

## **Associations between sleep parameters, non-communicable diseases, HIV status and medications in older, rural South Africans**

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## INTRODUCTION

While the global prevalence of non-communicable diseases (NCDs) continues to increase, the burden of NCDs is growing at a faster rate in developing countries. Historically, infectious diseases have represented the primary burden in South Africa, culminating in the HIV epidemic. National data indicated that NCDs such as heart disease, cancer, diabetes and stroke were responsible for 56% of all deaths occurring in 2015. Type 2 diabetes mellitus (T2DM) is now the second most common cause of death in South Africa (5.4%), after tuberculosis (7.2%)<sup>1</sup>. Because a major risk factor for cardiovascular diseases (CVD) and T2DM is obesity, it is concerning that one third of South African males and two thirds of South African females are overweight or obese<sup>2</sup>.

Although sleep is affected by and affects both infectious diseases and NCDs, it is a frequently neglected aspect of health and well-being. Sleep has been reported to be affected by HIV infection and some of the anti-retroviral treatments (ART) prescribed to treat it<sup>3 4 5 6 7</sup>.

Insufficient and/or mistimed sleep is also a major risk factor for obesity and NCDs such as CVD and T2DM<sup>8</sup>. Several prospective cohort studies indicate that both short and long sleep are associated with higher mortality rates and increased risk for CVD<sup>9 10 11 12</sup>. US National Health Interview Survey data indicate that relative to sleeping 7-8h per night, self-reported short ( $\leq 6$ h) and long sleep ( $> 9$ h) duration are independently associated with increased obesity, T2DM, hypertension, and CVD<sup>13</sup>. An added complication is the association between obesity and obstructive sleep apnea (OSA), a known cardiovascular risk factor that is additive to the effects of obesity alone<sup>14</sup>.

Few studies have investigated the sleep habits of South Africans and other Africans, let alone the interactions between sleep and the increasingly common chronic conditions associated with HIV and NCDs. The assumption that changes in sleep patterns coincided with the other lifestyle changes underlying epidemiologic transitions is one reason why sleep in communities that are at different stages of the urbanization process is of considerable interest.

Older individuals from the Agincourt Health and Demographic Surveillance System<sup>15</sup> were asked two questions to establish the severity of any nocturnal sleep problems and the extent to which the quality and/or quantity of their sleep affected their daytime function. A third of the population (30.2%) reported having severe/extreme nocturnal sleep problems, and 17.9% indicated that their daytime function was severely/extremely affected by their nocturnal sleep problems. Males who reported feeling unrested or unrefreshed during the day had a 2-fold increased mortality risk<sup>16</sup>.

The Health and Aging in Africa: A Longitudinal Study of an INDEPTH Community in South Africa (HAALSI) study investigates NCDs in a similar ageing segment of the Agincourt cohort<sup>17</sup>. Responses to a modified version of the Pittsburgh Sleep Quality Index (PSQI) questionnaire<sup>18</sup> were captured during this study. The responses to these questions are presented here, and have allowed us to derive information about sleep quality and duration, and relate these to NCDs, as well as HIV status and medication use. Therefore, the aims of this study were to (i) describe aspects of self-reported sleep duration and quality within this cohort of older, rural, black South Africans, and (ii) explore relationships between self-reported sleep duration, timing and quality and HIV status, ART, and NCDs.

## **METHODS**

### **Setting and participants**

The HAALSI study <sup>17</sup> was implemented in the Agincourt sub-district in Mpumalanga Province, South Africa, where the MRC/Wits Rural Public Health and Health Transitions Research Unit has been running the Agincourt Health and Demographic Surveillance System (Agincourt HDSS) site since 1992 <sup>15</sup>.

A sample of 6281 individuals who met the inclusion criteria was selected from the MRC/Wits Agincourt Unit's annual census of 2013. Of these, 391 individuals were excluded (deceased or had migrated). The response rate of the 5890 eligible individuals was 85.9%, resulting in a final sample size of 5059 <sup>17</sup>. All participants belonged to the Shangaan ethnic group.

The socio-demographic questions included information on age, sex, years of completed education, marital status, employment status, and socio-economic status (SES) as household wealth index quintiles <sup>19</sup>.

Anthropometric measurements included height (m), weight (kg), used to calculate BMI, waist and hip circumferences (cm). We collected blood pressure (BP) Blood was collected using the finger prick technique for dried blood spots (DBS) and point of care measurements were taken for glucose, lipids and haemoglobin.

HIV status was determined by testing DBS for HIV antibodies with enzyme-linked immunosorbent assays and confirmed using the Elecsys<sup>®</sup> HIV combi PT assay and the ADVIA Centaur<sup>®</sup> HIV Ag/Ab Combo assay. Among those who tested HIV positive, assays were performed for viral load and to detect presence of ART.

A subset of the major individual components of the Pittsburgh Sleep Quality index (PSQI) <sup>18</sup> were analysed in this study, in addition to a number of additional questions. All questions were translated from English to Shangaan and then back translated to English for consistency. The questionnaire in English is listed in Table 5. For the purposes of this study the question "Over the past 4 weeks, how many hours do you think you actually slept each day?" was used to determine self-reported sleep duration.

### **Data and statistical analyses**

Data collected in the field were checked regularly for quality and completeness following HAALSI standard operating procedures. Descriptive data are presented as mean  $\pm$  standard deviation, median (interquartile range) or count (%). Sex comparisons were carried out using an independent t-test, a Mann-Whitney U test or a Fisher's Exact test. The association of demographic variables and sleep parameters were measured using logistic regression. Models for continuous variables were estimated using ordered logistic regression, with sleep duration, bedtime and wake time quartiles as the dependent variables. We then modelled the association of sleep parameters and health conditions (hypertension, dyslipidaemia, diabetes, anaemia and HIV) also using logistic regression. In these analyses, each sleep parameter was evaluated in a separate model, adjusted for BMI and demographic characteristics (age group, sex, education group, employment status, marital status, wealth index quintile). For those participants who were HIV positive, we studied the association of being on ART and viral load on the main sleep variables (duration, quality, quantity, restless, awaking at night, snoring, gasping, nocturnal apnea). These models were adjusted for BMI and demographic characteristics (age group, sex, education group, employment status, marital status, wealth index quintile). Data were analysed using SAS software v9.3, and significance was accepted for  $p < 0.05$ .

