


SHORT REPORT

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# Association between cardiometabolic health and objectively-measured, free-living sleep parameters: a pilot study in a rural African setting

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## Abstract

**Objectives:** To investigate the relationship between objectively-measured, free-living sleep quantity and quality, and cardiometabolic health, in a rural African setting in 139 adults ( $\geq 40$  years, female:  $n = 99$ , male:  $n = 40$ ). Wrist-mounted, tri-axial accelerometry data was collected over 9 days. Measures of sleep quantity and quality, and physical activity were extracted from valid minute-by-minute data. Self-reported data included behavioural, health and socio-demographic variables. Biological data included body composition, resting blood pressure and fasting blood glucose, insulin and lipids. Logistic regression models were constructed with insulin resistance (IR) and cardiometabolic (CM) risk, as dependent variables, adjusting for socio-demographic, behavioural and biological factors.

**Results:** Nocturnal sleep time was longer in females ( $p = 0.054$ ) and sleep quality was better in males ( $p \leq 0.017$ ). Few participants slept  $> 9$  h/night (4–5%), and 46–50% slept  $< 7$  h/night. IR and CM risk was higher in females ( $p \leq 0.006$ ). In adjusted models, sleep variables were independently associated with IR ( $p < 0.05$ ). Sleep quantity was non-linearly associated with CM risk ( $p \leq 0.0398$ ), and linearly associated with IR ( $p \leq 0.0444$ ). Sleep quality was linearly related with CM risk and IR ( $p \leq 0.0201$ ). In several models, sleep quantity and sleep quality measures were concurrently and significantly associated with IR ( $p \leq 0.044$ ).

**Keywords:** Insulin resistance, Metabolic syndrome, Anthropometry, Accelerometer, Actigraphy, Movement monitor, Measurement

## Introduction

Sleep health is closely linked to metabolic health with several mechanisms linking poor sleep health to insulin resistance and the metabolic syndrome (Smiley et al. 2019). Although there is extensive literature from industrialised settings (Anothaisintawee et al. 2016), there is a paucity of data from African settings, especially free-living, objective measures of sleep (Cole et al. 2017).

Within the South African context, self-reported long sleep duration is associated with poor cardiometabolic health in mainly urban settings (Rae et al. 2018; Rae et al. 2020). Given the lack of objectively-measured, free-living sleep parameters in any South African setting, the objective of this study was to use wrist-actigraphy to investigate the association between sleep parameters and cardiometabolic health in a rural African setting during a cross-sectional survey, and thus extend the findings of self-report sleep duration and cardiometabolic health (Rae et al. 2018; Rae et al. 2020; Mashinya et al. 2018).

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## Main text

### Methods

#### *Dikgale health and demographic surveillance system site (DHDSS) sample*

A convenience sample of 167 adults was recruited from the DHDSS site (April 2016 – October 2017) (Alberts et al. 2015). These participants formed part of a larger study cohort ( $\geq 40$  years) (Mashinya et al. 2018; Ali et al. 2018). Trained field workers collected self-reported and measured data from participants by means of questionnaires translated to the local vernacular (Sepedi), anthropometry, oscillometric blood pressure measurement, ultrasound scans, and venipuncture (Mashinya et al. 2018; Ali et al. 2018). We calculated body mass index (BMI,  $\text{kg}/\text{m}^2$ ), and Conicity Index (CI) (Valdez et al. 1993). Questionnaire data included behavioural, health and socio-demographic variables (Mashinya et al. 2018; Ali et al. 2018). Nine day, free-living, wrist-mounted accelerometry data was collected (Cook et al. 2020). The ultrasound scans were not considered for this analysis.

#### *Blood sample collection and analysis*

A registered nurse collected fasting blood samples. The samples were analysed centrally; procedures and calculations are described in detail elsewhere (Ali et al. 2018). The Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) was calculated from fasting blood glucose and insulin (Matthews et al. 1985).

#### *Criteria for metabolic syndrome*

In accordance with the harmonized Joint Interim Statement (JIS) definition (Alberti et al. 2009), the presence of the Metabolic Syndrome (MetS) required three of the following components, with waist circumference not a prerequisite: elevated waist circumference (WC): females  $\geq 92$  cm, males  $\geq 86$  cm; elevated triglycerides (TG):  $\geq 1.7$  mmol/l; reduced high-density lipoprotein cholesterol (HDL-C): men  $< 1.0$  mmol/l, women  $< 1.3$  mmol/l; elevated resting blood pressure  $\geq 130/85$  mmHg or on hypertension treatment; and elevated fasting glucose (GC)  $\geq 5.6$  mmol/l or on diabetes treatment. For this study population-specific WC cut-points were chosen (Motala et al. 2011).

Using the five criteria from the JIS definition for MetS (JIS-MetS), we calculated sex-specific z-scores for HDL-C, TG, GC, WC and MAP (Mean Arterial Pressure), which were summed to create a MetS z-Score (MetSz) (Lee et al. 2019).

#### *Accelerometer data collection and data reduction*

Participants wore a small, light-weight, wrist-worn tri-axial accelerometer for 9 days (ActiGraph wGT3X-BT, Actigraph, LLC, Pensacola, FL, 2013) (Whitaker et al. 2018; Migueles et al. 2017; Slater et al. 2015; Full et al.

2018). The preparation, initialization, mounting, data processing and extraction of physical activity (PA) and sleep parameters are described in detail elsewhere (Cook et al. 2020).

