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Sleep problems and mortality in rural South Africa: novel evidence from a low-resource setting

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ABSTRACT

Objective: Sleep problems are associated with mortality in Western populations. In low-resource settings, evidence of sleep problems and their potential association with mortality is lacking. Our study aimed to fill this gap by examining the prospective association of sleep problems with mortality among older adults in rural South Africa, as well as potential sex differences in this association.
Methods: The study was conducted in 2006 in Agincourt (South Africa), as part of the Health and Demographic Surveillance System. A community-wide sample of 4044 men and women aged 50 years or older participated in the survey. Two measures of sleep quality over the last 30 days were assessed alongside sociodemographic variables, measures of quality of life (QoL), and functional ability. Cox proportional hazard models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI) for mortality risk over time associated with the two sleep measures at baseline, while allowing adjustment for other covariates.
Results: Overall, 394 deaths occurred during 3 years of follow-up. Both men and women reporting severe/extreme nocturnal sleep problems (vs none/mild/moderate) experienced a significantly greater mortality risk in models adjusted for sociodemographic variables only (HR, 1.65 [95% CI, 1.18–2.31] and HR, 1.42 [95% CI, 1.07–1.88], respectively). However, these associations were nonsignificant in fully adjusted models (HR, 1.23 [95% CI, 0.85–1.79] and HR, 1.07 [95% CI, 0.78–1.47], respectively).

Men who reported severe/extreme difficulty related to daytime function (vs none/mild/moderate) experienced a 2-fold increased mortality risk (HR, 2.01 [95% CI, 1.32–3.07]) in fully adjusted models, whereas no significant association was observed for women (1.16 [95% CI, 0.80–1.67]).
Conclusions: In this population, nocturnal sleep problems were not associated with mortality once analyses were adjusted for QoL, functional ability, and psychologic comorbidities. By contrast, severe or extreme problems with feeling unrested or unrefreshed during the day were associated with a 2-fold increased mortality risk, but this association was only significant in men.
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1. Introduction

Sleep problems represent an unmet public health problem affecting large segments of the population, especially middle-aged and older adults, with substantial costs to society in Western countries [1–4]. Sleep problems also are associated with adverse health outcomes in later life, including cardiovascular disease (CVD), psychiatric comorbidities, lower health-related quality of life (QoL), and reduced longevity [5–8]. In particular, there is a large body of evidence on the association of sleep duration, one dimension of sleep patterns, with mortality across several populations from Western countries [8–14]. Moreover, insomnia and daytime sleepiness have been associated with increased risks for all-cause mortality and CVD among older adults from high-income settings [15,16].

Whether or not these relationships are causal remains uncertain owing to the possibility of residual confounding by comorbidities of sleep problems, particularly in aging populations [17]. However, it is possible that sleep disturbances may represent a risk marker for poorer health outcomes [18].

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Importantly, most of the evidence to date comes from selected populations in high-income countries and in middle-aged individuals [13,14]. To our knowledge, there is no study that has reported on the prospective association of sleep problems with mortality outcomes among older adults from low-resource settings. Indeed, sleep problems might represent an unrecognized public health issue in many developing countries, especially in aging populations, as recently observed in several African and Asian settings [19] given the ongoing epidemiologic transition and population aging at the global level [20,21]. Moreover, factors contributing to poor sleep patterns in older adults from low-resource settings might differ from those characteristic of Western societies [19].

The Agincourt Study, part of the International Network for the Demographic Evaluation of Populations and their Health (INDEPTH) and the World Health Organization (WHO) Study on Global Aging and Adult Health (SAGE) multicenter collaboration on global aging and adult health [19], offers an unique opportunity to fill these gaps by examining the prospective relationship of sleep problems with mortality in a large population-based sample of older adults from rural South Africa while accounting for a number of sociodemographic variables measures of QoL, functional ability, and psychologic comorbidities [19,22].

There is a considerable body of literature suggesting potential sex differences in the health implications of sleep disturbances [15,23–26]; therefore, we investigated the associations of sleep problems with mortality separately in men and women.