### **Ethics approval**

This investigation was approved by the University of the Witwatersrand Human Research Ethics Committee (#M141159), the Harvard T.H. Chan School of Public Health Office of Human Research Administration (#13-1608), and the Mpumalanga Provincial Research and Ethics Committee. Written informed consent was obtained from all participants. For illiterate participants a witness not linked to the study was present during the consenting process.

## **RESULTS**

### **Characteristics of the study cohort**

Descriptive data for the 5059 rural participants included in this study are presented in Table 1. Males had on average received more years of education than females ( $p<0.001$ ), and more male participants were currently married ( $p<0.001$ ), lived in smaller households ( $p=0.004$ ) and were employed ( $p<0.001$ ). One third of this cohort was classified as obese, 58% hypertensive, 11% diabetic, 23% HIV positive, and almost 15% were taking ART. Females had higher BMIs ( $p<0.001$ ) and were more likely to be obese ( $p<0.001$ ), hypertensive ( $p<0.001$ ) and anaemic ( $p<0.001$ ) than the males. Although 94% of this cohort reported having good sleep quality, 32% took longer than 30 minutes to fall asleep at night, 36% felt that their self-reported sleep duration was insufficient, 33% experienced restless sleep, 40% were aware of nocturnal awakenings, 20% reported snoring, 12% reported gasping, and 7% reported that they stop breathing for brief periods in the night. Sleep habits also differed between sexes. Females reported shorter sleep durations ( $p<0.001$ ), going to bed earlier ( $p=0.023$ ), and waking earlier ( $p<0.001$ ) compared to males. Fewer females reported getting sufficient sleep each night ( $p=0.005$ ), more females experienced restless sleep ( $p<0.001$ ) and nocturnal awakenings ( $p=0.008$ ) than males, and more males reported snoring than females ( $p=0.008$ ). Figure 1 shows the sex-stratified distributions of bedtime, wake-up time, sleep and total sleep time for all participants.

### **Sleep parameter associations**

Table 2 displays associations between demographic and sleep parameters. Self-reported sleep duration was associated with age, sex, employment, marital status, and wealth quintile.

Self-reported bedtime was associated with age, BMI, education level, marital status and wealth quintile. Individuals aged 70-79y ( $p=0.058$ ) and  $\geq 80$ y ( $p<0.001$ ) had earlier bedtimes than those aged 40-49y; underweight participants had earlier bedtimes than normal weight participants ( $p=0.006$ ); individuals with 1-7y ( $p=0.005$ ) or  $>12$ y ( $p=0.002$ ) of education had later bedtimes than those with no formal education; widowed individuals had earlier bedtimes than married individuals ( $p=0.001$ ); middle, upper-middle and upper income individuals had later bedtimes than those in the lowest wealth quintile ( $p=0.002$ ,  $p<0.001$  and  $p<0.001$  respectively). Waking time was associated with age, sex, employment status and marital status. Participants aged 50-69y woke earlier than 40—49-year-olds ( $p<0.001$ ), females woke earlier than males ( $p<0.001$ ), employed individuals woke earlier than others ( $p<0.001$ ), and currently married individuals woke earlier than those not married ( $p<0.001$ ), separated / divorced ( $p<0.001$ ), or widowed ( $p=0.009$ ).

Ratings of insufficient sleep were associated with age, BMI, level of education, and employment status. Participants older  $\geq 80$ y were more likely to rate their sleep duration as being insufficient compared to 40—49-year-olds ( $p=0.025$ ); obese individuals were more likely to rate their sleep as being insufficient compared to normal weight individuals ( $p=0.001$ ); those with 8 to 11 years of education ( $p=0.001$ ) and those with 12+ years of education ( $p=0.017$ ) were less likely to rate their sleep as being insufficient compared to

those with no formal education; and homemakers were less likely to rate their sleep as being insufficient compared to those not working ( $p<0.001$ ).

Ratings of restless sleep were associated with age, sex, education level, employment and marital status. Individuals  $\geq 50$ y were more likely to report restless sleep compared to those aged 40-49y ( $p<0.001$ ); females were more likely to report restless sleep than males ( $p=0.001$ ); those with  $\geq 12$  years of education were less likely to report restless sleep compared to those with no formal education ( $p<0.001$ ); employed individuals were less likely to report restless sleep compared to those not working ( $p=0.011$ ); and separated/divorced ( $p=0.002$ ) and widowed ( $p<0.001$ ) participants were more likely to report restless sleep compared to married participants.

Self-reported snoring was associated with age, sex, BMI, education level and marital status. Participants  $\geq 50$ y were more likely to report snoring than 40–49-year-olds ( $p=0.044$  for 50-59y,  $p<0.001$  for 60-69y,  $p=0.004$  for 70-79y,  $p<0.001$  for  $\geq 80$ y); overweight ( $p=0.009$ ) and obese ( $p<0.001$ ) individuals were more likely to report snoring compared to normal weight individuals; males were more likely to report snoring than females ( $p<0.001$ ); those with 1-7y of education were more likely to report snoring compared to those with no formal education ( $p=0.005$ ); and separated/divorced ( $p=0.031$ ) and widowed ( $p<0.001$ ) participants were less likely to report snoring compared to those currently married.

### **Sleep and health outcomes**

Associations between self-reported sleep parameters and health outcomes are presented in Table 3. Obesity was associated with self-reported bedtime, wake time, insufficient sleep, snoring, gasping and periods of stopping breathing during sleep. Hypertension was associated with self-reported sleep duration, bedtime, wake time, sleep quality, restless sleep, and periods of stopping breathing during the night. Diabetes was associated with bedtime, restless sleep, and snoring. Those reporting restless sleep were more likely to have diabetes ( $p=0.015$ ); and those reporting snoring were more likely to have diabetes ( $p=0.003$ ). Dyslipidaemia was only associated with sleep sufficiency such that those reporting insufficient sleep were more likely to have dyslipidemia compared to those who felt they were obtaining sufficient sleep ( $p=0.032$ ). Anaemia was associated with self-reported sleep duration such that individuals in the shortest (4-7h,  $p=0.041$ ) and longest ( $\geq 10$ h,  $p=0.007$ ) sleep quartiles were more likely to have anaemia compared to those in the second sleep quartile (8h). HIV infection was associated with bedtime only: participants with moderately early bedtimes (20:00 to  $<21:00$ ) were more likely to be HIV positive compared to those with the earliest bedtimes ( $<20:00$ ,  $p=0.025$ ).