Vector Magnitude (VM)- and Ambulation-defined PA variables were defined as counts/day and steps/day, respectively (Wenman et al. 2019). Sleep indices included Total Sleep Time (TST), Nocturnal Sleep Time (NST), Sleep Efficiency (SE), Wake After Sleep Onset (WASO), Activity Counts during sleep (AC), Sleep Fragmentation Index (SFI) and sleep variation across days (within-person total sleep time SD) (Ancoli-Israel et al. 2015; Chung et al. 2016; Ko and Lee 2018). Nocturnal periods were defined as 18 h01-05 h59. Sufficient sleep quantity and quality was defined as 7–9 h (Hirshkowitz et al. 2015) and  $\geq 85\%$  (Fung et al. 2013), respectively.

#### *Statistical analysis*

Descriptive statistics comprised means (one standard deviation), medians (inter-quartile range), variances (maximum, minimum) and frequencies. Relationships between categorical variables were examined through Fisher's Exact Test. For continuous data, independent *t* tests and Levene's test examined differences between sexes and risk groups. Where required a non-parametric test was employed. Bi-variate relationships were examined using linear regression.

Forced-entry binary logistic regression models were constructed to examine the relationship between MetS risk (low/high) according to the JIS definition (Alberti et al. 2009), and tertiles (Q1 = low/Q2/Q3 = high) of sleep quantity and quality variables. Models were also constructed to examine the relationship between MetS risk and sleep quantity and quality categories (Hirshkowitz et al. 2015; Fung et al. 2013). Models were adjusted for socio-demographic (age, socio-economic status), behavioural (fruit and vegetable intake, sugar-sweetened beverages, tobacco and alcohol usage, physical activity) and biological (sex, HIV status) variables. CI was not included as an independent variable because WC formed part of the JIS risk definition.

Forced-entry ordinal logistic regression models were constructed to examine the relationship between HOMA-IR levels (tertiles), and tertiles of sleep quantity and quality variables. Additional models were constructed to examine the relationship between HOMA-IR tertiles and sleep quantity and quality categories (Hirshkowitz et al. 2015; Fung et al. 2013). Models were adjusted for socio-demographic (age, socio-economic status), behavioural (fruit and vegetable intake, sugar-sweetened beverages, tobacco and alcohol usage, physical activity) and biological (sex, CI, HIV status) variables.

All covariates were entered as quantiles. Regression coefficients were expressed as odds ratios ( $OR \pm 95\%$  confidence intervals).

Goodness of fit criteria included Akaike's Information Criteria (AIC) (all models), pseudo  $R^2$  (all models), Hosmer-Lemeshow test (Binary logistic) and Area Under the Curve (AUC) (Binary Logistic). Multicollinearity was assessed using Variance Inflation Factors (VIF) and Tolerance.

*Post-hoc* contrasts were run for binary and ordinal logistic regression models to test for linear and non-linear trends, and pairwise comparison of groups (Bonferroni correction).

Data were analysed using appropriate statistical software (Stata/SE for Windows: Release 15.1. College Station, TX: StataCorp LP, 2020). Significance for all inferential statistics was set at  $p < 0.05$ .

## Results

Of the 167 raw accelerometry data files, 157 had valid data for at least one weekday and one weekend day. Once combined with the questionnaire and biological data, 139 participants had complete data.

Females consumed more sugar-sweetened beverages (SSB), experienced poorer sleep quality, and were more physically active and insulin resistant (Table 1,  $p \leq 0.07$ ). Males were leaner, used more alcohol and tobacco products and experienced lower people-to-bedroom density ( $p \leq 0.040$ ). The JIS high risk group had a higher socioeconomic status (SES), a lower HIV+ prevalence, were mostly obese, more insulin resistant, and likely to be in a partnered relationship (Table 1,  $p \leq 0.040$ ).

In bi-variate analysis, sex, SES, CI, WC, BMI, SSB and WASO were significantly associated with HOMA-IR ( $p \leq 0.05$ ). SES, BMI, CI, WC and HIV status were significantly related to MetSz ( $p \leq 0.027$ ).

All models were significant (Fig. 1a-f, Fig. 2a-f, see Additional file 1 for Fig. S1A-B,  $p \leq 0.00191$ ) and there was no evidence of multicollinearity ( $VIF < 1.5$ , Tolerance  $> 0.75$ ). The binary logistic regression models (Fig. 1a-c, Fig. 2a-c, Additional file 1: Fig. S1A) showed good fit (Hosmer-Lemeshow:  $p \geq 0.2223$ ; AUC: 0.808–0.877). The full models ( $OR \pm 95\%$  confidence intervals) for Fig. 1a-f, Fig. 2a-f and Additional file 1: Fig. S1A-B are available in Additional file 2.

In binary logistic regression models (Fig. 1a-c, Additional file 1: Fig. S1A) males had significantly lower odds for JIS-MetS high risk ( $OR \approx 0.15$ ,  $p \leq 0.006$ ), and similarly for HIV+ status in the NST and SFI models ( $OR = 0.25$ ,  $p \leq 0.0035$ ). Once adjusted for adiposity (CI), sex was no longer a significant factor ( $p \geq 0.097$ ). However, HIV+ status remained a significant factor in most models ( $OR \approx 0.26$ ,  $p \leq 0.048$ ) (Fig. 1a-c).

There was a significant non-linear trend (U-shaped) between JIS-MetS risk and NST ( $p = 0.0196$ ) (Fig. 1a), such that for NST Q2, there was 80% less likelihood of being at high risk for JIS-MetS. There was also a significant difference in frequencies between NST Q1 and Q2 ( $p = 0.021$ ) (Fig. 1a).

