sup>. As recommended by 

Page 9 of 31

### **BMJ** Open

McCarthy et al. <sup>36</sup>, for boys and girls below 18 years, high body fat percentage (BF%) was set at  $\geq$ 85th percentile. For adults above 18 years, high BF% was defined as  $\geq$ 20 % for men and  $\geq$ 32 % for women <sup>37</sup>. The cut-offs and references are listed in Table 1.

190 <u>Cardio-metabolic risk factors</u>

All blood samples were drawn after overnight fasting and were collected from all eligible participants over 5 years of age by venepuncture <sup>38</sup>. To reduce pain, children below 10 years of age were given a local anaesthetic plaster before blood drawing, which motivated the children to participate. Before blood drawing, the procedure was once again explained to all participants in easy language and they were informed that they still could refuse to participate. For children weighing 10kg, the blood collection was restricted to 1%, corresponding to approximately 8 mL. For healthy, non-pregnant adults weighing at least 50 kg, a maximum of 20.5 mL venous blood was drawn. Collection, processing and storage of blood samples are described elsewhere <sup>25</sup>. 

Metabolic parameters were categorized for investigating the prevalence of cardio-metabolic disorders in the study population. Due to the wide range of age groups in this study population, different cardio-metabolic risk definitions and cut-offs were used (Table 1). Cardio-metabolic risk for children between 5-10 years was defined according to age-sex-specific cut-offs. The parameters, including hypertension (Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP)), blood lipids (high Total Cholesterol (TC), high Triglycerides (TG), Low-Density-Lipoprotein Cholesterol (LDL-C) and High-Density-Lipoprotein Cholesterol (HDL-C)), blood glucose/insulin (Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) and elevated Fasting Plasma Glucose (FPG), were defined according to the IDEFICS Study <sup>34 39</sup>. Glycated haemoglobin (HbA1c) was defined according to Rodoo et al. <sup>40</sup> for children under 17 years. For children and adolescents between 10 years and 16 years, hypertension was defined according to age-sex-specific cut-offs as 

recommended <sup>41</sup>; for adolescents and adults above 16 years hypertension was defined as recommended <sup>42</sup>. Blood lipids (TC and LDL-C) were defined according to the National Cholesterol Education Program (NCEP) 11 and TG, HDL-C and FPG according to the International Diabetes Federation (IDF) <sup>35</sup>. HbA1c for participants above 17 years was defined according to Stern et al. 43 and insulin resistance was estimated as HOMA-IR according to the reference value of HOMA-IR as recommended by Shashaj et al. 44. In the present study, the 75th percentile cut-off was used for children and adolescents from 10 to 17 years. For participants above 17 years, HOMA-IR was defined according to von Eyben et al <sup>45</sup>. HOMA-IR was calculated from glucose (mmol/l)) and insulin ( $\mu$ U/ml) concentrations using the formula: HOMA-IR=(fasting insulin×fasting glucose/22.5)<sup>46</sup>. 

222	
223	Table 1. Cardio-metabolic risk definitions and references

Age group	Obesity Indices and Blood Pressure	Blood lipids	Blood Glucose/Insulin
Children:	BMI $\geq 75^{\text{th}}$ percentile <sup>1</sup>	TC $\geq 90^{\text{th}}$ percentile <sup>2</sup>	$HbA1c \ge 97.5^{th} percentile^{10}$
≤10y	WC $\geq$ 90 <sup>th</sup> percentile <sup>2</sup>	TG $\geq$ 90 <sup>th</sup> percentile <sup>2</sup>	HOMA-IR $\ge$ 95 <sup>th</sup> percentile <sup>2</sup>
	BF %≥85 <sup>th</sup> percentile <sup>3</sup>	HDL-C $\leq 10^{\text{th}}$ percentile <sup>2</sup>	FPG $\ge$ 95 <sup>th</sup> percentile <sup>2</sup>
	SBP $\geq$ 90 <sup>th</sup> centile or DBP $\geq$ 90 <sup>th</sup> centile <sup>2</sup>	LDL $\geq 90^{\text{th}}$ percentile <sup>2</sup>	
Adolescents:	BMI $\geq$ 75 <sup>th</sup> percentile <sup>1</sup>	TC $\geq$ 5.2 mmol/L <sup>6</sup>	HbA1c $\geq$ 97.5 <sup>th</sup> percentile <sup>10</sup>
>10 to	WC $\geq$ 90 <sup>th</sup> percentile <sup>4</sup>	TG $\geq$ 1.7mmol/L <sup>4</sup>	HOMA-IR $\geq 75^{\text{th}}$ percentile <sup>9</sup>
<16 y	BF %≥85 <sup>th</sup> percentile <sup>3</sup>	HDL-C < 1.03 <sup>4</sup>	$FPG \ge 5.6 mmol/L^4$
	SBP≥140mmHg or DBP≥90mmHg <sup>11</sup>	LDL $\geq$ 3.4mmol/L <sup>6</sup>	
Adults:	$BMI \ge 25 \ kg/m^1$	TC ≥5.2 mmol/l <sup>6</sup>	HbA1c $\ge$ 6.1% <sup>5</sup>
≥16y	WC $\ge$ 94 cm male, $\ge$ 80cm female <sup>4</sup>	TG ≥1.7mmol/L, <sup>4</sup>	HOMA-IR >4.65 or HOMA- IR >3.60 and BMI >27.5 kg/m <sup>2 7</sup>
	BF % $\geq$ 20 % male and	HDL-C < 1.03 male,< 1.29	$FPG \ge 5.6 mmol/L^4$

	≥32 %	female <sup>8</sup>	female <sup>4</sup>	
		140mmHg or 90mmHg <sup>12</sup>	LDL $\geq$ 3.4mmol/L <sup>6</sup>	
224				
225	1 WHO			
226	2 IDEFICS Study			
227	3 McCarthy, H.D., et a	I. (2006)		
228	4 IDF 5 Stern, S.E., et al (200	)?) for adulta above	17 voor	
229 230	6 NCEP	<i>(</i> ) 101 adults abov	e 17 years	
230	7 von Eyben, F.E., et a	1 (2005)		
232	8 Gallagher, D., et al (			
232	<b>e</b>		dolescents under 17 years	
234	10 Rodoo P et al. (201			
235			d 7 <sup>th</sup> report respectively	
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237	Inclusion criteria for	study sample		
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238	Of 1,443 individuals	who participate	d in this study, 1,314 fulfille	d the inclusion criteria (age,
	• • • • • • •	0 1 11		
239	sex, weight, height)	for the overall s	tudy analysis. Of the 1,314	participants, 1,234 provided
240	complete waist circ	sumference and	body fat percent measure	ements. Among these, 557
241	provided complete b	lood samples for	the cardio-metabolic risk an	alysis and only 505 were on
242	fasting status. To re	duce bias while	estimating mean and SD in	the regression analysis, we
243	excluded the top 1%	of individuals v	with extremely high values for	or cardio-metabolic risk and
244	obesity indices, leav	ng us with a con	nplete sample of 470 particip	ants for the analysis.
	-	-		5
245	Statistical analysis			
	<b>.</b>			
246	Descriptive analysis	was conducted t	to calculate the mean standar	rd deviation (SD) and range
247	(minimum maximu	n) for continuou	s variables as well as the di	istribution of the categorical
247	(IIIIIIIIaIII, IIIaxiiia		s variables, as well as the a	surbution of the categorical
710	data in N and parag	$n_{1}$	part of the regression analys	sig we tested the peasenry
248	uata ili în allu perce	mages (70). As	part of the regression analys	sis, we tested the necessary
240	accumentions in terms	a of any and at the o	nd normality using residual	plata and O.O. Plata Mixed
249	assumptions in term	s of symmetry a	nd normality using residual-	plots and Q-Q-Plots. Mixed
250	logistic regression n	odels were used	to analyse the association l	between obesity indices and
	cardio-metabolic ris	sk factors. In a	addition, potential clusterir	ng within households was
251				
251				
251 252	considered in terms	of a random inter	rcept. Following the hierarch	y of the municipal structure

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in Zanzibar, we conducted sensitivity analysis modelling either Shehias or households within Shehias as a random intercept in the models. Since the results of the models only showed marginal differences, we only considered the household as a random intercept in our analyses. First, mixed logistic regression models were conducted to estimate the association between each of the three obesity indicators (BMI, WC and BF%) as exposure variables and each of the eight risk factors (hypertension, TC, TG, HDL-C, LDL-C, HbA1c, FPG and HOMA-IR) as dependent variables, in terms of odds ratios (OR) and 95% confidence limits (CI). Since BMI, WC and BF% are interrelated, the strongest relationship with cardio-metabolic risk factors was investigated by conducting mixed logistic regression models. This was done by estimating the association (ORs and 95% CIs) between all three obesity indices as dependent variables in one model and each of the eight risk factors as outcome variables. All models were adjusted for potential confounders and covariates such as gender, age, education level (ISCED), area of residence and utilization of hypertension medication. Statistical analysis was performed using SAS 9.3 (SAS Institute. Cary. NC. U SA); mixed logistic regression models were conducted based on the GLIMMIX procedure; statistical significance was set at  $\alpha = 0.05$ . 

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## **Results**

# 270 Distribution of obesity and cardio-metabolic risk and characteristics of the study population 271 by age groups (n=470)

The mean age was 29 ( $\pm 18$ ) years, with the highest proportion being in the age group ( $\geq 18$  to <45 years) (Table 2). The overall mean values for BMI, WC and BF% were as follows: BMI 22 (± 5.2) kg/m<sup>2</sup>, WC 75 (± 16) cm and BF% 22 (± 11) %. The mean BMI of 26 (± 5.7)  $kg/m^2$  for participants above 45 years was slightly higher than normal, indicating overweight. Mean diastolic blood pressure was in the normal range for all the age groups, but a higher mean value of systolic blood pressure,  $150 (\pm 280)$  mmHg, was observed among participants above 45 years. The mean values of most of the variables showed an increase with age group, except for HDL-C and diabetes markers (HbA1c, serum insulin, plasma glucose and HOMA-IR), which showed no specific trend. 

Of the 470 participants, more than half were women 52.6% (n=247), 51.9% (244) had higher education level and 73.4% (345) resided in urban area. Regarding education level, the majority of those with higher education level were aged  $\geq 18$ -<45 years (150/244 = 61%) (Table 3).