### **ART and viral load associations with sleep parameters**

While HIV positive individuals not on ART reported more awakenings during the night compared to those on ART ( $p=0.024$ ; Table 4), viral load amongst the HIV positive participants was not associated with any of the self-reported sleep parameters measured (Supplementary Table 1).

## **DISCUSSION**

This cohort of older, rural, black South African adults reported a longer sleep duration ( $8.2\pm 1.6$ h per night) than observed in other populations globally, despite the fact that one third described their sleep duration as being insufficient. A study of self-reported sleep duration and sleep problems in older adults found that participants from South Africa reported sleep durations of 8.6h ( $SD\pm 2.1$ ), and a greater proportion of rural dwelling participants than urban dwellers reported sleep durations  $>10$ h<sup>20</sup>. A review of data from 168 studies around the world ( $n=6052$ ) between 2010 and 2015 found total sleep time

(actigraphy- or PSG-derived) to range between 5.8 and 7.8h per night<sup>21</sup>. Other large-scale epidemiological studies have observed self-reported median sleep durations of 7-8h<sup>22 23 24 25</sup>. Although self-reported sleep duration is typically longer than objectively measured total sleep time, possible explanations for the longer self-reported sleep duration observed in this study may relate to differences in ethnicity (or tribal origin), geographical region, and socio-demographic factors.

Another point to consider relates to employment. A study of adults in the USA found that being employed had a strong effect on reducing self-reported sleep duration<sup>34</sup>. Since only 16% of the individuals in the present study were employed, the longer sleep durations are not unexpected, and indeed employed individuals from this cohort did report shorter sleep durations. Of interest, too, is that despite the lower proportion of females in paid employment in this study, they reported earlier rise times and shorter sleep durations than the males. This is the opposite of what was observed in Soweto, Finland, Norway, the UK and Canada<sup>27 22 28 29</sup>.

One might also argue that the longer sleep durations reported in this study relate to a rural living environment. Norwegian<sup>28</sup> and South African studies<sup>20</sup> have observed that individuals living in rural areas reported longer sleep durations than those in urban areas. However, the fact that an urban, albeit younger, population in Soweto, South Africa reported a longer sleep duration (8.8±1.7h)<sup>27</sup>, counters this argument. Generally, self-reported sleep durations from native Africans living in South Africa — those reported in the Soweto cohort<sup>27</sup>, the black African participants from the SAGE cohort<sup>20</sup> and the black South Africans from the Modelling the Epidemiological Transition Study (METS) cohort<sup>30</sup> — are all similar to those reported in the present study.

Data from the WHO indicate that the two strongest contributing risk factors to NCD-related deaths in South Africa are elevated blood pressure (33.7%) and obesity (31.3%)<sup>31</sup>. This sample of rural, older, longer sleeping adults was on average overweight, and had a high prevalence of obesity (30%) and hypertension (58%). Similar to the SA-NHANES report<sup>2</sup>, the incidence of obesity and hypertension was higher in the females in this study than in the males. The females also had higher incidences of depression and anaemia than the males. This higher burden of disease in the females was coincident with less formal education, larger households and lower employment. Since they also spent fewer hours in bed, had earlier wake times and reported more restless sleep and nocturnal awakenings than the males, one might speculate that their shorter, poorer quality sleep places them at higher risk for cardiometabolic diseases.

Prospective cohort studies indicate that both long- and short-total sleep times are associated with higher mortality rates and risk for cardiometabolic diseases<sup>9 10 11 12 32</sup>. In a recent large-scale study in the USA, 7h of sleep was associated with the lowest risk for cardiometabolic disease in all ethnic groups except non-Hispanic blacks, in whom 8h of sleep was associated with the lowest risk score for cardiometabolic disease<sup>33</sup>. As in previous studies<sup>34 35</sup>, the long sleepers (>10h) in the present study had a lower incidence of hypertension than the shorter sleepers (<7h). Sleep timing and ratings of sufficiency also appear to be important contributors to obesity in this cohort, since we observed an association between later bedtimes, ratings of insufficient sleep and obesity. A previous study in a cohort of black South Africans living in Soweto reported that a longer total sleep time and naps appeared to be protective against a high BMI in older females and high blood pressure, BMI and abdominal obesity in males<sup>27</sup>. Collectively, these data suggest that optimal sleep need may well differ by ethnicity in the context of minimising risk for NCDs. It

is also worth noting that although we did not assess sleep apnoea, there are indications that this cohort may suffer from the condition, which may be contributing to poorer health since those reporting snoring, gasping or having breathing pauses during the night were more likely to be obese.

The relationship between HIV infection, and its treatment, is complex. Sleep disturbances are a known effect of HIV infection<sup>3</sup>. This occurs already at an early stage of the infection, and has been suggested to be associated with chronic activation of the immune system<sup>4 36</sup>. HIV infection in itself has neurotoxic effects, quite apart from the effects of any opportunistic pathogens<sup>37</sup>. It is also well known that patients taking efavirenz, one of the common ART for HIV, experience insomnia and other sleep disturbances such as longer sleep onset latency and shorter sleep duration, in particular in the earlier stages of treatment<sup>5 6</sup>. Further, the immunoprotective effects of ART have a paradoxical effect when successful treatment commences at an advanced stage of the infection. It has been shown that a high increase in CD4 counts, although a sign of restored immune function, also associates with lower sleep quality (as well as higher incidence of pain and depression)<sup>36</sup>. Our finding that participants with untreated HIV infection and a high viral load reported more nocturnal awakenings than HIV negative participants ( $p=0.024$ ) is consistent with previous reports of an effect of the infection on sleep quality. Our finding of less self-reported sleep disturbance in treated than in untreated HIV positive participants are not suggestive of a negative net effect on sleep of ART treatment, either via the effects of the ART drugs or via an associated CD4 rebound, in this older population.