There was a significant positive, linear trend between JIS-MetS risk and SFI ( $p = 0.0001$ ) (Fig. 1c). The odds of high risk JIS-MetS for SFI Q3 was high ( $OR = 69.81$ , 8.44; 577.63), however the confidence intervals were wide. There were significant differences between the frequencies for Q3 versus Q1 and Q2 ( $p < 0.001$ ) (Fig. 1c).

Being a current user of both alcohol and tobacco products carried a significant higher odds for JIS-MetS high risk in the NST ( $OR = 4.51$ ,  $p = 0.034$ ) and SFI ( $OR = 6.55$ ,  $p = 0.023$ ) models (Fig. 1a-c).

In ordinal logistic regression models (Fig. 1d-f, Additional file 1: Fig. S1B), being in the VM Q2 level, significantly decreased the odds of being in HOMA-IR Q3 by a factor of  $\approx 0.31$  ( $p \leq 0.039$ ). In contrast, for both CI Q2 and Q3 levels, the odds of being in HOMA-IR Q3 were significantly increased; Q2  $OR \approx 2.9$  and Q3  $OR \approx 3.8$ , respectively ( $p \leq 0.045$ ) (Fig. 1d-f, Additional file 1: Fig. S1B).

There was a significant linear trend between TST and HOMA-IR levels ( $p = 0.0444$ ) (Fig. 1d). Compared to TST Q1 and Q2, being in TST Q3 (longest sleep time) increased the odds of being in the highest HOMA-IR level (Q3) by a factor of 2.84 ( $p = 0.044$ ) (Fig. 1d).

There were significant linear relationships between SE and WASO, and HOMA-IR ( $p \leq 0.007$ ) (Fig. 1e). A high SE (Q3) was 85% less likely to result in HOMA-IR Q3 ( $p = 0.001$ ). Being in WASO Q2 and Q3 significantly increased the odds for HOMA-IR Q3;  $OR = 3.17$  and  $OR = 6.75$ , respectively ( $p \leq 0.019$ ).

SFI and AC were significantly associated with increasing HOMA-IR levels ( $p \leq 0.0201$ ) (Fig. 1f). Being in SFI Q2 and Q3 significantly increased the odds for HOMA-IR Q3,  $OR = 4.67$  ( $p = 0.004$ ) and  $OR = 10.91$  ( $p < 0.001$ ), respectively. For AC Q3 the odds of being in the HOMA-IR Q3 was 3.01 ( $p = 0.020$ ) (Fig. 1f).

In the TST, NST, SE, WASO and AC models (Fig. 1d-e), being in SSB Q2 and Q3, increased the likelihood for being in HOMA-IR Q3 by a factor of 3.51 to 4.77, but did not reach statistical significance ( $p = 0.068$  to  $p = 0.098$ ).

Sleep quantity and quality measures featured concurrently and significantly in the TST, SE and SFI models (Fig. 1d-f) ( $p \leq 0.044$ ).

Expressing sleep quantity and quality parameters in terms of sleep health guidelines, we found significant non-linear associations with JIS-MetS risk ( $p \leq 0.0308$ ) (Fig. 2a-f). The relationship between sleep categories for both TST and NST, and JIS-MetS risk were U-shaped, the nadir at 7–9 h of sleep (Fig. 2a-b).

**Table 1** Descriptive statistics of demographic, behavioural and biological characteristics by sex and cardio-metabolic risk