Table 2: Distribution of obesity and cardio-metabolic risk in the study population (n=470) by
age group (means and standard deviation (SD))

	$\geq 5$ to $<18$	years	$\geq$ 18 to <4	15 years	45+y	/ears	Total		
	(n=16	5)	(n=1	95)	(n=)	110)	(n=470)		
	Mean	Range	Mean	Range	Mean	Range	Mean	Range	
	(SD)		(SD)	_	(SD)		(SD)		
Age (years)	12 (3.4)	4.9 -18	28 (8.1)	18-44	57 (9.8)	45-95	29 (18)	4.9-95	
BMI (kg/m)	17 (3.4)	11-34	23 (4.5)	16-37	26 (5.7)	15-49	22 (5.7)	11-49	
WC (cm)	61 (11)	12-103	79 (12)	37-111	88 (0.2)	35-126	75 (16)	12-126	
BF (%)	15 (7.0)	1.6-45	23 (11)	3.0-53	28 (10)	6.2-53	22 (11)	1.6-53	

[	1	1	1	1	1	1	1	
DBP (mmHg)	67 (9.8)	44-97	76 (10)	53-126	88 (15)	62-140	75 (14)	44-140
SBP (mmHg)	110 (13)	69-152	123 (16)	72-197	150 (28)	100-229	125 (24)	69-229
TC (mmol/l)	3.7 (0.7)	1.8-5.9	3.9 (0.8)	2.1-6.0	4.2 (0.8)	0.2-5.9	3.9 (0.8)	0.2-6.0
TG (mmol/l)	0.8 (0.3)	0.3-2.5	0.9 (0.4)	0.0-2.6	1.0 (0.4)	0.4-2.7	0.9 (0.4)	0.0-2.7
HDL-C (mmol/l)	1.4 (0.5)	0.7-3.3	1.5 (0.5)	0.6-3.7	1.4 (0.4)	0.6-3.6	1.4 (0.5)	0.6-3.7
LDL-C (mmol/l)	2.3 (0.9)	0.0-5.0	2.5 (0.9)	0.7-5.1	3.0 (1.0)	0.6-5.1	2.5 (1.0)	0.0-5.
HbA1c (%)	5.7 (0.5)	4.2-8.5	5.6 (0.6)	3.9-9.4	6.0 (0.8)	4.4-10	5.8 (0.6)	3.9-10
Serum Insulin (mmol/l)	4.3 (3.1)	0.4-18	4.8 (2.8)	0.8-17	3.6 (2.3)	0.4-17	4.4 (2.8)	0.4-18
FPG (mmol/l)	4.9 (0.8)	2.0-7.7	4.8 (0.9)	0.5-9.4	5.1 (1.3)	0.2-13	4.9 (1.0)	0.2-13
HOMA-IR	1.0 (0.7)	0.1-4.6	1.1 (0.7)	0.0-4.3	0.9 (0.6)	0.0-4.0	1.0 (0.7)	0.0-4.

> The overall proportion of overweight/obesity with regard to BMI, WC and BF % was 26.4%, 24.9% and 31.1% respectively, and increased with age (Table 2). The highest proportion was observed among participants above 45 years. We observed different trends in the prevalence of metabolic parameters and hypertension across age groups. The prevalence of hypertension, high total cholesterol, LDL-C and HbA1c increased with age, while that for triglycerides and HOMA-IR decreased with age. The most prevalent factors were reduced HDL-C (29.4%), hypertension (24.5%) as well as raised LDL-C (21.3%) and HbA1c levels (19.1%). Although hypertension was more prevalent among participants above 45 years, only about 9.4% (10) of the participants in this age group were on hypertension medication. Further, high LDL-C and HbA1c were more prevalent among participants above 45 years, and low HDL-C was most prevalent among  $\geq 18$  to <45 year olds.

301	Table 3: Characteristics of the study population ( $n=470$ ) by age group ( $n/9$	6)
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			≥18 to years	<45	45+ y	ears	Total		
	n	(%)	n	(%)	n	(%)	n	(%)	
All	165	(100)	195	(100)	110	(100)	470	(100)	
Gender									
Male	85	(51.5)	86	(44.1)	52	(47.3)	223	(47.4)	

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Page 15 of 31

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	≥5 to years		≥18 to <45 years		45+ years		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Female	80	(48.5)	109	(55.9)	58	(52.7)	247	(52.6
Education level								
Low	122	(73.9)	45	(23.1)	59	(53.6)	226	(48.1
High	43	(26.1)	150	(76.9)	51	(46.4)	244	(51.9
Area of residence								
Rural	43	(26.1)	49	(25.1)	33	(30.0)	125	(26.6
Urban	122	(73.9)	146	(74.9)	77	(70.0)	345	(73.4
Obesity Indices								
BMI								
Underweight	83	(50.3)	29	(14.9)	9	(8.18)	121	(25.7
Normal weight	73	(44.2)	106	r í	46	, í	225	(47.9
Overweight/obese	9	(5.45)	60	(30.8)	55	(50.0)	124	(26.4
Waist circumference								
Normal	165	(100)	141	(72.2)	47	(42.7)	353	(75.1
High <sup>a</sup>	0	(0)	54		63	(57.3)	117	(24.9
Body fat %								
Normal	157	(95.2)	121	(62.1)	46	(41.8)	324	(69.0
High <sup>b</sup>	8	(4.86)	74		64	(58.2)	146	(31.1
Hypertension					•			
Normal	123	(74.5)	76	(39.0)	10	(9.09)	209	(44.5
Pre-hypertension	25	(15.8)	89	(45.6)	31	(28.2)	146	(31.1
Hypertension	16	(9.70)	30	(15.4)	69	(62.7)	115	(24.5
Hypertension medication <sup>c</sup>								
Yes	1	(0.61)	12	(6.38)	10	(9.43)	23	(5.02
No	163	(99.4)	176	(93.6)	96	(90.6)	435	(95.0
Dyslipidaemia <sup>d</sup>								
Total cholesterol								•
Normal	161	(97.6)	183	(93.8)	102	(92.7)	446	(94.9
High	4	(2.42)	12	(6.15)	8	(7.27)	24	(5.11
Triglycerides		()		()				
Normal	157	(95.2)	186	(95.4)	105	(95.5)	448	(95.3
High	8	(4.85)	9	(4.62)	5	(4.55)	22	(4.68
HDL-cholesterol		(		(		(		1.00
Normal	126	(76.4)	128	(65.6)	78	(70.9)	332	(70.5
Low	39	(23.6)	67	(34.4)	32	(29.1)	138	(29.4
LDL-cholesterol		(23.0)				<u>(</u> <u></u>	150	(2)
Normal	141	(85.5)	163	(83.6)	66	(60.0)	370	(78.7
High	24		32		44	(40.0)	100	(21.3

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1 2 3					1				1		1
5 4 5			≥5 to years		≥18 to years	<45	45+ y	vears	Tota	l	
6			n	(%)	n	(%)	n	(%)	n	(%)	-
7 8		Diabetes Markers <sup>e</sup>									
9 10		HbA1c									-
11		Normal	142	(86.1)	166	(85.1)	72	(65.5)	380	(80.9)	
12 13		High	23	(13.9)	29	(14.9)	38	(34.5)	90	(19.1)	
13 14		Plasma glucose									
15		Normal	136	(82.4)	167	(85.6)	88	(80.0)	391	(83.2)	
16 17		High	29	(17.6)	28	(14.4)	22	(20.0)	79	(16.8)	
18		HOMA-IR									
19 20		Normal	162	(98.2)	193	(99.0)	109	(99.1)	464	(98.7)	_
21		High	3	(1.82)	2	(1.03)	1	(0.91)	6	(1.28)	
22 22	302			, ooth		0 1			10 24		
23 24	303 304	<sup>a</sup> High WC was defined a between 10-16 years and									
25	304 305	according to IDF cut-off		sauove	10 year	SWC-	- 94 C	11 101 11		u / ou (	in for wonnen
26 27	306	<sup>b</sup> High BF% for adults (o		ight/ob	$ese) \ge 20$	) for me	en and	l≥32 fo	r won	nen acco	ording to
27	307	(NIH/WHO) BMI guidel									C
29	308	<sup>c</sup> Missing information fro									
30 31	309	<sup>d</sup> High dyslipidemia for a									
32	310	LDL-cholesterol (≥3.4mi									
33	311 312	women high and hypertri IDEFICS study <sup>34</sup>	giycei	ndemia	(≥1.7 fi	1mol/1)		l lor chi	lidren	accordi	ng to
34 35	313	<sup>e</sup> High diabetes risk mark	ers: h	igh Hb/	A1c (>6	.1%) 45	. high	fasting	plasm	na gluco	ose (>5.6
36	314	mmol/l) <sup>35</sup> and HOMA-in									
37	315	>3.60 and BMI >27.5 kg	$/m^{2} 43$	and for	childre	n high I	HbA1	c (≥97.5	5 <sup>th</sup> per	centile)	, high fasting
38 39	316	plasma glucose ≥95 <sup>th</sup> per	centile	e and H	OMA-I	$R \ge 95^{th}$	perce	ntile.			
40	317										
41	318	Association between obe	sity in	dices a	nd cardi	o-meta	bolic	risk fact	tors		
42 43			-								
44	319	Obesity indices (BMI, W	/C and	1 BF %	) were o	observe	d to b	e assoc	iated	with on	e or more risk
45 46 47	320	factors. Participants with	high	BMI (C	)R=2.41	(1.33,	4.47))	), high '	WC (O	OR=3.6	8 (1.81, 7.52))
48 49	321	or high BF% (OR=2.51	(1.40,	4.51))	were m	ore like	ely to	be hype	ertensi	ive (Tal	ble 4). Having
50 51 52	322	high WC (OR=2.52 (1.2	4, 5.1	3)) or ł	nigh BF	% (OR	=1.91	(1.02,	3.58))	) was as	ssociated with
52 53 54	323	higher chances of havin	g higł	n LDL-	C. Furt	hermor	e, BM	II (OR=	=2.08	(1.15-3	.79)) and WC
55 56	324	(OR=3.01 (1.51-6.03)) v	vere a	ssociate	ed with	HbA1	c leve	ls. We	furthe	er obser	rved increased
57 58 59	325	OR for obesity indices v	with re	gard to	high to	otal cho	lester	ol, high	trigly	cerides	, low HDL-C
60	326	elevated glucose and HC	MA-I	R. As t	the prop	ortion	of ind	ividual	s with	high H	IOMA-IR was

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very small in our sample (1,28%/n=6), the results was not considered in the final regression
analysis. Regarding goodness of fit of the models, values of the Akaike Information Criterion
(AIC), which estimates the quality of each model relative to that of each of the other models,
showed that models including WC as an obesity index tended to have a slightly stronger
relationship compared to those including BMI and BF%.