In conclusion, this cohort has the potential to address a number of important questions of current high interest. What is not known is whether the longer total sleep time, and higher prevalence of long sleep (9h or more) seen in this and other South African studies (i) reflects a greater sleep need, (ii) is a consequence of higher levels of unemployment, (iii) is protective against NCDs, and/or (iv) is underpinned by society-specific beliefs or value placed on sleep in South Africans of African origin. The data presented here provide a basis for further objective studies of the relationship between sleep quality and quantity to other risk factors in South African populations, a complex and underexplored area of research<sup>48</sup>. On a more general note, it also provides valuable data about sleep habits in Africa, with the potential for future analysis of how it is affected by urbanisation and industrialisation. Finally, it offers a unique opportunity for a population-based comparison of the effects of treated and untreated HIV infection, which is increasingly unavailable elsewhere.

## REFERENCES

- 1 Statistics South Africa. Mortality and causes of death in South Africa, 2015: Findings from death notification. 1-132 (Pretoria, 2015).
- 2 Shisana, O. et al. The South African National Health and Nutrition Examination Survey, 2012: SANHANES-1: the health and nutritional status of the nation. (Pretoria, 2013).
- 3 Darko, D. F., McCutchan, J. A., Kripke, D. F., Gillin, J. C. & Golshan, S. Fatigue, sleep disturbance, disability, and indices of progression of HIV infection. *Am J Psychiatry* 149, 514-6520 (1992).
- 4 Norman, S. E. et al. Sleep disturbances in men with asymptomatic human immunodeficiency (HIV) infection. *Sleep* 15, 150-155 (1992).
- 5 Gallego, L. et al. Analyzing sleep abnormalities in HIV-infected patients treated with Efavirenz. *Clin Infect Dis* 38, 430-432, <https://doi.org/10.1086/380791> (2004).
- 6 Nunez, M. et al. Higher efavirenz plasma levels correlate with development of insomnia. *J Acquir Immune Defic Syndr* 28, 399-400 (2001).
- 7 Koppel, B. S. & Bharel, C. Use of amitriptyline to offset sleep disturbances caused by efavirenz. *AIDS Patient Care STDS* 19, 419-420, <https://doi.org/10.1089/apc.2005.19.419> (2005).
- 8 Lucassen, E. A., Rother, K. I. & Cizza, G. Interacting epidemics? Sleep curtailment, insulin resistance, and obesity. *Ann N Y Acad Sci* 1264, 110-134, <https://doi.org/10.1111/j.1749-6632.2012.06655.x> (2012).
- 9 Chien, K. L. et al. Habitual sleep duration and insomnia and the risk of cardiovascular events and all-cause death: report from a community-based cohort. *Sleep* 33, 177-184 (2010).
- 10 Magee, C. A., Holliday, E. G., Attia, J., Kritharides, L. & Banks, E. Investigation of the relationship between sleep duration, all-cause mortality, and preexisting disease. *Sleep medicine* 14, 591-596, <https://doi.org/10.1016/j.sleep.2013.02.002> (2013).
- 11 Li, Y. et al. Association between insomnia symptoms and mortality: a prospective study of U.S. men. *Circulation* 129, 737-746, <https://doi.org/10.1161/CIRCULATIONAHA.113.004500> (2014).
- 12 Yeo, Y. et al. A prospective cohort study on the relationship of sleep duration with all-cause and disease-specific mortality in the Korean Multi-center Cancer Cohort study. *J Prev Med Public Health* 46, 271-281, <https://doi.org/10.3961/jpmph.2013.46.5.271> (2013).
- 13 Buxton, O. M. et al. Sleep restriction for 1 week reduces insulin sensitivity in healthy men. *Diabetes* 59, 2126-2133, <https://doi.org/10.2337/db09-0699> (2010).
- 14 Kasai, T., Floras, J. S. & Bradley, T. D. Sleep apnea and cardiovascular disease: a bidirectional relationship. *Circulation* 126, 1495-1510, <https://doi.org/10.1161/CIRCULATIONAHA.111.070813> (2012).
- 15 Kahn, K. et al. Profile: Agincourt health and socio-demographic surveillance system. *Int J Epidemiol* 41, 988-1001, <https://doi.org/10.1093/ije/dys115> (2012).
- 16 Gomez-Olive, F. X. et al. Sleep problems and mortality in rural South Africa: novel evidence from a low-resource setting. *Sleep medicine* 15, 56-63, <https://doi.org/10.1016/j.sleep.2013.10.003> (2014).
- 17 Gomez-Olive, F. X. et al. Cohort Profile: Health and Ageing in Africa: a Longitudinal Study of an INDEPTH Community in South Africa (HAALSI). *Int J Epidemiol*,