	Sex			Cardio-metabolic Risk (IJS Harmonized definition)		
	Females (n = 99)	Males (n = 40)	<i>p</i> -values	Low Risk (< 3 factors) (n = 90)	High Risk (≥ 3 factors) (n = 49)	<i>p</i> -values
<b>Socio-demographic</b>						
Age (years)	52.0 (6.9)	53.9 (7.5)	0.165	51.9 (7.4)	53.9 (6.3)	0.112
Marital status (Married/Co-habiting) <sup>b</sup>	54.5 (54)	55.0 (22)	0.648	46.7 (42)	69.4 (34)	<b>0.040</b>
Level of education (formal education) <sup>b</sup>	94.9 (94)	97.5 (39)	0.978	95.6 (96)	95.9 (47)	0.766
Employed (Yes) <sup>b</sup>	27.3 (27)	27.5 (11)	0.567	73.3 (66)	71.4 (35)	0.844
SES Quintile	3.6 (1.3)	3.5 (1.3)	0.652	3.4 (1.3)	4.0 (1.3)	<b>0.008</b>
Housing density <sup>a</sup>						
People/room	0.86 (0.75)	0.69 (0.78)	0.065	0.79 (0.75)	0.83 (0.88)	0.220
People/bedroom	1.67 (1.25)	1.37 (1.00)	<b>0.040</b>	1.50 (1.25)	1.67 (1.0)	0.330
<b>Behavioural</b>						
<b>Diet<sup>a</sup></b>						
Fruit and vegetable intake (servings/day)	1.29 (1.00)	1.14 (0.00)	0.070	1.14 (1.00)	1.29 (2)	0.194
Sugar sweetened beverages (servings/day)	0.29 (0.10)	0.29 (0.00)	<b>0.010</b>	0.29 (0.00)	0.29 (1.00)	0.131
<b>Health-compromising</b>						
Alcohol & Tobacco use (both current; Yes)	8.1 (8)	45.0 (18)	<b>&lt; 0.001</b>	18.9 (17)	18.4 (9)	0.972
<b>Objectively-measured Sleep</b>						
<i>Quantity</i>						
Sleep Time (minutes/day)						
Total	458 (67)	456 (106)	0.901	456 (73)	460 (92)	0.818
Nocturnal <sup>a</sup>	434 (61)	411 (72)	0.054	425 (60)	431 (73)	0.639
Sufficient sleep categories <sup>b</sup>						
Total sleep time						
< 7 h/day	32.3 (32)	40.0 (16)	0.666	31.1 (28)	40.8 (20)	0.115
7–9 h/day	52.5 (52)	45.0 (18)		56.7 (51)	38.8 (19)	
> 9 h/day	15.2 (15)	15.0 (6)		12.2 (11)	20.4 (10)	
Nocturnal sleep time						
< 7 h/night	45.5 (45)	50.0 (22)	0.546	45.6 (41)	53.1 (26)	0.122
7–9 h/night	50.5 (50)	40.0 (16)		52.2 (47)	38.8 (19)	
> 9 h/night	4.0 (4)	5.0 (2)		2.2 (2)	8.2 (4)	
<i>Quality</i>						
Wake after sleep onset (minutes)	54 (16)	44 (17)	<b>0.001</b>	51 (18)	51 (15)	0.839
Sleep efficiency (%)	87.6 (4.2)	89.5 (4.6)	<b>0.017</b>	88.2 (4.6)	88.0 (3.9)	0.789
Achieved ≥85% <sup>b</sup>	79.8 (79)	82.5 (33)	0.816	80.0 (72)	81.6 (40)	1.000
Activity counts during sleep (counts)	35,057 (9223)	27,448 (9223)	<b>0.001</b>	32,633 (9223)	33,298 (9223)	0.761
Sleep fragmentation index (%)	26.7 (7.0)	28.2 (6.6)	0.243	26.5 (6.9)	28.3 (6.8)	0.151
Within-person total sleep time SD (minutes) <sup>a</sup>	85 (51)	91 (92)	0.266	86 (53)	88 (63)	0.968
<b>Objectively-measured Physical Activity</b>						
VM counts/day (× 10 <sup>6</sup> )	2.49 (0.63)	2.00 (0.77)	<b>&lt; 0.001</b>	2.33 (0.75)	2.38 (0.60)	0.669
Ambulation (steps/day)	14,288 (3691)	15,132 (6492)	0.443	14,470 (432)	14,681 (4378)	0.838
<b>Biological</b>						
Females (Yes)	–	–	–	65.6 (59)	81.6 (40)	0.052
Waist circumference (cm)	93.0 (16.3)	80.8 (9.7)	<b>&lt; 0.001</b>	83.5 (14.0)	100.7 (12.4)	<b>&lt; 0.001</b>