Table 4: Associations between obesity indices (independent) and cardio-metabolic risk factors (dependent), adjusted for gender, age, education level, area of residence, and hypertension medication (n=470)

Obesity indices High BMI					High WC				High BF%				
Risk factors	OR	(95%	CI)	AIC	OR	(95% CI)		AIC	OR	(95% CI)		AIC	
Hypertension	2.41	1.33	4.47	504.86	3.68	1.81	7.52	499.79	2.51	1.40	4.51	503.46	
High Total cholesterol	1.13	0.40	3.19	192.74	0.84	0.27	2.66	192.71	1.05	0.37	2.95	192.79	
High Triglycerides	1.79	0.55	5.77	189.88	2.23	0.58	8.66	189.38	1.64	0.52	5.14	190.11	
Low HDL cholesterol	1.21	0.62	2.37	516.08	1.15	0.55	2.42	516.25	1.06	0.54	2.05	516.37	
High LDL cholesterol	1.45	0.78	2.69	457.62	2.52	1.24	5.13	452.23	1.91	1.02	3.58	454.77	
High HbA1c	2.08	1.15	3.79	442.70	3.01	1.51	6.03	438.53	1.75	0.96	3.18	445.23	
High Glucose	2.04	0.93	4.50	397.36	2.07	0.84	5.07	397.98	1.76	0.80	3.87	398.56	

Table 5 presents results of mixed logistic regression models including all three obesity indices to investigate the association with single cardio-metabolic risk factors. Compared to the separate regression models, the ORs for most of the associations were attenuated. However, having high WC was again associated with a higher chance of having hypertension (OR=2.62 (1.14, 6.06)) and having high HbA1c levels (OR=2.62 (1.12, 6.15)). Again, as the proportion of individuals with high HOMA-IR levels was very small in our sample (1,28%/n=6), HOMA-IR was not considered in the final regression analysis.

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344	Table 5: Associations between obesity indices (independent) and cardio-metabolic risk
345	factors (outcome) adjusted by gender, age, education level and area of residence (n=470)

	Combined Obesity Indices						AIC			
Obesity indices		BMI			WC			BF%		total
Risk Factors	OR	(95%	CI)	OR	(95%	6 CI)	OR	(95%)	CI)	
Hypertension	1.19	0.48	2.95	2.62	1.1	6.06	1.48	0.63	3.51	501.3
High Total	1.31	0.25	6.79	0.71	0.1	2.92	1.01	0.19	5.32	196.5
High Triglycerides	1.34	0.25	7.16	1.90	0.3	9.52	1.02	0.19	5.52	193.2
Low HDL	1.35	0.48	3.76	1.09	0.4	2.67	0.82	0.98	2.25	519.9
High LDL	0.63	0.24	1.65	2.34	0.9	5.50	1.81	0.70	4.70	454.6
High HbA1c	1.53	0.61	3.81	2.62	1.1	6.15	0.82	0.32	2.10	441.6
Elevated Glucose	1.67	0.55	5.06	1.54	0.5	4.44	1.03	0.33	3.17	400.6
			5.06							

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### **Discussion**

This study is the first population-based survey in Unguja Island that investigated the association between multiple obesity indices (BMI, WC and BF%) and multiple cardio-metabolic risk factors in a representative Zanzibari population, aged 5-95 years. This study population, as in many other LMICs, is undergoing a coexistence of the double burden of underweight children and overweight/obese adults. Generally, about a quarter of the study population were overweight/obese, and obesity increased with age. This observation has also been reported in demographic health surveys from seven sub-Saharan African countries <sup>47</sup>. In the adult population, the prevalence of overweight/obesity was lower than that in Ghana<sup>7</sup>, but higher than in Nigeria<sup>2</sup> and Benin<sup>48</sup>. On the other hand, more than 50% of the children in this study were underweight, a proportion higher than that in other sub-Saharan African countries (Kenya, Nigeria, South Africa, Equatorial Guinea and Cameroon)<sup>49</sup>.

Dyslipidemia is a risk factor for a variety of cardiovascular diseases and is becoming more prevalent in sub-Saharan Africa, particularly the form of low HDL-C <sup>50 51</sup>. Despite the relatively normal levels of total cholesterol and triglycerides, low HDL-C affected about 29% of the overall population, an indication that low HDL-C affects a large proportion of adults above 18 years.. The low HDL-C levels observed in our study population might therefore be indicative of a notable and evolving cardiovascular risk in the study region. Our results are in line with a recent study in sub-Saharan Africa and Middle East with 30% of the participant having low HDL-C <sup>52</sup>. Other studies in sub-Saharan Africa reported even higher prevalence of low HDL-C, 43.1% in Nigeria<sup>2</sup> and 80% in Botswana<sup>53</sup>, mostly affecting individuals between 35-54 years. 

In the present study, a high proportion of participants with high HbA1c (14%) and elevated fasting glucose (18%) are children below 18 years. Since diabetes in children in LMICs has 

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not received much attention, it is likely that there is a high number of children with sub-clinical complications due to delayed or missed diagnosis as well as a lack of regular monitoring. The high proportions observed in this study are a possible indication that a large proportion of diabetic participants are not aware of their status and are hence not monitored or treated. The fact that diabetes medication was not reported in this sample supports this assumption. However, when using WHO diabetes diagnostic criteria <sup>54</sup>, i.e. HbA1c cut-off  $\geq 6.5\%$  and FPG  $\geq 7.0$  mmol/l, the prevalence of diabetes in participants above 18 years decreased to 8.14% and 3.05%, respectively (data not shown). The most intriguing result however is the high proportion of children between 5 and <18 years being at high risk for diabetes with elevated FPG levels when using cut-off of  $\geq$ 5.6mmol/l. Our results showed that the prevalence of FPG and HOMA-IR in children and adolescents below 18 years was in general higher than that of adults above 18 years, but less than that of adults above 45 years. Results from previous cross-sectional studies have shown that physiological transient insulin resistance develops in children during puberty<sup>55</sup> and decreases again by the end of puberty, regardless of obesity. The decrease in insulin sensitivity in the pubertal period is said to lead to an increase in glucose-stimulated insulin secretion<sup>56</sup>. The high prevalence of FPG and HOMA-IR observed in children and adolescents in our study could hence be due to physiological changes in children and adolescents during pre-pubertal period and puberty. They could however also be due to misreporting (children did not report having eaten prior to the blood drawing), or to a true high risk within this age group. Considering this, we adjusted for age in the regression models in order to control for possible confounding effects of physiological changes through maturation and aging. Interestingly, the prevalence of high FPG decreased from approximately 18% to 0.61% when we used the WHO <sup>54</sup> diabetes diagnostic criteria (FPG  $\geq$ 7mmol/l) for the same age group (data not shown). This, in our opinion, indicates that the majority of the children are at risk for diabetes, and that the cut-off 

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for HbA1c  $\geq$ 6.1% as well as elevated FPG $\geq$ 5.6 mmol/l seem to be better screening tools for identifying those at risk, earlier.

Our study showed a strong association between BMI, WC and BF% and hypertension in the study population. These findings are in agreement with other studies that also reported an association between hypertension/pre-hypertension, BMI and WC 57 as well as BF% 7. Moreover, the association between hypertension and high WC was twice as strong as that with high BMI and high %BF. This result suggests that central obesity may be a better indicator for the risk of hypertension and other cardiovascular diseases in our study population. Thus, optimal body weight control and reduced central obesity risk may have beneficial effects on hypertension control in this population. This study also observed a strong association between WC and LDL-C levels. Obirikorang also reported similar associations in a comparative cross-sectional study conducted in Ghana<sup>7</sup>.

In the separate models, strong associations were observed between BMI, WC and HbA1c levels, which can be explained by the interrelation of the two indices, since abdominal fat accumulation increases in proportion to BMI <sup>58</sup> and BMI is one of the main risk factors for diabetes and pre-diabetes <sup>59</sup>. However, when all three obesity indices were combined, it is only the association between WC and HbA1c levels and hypertension that remained strong. Excessive visceral fat in abdominal obesity is the main source of free fatty acids and inflammatory cytokines, which, according to the literature, might lead to insulin resistance and type 2 diabetes mellitus<sup>60</sup>. This probably explains why WC was strongly associated with diabetes and hypertension in our study population. Therefore, measuring WC using optimal WC cut-off values as was done in this study would be a feasible, less time consuming and cost-effective screening tool to identify at-risk individuals in the Zanzibari population. 

This study has some limitations that should be considered. First, this study investigated the
 association between obesity indices and cardio-metabolic risk factors using cross-sectional

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data; thus we were not able to examine the impact of changes in obesity indices on risk factors. Second, as is done in many epidemiological studies and clinical trials, we used Bioelectrical Impedance Analysis (BIA) to estimate body fat percentage. However, compared to skinfold measurements, BIA measurements may underestimate adiposity in children <sup>61</sup>. Third, even though we excluded participants who reported food or beverage intake prior to blood drawing during the data cleaning process, we cannot entirely rule out misreporting of the "fasting status". According to our power calculation, our sample size of 1,314 individuals would have been enough to reach a statistical power. However, our study sample decreased to 470 due to the individual opt-out option for particular examinations as well as the exclusion of outliers and the requirement of completeness of variables of interest. We nevertheless believe that our findings provide important information for public health stakeholders, policy makers and researchers, despite the fact that some of the detected associations did not reach the significance threshold due to the small sample size. 

The results of this research can be used for the development of interventions or policies by researchers, stakeholders and government officials. The random selection of the study participants and the standardised assessment of anthropometrical and laboratory measurements are main strengths of the present study. Moreover, we consequently applied age- and sex-specific cut-offs that take into account the physiological development characteristic of the young age group, rather than applying the fixed cut-offs used in the adult population. There is little information on the association of multiple obesity indices with multiple cardio-metabolic risk factors in this population; hence, our study provides an important contribution towards filling this gap. 

## 444 Conclusion

This study adds to the literature on the association of obesity with higher risks for hypertension, dyslipidemia and type 2 diabetes mellitus, but for the first time in a Zanzibari population. Based on our findings, we recommend that similar epidemiological studies including children, adolescents, adults and elderly set diabetes and/or pre-diabetes cut-offs of HbA1c at  $\geq 6.1\%$  and/or elevated fasting glucose at  $\geq 5.6$ mmol/l. Where feasible, BF% and WC should be used in addition to BMI for screening and monitoring for dyslipidemia and hypertension. We further conclude that there is a need for effective interventions to create awareness as well as for primary prevention strategies for cardio-metabolic risks and its complications in Unguja Island, using local multidisciplinary approaches in the local language, Swahili. Additionally, there is a need for health surveillance initiatives that particularly target the age group  $\geq 18$  to  $\leq 45$  years. These can also be used to help monitor prevention activities. 

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473 since a follow-up study is planned.