2. Material and methods

2.1. Study setting and population

The MRC/Wits (Medical Research Council/Witwatersrand) Rural Public Health and Health Transitions Research Unit (Agincourt) is located in the Agincourt subdistrict of Bushbuckridge, Mpumalanga Province, northeast South Africa, which is close to the border of Mozambique. Although South Africa as a whole is considered as an upper middle income country, the study setting is a former homeland (Bantustan) and remains under resourced. Since the first democratically elected government, there has been substantial development in certain services such as electrification. For example, 89% of households had electricity while 60% owned a television in 2005; however, other key infrastructure remained poor, including provision of water and sanitation. The unemployment rate is high (36%) sustaining prior high levels of male labor migration, leading to increased migration of young women [27]. The South African noncontributory old-age pension provides critical income for women older than the age of 60 years and men older than 65 years [28].

The Agincourt health and sociodemographic surveillance system (HDSS) has been annually updated since 1992. The annual census update involves collection of basic demographic data (pregnancy outcomes, deaths, in- and out-migrations) on every individual in each household [25,26]. Although the surveillance system includes information on all deaths, there is incomplete official death notification, and hence a verbal autopsy is conducted on every death reported [29,30].

The Agincourt HDSS is supplemented by additional data collected through special add-on modules administered at less frequent but regular time intervals, including labor participation, household assets, healthcare utilization, and physical and cognitive function of older adults. The latter module provides the core data for our paper.

The total population under surveillance in 2006 was approximately 70,000 individuals living in 21 villages. In August 2006 there were 8429 men and women aged 50 years or older. From these, we excluded those who did not live permanently in the area ($n = 1648$) and individuals who had participated in previous studies ($n = 575$). The 6206 individuals living permanently in the area were invited to participate in the Agincourt Study on Ageing during the 2006 census update. Each individual was visited up to 3 times in an effort to complete the interview, resulting in 4047 out of 6206 (65.2%) individuals who agreed to participate and complete the questionnaire. Reasons for nonparticipation in the study included being absent at time of interview ($n = 1616$; 26.0%), death ($n = 218$; 3.5%), declining to take part in the study ($n = 47$; 0.75%), or unable to answer the questions mainly due to poor health ($n = 240$; 3.9%). There were 38 participants (0.9%) who were lost to follow-up and were not included in these analyses. Three other individuals were excluded because they did not answer the questions related to sleep quality; thus, the final sample of participants with a complete set of data for these analyses included 4044 individuals.

Ethical clearance was granted by the Committee for Research on Human Subjects (Medical) of the University of the Witwatersrand, Johannesburg, South Africa for both the MRC/Wits Rural Public Health and Health Transitions Research Unit's (Agincourt) Health and Socio-Demographic Surveillance System and add-on modules (Ref no. M960720), and the Agincourt-INDEPTH-WHO Study on Global Ageing and Adult Health (Ref no.R14/49).

2.2. Data collection

The data collection tool was adapted and shortened as part of the INDEPTH WHO-SAGE. The study background has been described in detail in previous reports [19,22]. It included questions on self-health assessment, functionality, sleep and energy, depression and anxiety, well-being, and QoL.

The questionnaire was back-translated to the local language (Shangaan). Certain amendments were made to the questionnaire following a pilot study. Fieldwork quality control followed routine systems established for the annual census update and included three levels: cross checking of forms by other fieldworkers, supervisor's check, and quality checkers' revision [22]. The short INDEPTH-SAGE module was administered by trained local field workers. As part of the census update routine, verbal informed consent was obtained from the participants prior to the interview.

Additional demographic data, including sex, age, marital status, nationality, and level of education were extracted from the Agincourt HDSS (2006 census update). Household asset score was extracted from 2005 data, as these were the most recent data available.

2.3. Follow-up

The 4044 participants in the 2006 study were followed up at the annual census update from 2007 to 2009, providing information on deaths up to July 31st, 2009. Participants were included in the analysis until out-migration, death, or July 31st, 2009, whichever came first. All efforts were made to follow-up on individuals who were reported to be dwelling within the Agincourt subdistrict; however, those not found in the new dwelling were censored from follow-up at the date of the move ($n = 48$; 1.2%), and those who left the study area ($n = 56$; 1.4%) were censored at the out-migration date. The main reasons for out-migration were moving to a new house, change of marital status, and study- or work-related opportunities.