**Table 1** Descriptive statistics of demographic, behavioural and biological characteristics by sex and cardio-metabolic risk (Continued)

	Sex			Cardio-metabolic Risk (JIS Harmonized definition)		
	Females (n = 99)	Males (n = 40)	p-values	Low Risk (< 3 factors) (n = 90)	High Risk (≥ 3 factors) (n = 49)	p-values
Body mass index (kg/m <sup>2</sup> )	30.4 (7.6)	21.7 (3.8)	< 0.001	25.3 (6.9)	32.6 (7.2)	< 0.001
Body mass index categories <sup>b</sup>						
Under- weight (< 18.5 kg/m <sup>2</sup> )	3.0 (3)	17.5 (7)	< 0.001	10.0 (9)	2.0 (1)	< 0.001
Normal weight (18.5–24.9 kg/m <sup>2</sup> )	21.2 (21)	55.0 (22)		43.3 (39)	8.2 (4)	
Overweight (25–29.99 kg/m <sup>2</sup> )	23.2 (23)	27.5 (11)		24.4 (22)	24.5 (12)	
Obese (≥30 kg/m <sup>2</sup> )	52.5 (52)	0.0 (0.0)		22.2 (20)	65.3 (32)	
Conicity Index	1.23 (0.10)	1.23 (0.08)	0.940	1.20 (0.09)	1.29 (0.08)	< 0.001
HIV status (Yes) <sup>b</sup>	22.2 (22)	25.0 (10)	0.824	28.9 (26)	12.2 (6)	0.034
Resting SBP (mmHg)	126 (20)	126 (24)	0.870	120 (17)	138 (22)	< 0.001
Resting DBP (mmHg)	81 (11)	78 (13)	0.157	77 (11)	86 (12)	< 0.001
MAP (mmHg)	96 (13)	94 (16)	0.384	91 (12)	104 (14)	< 0.001
Parity <sup>a,d</sup>	4 (2)	–	–	4 (2)	4 (3)	0.775
<b>Cardio-metabolic</b>						
Total Cholesterol (mmol/l)	4.10 (1.36)	3.72 (1.30)	0.139	4.00 (1.44)	3.98 (1.15)	0.972
HDL-Cholesterol (mmol/l)	1.10 (0.47)	1.07 (0.52)	0.865	1.16 (0.53)	0.95 (0.34)	0.007
LDL-Cholesterol (mmol/l)	2.51 (1.10)	2.15 (0.96)	0.072	2.40 (1.14)	2.40 (0.95)	0.997
Triglyceride (mmol/l)	1.10 (0.58)	1.10 (0.61)	0.959	0.95 (0.47)	1.38 (0.68)	< 0.001
Glucose (mmol/l)	5.32 (1.89)	5.41 (1.86)	0.811	4.85 (1.26)	6.26 (2.42)	< 0.001
Insulin (μU/ml) <sup>a</sup>	6.91 (7.75)	3.14 (5.61)	0.001	4.12 (6.27)	7.60 (7.05)	0.001
HOMA-IR <sup>a</sup>	1.51 (1.91)	0.71 (1.72)	0.003	0.90 (1.53)	2.09 (1.96)	0.003
HOMA-IR categories <sup>b</sup>						
Q1 (≤0.82)	–	–	–	42.2 (38)	16.3 (8)	0.002
Q2 (0.83–2.09)	–	–	–	33.3 (30)	34.7 (17)	
Q3 (2.10)	–	–	–	24.4 (22)	49.0 (24)	
Metabolic Syndrome (JIS Harmonised definition) <sup>b</sup>						
No risk factor	11.1 (11)	12.5 (5)	0.006	–	–	–
1 risk factor	15.2 (15)	42.5 (17)		–	–	
2 risk factors	33.3 (33)	22.5 (9)		–	–	
≥ 3 risk factors	40.4 (40)	22.5 (9)		–	–	
Waist circumference (male: ≥86 cm, females: ≥92 cm)	58.6 (58)	35.0 (14)	0.015	31.1 (28)	89.8 (44)	< 0.001
Blood pressure (SBP: ≥135 mmHg, DBP: ≥85 mmHg)	42.4 (42)	50.0 (20)	0.266	27.8 (25)	75.5 (37)	< 0.001
HDL-Cholesterol (male:< 1 mmol/l, female< 1.3 mmol/l)	72.7 (72)	45.0 (18)	0.003	53.3 (48)	85.7 (42)	< 0.001
Triglyceride ≥1.7 mmol/l)	15.2 (15)	7.5 (3)	0.276	5.6 (5)	26.5 (13)	0.001
Glucose (≥5.6 mmol/l)	19.2 (19)	27.5 (11)	0.362	11.1 (10)	40.8 (20)	< 0.001
Metabolic Syndrome z-score	7.7 (–7.3; 9.4) <sup>c</sup>	6.1 (–4.5; 6.6)	< 0.001	–1.17 (2.50) <sup>a</sup>	2.21 (1.97)	0.599