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	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract
		Cross-sectional study
		(b) Provide in the abstract an informative and balanced summary of what was done
		and what was found
		Completed in the abstract, please refer to line 27-53
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
		This has been explained in the Introducion section .
Objectives	3	State specific objectives, including any prespecified hypotheses
		-To determine the prevalence of obesity indices (body mass index (BMI), waist
		circumference (WC), body fat percent (BF%)) and cardio-metabolic risk factors.
		-To investigate the association between obesity indices and cardio-metabolic risk
		factors in a Zanzibari population.
Methods		
Study design	4	Present key elements of study design early in the paper
		This has been presented in the abstract, please refer to line 31-34.
		Key elements of study design : cross-sectional survey , in a representative
		population sample in Unguja Island, Zanzibar, households were randomly selecet
		and all household members were invited for the examination.
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment,
		exposure, follow-up, and data collection
<b>D</b>		This has been described in the method section, please refer to <i>line 115-125</i>
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of
		participants
		This has been described in the method section, refere to line 116-124
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect
		modifiers. Give diagnostic criteria, if applicable
		This has been defined in the method section, refer to <i>line 150-225</i> including Table 1
		line 225-237
		Since clinical patients were not included, diagnostic criteris is not applicable
Data sources/	8*	For each variable of interest, give sources of data and details of methods of
measurement		assessment (measurement).
		-Please refer to method section <i>line 161-225</i>
		Describe comparability of assessment methods if there is more than one group
		Deserve comparating of assessment methods if there is more than the group

	2	
Bias	9	Describe any efforts to address potential sources of bias
		This was described in the inclusion criteria were outliers were deleted from the
		sample in order to reduce bias. Refer to line 246
Study size	10	Explain how the study size was arrived at
		This has been described in <i>line 119-122</i>
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable,
		describe which groupings were chosen and why
		-Quantitative variables were grouped into categories according to the given cut-of
		please refer to method sections anthropometric measurements and cardiometaboli
		risk factors
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confoundin
		(b) Describe any methods used to examine subgroups and interactions
		(c) Explain how missing data were addressed
		( <i>d</i> ) If applicable, describe analytical methods taking account of sampling strategy
		( <u>e</u> ) Describe any sensitivity analyses
		-all the above points have been discussed in the statistical analysis, refer to line 22
		272
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially
		eligible, examined for eligibility, confirmed eligible, included in the study,
		completing follow-up, and analysed
		This has been described in <i>line 242-246</i>
		(b) Give reasons for non-participation at each stage
		This has been described in <i>line 242-246</i>
		(c) Consider use of a flow diagram
		-Not feasible because of differet age groups
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and
		information on exposures and potential confounders
		Please refer to line 277-304 and Tables 2 and 3
		(b) Indicate number of participants with missing data for each variable of interest
		-This was not described in the manuscript, the missing data for each variable of
		interest were deleted during data cleaning and before running the statistical analys
		Please refer to the inclusion criteria section for general overview, line 242-248
Outcome data	15*	Report numbers of outcome events or summary measures
		-Please refer to result sections table 3
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates an
		their precision (eg, 95% confidence interval). Make clear which confounders were

		adjusted for and why they were included
		(b) Report category boundaries when continuous variables were categorized
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a
		meaningful time period . Not relevant
		-Please refer to result section tables 4 and 5
Other analyses	17	Report other analyses done-eg analyses of subgroups and interactions, and
		sensitivity analyses
		-This is was not applied to this manuscript.
Discussion		
Key results	18	Summarise key results with reference to study objectives
		-This has been decribed in the discussion section, please refer to line 348 onwards
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or
		imprecision. Discuss both direction and magnitude of any potential bias
		-Limitations of the study have been described in line 427-441
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations
		multiplicity of analyses, results from similar studies, and other relevant evidence
		-Please refer to the conclusion section from <i>line 353 onwards</i>
Generalisability	21	Discuss the generalisability (external validity) of the study results
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		-Based on the findings of the study, similar epidemiological surveys could be
		conducted in the rest of the Island. Please refer to the conclusion section.
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if
		applicable, for the original study on which the present article is based
		-This work was supported by the Leibniz-Gemeinschaft grant number SAW-2012
		ZMT-4. See line 483
		-The present article is based on the "Access to Food and Nutritional Status of the
		Zanzibari population" study, <i>please refer to reference no.25</i>

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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## **BMJ Open**

### Association between cardio-metabolic risk factors and body mass index, waist circumferences and body fat in a Zanzibari cross-sectional study

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SCHOLARONE<sup>™</sup> Manuscripts

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## 26 Abstract

 Objectives: To determine the prevalence of obesity indices (body mass index (BMI), waist
circumference (WC), body fat percent (BF%)) and cardio-metabolic risk factors. To
investigate the association between obesity indices and cardio-metabolic risk factors in a
Zanzibari population.

**Designs:** Cross-sectional study.

Settings: Participants randomly selected from 80 Shehias (wards) in Unguja, Zanzibar in
2013.

Participants: A total of 470 participants between 5-95 years were examined. Data on socioeconomic status, area of residence, anthropometry and venous blood were collected. Associations between obesity indices and cardio-metabolic risk factors were investigated using multilevel logistic regression analyses in two steps: first, each obesity indicator was tested independently; second, all indicators combined in one model were tested for their association with cardio-metabolic risk factors.

**Results:** The proportion of overweight/obese individuals was 26.4%, high WC (24.9%) and high BF% (31.1%). Cardio-metabolic risk factors with highest prevalence of abnormal values included hypertension (24.5%), low HDL-C (29.4%), high LDL-C (21.3%) and high HbA1c (19.1%). Obesity and hypertension increased with age, and were most prevalent in participants aged 45 years and above. Low HDL-C was most prevalent among participants  $\geq$ 18 to < 45 years old, while high LDL-C was more prevalent in those above 45 years. High WC and high BF% were associated with high levels of LDL-C (OR=2.52 (1.24, 5.13), OR=1.91 (1.02, 3.58), respectively). Additionally, BMI and WC were associated with high levels of HbA1c (OR=2.08 (1.15, 3.79), OR=3.01 (1.51, 6.03), respectively). In the combined regression model WC was associated with higher chances for hypertension (OR=2.62 (1.14, 6.06)) and for high levels of HbA1c (OR=2.62 (1.12, 6.15)). Conclusion: High BMI, WC 

3 4	51	and BF% were strongly associated with hypertension, with individuals with high WC being
5 6 7	52	twice more likely to have hypertension; this calls for early and effective screening strategies
7 8 9	53	for this study population.
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12 13 14	55	Key words: hypertension, diabetes, children, adolescents, adults, sub-Saharan Africa
15 16 17 18	56	
19 20 21	57	Strengths and limitations of this study
22 23	58	• This is the first study to report the associations between obesity indices and cardio-
24 25 26	59	metabolic risk factors in Zanzibar.
27 28	60	• The household-based approach, which involved visiting the families in the home setting,
29 30 31	61	resulted in a high individual response rate, thus minimising risk of selection bias.
32 33	62	• The cross-sectional design prevents us from drawing conclusions regarding the impact of
34 35	63	changes in obesity indices on risk factors.
36 37 38	64	• Bioelectrical Impedance Analysis (BIA) was used to estimate body fat percentage, which
39 40	65	might have underestimated adiposity in children.
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## Introduction

Worldwide, cardiovascular diseases (CVDs) are not only the leading cause of death<sup>1</sup>, they are also emerging as a notable public health problem in sub-Saharan African countries <sup>2</sup>. These countries are undergoing epidemiological transitions from communicable to non-communicable diseases (NCDs) that have been closely linked to increased urbanization and rural-urban migration, which has led to unhealthy behaviours, including poor dietary habits and sedentary lifestyles <sup>23</sup>. According to the International Diabetes Federation (IDF), about 12 million people in Africa are estimated to have type 2 diabetes mellitus <sup>4</sup>, with the prevalence ranging from 1% in rural Uganda to 12 % in urban Kenya <sup>56</sup>. Overweight and obesity have been found to be modifiable risk factors for cardio-metabolic and other chronic diseases <sup>7</sup> including hypertension <sup>8</sup>, diabetes <sup>9</sup> and dyslipidemia <sup>10</sup>. The third report of the National Cholesterol Education Program-Adult treatment Panel (NCEP-ATP III) also identified central obesity, dyslipidemia (hypertriglyceridemia and low levels of high-density lipoprotein cholesterol [HDL-C]), impaired glucose tolerance, and elevated blood pressure as cardio-metabolic risk factors<sup>11</sup>. 

Multiple obesity indices such as BMI, Waist Circumference (WC), Body fat percent (BF%) and Waist to Hip Ratio (WtHR) have been widely used to screen individuals for cardiometabolic risk in clinical and research settings<sup>12-14</sup> due to their low-cost and ease of administration. The performance of anthropometric indices may however vary according to different factors, including ethnicity, age, geographical area and population<sup>13</sup><sup>15</sup>. BMI, which is based on weight and height, is the most widely used marker to assess body mass. In children and adolescents, the z-scores are used to classify obesity status <sup>16</sup>, which is linked to metabolic risk, e.g. in South African youth<sup>17</sup>. However, BMI does not distinguish well between lean mass and fat mass<sup>18</sup>. In contrast, WC is a measure of total body and abdominal fat accumulation and is better correlated with visceral adipose tissues than BMI. The 

Page 5 of 32

### **BMJ** Open

correlation on the other hand varies significantly across ethnicities <sup>19 20</sup>. Another approach for measuring body fat is through bioelectrical impedance analysis, which has also been done in several epidemiological studies<sup>21</sup>. The use of different anthropometric measurements might also provide complementary information which can be used to aid screening for cardio-metabolic risk in different population settings <sup>22</sup> <sup>23</sup>. 

Few studies have investigated the performance of different obesity indices in association with cardio-metabolic risk factors in sub Saharan African populations <sup>2 7 18</sup>. Data from mainland Tanzania have shown an increasing prevalence of overweight and obesity in urban, peri-urban and rural areas <sup>24</sup>. However, there is still a dearth of population-based studies investigating the associations of cardio-metabolic risk factors with obesity indices in Tanzania mainland and Zanzibar. To help fill this gap, this study uses cross-sectional data of 470 individuals between 5-95 years who were examined in 2013 in Unguja Island, Zanzibar, to describe the prevalence of overweight/obesity and cardio-metabolic risk factors in three age groups ( $\geq 5$  to <18 years,  $\geq 18$  to <45 years and above 45 years). The aim of the study was to identify vulnerable groups in the Zanzibari population with respect to cardio-metabolic risk. Consequently, we investigated the association of BMI, WC and BF% with cardio-metabolic risk factors (hypertension, total cholesterol, triglycerides, high-density-lipoprotein, low-density-lipoprotein, glycated HbA1c, fasting plasma glucose and HOMA-IR). We considered the three obesity indices independently as well as combined, thereby reflecting different aspects of body composition.