2.4. Sleep variables

Sleep problems were assessed by two questions: (1) "Overall in the last 30 days, how much of a problem did you have with sleeping, such as falling asleep, waking up frequently during the night or waking up too early in the morning?" (Q1016 of the questionnaire, see appendix). (2) "Overall in the last 30 days, how much of a problem did you have due to not feeling rested and refreshed during the day (e.g., feeling tired or not having energy)?" (Q1017 of the questionnaire).

The first question describes the severity of nocturnal sleep problems; the second question denotes severity of difficulty related to daytime function. Both questions had five possible responses: none, mild, moderate, severe, and extreme. Responses were collapsed into two categories: none/mild/moderate and severe/extreme, which is in line with a previous report [19].

2.5. Covariates

Age at interview was calculated from the date of birth, taken from the national ID book in over 80% of individuals, or was otherwise self-reported. Age was divided into four groups: 50–59, 60–69, 70–79, and 80 years and older. Education was categorized according to WHO levels: no formal education, less than 6 years of formal education, and 6 years or more of formal education. This information was obtained from the Agincourt HDSS database, using the most recent 2006 update.

Because many unions are traditional rather than civic and polygamy is practiced by some individuals, we categorized marital status into two groups: (1) currently married or living as married; and (2) single, including anyone without a current partner (i.e., those who were never married, were separated, or were divorced or widowed).

To evaluate socioeconomic status, we used a household asset score. This score was developed using principal component factor analysis and 34 variables derived from the 2005 HDSS questionnaire. The assets were categorized in five groups which included information on modern assets, power supply, water and sanitation, housing quality, and livestock. Each asset variable was coded to assure that increasing values corresponded to greater SES. Each asset was given equal weight by rescaling so that all values of a given asset variable fell within the range (0, 1). For each household and for each asset group, the rescaled asset values were added and then rescaled to get a specific value in the range (0, 1). Finally, for each household these five group-specific scaled values were added to get an overall asset score, which had a value in the range (0, 5). This score was then divided in quintiles by household [31].

Table 1
Baseline characteristics of the study population by vital status at follow-up (2006–2009). Agincourt Study, Health and Socio-demographic Surveillance System.

	Men		*P* value	Women		*P* value
	Alive	Dead		Alive	Dead	
N = 4044	838	164		2812	230	
Age (y); mean ± SD = 66 ± 11	65.7 (10.3)	69.8 (12.0)		67.2 (10.5)	70.9 (11.1)	<.001
50–59	245 (29.2)	27 (16.5)	<.001	953 (33.9)	60 (26.1)	<.001
60–69	261 (31.1)	59 (36.0)		840 (29.9)	56 (24.4)	
70–79	228 (27.2)	39 (23.8)		739 (26.3)	62 (27.0)	
⩾80	105 (12.5)	39 (23.8)		282 (10.0)	52 (22.6)	
Education levels						
No formal	437 (54.6)	108 (66.7)	.011	1867 (68.3)	168 (76.4)	.038
At most 6 years	179 (22.4)	31 (19.1)		506 (18.5)	33 (15.0)	
More than 6 years	185 (23.1)	23 (14.2)		360 (13.2)	19 (8.6)	
Marital status						
In partnership	659 (78.6)	109 (66.5)	.001	1032 (36.7)	50 (21.7)	<.001
Single	180 (21.5)	55 (33.5)		1782 (63.3)	180 (78.3)	
Household socioeconomic status						
First quintile (lowest)	121 (14.8)	32 (20.4)	.11	392 (14.4)	50 (22.5)	.004
Second quintile	118 (14.4)	29 (18.5)		512 (18.8)	45 (20.3)	
Third quintile	154 (18.8)	31 (19.8)		544 (20.0)	42 (18.9)	
Fourth quintile	170 (20.8)	29 (18.5)		614 (22.6)	50 (22.5)	
Fifth quintile (highest)	256 (31.3)	36 (22.9)		659 (24.2)	35 (15.8)	
WHO quality of life rating						
First quintile (best functionality)	223 (26.6)	20 (12.2)	<.001	531 (18.9)	29 (12.6)	<.001
Second quintile	179 (21.4)	38 (23.2)		583 (20.7)	33 (14.4)	
Third quintile	140 (16.7)	26 (15.9)		567 (20.2)	33 (14.4)	
Fourth quintile	144 (17.2)	24 (14.6)		615 (21.9)	58 (25.2)	
Fifth quintile (worst functionality)	151 (18.0)	56 (34.2)		516 (18.4)	77 (33.5)	
WHODAS quintiles						
First quintile (best functionality)	298 (35.5)	29 (17.7)	<.001	662 (23.5)	35 (15.2)	<.001
Second quintile	157 (18.7)	24 (14.6)		512 (18.2)	24 (10.4)	
Third quintile	140 (16.7)	24 (14.6)		489 (17.4)	32 (13.9)	
Fourth quintile	123 (14.7)	34 (20.7)		589 (20.9)	48 (20.9)	
Fifth quintile (worst functionality)	121 (14.4)	53 (32.3)		562 (20.0)	91 (39.6)	
Reported depression*	88 (10.5)	33 (20.1)	.001	441 (15.7)	46 (20.1)	.082
Reported anxiety*	172 (20.7)	45 (27.8)	.046	726 (26.2)	74 (32.6)	.035
Nocturnal sleep problems*, [a]	211(25.2)	62 (37.8)	.001	893 (31.8)	94 (40.9)	.005
Difficulty related to daytime function*, [b]	111 (13.3)	47 (28.7)	<.001	506 (18.0)	58 (25.2)	.007