Data reported as mean (SD), <sup>a</sup> median (IQR), <sup>b</sup> % (n) or <sup>c</sup> variance (minimum; maximum); <sup>d</sup> low risk: n = 59, high risk: n = 40; DBP Diastolic Blood Pressure, HOMA-IR Homeostasis Model Assessment of Insulin Resistance, HIV Human Immunodeficiency Virus, JIS Joint Interim Statement, MAP Mean Arterial Pressure =  $\frac{2}{3}DBP + \frac{1}{3}SBP$

SBP, Nocturnal 18 h01 - 05 h59, SES Socio-Economic Status, SBP Systolic Blood Pressure, VM Vector Magnitude

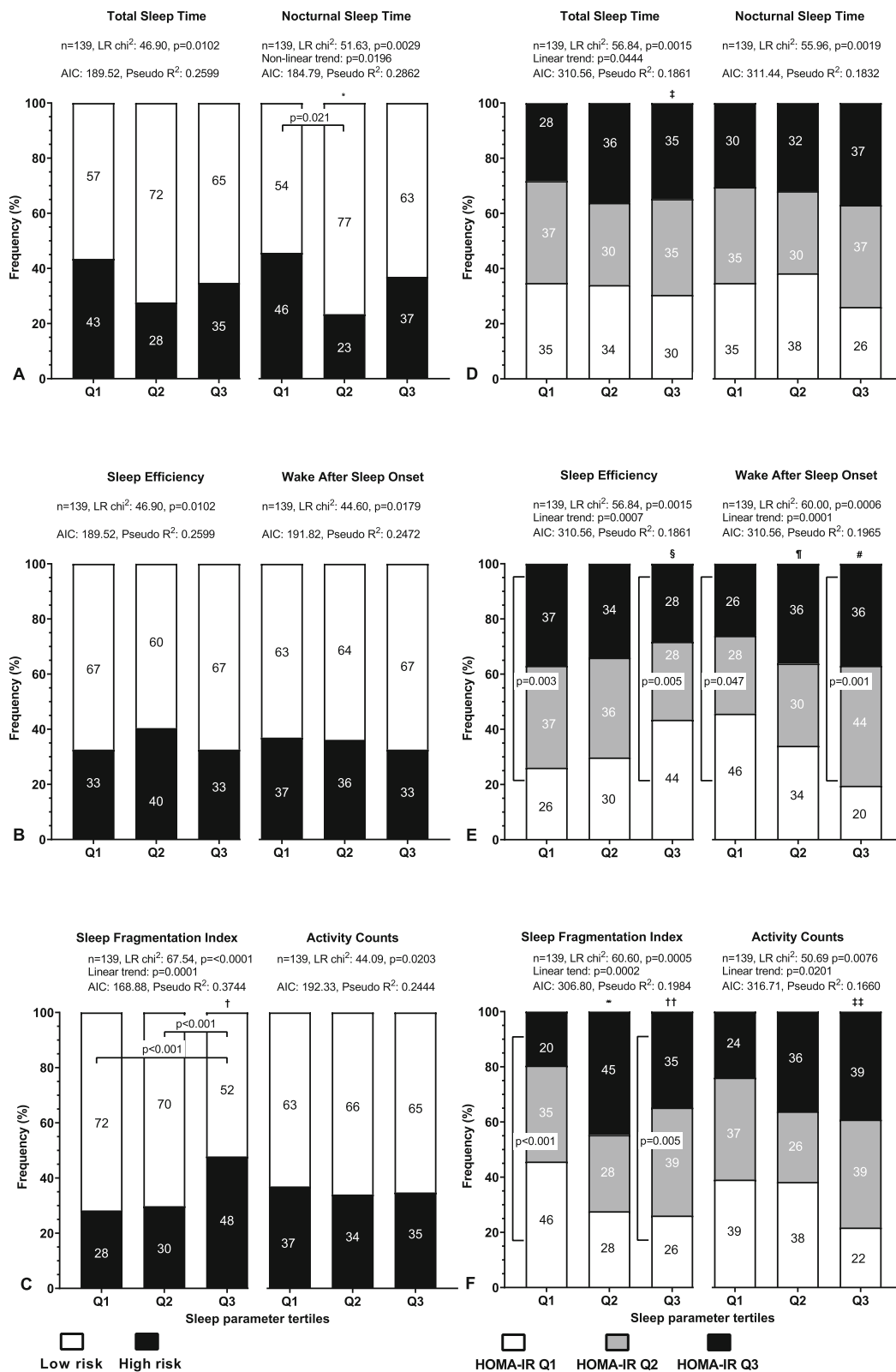


Fig. 1 (See legend on next page.)



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**Fig. 1** Cardiometabolic risk categories across quantiles of accelerometry-derived sleep-quantity and -quality measures. **a-c** Binary risk categories for the JIS Harmonised Definition. Nocturnal sleep time (minutes) and Total sleep time (minutes), \* OR 0.20 (0.05, 0.71); **b** Sleep efficiency (percentage) and Wake after sleep onset (minutes); **c** Sleep fragmentation index (%) and Activity counts during sleep (counts), †OR 69.80 (8.44, 577.63). Fully-adjusted binary logistic regression models (socio-demographic, behavioural, biological), excluding body composition measures (see Additional file 1). **d-f** Tertiles of HOMA-IR. **d** Nocturnal sleep time (minutes) and Total sleep time (minutes), ‡ OR 2.84 (1.03, 7.83); **e** Sleep efficiency (percentage) and Wake after sleep onset (minutes), § OR 0.15 (0.05, 0.45), ¶ OR 3.17 (1.21, 8.32), # OR 6.75 (2.54, 17.91); **f** Sleep fragmentation index (%) and Activity counts during sleep (counts), \*\* OR 4.67 (1.64, 13.30), †† OR 10.91 (3.11, 38.33), ††† OR 3.01 (1.19, 7.64). Fully-adjusted ordinal logistic regression models (socio-demographic, behavioural, biological), including body composition measures (Conicity Index) (see Additional file 1). The horizontal lines between the sleep parameter tertiles (Q1-Q3) and vertical lines between the HOMA-IR tertiles (HOMA-IR Q1/Q2/Q3) indicate significant post hoc differences between tertiles at either end of the line. Cut-points for sleep parameter quantiles (Q1/Q2/Q3) are presented in Table S1 (see Additional file 3)

In binary logistic regression models (Fig. 2a-c) males had significantly lower odds for JIS-MetS high risk (OR≈0.14,  $p = 0.004$ ), and similarly for HIV+ (OR≈0.26,  $p \leq 0.0034$ ). Once adjusted for adiposity (CI), sex was no longer a significant factor ( $p \geq 0.121$ ). However, HIV+ status remained a significant factor in most models (OR≈0.23,  $p \leq 0.045$ ) (Fig. 2a-c).

In ordinal logistic regression models (Fig. 2d-f) physical activity (VM Q2) significantly reduced the odds of being in HOMA-IR Q3 by a factor of ≈0.26 ( $p \leq 0.010$ ). For both CI Q2 and Q3 levels, the odds of being in HOMA-IR Q3 were significantly increased (Q2 OR≈3.16, Q3 OR≈3.89,  $p \leq 0.022$ ). For SE ≥85%, there was a 76% lower likelihood of being in HOMA-IR Q3 ( $p = 0.010$ ). Significantly more participants were classified as low HOMA-IR (Q1) in the SE ≥85% category (Fig. 2d).

In the TST, NST and SE models (Fig. 2d and f), being in SSB Q2, increased the odds for being in HOMA-IR Q3 by a factor of 3.24 to 3.65, but did not reach statistical significance ( $p = 0.074$ ).

## Discussion

This analysis is novel in that, as far as the authors are aware, this is the first free-living, actigraphy-measured sleep and cardiometabolic health study from a rural South African setting.

The main findings of this analysis were first that sleep quality and quantity measures were independently associated with HOMA-IR, and to a lesser extent JIS-MetS. Second, we found linear and non-linear (U-shaped) relationships between categories of sleep quantity and cardiometabolic risk. Third, except for sleep variability, all sleep quality measures were consistently associated with HOMA-IR.

The level of JIS-defined MetS within rural sub-Saharan African settings is 12.0% (95%CI: 4.0; 23.4) which is substantially lower than in our sample (35.3%) and is likely due to variations in levels of central adiposity, differing stages of the epidemiological transition and variations in the implementation of preventative programmes (Jaspers Faijer-Westerink et al. 2020). However, the mean

prevalence reported in a rural South African setting for the ≥45 year age groups (males: 17.9%; females: 42.2%) (Motala et al. 2011) is similar to our results (males: 22.5%; females: 40.4%).