### **Subjects and Methods**

#### Study population and design

We conducted a cross-sectional survey from September to December 2013 in a representative population sample in Unguja Island, Zanzibar. A total of 239 households were randomly selected and all household members were invited for the examination. As we also aimed to identify vulnerable groups within the families, we included young children and the elderly, who both normally depend on the family food environment. A two-staged sampling approach was used: (1) from a list of all 213 Shehias (wards), 80 Shehias were randomly selected; (2) households were randomly selected based on the Shehia's registration records. Participation agreement was requested from all members of a household. A total of 1,443 family members agreed to participate and completed anthropometric and blood pressure measurements, as well as interviewer-administered questionnaires. Venous blood was also collected. The subgroup examinations are described in detail below. The complete description of the study design and methods has been described in detail elsewhere <sup>25</sup>. The study was performed according to the Helsinki Declaration and the study protocol was evaluated and approved by the Ethics Committees of the University of Bremen and of the Zanzibar Ministry of Health and the Zanzibar Medical Research and Ethics Committee. All participants gave written informed consent and parents/guardians consented on behalf of their children in writing. 

#### Patient and Public Involvement

During the development of the survey tools, measurements and the study protocol, a meeting was held with the local partners, government officials and researchers in Zanzibar to discuss the needs and gaps of the nutrition and health survey planned in Zanzibar. The documents and instruments were then modified according to the needs of the Zanzibari population as recommended in the meeting. 

Page 7 of 32

### **BMJ** Open

A year after the survey, preliminary results on the major health outcomes and related risk factors were presented and discussed during a two days feedback workshop with the administrative leaders (e.g. Shehas, district commissioners), stakeholders (from health services, government officials, food safety) and our local partners in Zanzibar (academics and research). Each Sheha was handed a poster of the preliminary results, which was then displayed at their local offices for all Shehia members to see. District commissioners received a summary report on all Shehias of their districts. The preliminary results were further publicised on TV and print media. The same group of workshop participants was invited to a further workshop in 2018, whose aim was to identify target populations and channels for future nutrition education to address the aetiology and prevention of NCDs in the Zanzibari population, taking into consideration the survey results presented also in this study. 

148 This observational epidemiological study examined participants in their home environment149 and did not enrol clinical patients.

### 150 <u>Questionnaires and anthropometric measurements</u>

Questionnaires were developed in English, translated into Swahili, and then back translated to control for translation errors. Trained field staff collected the survey information. Parents reported their age and sex, as well as that of their children. Age was grouped into three categories  $\geq 5$  to <18 years,  $\geq 18$  to <45 years, and 45 years and above. In addition, parental highest educational level according to the International Standard Classification of Education (ISCED) <sup>26</sup> was used as a proxy indicator for socio-economic status (SES) of the family. Education was categorized into low education (no education and primary school) and high education (secondary school and above). To determine participants' area of residence, information on region, district and Shehia (the smallest administrative unit in Zanzibar) was recorded and two categories for area of residence were developed (urban and rural). Utilization of medication was also documented in the questionnaire. Regarding medication

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for obesity-related conditions, participants reported use of hypertension medication but not of diabetes or dyslipoproteinemia medication. Hence, the variable was later categorized as "hypertension medication" and "other medication" (e.g. anti-Malaria therapy or antipyretic products). To ensure a high quality of data collection, this study used proven examination methods and laboratory standards <sup>27</sup> <sup>28</sup>. All anthropometric measurements and physical examinations were adopted from the IDEFICS Study and conducted following standardized procedures <sup>29 30</sup>. Measurement of body weight was carried out to the nearest 0.1kg and body fat percent was determined using the bioelectrical impedance analysis (BIA) method using an electronic scale (TANITA BC-420 SMA, Germany). Height was measured using a SECA 213 stadiometer, UK, and waist circumference (WC) was measured midway between the lowest rib and the iliac crest, using an inelastic measuring tape (SECA 201). For all measurements, participants wore light clothing. The measures were recorded to the nearest 0.1cm. The complete description of the anthropometric measurements of the study is described elsewhere <sup>25</sup>. 

For children and adolescents, Body Mass Index (BMI) was calculated as kg/m<sup>2</sup> and then transformed to age-and sex-specific z-score and percentiles. Thereafter, categories for overweight (BMI between >75<sup>th</sup> and <95<sup>th</sup> percentile) and obesity (BMI >95<sup>th</sup> percentile) were built according to the WHO centile curves <sup>31 32</sup>. For adults, overweight/obesity was defined as BMI  $\geq 25 \text{kg/m}^2$  as recommended by WHO <sup>33</sup>. For statistical analysis, the BMI categories were merged into two 1) under-weight/ normal weight ( $\leq 75^{\text{th}}$  percentile for children and adolescents and  $< 25 \text{kg/m}^2$  for adults) and 2) overweight/obesity (>75<sup>th</sup> percentile and  $\geq 25 \text{kg/m}^2$ ). Regarding waist circumference (WC), high abdominal obesity was defined as WC  $\geq$ 90<sup>th</sup> percentile for children below 10 years <sup>34</sup>;WC  $\geq$ 90<sup>th</sup> percentile for adolescents aged 10 - <16 years; and WC >94 cm for men and > 80 cm for women for participants 16 years and older, as recommended by the IDF <sup>35</sup>. As recommended by 

Page 9 of 32

### **BMJ** Open

187 McCarthy et al. <sup>36</sup>, for boys and girls below 18 years, high body fat percentage (BF%) was set 188 at  $\geq$ 85th percentile. For adults above 18 years, high BF% was defined as  $\geq$ 20 % for men and 189  $\geq$ 32 % for women <sup>37</sup>. The cut-offs and references are listed in Table 1.

190 <u>Cardio-metabolic risk factors</u>

All blood samples were drawn after overnight fasting and were collected from all eligible participants over 5 years of age by venepuncture <sup>38</sup>. To reduce pain, children below 10 years of age were given a local anaesthetic plaster before blood drawing, which motivated the children to participate. Before blood drawing, the procedure was once again explained to all participants in easy language and they were informed that they still could refuse to participate. For children weighing 10kg, the blood collection was restricted to 1%, corresponding to approximately 8 mL. For healthy, non-pregnant adults weighing at least 50 kg, a maximum of 20.5 mL venous blood was drawn. Collection, processing and storage of blood samples are described elsewhere <sup>25</sup>. 

Metabolic parameters were categorized for investigating the prevalence of cardio-metabolic disorders in the study population. Due to the wide range of age groups in this study population, different cardio-metabolic risk definitions and cut-offs were used (Table 1). Cardio-metabolic risk for children between 5-10 years was defined according to age-sex-specific cut-offs. The parameters, including hypertension (Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP)), blood lipids (high Total Cholesterol (TC), high Triglycerides (TG), Low-Density-Lipoprotein Cholesterol (LDL-C) and High-Density-Lipoprotein Cholesterol (HDL-C)), blood glucose/insulin (Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) and elevated Fasting Plasma Glucose (FPG), were defined according to the IDEFICS Study <sup>34 39</sup>. Glycated haemoglobin (HbA1c) was defined according to Rodoo et al. <sup>40</sup> for children under 17 years. For children and adolescents between 10 years and 16 years, hypertension was defined according to age-sex-specific cut-offs as 

recommended <sup>41</sup>; for adolescents and adults above 16 years hypertension was defined as recommended <sup>42</sup>. Blood lipids (TC and LDL-C) were defined according to the National Cholesterol Education Program (NCEP) 11 and TG, HDL-C and FPG according to the International Diabetes Federation (IDF) <sup>35</sup>. HbA1c for participants above 17 years was defined according to Stern et al. 43 and insulin resistance was estimated as HOMA-IR according to the reference value of HOMA-IR as recommended by Shashaj et al. 44. In the present study, the 75th percentile cut-off was used for children and adolescents from 10 to 17 years. For participants above 17 years, HOMA-IR was defined according to von Eyben et al <sup>45</sup>. HOMA-IR was calculated from glucose (mmol/l)) and insulin ( $\mu$ U/ml) concentrations using the formula: HOMA-IR=(fasting insulin×fasting glucose/22.5)<sup>46</sup>. 

222	
223	Table 1. Cardio-metabolic risk definitions and references

Age group	Obesity Indices and Blood Pressure	Blood lipids	Blood Glucose/Insulin
Children: BMI $\geq$ 75 <sup>th</sup> percentile <sup>1</sup>		TC $\geq$ 90 <sup>th</sup> percentile <sup>2</sup>	$HbA1c \ge 97.5^{th} percentile^{10}$
≤10y	WC $\geq$ 90 <sup>th</sup> percentile <sup>2</sup>	TG $\geq$ 90 <sup>th</sup> percentile <sup>2</sup>	HOMA-IR $\geq$ 95 <sup>th</sup> percentile <sup>2</sup>
	BF %≥85 <sup>th</sup> percentile <sup>3</sup>	HDL-C $\leq 10^{\text{th}}$ percentile <sup>2</sup>	$FPG \ge 95^{th}$ percentile <sup>2</sup>
	SBP $\geq$ 90 <sup>th</sup> centile or DBP $\geq$ 90 <sup>th</sup> centile <sup>2</sup>	$LDL \ge 90^{th}$ percentile <sup>2</sup>	
Adolescents:	BMI $\geq$ 75 <sup>th</sup> percentile <sup>1</sup>	TC ≥5.2 mmol/L <sup>6</sup>	HbA1c $\geq$ 97.5 <sup>th</sup> percentile <sup>10</sup>
>10 to	WC $\geq$ 90 <sup>th</sup> percentile <sup>4</sup>	TG $\geq$ 1.7mmol/L <sup>4</sup>	HOMA-IR $\geq$ 75 <sup>th</sup> percentile <sup>9</sup>
<16 y	BF %≥85 <sup>th</sup> percentile <sup>3</sup>	HDL-C < 1.03 <sup>4</sup>	FPG $\geq$ 5.6mmol/L <sup>4</sup>
	SBP≥140mmHg or DBP≥90mmHg <sup>11</sup>	LDL $\geq$ 3.4mmol/L <sup>6</sup>	
Adults:	$BMI \ge 25 \ kg/m^1$	TC ≥5.2 mmol/l <sup>6</sup>	$HbA1c \ge 6.1\%^{5}$
≥16y	WC $\geq$ 94 cm male, $\geq$ 80cm female <sup>4</sup>	$TG \ge 1.7 \text{mmol/L},^4$	HOMA-IR >4.65 or HOMA- IR >3.60 and BMI >27.5 kg/m <sup>2 7</sup>
	BF % $\geq$ 20 % male and	HDL-C < 1.03 male,< 1.29	$FPG \ge 5.6 mmol/L^4$