Abbreviations: y, years; SD, standard deviation; WHO, World Health Organization; WHODAS, World Health Organization Disability Schedule.
Significance levels (*P* values) for χ^2 tests comparing dead and alive are provided.
* For depression, anxiety, nocturnal sleep problems, and difficulty related to daytime function, the responses were collapsed in two categories: none/mild/moderate and severe/extreme.
[a] Sleep problems were based on the following question (Q1016): "Overall in the last 30 days, how much of a problem did you have with sleeping, such as falling asleep, waking up frequently during the night or waking up too early in the morning?"
[b] Sleep problems were based on the following question (Q1017): "Overall in the last 30 days, how much of a problem did you have due to not feeling rested and refreshed during the day (e.g., feeling tired or not having energy)?"

Self-rated QoL of each participant was measured using the WHOQOL (Word Health Organization Quality of Life) scale assessing the individual's satisfaction with his or her life, and physical functionality or disability was measured using the WHODAS (World Health Organization Disability Assessment Schedule) scale. For both scales, a higher score indicated a poorer outcome (WHOQOL range, 8–40; WHODAS range, 1–100). Further details on these instruments can be found in previous reports [32,33]. For both measurements, the sample was divided in quintiles to include approximately 20% of the respondents in each category.

Feelings of depression and anxiety were elicited using the questions: (1) "Overall in the last 30 days, how much of a problem did you have with feeling sad, low or depressed?" (2) "Overall in the last 30 days, how much of a problem did you have with worry or anxiety?" Responses were collapsed in two categories: none/mild/moderate and severe/extreme [19].

2.6. Statistical analysis

Data were entered using CSPro 3.1 data entry program, which included validation checks (http://www.census.gov/ipc/www/cspro/index.html). For descriptive purposes, all the selected variables were first analyzed in both men and women by vital status (alive vs dead) at follow-up (Table 1). For categorical variables, χ^2 tests were used to determine the statistical significance of any difference in the distribution of baseline variables between these two categories in both men and women.

Cox proportional hazard models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI) for mortality risk over time associated with the two sleep measures at baseline, allowing adjustment for other covariates separately in men and women. Sleep variables were collapsed in two categories: none/mild/moderate and severe/extreme [19]. Reference categories for other covariates were the following: 50–59 years (age); >6 years (education); living in partnership (marital status); fifth quintile (household socioeconomic status); first quintile (WHOQOL and WHODAS); and none/mild/moderate (depression and anxiety).

For each sleep measure, three sets of Cox regression analyses were performed (Tables 2 and 3). The first two sets (reduced models) were either adjusted for age or adjusted for all sociodemographic variables (age, education, marital status, and household socioeconomic status); the third set (fully adjusted models) was adjusted for the full range of selected covariates (sociodemographics, WHOQOL, WHODAS, depression, and anxiety). Selection of covariates was based on previous literature [19] and on their correlation with the sleep measures in bivariate analyses. Proportional analysis was performed using proportion hazard assumption. We performed a test of proportionality for each predictor using the Schoenfeld and scaled Schoenfeld residuals. If the tests were not significant ($P > .05$), proportionality was not rejected and we assumed that there was no violation of the proportional assumption. All statistical analyses were conducted with STATA version 10.0 [34].