- <https://doi.org/10.1093/ije/dyx247> (2018).
- 18 Buysse, D. J., Reynolds, C. F., 3rd, Monk, T. H., Berman, S. R. & Kupfer, D. J. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res* 28, 193-213 (1989).
- 19 Collinson, M. A. et al. The Dynamics of Poverty and Migration in a Rural South African Community,. (Center for Statistics and the Social Sciences, University of Washington, Seattle, WA, 2009).
- 20 Peltzer, K. Sociodemographic and health correlates of sleep problems and duration in older adults in South Africa. *S Afr J Psych*. 5, a369 (2012).
- 21 Youngstedt, S. D. et al. Has adult sleep duration declined over the last 50+ years? *Sleep Med Rev* 28, 69-85, <https://doi.org/10.1016/j.smrv.2015.08.004> (2016).
- 22 Kronholm, E., Harma, M., Hublin, C., Aro, A. R. & Partonen, T. Self-reported sleep duration in Finnish general population. *J Sleep Res* 15, 276-290, <https://doi.org/10.1111/j.1365-2869.2006.00543.x> (2006).
- 23 Hale, L. Who has time to sleep? *J Public Health (Oxf)* 27, 205-211 (2005).
- 24 Krueger, P. M. & Friedman, E. M. Sleep duration in the United States: a cross-sectional population-based study. *Am J Epidemiol* 169, 1052-1063, <https://doi.org/10.1093/aje/kwp023> (2009).
- 25 Stranges, S. et al. Correlates of short and long sleep duration: a cross-cultural comparison between the United Kingdom and the United States: the Whitehall II Study and the Western New York Health Study. *Am J Epidemiol* 168, 1353-1364, <https://doi.org/10.1093/aje/kwn337> (2008).
- 26 Basner, M., Spaeth, A. M. & Dinges, D. F. Sociodemographic characteristics and waking activities and their role in the timing and duration of sleep. *Sleep* 37, 1889-1906, <https://doi.org/10.5665/sleep.4238> (2014).
- 27 Pretorius, S. et al. Is There an Association between Sleeping Patterns and Other Environmental Factors with Obesity and Blood Pressure in an Urban African Population? *PLoS One* 10, e0131081, <https://doi.org/10.1371/journal.pone.0131081> (2015).
- 28 Ursin, R., Bjorvatn, B. & Holsten, F. Sleep duration, subjective sleep need, and sleep habits of 40- to 45-year-olds in the Hordaland Health Study. *Sleep* 28, 1260-1269 (2005).
- 29 Grandner, M. A. & Kripke, D. F. Self-reported sleep complaints with long and short
- 30 Sani, M. et al. Daily activity patterns of 2316 men and women from five countries differing in socioeconomic development. *Chronobiol Int* 32, 650-656, <https://doi.org/10.3109/07420528.2015.1038559> (2015).
- 31 World Health Organisation. WHO Global Health Observatory data, <http://www.who.int/gho/en> (2017).
- 32 Yin, J. et al. Relationship of Sleep Duration With All-Cause Mortality and Cardiovascular Events: A Systematic Review and Dose-Response Meta-Analysis of Prospective Cohort Studies. *J Am Heart Assoc* 6, <https://doi.org/10.1161/JAHA.117.005947> (2017).
- 33 Kanagasabai, T. & Chaput, J. P. Sleep duration and the associated cardiometabolic risk scores in adults. *Sleep Health* 3, 195-203, doi:10.1016/j.sleh.2017.03.006 (2017).
- 34 Knutson, K. L. et al. Association between sleep and blood pressure in midlife: the CARDIA sleep study. *Arch Intern Med* 169, 1055-1061, <https://doi.org/10.1001/archinternmed.2009.119> (2009).

- 35 Altman, N. G. et al. Sleep duration versus sleep insufficiency as predictors of cardiometabolic health outcomes. *Sleep medicine* 13, 1261-1270, <https://doi.org/10.1016/j.sleep.2012.08.005> (2012).
- 36 Redman, K. N., Karstaedt, A. S. & Scheuermaier, K. Increased CD4 counts, pain and depression are correlates of lower sleep quality in treated HIV positive patients with low baseline CD4 counts. *Brain Behav Immun* 69, 548-555 (2018).
- 37 Low, Y., Goforth, H., Preud'homme, X., Edinger, J. & Krystal, A. Insomnia in HIV-infected patients: Pathophysiologic implications. *AIDS Rev* 16, 3-13 (2014).

**TABLES**

**Table 1. Descriptive, demographic, health and sleep characteristics of the cohort.**

	<b>All (n=5059)</b>	<b>Females (n=2714)</b>	<b>Males (n=2345)</b>	<b>p-value</b>
<b>Age (y)</b>	61 (52-71)	60 (51-71)	61 (52-71)	0.594
<b>Years of education</b>	4 (1-9)	3 (1-9)	5 (1-9)	<0.001
<b>Married/ cohabiting</b>	2575 (50.9%)	973 (35.9%)	1602 (68.3%)	<0.001
<b>Number of people in household</b>	5.3 ±3.3	5.5 ±3.3	5.2 ±3.4	0.004
<b>Employed</b>	805 (16.0%)	362 (13.4%)	443 (19.0%)	<0.001
<b>Household wealth quintile:</b>				
1 (poorest)	1046 (20.7%)	544 (20.0%)	502 (21.4%)	0.614
2	1001 (19.8%)	546 (20.1%)	455 (19.4%)	
3	991 (19.6%)	541 (19.9%)	450 (19.2%)	
4	1007 (19.9%)	550 (20.3%)	457 (19.5%)	
5 (wealthiest)	1014 (20.0%)	533 (19.6%)	481 (20.5%)	
<b>BMI (kg·m<sup>-2</sup>)</b>	27.2 ±6.9	29.3 ±7.4	24.9 ±5.4	<0.001
<b>Obese</b>	1384 (29.5%)	1043 (41.2%)	341 (15.8%)	<0.001
<b>Hypertension</b>	2884 (58.4%)	1645 (61.8%)	1239 (54.5%)	<0.001
<b>Dyslipidemia</b>	1861 (43.8%)	1000 (42.9%)	861 (44.9%)	0.203
<b>Diabetes</b>	495 (10.7%)	288 (11.5%)	207 (9.7%)	0.050
<b>Anemia</b>	779 (17.3%)	544 (22.5%)	235 (11.4%)	<0.001
<b>HIV positive</b>	1048 (23.0%)	565 (22.9%)	483 (23.0%)	0.944
<b>HIV+ and on ART</b>	663 (64.0%)	346 (61.8%)	317 (66.6%)	0.108
<b>Sleep duration* (h)</b>	8.23 ±1.6	8.15 ±1.6	8.33 ±1.7	<0.001
<b>Bedtime (h:min)</b>	20:48 ±1:15	20:46 ±1:13	20:51 ±1:18	0.023
<b>Wake time (h:min)</b>	05:31 ±1:05	05:22 ±1:00	05:41 ±1:10	<0.001
<b>Good sleep quality<sup>1</sup></b>	4724 (93.5%)	2527 (93.2%)	2197 (93.8%)	0.458