	<u> </u>	32 % female <sup>8</sup>	female <sup>4</sup>					
		BP≥140mmHg or BP≥90mmHg <sup>12</sup>	LDL $\geq$ 3.4mmol/L <sup>6</sup>					
224								
225	1 WHO							
226	5	2 IDEFICS Study						
227 228	3 McCarthy, H.D., et al. (2006) 4 IDF							
229		5 Stern, S.E., et al (2003) for adults above 17 years						
230								
231	7 von Eyben, F.E., et al (2005)							
232	8 Gallagher, D., et al (200)							
233	9 Shashaj et al. (2015) for children and adolescents under 17 years							
234	10 Rodoo P et al. (2013)							
235	11, 12 National Institute of Health 3 <sup>rd</sup> and 7 <sup>th</sup> report respectively							
236								
237	Inclusion criteria	Inclusion criteria for study sample						
237	inclusion enteria for study sample							
238	Of 1 443 individ	f 1,443 individuals who participated in this study, 1,314 fulfilled the inclusion criteria (age,						
200	01 1,110 marvie	or i, i is marviduals who participated in this study, 1,514 furnited the inclusion criteria (age,						
239	sex weight hei	sex, weight, height) for the overall study analysis. Of the 1,314 participants, 1,234 provided						
255								
240	complete waist straumforence and hady for noreant maggingments. Among these is							
240	complete waist circumference and body fat percent measurements. Among these, 557							
241	provided compl	provided complete blood complex for the condia metabolic risk surfaces and surfaces 505						
241	provided complete blood samples for the cardio-metabolic risk analysis and only 505 were on							
242	forting status. To make a king while actimating ways and CD in the manual in the							
242	lasting status. I	fasting status. To reduce bias while estimating mean and SD in the regression analysis, we						
242	excluded the top 1% of individuals with extremely high values for cardio-metabolic risk and							
243								
244	obesity indices, leaving us with a complete sample of 470 participants for the analysis.							
245	Statistical analys	Statistical analysis						
246	Descriptive analysis was conducted to calculate the mean standard deviation (SD) and range							
247	(minimum, max	minimum, maximum) for continuous variables, as well as the distribution of the categorical						
248	data in N and p	data in N and percentages (%). As part of the regression analysis, we tested the necessary						
	1			2				
249	assumptions in terms of symmetry and normality using residual-plots and Q-Q-Pl							
		······································						
250	logistic regressi	on models were used t	to analyse the association betw	veen obesity indices and				
250	10515110 10510551	shi models were used	to analyse the association betw	veen obesity marces and				
251	cardio metaboli	cardio-metabolic risk factors. In addition, potential clustering within households was						
251	caruio-inclauoin	2 115K 1001015. 111 ac	iunion, potential clustering	within nouscholus was				
252	considered in to	considered in terms of a random intercept. Following the hierarchy of the municipal structure						
252	considered in terms of a random intercept. Fonowing the merarchy of the multicipal sut							

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in Zanzibar, we conducted sensitivity analysis modelling either Shehias or households within Shehias as a random intercept in the models. Since the results of the models only showed marginal differences, we only considered the household as a random intercept in our analyses. First, mixed logistic regression models were conducted to estimate the association between each of the three obesity indicators (BMI, WC and BF%) as exposure variables and each of the eight risk factors (hypertension, TC, TG, HDL-C, LDL-C, HbA1c, FPG and HOMA-IR) as dependent variables, in terms of odds ratios (OR) and 95% confidence limits (CI). Since BMI, WC and BF% are interrelated, the strongest relationship with cardio-metabolic risk factors was investigated by conducting mixed logistic regression models. This was done by estimating the association (ORs and 95% CIs) between all three obesity indices as dependent variables in one model and each of the eight risk factors as outcome variables. All models were adjusted for potential confounders and covariates such as gender, age, education level (ISCED), area of residence and utilization of hypertension medication. Statistical analysis was performed using SAS 9.3 (SAS Institute. Cary. NC. U SA); mixed logistic regression models were conducted based on the GLIMMIX procedure; statistical significance was set at  $\alpha = 0.05$ . 

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## **Results**

# 270 Distribution of obesity and cardio-metabolic risk and characteristics of the study population 271 by age groups (n=470)

The mean age was 29 ( $\pm 18$ ) years, with the highest proportion being in the age group ( $\geq 18$  to <45 years) (Table 2). The overall mean values for BMI, WC and BF% were as follows: BMI 22 (± 5.2) kg/m<sup>2</sup>, WC 75 (± 16) cm and BF% 22 (± 11) %. The mean BMI of 26 (± 5.7)  $kg/m^2$  for participants above 45 years was slightly higher than normal, indicating overweight. Mean diastolic blood pressure was in the normal range for all the age groups, but a higher mean value of systolic blood pressure,  $150 (\pm 280)$  mmHg, was observed among participants above 45 years. The mean values of most of the variables showed an increase with age group, except for HDL-C and diabetes markers (HbA1c, serum insulin, plasma glucose and HOMA-IR), which showed no specific trend. 

Of the 470 participants, more than half were women 52.6% (n=247), 51.9% (244) had higher education level and 73.4% (345) resided in urban area. Regarding education level, the majority of those with higher education level were aged  $\geq 18$ -<45 years (150/244 = 61%) (Table 3).

Table 2: Distribution of obesity and cardio-metabolic risk in the study population (n=470) by
age group (means and standard deviation (SD))

		$\geq$ 5 to <18 years (n=165)		15 years		years 110)	Total (n=470)	
	Mean	Range	(n=1 Mean	Range	Mean	Range	Mean	Range
	(SD)		(SD)		(SD)		(SD)	
Age (years)	12 (3.4)	4.9 -18	28 (8.1)	18-44	57 (9.8)	45-95	29 (18)	4.9-95
BMI (kg/m)	17 (3.4)	11-34	23 (4.5)	16-37	26 (5.7)	15-49	22 (5.7)	11-49
WC (cm)	61 (11)	12-103	79 (12)	37-111	88 (0.2)	35-126	75 (16)	12-126
BF (%)	15 (7.0)	1.6-45	23 (11)	3.0-53	28 (10)	6.2-53	22 (11)	1.6-53

DBP (mmHg)	67 (9.8)	44-97	76 (10)	53-126	88 (15)	62-140	75 (14)	44-140
SBP (mmHg)	110 (13)	69-152	123 (16)	72-197	150 (28)	100-229	125 (24)	69-229
TC (mmol/l)	3.7 (0.7)	1.8-5.9	3.9 (0.8)	2.1-6.0	4.2 (0.8)	0.2-5.9	3.9 (0.8)	0.2-6.0
TG (mmol/l)	0.8 (0.3)	0.3-2.5	0.9 (0.4)	0.0-2.6	1.0 (0.4)	0.4-2.7	0.9 (0.4)	0.0-2.7
HDL-C (mmol/l)	1.4 (0.5)	0.7-3.3	1.5 (0.5)	0.6-3.7	1.4 (0.4)	0.6-3.6	1.4 (0.5)	0.6-3.7
LDL-C (mmol/l)	2.3 (0.9)	0.0-5.0	2.5 (0.9)	0.7-5.1	3.0 (1.0)	0.6-5.1	2.5 (1.0)	0.0-5.1
HbA1c (%)	5.7 (0.5)	4.2-8.5	5.6 (0.6)	3.9-9.4	6.0 (0.8)	4.4-10	5.8 (0.6)	3.9-10
Serum Insulin (mmol/l)	4.3 (3.1)	0.4-18	4.8 (2.8)	0.8-17	3.6 (2.3)	0.4-17	4.4 (2.8)	0.4-18
FPG (mmol/l)	4.9 (0.8)	2.0-7.7	4.8 (0.9)	0.5-9.4	5.1 (1.3)	0.2-13	4.9 (1.0)	0.2-13
HOMA-IR	1.0 (0.7)	0.1-4.6	1.1 (0.7)	0.0-4.3	0.9 (0.6)	0.0-4.0	1.0 (0.7)	0.0-4.6

> The overall proportion of overweight/obesity with regard to BMI, WC and BF % was 26.4%, 24.9% and 31.1% respectively, and increased with age (Table 2). The highest proportion was observed among participants above 45 years. We observed different trends in the prevalence of metabolic parameters and hypertension across age groups. The prevalence of hypertension, high total cholesterol, LDL-C and HbA1c increased with age, while that for triglycerides and HOMA-IR decreased with age. The most prevalent factors were reduced HDL-C (29.4%), hypertension (24.5%) as well as raised LDL-C (21.3%) and HbA1c levels (19.1%). Although hypertension was more prevalent among participants above 45 years, only about 9.4% (10) of the participants in this age group were on hypertension medication. Further, high LDL-C and HbA1c were more prevalent among participants above 45 years, and low HDL-C was most prevalent among  $\geq 18$  to <45 year olds.