Table 2
Hazard ratios and 95% confidence intervals for mortality risk over time associated with nocturnal sleep problems* from Cox proportional hazard models.

Variables	HR (95% CI)			
	Reduced models		Fully adjusted models	
	Men	Women	Men	Women
Nocturnal sleep problems*	1.64 (1.18–2.28)	1.37 (1.04–1.79)		
	1.65 (1.18–2.31)	1.42 (1.07–1.88)	1.23 (0.85–1.79)	1.07 (0.78–1.47)
Age (y)				
50–59	Reference category		Reference category	
60–69	1.93 (1.20–3.10)	1.08 (0.73–1.61)	1.92 (1.19–3.10)	1.14 (0.76–1.70)
70–79	1.21 (0.72–2.04)	1.19 (0.79–1.77)	1.20 (0.71–2.05)	1.07 (0.71–1.62)
⩾80	2.29 (1.35–3.87)	2.25 (1.46–3.47)	1.98 (1.16–3.40)	1.67 (1.06–2.63)
Education levels				
No formal	1.25 (0.71–2.18)	1.23 (0.68–2.25)	1.28 (0.73–2.25)	1.21 (0.66–2.22)
At most 6 years	1.47 (0.91–2.39)	1.24 (0.72–2.12)	1.38 (0.85–2.24)	1.15 (0.67–1.99)
More than 6 years	Reference category		Reference category	
Marital status: single	1.57 (1.10–2.24)	1.62 (1.14–2.31)	1.44 (1.00–2.07)	1.60 (1.12–2.28)
Household socioeconomic status				
First quintile (lowest)	1.12 (0.67–1.86)	1.30 (0.83–2.04)	1.12 (0.67–1.87)	1.32 (0.84–2.10)
Second quintile	1.23 (0.74–2.02)	1.23 (0.77–1.97)	1.26 (0.76–2.09)	1.28 (0.79–2.07)
Third quintile	1.48 (0.89–2.46)	1.22 (0.76–1.96)	1.50 (0.89–2.52)	1.20 (0.75–1.94)
Fourth quintile	1.50 (0.91–2.48)	1.87 (1.18–2.96)	1.50 (0.90–2.52)	1.97 (1.23–3.15)
Fifth quintile (highest)	Reference category		Reference category	
WHO quality of life rating				
First quintile (best quality of life)			Reference category	
Second quintile			1.65 (0.92–2.98)	0.80 (0.46–1.38)
Third quintile			1.47 (0.78–2.77)	0.81 (0.47–1.41)
Fourth quintile			0.91 (0.45–1.82)	1.14 (0.68–1.92)
Fifth quintile (worst quality of life)			1.72 (0.91–3.24)	1.41 (0.83–2.39)
WHODAS quintiles				
First quintile (best functionality)			Reference category	
Second quintile			1.33 (0.74–2.38)	0.71 (0.40–1.28)
Third quintile			1.44 (0.81–2.58)	1.05 (0.61–1.79)
Fourth quintile			1.84 (1.05–3.21)	1.26 (0.77–2.07)
Fifth quintile (worst functionality)			2.55 (1.45–4.49)	2.00 (1.22–3.30)
Reported depression			1.05 (0.62–1.76)	1.00 (0.65–1.54)
Reported anxiety			1.18 (0.77–1.82)	1.00 (0.69–1.45)

Abbreviations: HR, hazard ratios; CI, confidence intervals; y, years; WHO, World Health Organization; WHODAS, World Health Organization Disability Schedule.
* For nocturnal sleep problems, reduced models were either adjusted for age (first row) or adjusted for all sociodemographic variables (second row).

3. Results

The study population consisted of 4044 adults aged 50 years and older, 75% of whom were women. Nearly one-third (30.2%) of the participants reported severe/extreme nocturnal sleep problems, while 17.9% reported severe/extreme difficulty related to daytime function. Moreover, 15.1% of participants reported severe/extreme feelings of depression and 25.5% reported experiencing anxiety.

Table 1 shows the general characteristics of the study population for both men and women by vital status at follow-up. After 3 years of follow-up, 394 (9.7%) of the participants had died. There was a mortality peak for men in their sixties and for women in their seventies. Among men, higher mortality was significantly associated with older age, lower education, single marital status, lower functionality and QoL, severe/extreme feelings of depression and anxiety, severe/extreme nocturnal sleep problems, and difficulty related to daytime function. A similar pattern of associations was observed among women. However, higher mortality was significantly associated with living in partnership in women than with living alone in men.