<b>Latency &gt;30 min<sup>2</sup></b>	1603 (31.8%)	861 (31.9%)	742 (31.8%)	0.952
<b>Sufficient sleep<sup>3</sup></b>	3241 (64.2%)	1691 (62.4%)	1550 (66.2%)	0.005
<b>Restless sleep</b>	1626 (32.9%)	964 (36.3%)	662 (28.9%)	<0.001
<b>Nocturnal awakenings<sup>3</sup></b>	2036 (40.3%)	1139 (42.0%)	897 (38.3%)	0.008
<b>Snoring<sup>4</sup></b>	979 (19.5%)	488 (18.1%)	491 (21.1%)	0.008
<b>Gaspings<sup>4</sup></b>	624 (12.4%)	313 (11.6%)	311 (13.4%)	0.065
<b>Breathing stops<sup>4</sup></b>	352 (7.0%)	177 (6.6%)	175 (7.5%)	0.203

Data are presented as mean  $\pm$  standard deviation, median (interquartile range) or count (%). BMI: body mass index; ART: antiretroviral therapy. \* Self-reported sleep duration. <sup>1</sup> “Very good” or “Fairly good”; <sup>2</sup> Once a week or more; <sup>3</sup> “Often” or “Very often”; <sup>4</sup> “Yes”. The p-values represent differences between the two gender groups analyzed using an independent t-test, a Mann-Whitney U test or a Fisher’s Exact test.

**Table 2.** Logistic regression models for associations between demographic and sleep variables. Each of the six sleep parameters (dependent variables) was evaluated in a separate model with the demographic variables serving as independent variables.

		Self-reported sleep duration	Bedtime	Wake time	Insufficient sleep	Restless sleep	Snoring
		Quartile 1 - Quartile 4	Quartile 1 - Quartile 4	Quartile 1 - Quartile 4	Sometimes/ Rarely/ Never sufficient vs. Often/ Very often sufficient	Yes vs. No	Yes vs. No
		OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
<b>Age group (y)</b>	50-59 vs 40-49	0.83 (0.70, 0.98)	1.00 (0.85, 1.17)	0.76 (0.64, 0.89)	1.13 (0.93, 1.37)	1.39 (1.12, 1.72)	1.28 (1.00, 1.63)
	60-69 vs 40-49	0.78 (0.65, 0.94)	0.99 (0.83, 1.19)	0.61 (0.51, 0.73)	1.04 (0.84, 1.29)	1.79 (1.42, 2.25)	1.64 (1.26, 2.13)
	70-79 vs 40-49	0.93 (0.76, 1.15)	0.75 (0.61, 0.92)	0.85 (0.69, 1.04)	1.15 (0.91, 1.47)	1.97 (1.53, 2.54)	1.54 (1.14, 2.07)
	80+ vs 40-49	1.24 (0.97, 1.59)	0.53 (0.41, 0.67)	1.18 (0.93, 1.51)	1.37 (1.04, 1.81)	2.46 (1.84, 3.29)	1.80 (1.27, 2.55)
<b>Sex</b>	Female vs Male	0.73 (0.64, 0.83)	0.93 (0.82, 1.05)	0.50 (0.44, 0.57)	1.05 (0.91, 1.21)	1.28 (1.10, 1.49)	0.74 (0.62, 0.88)
<b>BMI</b>	Underweight vs normal	1.01 (0.79, 1.30)	0.71 (0.55, 0.90)	1.06 (0.83, 1.35)	1.09 (0.82, 1.44)	1.27 (0.95, 1.69)	1.34 (0.94, 1.89)
	Overweight vs normal	1.03 (0.90, 1.19)	0.97 (0.84, 1.11)	0.91 (0.79, 1.04)	1.14 (0.97, 1.33)	1.14 (0.97, 1.34)	1.30 (1.07, 1.60)
	Obese vs normal	1.08 (0.93, 1.24)	1.06 (0.92, 1.22)	1.10 (0.95, 1.26)	1.30 (1.11, 1.53)	1.02 (0.86, 1.20)	2.50 (2.05, 3.05)
<b>Education</b>	1-7 years vs No formal education	0.89 (0.78, 1.02)	1.19 (1.05, 1.35)	1.02 (0.9, 1.16)	0.93 (0.81, 1.08)	0.94 (0.81, 1.09)	1.29 (1.08, 1.53)
	8-11 years vs No formal education	0.96 (0.79, 1.16)	1.18 (0.97, 1.43)	1.17 (0.97, 1.42)	0.67 (0.53, 0.85)	0.82 (0.64, 1.04)	1.09 (0.83, 1.44)

	12+ years vs No formal education	0.82 (0.64, 1.03)	1.45 (1.15, 1.83)	0.81 (0.64, 1.02)	0.71 (0.54, 0.94)	0.50 (0.36, 0.70)	1.23 (0.89, 1.70)
<b>Employment</b>	Employed vs Not working	0.57 (0.48, 0.67)	1.00 (0.86, 1.18)	0.43 (0.36, 0.50)	0.94 (0.78, 1.13)	0.76 (0.62, 0.94)	0.99 (0.79, 1.24)
	Homemaker vs Not working	0.45 (0.37, 0.54)	0.88 (0.74, 1.05)	0.96 (0.80, 1.14)	0.34 (0.27, 0.43)	0.86 (0.70, 1.06)	1.20 (0.95, 1.52)
<b>Marital status</b>	Never married vs Currently married	1.18 (0.92, 1.51)	0.95 (0.75, 1.20)	1.57 (1.24, 1.99)	1.10 (0.84, 1.46)	1.14 (0.83, 1.56)	0.82 (0.57, 1.17)
	Separated / divorced vs Currently married	1.20 (1.01, 1.43)	0.85 (0.71, 1.00)	1.35 (1.13, 1.59)	1.15 (0.94, 1.40)	1.38 (1.12, 1.69)	0.76 (0.59, 0.97)
	Widowed vs Currently married	1.23 (1.07, 1.42)	0.79 (0.69, 0.91)	1.20 (1.04, 1.38)	1.13 (0.96, 1.33)	1.33 (1.13, 1.57)	0.66 (0.54, 0.81)
<b>Wealth quintile</b>	2 vs 1 (lowest)	0.94 (0.79, 1.11)	1.21 (1.03, 1.44)	0.92 (0.77, 1.08)	1.11 (0.92, 1.35)	0.91 (0.75, 1.11)	0.86 (0.68, 1.10)
	3 vs 1	0.81 (0.68, 0.97)	1.31 (1.11, 1.56)	0.90 (0.76, 1.07)	0.93 (0.76, 1.14)	1.09 (0.89, 1.33)	0.93 (0.73, 1.18)
	4 vs 1	0.73 (0.61, 0.87)	1.66 (1.40, 1.97)	0.99 (0.83, 1.18)	1.03 (0.84, 1.26)	1.05 (0.85, 1.29)	0.92 (0.72, 1.18)
	5 vs 1	0.76 (0.63, 0.92)	1.83 (1.52, 2.19)	0.99 (0.83, 1.19)	1.05 (0.85, 1.30)	0.89 (0.72, 1.11)	0.88 (0.68, 1.14)