Our findings are in agreement with the linear relationship between sleep duration and HOMA-IR in black, urban women, although we found far more women had short sleep time compared with self-report measures (Rae et al. 2018). A recent study from the METS group found long sleep duration in a black, urban South African sample (Rae et al. 2020). The accuracy with which sleep is self-reported, and how sleep questions are interpreted across different South African populations is unknown (Rae et al. 2018; Rae et al. 2020).

Unadjusted sleep quantity did not differ significantly across the sexes, which is in contrast to self-report measures (Rae et al. 2018). Sleep quality was poorer in females, although sex did not reach significance in most HOMA-IR models. Poor sleep quality in females is likely due to environmental and social determinants (Cook et al. 2020).

Some have speculated that poor sleep quality might be underpinning the long self-reported sleep durations in South African settings and hence the poorer cardiometabolic health associated with long sleep (Rae et al. 2018; Rae et al. 2020). Our results suggest that fragmented, poor sleep quality, independent of sleep duration might be more important than sleep duration. In young adolescents objectively-measured sleep quality, independent of sleep duration, was associated with cardiometabolic risk, such that increasing sleep duration and better sleep quality were associated with better cardiometabolic health (Feliciano et al. 2018). Future analyses need to explore the effect of the interaction between sleep quantity and quality, and cardiometabolic health (Lu et al. 2020).

Higher sleep variability for objectively-measured sleep quantity and quality measures has been shown to be associated with less favourable cardiometabolic health (Baron et al. 2017). In contrast, we found no association between sleep variability in total sleep time and cardiometabolic health. Median sleep variability was 22 min higher in our rural study compared with an

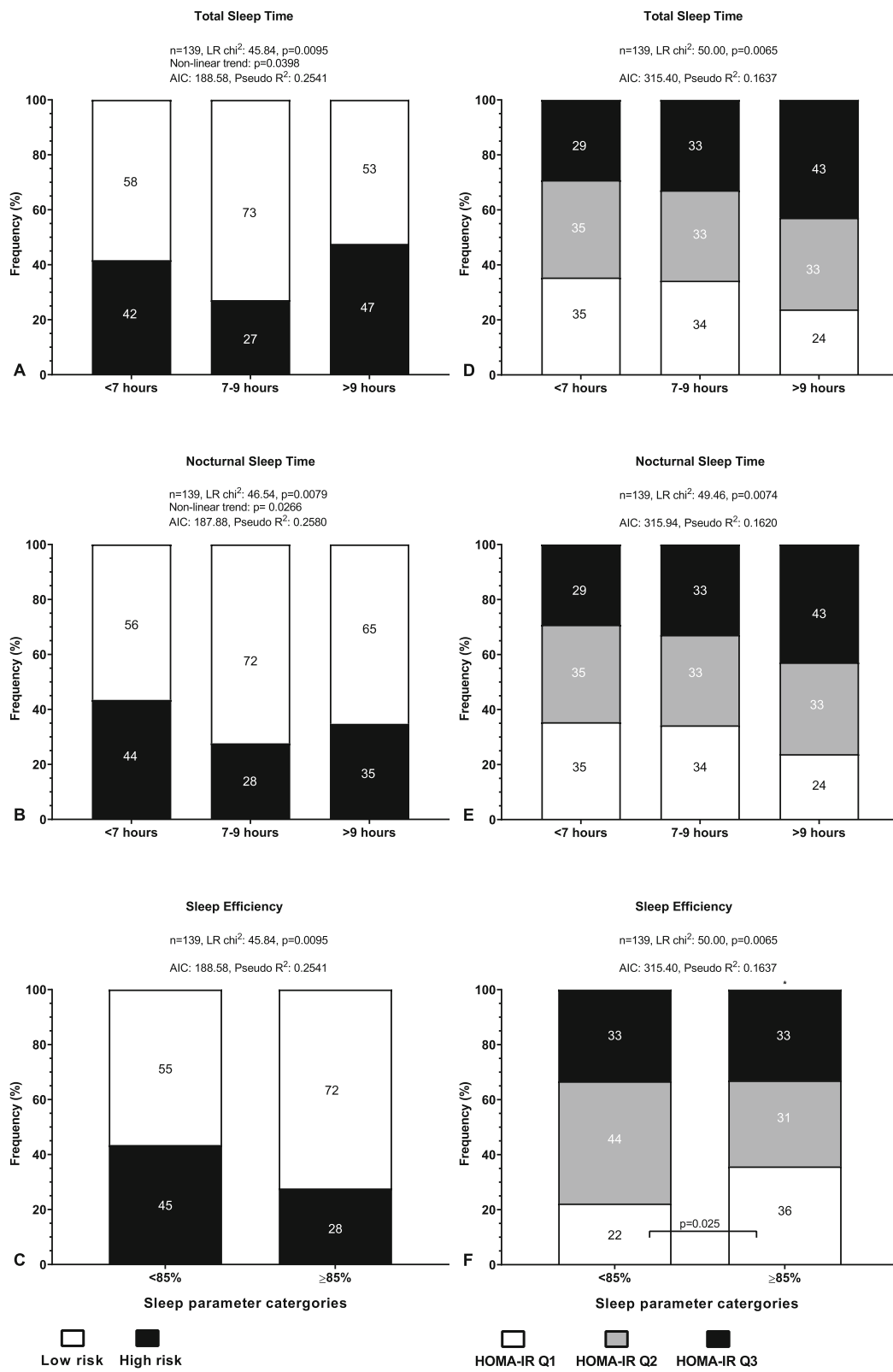


Fig. 2 (See legend on next page.)