In Figs. 1 and 2, Kaplan–Meir survival curves are presented for the risk for mortality over time associated with severe/extreme nocturnal sleep problems (Fig. 1) and difficulty related to daytime function (Fig. 2) in both women (left graphs) and men (right graphs). Unadjusted HR for mortality for those who reported severe/extreme nocturnal sleep problems were 1.75 (95% CI, 1.26–2.41) for men and 1.48 (95% CI, 1.13–1.93) for women. For those who reported severe/extreme difficulty related to daytime function, the unadjusted HR for mortality were 2.51 (95% CI, 1.78–3.55) and 1.60 (95% CI, 1.18–2.15) for men and women, respectively.

Table 2 shows adjusted HR and 95% CI for mortality risk over time associated with nocturnal sleep problems from Cox regression analyses. As described in the Methods section, we constructed two models, a reduced model only adjusted for sociodemographic variables and a fully adjusted model adjusted for the full set of selected covariates (i.e., sociodemographics, WHOQOL, WHODAS, depression, anxiety).

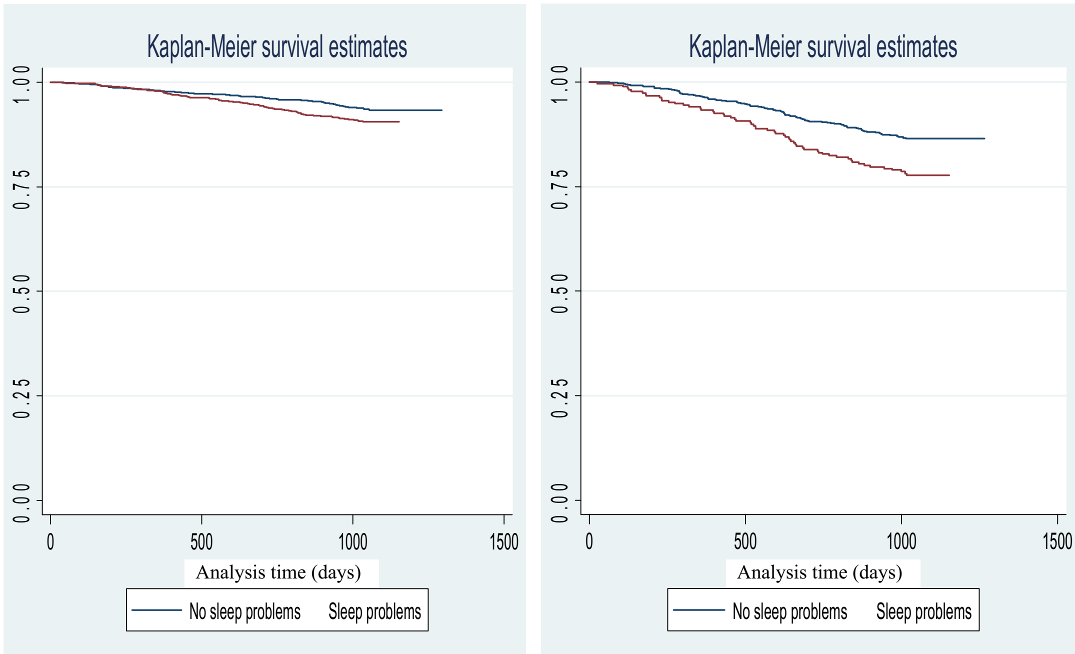
In reduced models both men and women who reported severe/extreme nocturnal sleep problems (vs none/mild/moderate) experienced greater mortality (HR, 1.65 [95% CI, 1.18–2.31] and HR, 1.42 [95% CI, 1.07–1.88], respectively). However, these associations were not significant in the fully adjusted model (HR, 1.23 [95% CI, 0.85–1.79 and HR, 1.07 [95% CI, 0.78–1.47], respectively). Table 3 shows adjusted HR and 95% CI for mortality risk over time associated with difficulty related to daytime function from Cox regression analyses.