OR: odds ratio, CI: confidence interval, BMI: body mass index.

**Table 3.** Logistic regression models for associations between sleep parameters and health conditions. Each of the six health conditions (dependent variables) was evaluated in a separate model for each off the 11 sleep variables (independent variables), adjusted for BMI category and demographic characteristics (age group, sex, education group, employment status, marital status, wealth index quintile). The obesity outcome was not adjusted for BMI.

		<b>Obesity</b>	<b>Hypertension</b>	<b>Dyslipidemia</b>	<b>Diabetes</b>	<b>Anemia</b>	<b>HIV</b>
		OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
<b>(1) Self-reported sleep duration</b>	Quartile 1 (4-7h) vs 2 (8h)	0.97 (0.82, 1.17)	1.18 (1.00, 1.39)	0.94 (0.79, 1.12)	1.12 (0.86, 1.47)	1.26 (1.01, 1.58)	1.05 (0.86, 1.29)
	Quartile 3 (9h) vs 2 (8h)	1.06 (0.87, 1.30)	1.12 (0.93, 1.35)	0.99 (0.82, 1.20)	1.02 (0.75, 1.38)	1.19 (0.92, 1.52)	1.19 (0.95, 1.49)
	Quartile 4 (10-14h) vs 2 (8h)	1.07 (0.86, 1.33)	0.84 (0.69, 1.03)	0.88 (0.72, 1.09)	1.31 (0.96, 1.79)	1.43 (1.10, 1.86)	1.08 (0.84, 1.38)
<b>(2) Bedtime</b>	Quartile 2 (8-<9pm) vs 1 (<8pm)	1.22 (0.96, 1.55)	1.15 (0.94, 1.42)	0.94 (0.75, 1.17)	1.01 (0.72, 1.40)	0.96 (0.73, 1.26)	1.35 (1.03, 1.76)
	Quartile 3 (9-9:30pm) vs 1 (<8pm)	1.36 (1.07, 1.73)	1.26 (1.02, 1.56)	1.10 (0.88, 1.37)	0.80 (0.57, 1.12)	0.99 (0.75, 1.30)	1.21 (0.93, 1.58)
	Quartile 4 (>9:30pm) vs 1 (<8pm)	1.24 (0.96, 1.60)	1.11 (0.89, 1.39)	0.96 (0.76, 1.22)	0.68 (0.47, 0.99)	0.96 (0.71, 1.28)	1.14 (0.86, 1.52)
<b>(3) Wake time</b>	Quartile 2 (5am) vs 1 (<5am)	1.15 (0.95, 1.40)	0.81 (0.68, 0.98)	1.01 (0.83, 1.22)	1.22 (0.91, 1.64)	0.95 (0.75, 1.21)	0.92 (0.74, 1.15)
	Quartile 3 (>5-6am) vs 1 (<5am)	1.27 (1.04, 1.55)	0.98 (0.81, 1.18)	1.07 (0.88, 1.30)	1.05 (0.77, 1.43)	1.00 (0.79, 1.28)	1.14 (0.91, 1.42)

	Quartile 4 (>6am) vs 1 (<5am)	1.23 (0.97, 1.57)	0.96 (0.77, 1.19)	1.02 (0.81, 1.27)	1.36 (0.96, 1.93)	1.14 (0.85, 1.51)	0.99 (0.75, 1.29)
<b>(4) Sleep quality</b>	Bad vs good	0.82 (0.61, 1.11)	1.43 (1.08, 1.90)	1.28 (0.98, 1.68)	1.08 (0.72, 1.64)	1.33 (0.96, 1.84)	0.76 (0.53, 1.09)
<b>(5) Latency &gt;30 min</b>	At least once/week vs <once/week	0.97 (0.84, 1.12)	1.08 (0.94, 1.23)	1.01 (0.88, 1.16)	1.10 (0.89, 1.36)	1.09 (0.91, 1.30)	0.93 (0.78, 1.09)
<b>(6) Insufficient sleep</b>	Sometimes/rarely/never sufficient vs often/very often sufficient	1.21 (1.05, 1.40)	1.10 (0.96, 1.26)	1.16 (1.01, 1.33)	0.89 (0.72, 1.10)	1.05 (0.88, 1.25)	0.93 (0.79, 1.09)
<b>(7) Restless sleep</b>	Yes vs no	0.95 (0.82, 1.10)	1.19 (1.04, 1.37)	1.06 (0.92, 1.22)	1.29 (1.05, 1.60)	1.04 (0.87, 1.25)	0.86 (0.72, 1.02)
<b>(8) Nocturnal awakenings</b>	At least once/week vs <once/week	0.96 (0.84, 1.10)	1.12 (0.98, 1.27)	0.97 (0.85, 1.10)	1.02 (0.83, 1.25)	0.99 (0.84, 1.18)	1.09 (0.93, 1.27)
<b>(9) Snoring</b>	Yes vs no	2.18 (1.85, 2.57)	1.15 (0.98, 1.35)	0.97 (0.82, 1.14)	1.41 (1.12, 1.78)	0.82 (0.65, 1.02)	0.89 (0.72, 1.09)
<b>(10) Gasping</b>	Yes vs no	2.13 (1.75, 2.59)	1.07 (0.88, 1.30)	0.93 (0.76, 1.13)	1.27 (0.97, 1.67)	0.90 (0.69, 1.18)	1.05 (0.82, 1.34)
<b>(11) Breathing stops</b>	Yes vs no	1.77 (1.37, 2.30)	1.42 (1.09, 1.85)	0.94 (0.72, 1.21)	1.29 (0.91, 1.83)	1.10 (0.79, 1.53)	0.85 (0.60, 1.20)

OR: odds ratio, CI: confidence interval, BMI: body mass index.