(See figure on previous page.)

**Fig. 2** Cardiometabolic risk categories across categories of accelerometry-derived sleep-quantity and -quality measures. **a-c** Binary risk categories for the JIS Harmonised Definition. Total sleep time (minutes); **b** Nocturnal sleep time (minutes); **c** Sleep efficiency (percentage). Fully-adjusted binary logistic regression models (socio-demographic, behavioural, biological), excluding body composition measures (see Additional file 1). **d-f** Tertiles of HOMA-IR. **d** Total sleep time (minutes); **e** Nocturnal sleep time (minutes); **f** Sleep efficiency (percentage), \* OR 0.24 (0.08, 0.71). Fully-adjusted ordinal logistic regression models (socio-demographic, behavioural, biological), including body composition measures (Conicity Index) (see Additional file 1). The horizontal lines between the sleep parameter tertiles (Q1-Q3) indicate significant post hoc differences between tertiles at either end of the line

industrialised, urban, adult sample; 87 min vs. 65 min, respectively (DeSantis et al. 2019).

Future investigations into the sleep and cardiometabolic health of this rural group will require the construction of a composite sleep health score as opposed to relying solely on individual sleep dimensions (DeSantis et al. 2019).

In contrast with some self-reported PA studies (Rae et al. 2018), we found PA volume to be significantly and independently related to HOMA-IR, but not associated with JIS-MetS risk as in other self-report studies (Rae et al. 2020). Interestingly, other lifestyle factors such as concurrent alcohol and tobacco use, and the consumption of SSB were independently associated with poor cardiometabolic health. The concurrent use of alcohol and tobacco is associated with poorer cardiometabolic health through dyslipidemia and abdominal obesity (Slagter et al. 2014). Although the association with SSB did not quite reach statistical significance, there is evidence that the consumption of SSB is linked with poor cardiometabolic health through insulin resistance, visceral adiposity, dyslipidemia and inflammation, even within rural environments (Vorster et al. 2014).

## Conclusion

We found objectively-measured sleep quality indices were significantly associated with HOMA-IR in a rural South African sample. Future research in this population should include composite sleep health indices, and detailed data for environmental and social factors which impact sleep health. This study suggests that poor sleep quality, independent of sleep duration, may be an important risk factor for the development insulin resistance. Identifying and addressing factors which influence sleep quality should be considered as integral to strategies and interventions aimed at addressing cardiometabolic health in this rural population.

## Limitations

Due to the small sample size and cross-sectional, convenience sampling in this study, the results cannot be readily generalized, nor can causality be shown.

## Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s41606-020-00054-y>.

**Additional file 1.** Cardiometabolic risk categories across categories of accelerometry-derived sleep variability. **A: Binary risk categories for the JIS Harmonised Definition.** Total sleep time SD (minutes). Fully-adjusted binary logistic regression model (socio-demographic, behavioural, biological), excluding body composition measures (see Additional file 1). **B: Tertiles of HOMA-IR.** Total sleep time SD (minutes). Fully-adjusted ordinal logistic regression model (socio-demographic, behavioural, biological), including body composition measures (Conicity Index) (see Additional file 1). Cut-points for sleep parameter quantiles (Q1/Q2/Q3) are presented in Additional file 3: Table S1 (see Additional file 3)

**Additional file 2.** Models. Full logistic regression models for Fig. 1a-f, Fig. 2a-f and Additional file 1: Fig. S1A-B.

**Additional file 3: Table S1.** Cut-points for quantiles of sleep parameters.

## Abbreviations

BMI: Body mass index; CI: Conicity Index; DHDSS: Dikgale Health and Demographic Surveillance System; GC: Glucose; HDL-C: High-density Lipoprotein Cholesterol; HIV: Human Immunodeficiency Virus; HOMA-IR: Homeostasis Model Assessment of Insulin Resistance; JIS: Joint Interim Statement; LDL-C: Low-density Lipoprotein Cholesterol; MAP: Mean Arterial Pressure; MetS: Metabolic Syndrome; MetSz: Metabolic Syndrome z-score; NST: Nocturnal Sleep Time; PA: Physical Activity; SE: Sleep Efficiency; SES: Socio-Economic Status; SFI: Sleep Fragmentation Index; SSB: Sugar sweetened beverages; TC: Total Cholesterol; TG: Triglyceride; TST: Total Sleep Time; VM: Vector Magnitude; WASO: Wake After Sleep Onset; WC: Waist circumference

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## Authors' contributions

IC was the principal investigator of the accelerometer data on which this manuscript is based, who initiated the research and obtained funding, co-wrote and edited the research proposal, supervised the data entry, analyzed the data and wrote the first draft manuscript. MM co-wrote and edited the research proposal, collected field data, supervised the field work, performed the data entry, commented on the manuscript. HMM commented on- and contributed to the manuscript. The authors read and approved the final manuscript.

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#### Availability of data and materials

The dataset analysed during the current study is available from the corresponding author on reasonable request.

#### Ethics approval and consent to participate

Ethics approval for the AWI-Gen Phase 1 survey data and the accelerometer data collection was obtained from the Medunsa Research and Ethics Committee of the University of Limpopo (MREC/HS/195/2014:CR). The participants recruited into the original studies were informed about the study objectives, expected outcomes, benefits and the risks associated with it. Written informed consent was obtained from the participants prior to interviews and measurements.

#### Consent for publication

Not applicable.

#### Competing interests

The authors declare no competing interests.

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