Table 3: Characteristics of the study population (n=470) by age group (n/%)

			≥18 to years	<45	45+ y	ears	Total		
	n	(%)	n	(%)	n	(%)	n	(%)	
All	165	(100)	195	(100)	110	(100)	470	(100)	
Gender									
Male	85	(51.5)	86	(44.1)	52	(47.3)	223	(47.4)	

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Page 15 of 32

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		≥5 to <18 years		<45	45+ years		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Female	80	(48.5)	109	(55.9)	58	(52.7)	247	(52.6)
Education level								
Low	122	(73.9)	45	(23.1)	59	(53.6)	226	(48.1
High	43	(26.1)	150	(76.9)	51	(46.4)	244	(51.9)
Area of residence								
Rural	43	(26.1)	49	(25.1)	33	(30.0)	125	(26.6
Urban	122	(73.9)	146	(74.9)	77	(70.0)	345	(73.4
Obesity Indices								
BMI								
Underweight	83	(50.3)	29	(14.9)	9	(8.18)	121	(25.7
Normal weight	73	(44.2)	106	<u>í</u>	46	(41.8)	225	(47.9
Overweight/obese	9		60	· ·	55	(50.0)	124	(26.4
Waist circumference								
Normal	165	(100)	141	(72.2)	47	(42.7)	353	(75.1
High <sup>a</sup>	0	(0)	54	È é é é é é é é é é é é é é é é é é é é	63	(57.3)	117	(24.9
Body fat %								
Normal	157	(95.2)	121	(62.1)	46	(41.8)	324	(69.0
High <sup>b</sup>	8	(4.86)	74		64	(58.2)	146	(31.1
Hypertension					•			
Normal	123	(74.5)	76	(39.0)	10	(9.09)	209	(44.5
Pre-hypertension	25		89	(45.6)	31	(28.2)	146	
Hypertension	16	(9.70)	30	(15.4)	69	(62.7)	115	(24.5
Hypertension medication <sup>c</sup>								
Yes	1	(0.61)	12	(6.38)	10	(9.43)	23	(5.02
No	163	(99.4)	176	(93.6)	96	(90.6)	435	(95.0
Dyslipidaemia <sup>d</sup>								
Total cholesterol								
Normal	161	(97.6)	183	(93.8)	102	(92.7)	446	(94.9
High	4	Ĺ Ó	12	(6.15)	8	(7.27)	24	
Triglycerides								
Normal	157	(95.2)	186	(95.4)	105	(95.5)	448	(95.3
High	8	(4.85)	9	(4.62)	5	(4.55)	22	(4.68
HDL-cholesterol								
Normal	126	(76.4)	128	(65.6)	78	(70.9)	332	(70.5
Low	39	Ĺ Ó	67	(34.4)	32	(29.1)	138	(29.4
LDL-cholesterol		()				()		
Normal	141	(85.5)	163	(83.6)	66	(60.0)	370	(78.7
High	24		32		44	, í	100	

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	_		≥18 to years	<45	45+ years		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Diabetes Markers <sup>e</sup>								
HbA1c								
Normal	142	(86.1)	166	(85.1)	72	(65.5)	380	(80.9)
High	23	(13.9)	29	(14.9)	38	(34.5)	90	(19.1)
Plasma glucose								
Normal	136	(82.4)	167	(85.6)	88	(80.0)	391	(83.2)
High	29	(17.6)	28	(14.4)	22	(20.0)	79	(16.8)
HOMA-IR								
Normal	162	(98.2)	193	(99.0)	109	(99.1)	464	(98.7)
High	3	(1.82)	2	(1.03)	1	(0.91)	6	(1.28)

<sup>a</sup> High WC was defined as WC  $\geq$ 90<sup>th</sup> percentile for children under 10y <sup>34</sup>. Adolescents

between 10-16 years and adults above 16 years WC > 94 cm for men and > 80 cm for women according to IDF cut-off  $^{35}$ 

<sup>306</sup> <sup>b</sup> High BF% for adults (overweight/obese)  $\geq 20$  for men and  $\geq 32$  for women according to <sup>307</sup> (NIH/WHO) BMI guidelines <sup>37</sup> and  $\geq 85^{\text{th}}$  percentile for children <sup>36</sup>

9 308 <sup>c</sup> Missing information from 12 participants (n=458)

 $^{30}$  309 <sup>d</sup> High dyslipidemia for adults; was defined as total serum cholesterol ( $\geq 6.2$ mmol/l) and

1 310 LDL-cholesterol ( $\geq$ 3.4mmol/l) <sup>11</sup> low HDL-C:<1.03 mmol/l in men or <1.29 mmol/l in 311 women high and hypertriglyceridemia ( $\geq$ 1.7 mmol/l) <sup>35</sup> and for children according to 312 IDEFICS study <sup>34</sup>

<sup>34</sup> <sup>312</sup> <sup>1</sup>DEFICS study <sup>41</sup> <sup>6</sup> High diabetes risk markers; high HbA1c (>6.1%) <sup>45</sup>, high fasting plasma glucose ( $\geq$ 5.6 <sup>36</sup> <sup>314</sup> mmol/l) <sup>35</sup> and HOMA-insulin resistance was defined as HOMA-IR >4.65. or HOMA-IR

7 315 >3.60 and BMI >27.5 kg/m<sup>2 43</sup> and for children high HbA1c ( $\geq$ 97.5<sup>th</sup> percentile), high fasting

<sup>38</sup> 316 plasma glucose  $\geq$  95<sup>th</sup> percentile and HOMA-IR  $\geq$  95<sup>th</sup> percentile.

318 Association between obesity indices and cardio-metabolic risk factors

319 Obesity indices (BMI, WC and BF %) were observed to be associated with one or more risk

5 320 factors. Participants with high BMI (OR=2.41 (1.33, 4.47)), high WC (OR=3.68 (1.81, 7.52))

<sup>3</sup> 321 or high BF% (OR=2.51 (1.40, 4.51)) were more likely to be hypertensive (Table 4). Having

322 high WC (OR=2.52 (1.24, 5.13)) or high BF% (OR=1.91 (1.02, 3.58)) was associated with

3 323 higher chances of having high LDL-C. Furthermore, BMI (OR=2.08 (1.15-3.79)) and WC

324 (OR=3.01 (1.51-6.03)) were associated with HbA1c levels. We further observed increased

 $^{7}_{\circ}$  325 OR for obesity indices with regard to high total cholesterol, high triglycerides, low HDL-C,

<sup>59</sup> <sub>60</sub> <sup>326</sup> elevated glucose and HOMA-IR. As the proportion of individuals with high HOMA-IR was

very small in our sample (1,28%/n=6), the results was not considered in the final regression
analysis. Regarding goodness of fit of the models, values of the Akaike Information Criterion
(AIC), which estimates the quality of each model relative to that of each of the other models,
showed that models including WC as an obesity index tended to have a slightly stronger
relationship compared to those including BMI and BF%.

Table 4: Associations between obesity indices (independent) and cardio-metabolic risk factors (dependent), adjusted for gender, age, education level, area of residence, and hypertension medication (n=470)

Obesity indices	Obesity indices High BMI					Hig	h WC		High BF%			
<b>Risk factors</b>	OR	(95%	CI)	AIC	C OR (95%		CI)	AIC	OR	(95% CI)		AIC
Hypertension	2.41	1.33	4.47	504.86	3.68	1.81	7.52	499.79	2.51	1.40	4.51	503.46
High Total cholesterol	1.13	0.40	3.19	192.74	0.84	0.27	2.66	192.71	1.05	0.37	2.95	192.79
High Triglycerides	1.79	0.55	5.77	189.88	2.23	0.58	8.66	189.38	1.64	0.52	5.14	190.11
Low HDL cholesterol	1.21	0.62	2.37	516.08	1.15	0.55	2.42	516.25	1.06	0.54	2.05	516.37
High LDL cholesterol	1.45	0.78	2.69	457.62	2.52	1.24	5.13	452.23	1.91	1.02	3.58	454.77
High HbA1c	2.08	1.15	3.79	442.70	3.01	1.51	6.03	438.53	1.75	0.96	3.18	445.23
High Glucose	2.04	0.93	4.50	397.36	2.07	0.84	5.07	397.98	1.76	0.80	3.87	398.56

Table 5 presents results of mixed logistic regression models including all three obesity indices to investigate the association with single cardio-metabolic risk factors. Compared to the separate regression models, the ORs for most of the associations were attenuated. However, having high WC was again associated with a higher chance of having hypertension (OR=2.62 (1.14, 6.06)) and having high HbA1c levels (OR=2.62 (1.12, 6.15)). Again, as the proportion of individuals with high HOMA-IR levels was very small in our sample (1,28%/n=6), HOMA-IR was not considered in the final regression analysis.

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> Table 5: Associations between obesity indices (independent) and cardio-metabolic risk 344 factors (outcome) adjusted by gender, age, education level and area of residence (n=470) 345

		Combined Obesity Indices								
Obesity indices		BMI			WC			BF%		total
Risk Factors	OR	(95%)	CI)	OR	(95%	o CI)	OR	(95%	CI)	
Hypertension	1.19	0.48	2.95	2.62	1.1	6.06	1.48	0.63	3.51	501.3
High Total	1.31	0.25	6.79	0.71	0.1	2.92	1.01	0.19	5.32	196.5
High Triglycerides	1.34	0.25	7.16	1.90	0.3	9.52	1.02	0.19	5.52	193.2
Low HDL	1.35	0.48	3.76	1.09	0.4	2.67	0.82	0.98	2.25	519.9
High LDL	0.63	0.24	1.65	2.34	0.9	5.50	1.81	0.70	4.70	454.6
High HbA1c	1.53	0.61	3.81	2.62	1.1	6.15	0.82	0.32	2.10	441.6
Elevated Glucose	1.67	0.55	5.06	1.54	0.5	4.44	1.03	0.33	3.17	400.6
	1.53									

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#### **Discussion**

This study is the first population-based survey in Unguja Island that investigated the association between multiple obesity indices (BMI, WC and BF%) and multiple cardio-metabolic risk factors in a representative Zanzibari population, aged 5-95 years. This study population, as in many other LMICs, is undergoing a coexistence of the double burden of underweight children and overweight/obese adults. Generally, about a quarter of the study population were overweight/obese, and obesity increased with age. This observation has also been reported in demographic health surveys from seven sub-Saharan African countries <sup>47</sup>. In the adult population, the prevalence of overweight/obesity was lower than that in Ghana<sup>7</sup>, but higher than in Nigeria<sup>2</sup> and Benin<sup>48</sup>. On the other hand, more than 50% of the children in this study were underweight, a proportion higher than that in other sub-Saharan African countries (Kenya, Nigeria, South Africa, Equatorial Guinea and Cameroon)<sup>49</sup>.

Dyslipidemia is a risk factor for a variety of cardiovascular diseases and is becoming more prevalent in sub-Saharan Africa, particularly the form of low HDL-C <sup>50 51</sup>. Despite the relatively normal levels of total cholesterol and triglycerides, low HDL-C affected about 29% of the overall population, an indication that low HDL-C affects a large proportion of adults above 18 years.. The low HDL-C levels observed in our study population might therefore be indicative of a notable and evolving cardiovascular risk in the study region. Our results are in line with a recent study in sub-Saharan Africa and Middle East with 30% of the participant having low HDL-C <sup>52</sup>. Other studies in sub-Saharan Africa reported even higher prevalence of low HDL-C, 43.1% in Nigeria<sup>2</sup> and 80% in Botswana<sup>53</sup>, mostly affecting individuals between 35-54 years. 