**Table 4.** Effect of HIV status and current antiretroviral therapy (ART) use on sleep characteristics among the entire cohort. Models were estimated using ordered logistic regression with the sleep variables treated as dependent variables in each of the 8 models. Models were adjusted for BMI and demographic characteristics (age group, sex, education group, employment status, marital status, wealth index quintile).

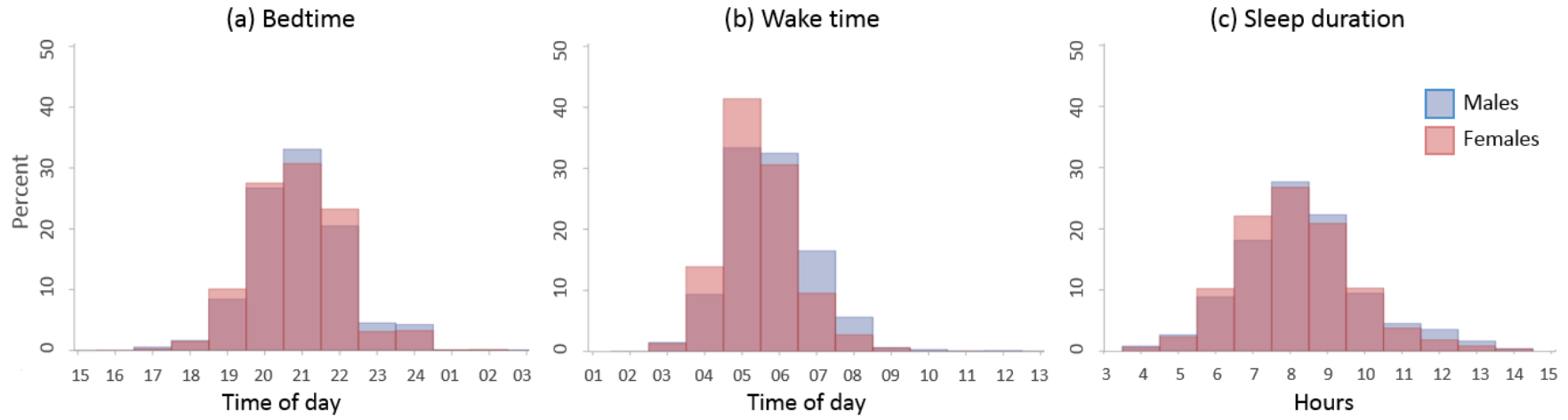
	<b>Self-reported sleep duration</b>	<b>Bad sleep quality</b>	<b>Insufficient sleep</b>	<b>Restless sleep</b>	<b>Awakenings</b>	<b>Snoring</b>	<b>Gasping</b>	<b>Breathing stops</b>
	Quartile 1 - Quartile 4	Very bad/ Bad vs Very good/ Good	Sometimes/ Rarely/ Never sufficient vs Often/ Very often sufficient	Yes vs No	At least once per week vs < Once per week	Yes vs No	Yes vs No	Yes vs No
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
<b>HIV+/ART+ vs HIV-</b>	1.10 (0.93, 1.29)	0.74 (0.49, 1.14)	0.99 (0.82, 1.20)	0.87 (0.71, 1.06)	1.00 (0.83, 1.21)	0.87 (0.68, 1.11)	1.06 (0.79, 1.41)	0.71 (0.46, 1.10)
<b>HIV+/ART- vs HIV-</b>	0.97 (0.79, 1.20)	0.84 (0.50, 1.42)	0.80 (0.62, 1.03)	0.88 (0.68, 1.13)	1.30 (1.04, 1.64)	0.91 (0.67, 1.23)	1.00 (0.68, 1.44)	1.09 (0.68, 1.74)

OR: odds ratio, CI: confidence interval.

**Table 5.** Questionnaire items used in this study, with response options in parentheses.

- Over the past 4 weeks, what time did you usually turn the lights off to go to sleep? (Hours, minutes)
- Over the past 4 weeks, what time did you usually get out of bed? (Hours, minutes)
- Over the past 4 weeks, how many hours do you think you actually slept each day? (Hours)
- During the past 4 weeks, how often did you wake up in the middle of the night or early morning? (“Never”/“Less than once per week”/“Once or twice a week”/“Three or more times a week”)
- During the past month, have you snored, or ever been told that you were snoring? (“Yes”/“No”)
- During the past month, have you snored loudly, or ever been told that you were snoring loudly? (“Yes”/“No”)
- During the last month, have you had, or ever been told that your breathing stops or you struggle for breath? (“Yes”/“No”)
- During the last month, have you had, or ever been told that you were snorting or gasping? (“Yes”/“No”)
- On a scale of 0 to 10, where 0 is “Does not interfere” and 10 is “Completely interferes”, select the one number that describes how, during the past 24 hours, pain has interfered with your sleep.
- Over the past 4 weeks, how would you rate your sleep quality overall? (“Very good”/“Fairly good”/“Fairly bad”/“Very bad”)
- During the past 4 weeks, how often could you not get to sleep within 30 minutes? (“Never”/“Less than once per week”/“Once or twice a week”/“Three or more times a week”)
- In your life, have you ever had any experience that was so frightening, horrible, or upsetting that, in the past 30 days you had more trouble than usual falling asleep or staying asleep?
- Much of the time in the past week, your sleep was restless. (“Yes”/“No”)
- How often during the past 4 weeks did you get enough sleep to feel rested upon waking up? (“Never”/“Rarely”/“Sometimes”/“Often”/“Very often”)

## FIGURES



**Figure 1.** Histograms of self-reported bedtime (a), wake time (b) and sleep duration (c), stratified by sex