In the present study, a high proportion of participants with high HbA1c (14%) and elevated fasting glucose (18%) are children below 18 years. Since diabetes in children in LMICs has 

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not received much attention, it is likely that there is a high number of children with sub-clinical complications due to delayed or missed diagnosis as well as a lack of regular monitoring. The high proportions observed in this study are a possible indication that a large proportion of diabetic participants are not aware of their status and are hence not monitored or treated. The fact that diabetes medication was not reported in this sample supports this assumption. However, when using WHO diabetes diagnostic criteria <sup>54</sup>, i.e. HbA1c cut-off  $\geq 6.5\%$  and FPG  $\geq 7.0$  mmol/l, the prevalence of diabetes in participants above 18 years decreased to 8.14% and 3.05%, respectively (data not shown). The most intriguing result however is the high proportion of children between 5 and <18 years being at high risk for diabetes with elevated FPG levels when using cut-off of  $\geq$ 5.6mmol/l. Our results showed that the prevalence of FPG and HOMA-IR in children and adolescents below 18 years was in general higher than that of adults above 18 years, but less than that of adults above 45 years. Results from previous cross-sectional studies have shown that physiological transient insulin resistance develops in children during puberty<sup>55</sup> and decreases again by the end of puberty, regardless of obesity. The decrease in insulin sensitivity in the pubertal period is said to lead to an increase in glucose-stimulated insulin secretion<sup>56</sup>. The high prevalence of FPG and HOMA-IR observed in children and adolescents in our study could hence be due to physiological changes in children and adolescents during pre-pubertal period and puberty. They could however also be due to misreporting (children did not report having eaten prior to the blood drawing), or to a true high risk within this age group. Considering this, we adjusted for age in the regression models in order to control for possible confounding effects of physiological changes through maturation and aging. Interestingly, the prevalence of high FPG decreased from approximately 18% to 0.61% when we used the WHO <sup>54</sup> diabetes diagnostic criteria (FPG  $\geq$ 7mmol/l) for the same age group (data not shown). This, in our opinion, indicates that the majority of the children are at risk for diabetes, and that the cut-off 

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for HbA1c  $\geq$ 6.1% as well as elevated FPG $\geq$ 5.6 mmol/l seem to be better screening tools for identifying those at risk, earlier.

Our study showed a strong association between BMI, WC and BF% and hypertension in the study population. These findings are in agreement with other studies that also reported an association between hypertension/pre-hypertension, BMI and WC 57 as well as BF% 7. Moreover, the association between hypertension and high WC was twice as strong as that with high BMI and high %BF. This result suggests that central obesity may be a better indicator for the risk of hypertension and other cardiovascular diseases in our study population. Thus, optimal body weight control and reduced central obesity risk may have beneficial effects on hypertension control in this population. This study also observed a strong association between WC and LDL-C levels. Obirikorang also reported similar associations in a comparative cross-sectional study conducted in Ghana<sup>7</sup>.

In the separate models, strong associations were observed between BMI, WC and HbA1c levels, which can be explained by the interrelation of the two indices, since abdominal fat accumulation increases in proportion to BMI <sup>58</sup> and BMI is one of the main risk factors for diabetes and pre-diabetes <sup>59</sup>. However, when all three obesity indices were combined, it is only the association between WC and HbA1c levels and hypertension that remained strong. Excessive visceral fat in abdominal obesity is the main source of free fatty acids and inflammatory cytokines, which, according to the literature, might lead to insulin resistance and type 2 diabetes mellitus<sup>60</sup>. This probably explains why WC was strongly associated with diabetes and hypertension in our study population. Therefore, measuring WC using optimal WC cut-off values as was done in this study would be a feasible, less time consuming and cost-effective screening tool to identify at-risk individuals in the Zanzibari population. 

This study has some limitations that should be considered. First, this study investigated the
 association between obesity indices and cardio-metabolic risk factors using cross-sectional

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data; thus we were not able to examine the impact of changes in obesity indices on risk factors. Second, as is done in many epidemiological studies and clinical trials, we used Bioelectrical Impedance Analysis (BIA) to estimate body fat percentage. However, compared to skinfold measurements, BIA measurements may underestimate adiposity in children <sup>61</sup>. Third, even though we excluded participants who reported food or beverage intake prior to blood drawing during the data cleaning process, we cannot entirely rule out misreporting of the "fasting status". The overall aim of the study was to estimate the prevalence of malnutrition in the Zanzibari population including possible correlates. Therefore, the initial sample size calculation was based on the following considerations: Assuming a prevalence of approximately 30% malnutrition in children <5 years of age, a sample size of 323 children <5 years of age was needed to estimate such a prevalence and a corresponding 95% confidence interval with a precision of  $\pm 5\%$  <sup>62</sup>. To recruit this number of children, we decided to include entire households. Therefore, 1,314 individuals are sufficient to estimate prevalences up to 30% within 5 absolute percentage points with 95% confidence (in children <5 years of age, but also their fathers and mothers). The present study consists of a sub sample of the study population providing all biomarkers of interest. Even though the decreased sample size may limit the scope of the results obtained - and we acknowledge this as a limitation -, we are convinced that the results, presented in the current paper, provide important information for public health stakeholders, policy makers and researchers. 

The results of this research can be used for the development of interventions or policies by researchers, stakeholders and government officials. The random selection of the study participants and the standardised assessment of anthropometrical and laboratory measurements are main strengths of the present study. Moreover, we consequently applied age- and sex-specific cut-offs that take into account the physiological development characteristic of the young age group, rather than applying the fixed cut-offs used in the adult

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population. There is little information on the association of multiple obesity indices with
multiple cardio-metabolic risk factors in this population; hence, our study provides an
important contribution towards filling this gap.

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#### Conclusion

This study adds to the literature on the association of obesity with higher risks for hypertension, dyslipidemia and type 2 diabetes mellitus, but for the first time in a Zanzibari population. Based on our findings, we recommend that similar epidemiological studies including children, adolescents, adults and elderly set diabetes and/or pre-diabetes cut-offs of HbA1c at  $\geq 6.1\%$  and/or elevated fasting glucose at  $\geq 5.6$  mmol/l. Where feasible, BF% and WC should be used in addition to BMI for screening and monitoring for dyslipidemia and hypertension. We further conclude that there is a need for effective interventions to create awareness as well as for primary prevention strategies for cardio-metabolic risks and its complications in Unguja Island, using local multidisciplinary approaches in the local language, Swahili. Additionally, there is a need for health surveillance initiatives that particularly target the age group  $\geq 18$  to  $\leq 45$  years. These can also be used to help monitor prevention activities. 

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24 25 26	473	design. AH, MAN and SK conducted data collection and developed study hypothesis. MAN
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38 39 40	479	The datasets generated and/or analysed during the current study are not publicly available
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	Item No	Recommendation
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract
		Cross-sectional study
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found
		Completed in the abstract, please refer to line 27-53
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
		This has been explained in the Introducion section.
Objectives	3	State specific objectives, including any prespecified hypotheses
		<ul> <li>To determine the prevalence of obesity indices (body mass index (BMI), waist circumference (WC), body fat percent (BF%)) and cardio-metabolic risk factors.</li> <li>To investigate the association between obesity indices and cardio-metabolic risk factors in a Zanzibari population.</li> </ul>
Methods		
Study design	4	Present key elements of study design early in the paper
		This has been presented in the abstract, please refer to line 31-34.
		<b>Key elements of study design</b> : cross-sectional survey , in a representative population sample in Unguja Island, Zanzibar, households were randomly selected and all household members were invited for the examination.
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment,
		exposure, follow-up, and data collection
		This has been described in the method section, please refer to <i>line 115-125</i>
Participants	6	( <i>a</i> ) Give the eligibility criteria, and the sources and methods of selection of participants
		This has been described in the method section, refere to <i>line 116-124</i>
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect
	·	modifiers. Give diagnostic criteria, if applicable
		This has been defined in the method section, refer to <i>line 150-225</i> including <b>Table 1</b> <i>line 225-237</i>
		Since clinical patients were not included, diagnostic criteris is not applicable
Data sources/	8*	For each variable of interest, give sources of data and details of methods of
measurement		assessment (measurement).
		-Please refer to method section <i>line 161-225</i>
		Describe comparability of assessment methods if there is more than one group
		r

		-Not applicable
Bias	9	Describe any efforts to address potential sources of bias
		This was described in the inclusion criteria were outliers were deleted from the
		sample in order to reduce bias. Refer to line 246
Study size	10	Explain how the study size was arrived at
		This has been described in <i>line 119-122</i>
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable,
		describe which groupings were chosen and why
		-Quantitative variables were grouped into categories according to the given cut-offs
		please refer to method sections anthropometric measurements and cardiometabolic
		risk factors
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding
		(b) Describe any methods used to examine subgroups and interactions
		(c) Explain how missing data were addressed
		( <i>d</i> ) If applicable, describe analytical methods taking account of sampling strategy
		( <i>e</i> ) Describe any sensitivity analyses
		-all the above points have been discussed in the statistical analysis, refer to <i>line 25</i> .
		272
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially
i uitioipuilis	15	eligible, examined for eligibility, confirmed eligible, included in the study,
		completing follow-up, and analysed
		completing follow up, and analysed
		This has been described in <i>line 242-246</i>
		(b) Give reasons for non-participation at each stage
		(b) Give reasons for non participation at each stage
		This has been described in <i>line 242-246</i>
		(c) Consider use of a flow diagram
		(,, , , , , , , , , , , , , , , , , , ,
		-Not feasible because of differet age groups
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and
1		information on exposures and potential confounders
		Please refer to <i>line 277-304</i> and <i>Tables 2 and 3</i>
		(b) Indicate number of participants with missing data for each variable of interest
		-This was not described in the manuscript, the missing data for each variable of
		interest were deleted during data cleaning and before running the statistical analysis
		Please refer to the inclusion criteria section for general overview, <i>line 242-248</i>
Outcome data	15*	Report numbers of outcome events or summary measures
		-Please refer to result sections table 3
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and

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		adjusted for and why they were included
		(b) Report category boundaries when continuous variables were categorized
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a
		meaningful time period . Not relevant
		-Please refer to result section tables 4 and 5
Other analyses	17	Report other analyses done-eg analyses of subgroups and interactions, and
		sensitivity analyses
		-This is was not applied to this manuscript.
Discussion		
Key results	18	Summarise key results with reference to study objectives
		-This has been decribed in the discussion section, please refer to line 348 onwards
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or
		imprecision. Discuss both direction and magnitude of any potential bias
		-Limitations of the study have been described in line 427-441
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations
		multiplicity of analyses, results from similar studies, and other relevant evidence
		-Please refer to the conclusion section from <i>line 353 onwards</i>
Generalisability	21	Discuss the generalisability (external validity) of the study results
		-Based on the findings of the study, similar epidemiological surveys could be
		conducted in the rest of the Island. Please refer to the conclusion section.
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if
		applicable, for the original study on which the present article is based
		-This work was supported by the Leibniz-Gemeinschaft grant number SAW-2012-
		ZMT-4. See line 483
		-The present article is based on the "Access to Food and Nutritional Status of the
		Zanzibari population" study, please refer to reference no.25

\*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.