In reduced models, both men and women reporting severe/extreme difficulty related to daytime function (vs none/mild/moderate) experienced greater mortality (HR, 2.49 [95% CI, 1.75–3.54 and HR, 1.54 [95% CI, 1.13–2.11], respectively). However, in fully adjusted models only men experienced a 2-fold increased risk for all-cause mortality (HR, 2.01 [95% CI, 1.32–3.07]), whereas no

Table 3
Hazard ratios and 95% confidence intervals for mortality risk over time associated with difficulty related to daytime function* from Cox proportional hazard models.

Correlates	HR (95% CI)			
	Reduced models		Fully adjusted models	
	Men	Women	Men	Women
Daytime lack of rest/energy*	2.46 (1.74–3.48)	1.49 (1.10–2.02)		
	2.49 (1.75–3.54)	1.54 (1.13–2.11)	2.01 (1.32–3.07)	1.16 (0.80–1.67)
Age (y)				
50–59	Reference category		Reference category	
60–69	1.90 (1.18–3.05)	1.09 (0.73–1.62)	1.91 (1.18–3.07)	1.14 (0.76–1.70)
70–79	1.21 (0.72–2.05)	1.21 (0.81–1.81)	1.21 (0.71–2.06)	1.08 (0.71–1.62)
⩾80	2.38 (1.41–4.02)	2.26 (1.47–3.49)	2.04 (1.19–3.48)	1.67 (1.06–2.63)
Education levels				
No formal	1.28 (0.73–2.23)	1.29 (0.71–2.36)	1.31 (0.75–2.30)	1.23 (0.67–2.25)
At most 6 years	1.49 (0.92–2.41)	1.27 (0.74–2.19)	1.38 (0.84–2.24)	1.17 (0.68–2.01)
More than 6 years	Reference category		Reference category	
Marital status: single	1.46 (1.03–2.09)	1.63 (1.15–2.32)	1.39 (0.97–2.00)	1.60 (1.12–2.28)
Household socioeconomic status				
First quintile (lowest)	1.10 (0.66–1.83)	1.30 (0.82–2.04)	1.09 (0.65–1.82)	1.32 (0.83–2.09)
Second quintile	1.25 (0.76–2.06)	1.24 (0.77–1.98)	1.27 (0.77–2.11)	1.28 (0.79–2.07)
Third quintile	1.49 (0.89–2.47)	1.23 (0.77–1.97)	1.46 (0.87–2.45)	1.20 (0.74–1.94)
Fourth quintile	1.60 (0.97–2.64)	1.90 (1.20–3.01)	1.55 (0.93–2.60)	1.97 (1.23–3.16)
Fifth quintile (highest)	Reference category		Reference category	
WHO quality of life rating				
First quintile (best quality of life)			Reference category	
Second quintile			1.70 (0.94–3.06)	0.80 (0.46–1.38)
Third quintile			1.46 (0.78–2.75)	0.81 (0.47–1.41)
Fourth quintile			0.91 (0.46–1.82)	1.16 (0.69–1.93)
Fifth quintile (worst quality of life)			1.59 (0.84–3.00)	1.39 (0.82–2.36)
WHODAS quintiles				
First quintile (best functionality)			Reference category	
Second quintile			1.20 (0.67–2.16)	0.71 (0.40–1.28)
Third quintile			1.40 (0.79–2.51)	1.05 (0.61–1.79)
Fourth quintile			1.80 (1.03–3.15)	1.26 (0.77–2.07)
Fifth quintile (worst functionality)			2.50 (1.42–4.41)	1.99 (1.21–3.28)
Reported depression			0.87 (0.51–1.49)	0.97 (0.63–1.51)
Reported anxiety			1.09 (0.70–1.69)	0.99 (0.69–1.44)

Abbreviations: HR, hazard ratios; CI, confidence intervals; y, years; WHO, World Health Organization; WHODAS, World Health Organization Disability Schedule.
* For difficulty related to daytime function, reduced models were either age-adjusted (first row) or adjusted for all sociodemographic variables (second row).



Log rank test P<.001 Log rank test P<.001.

Fig. 1. Kaplan–Meir survival curves by nocturnal sleep problems in women (left) and men (right).

significant association was observed for women (HR, 1.16 [95% CI, 0.80–1.67]).

Finally, there was no differential association between the two sleep questions and cause-specific mortality in subgroup analyses by primary cause of death (analyses in four categories: CVD, respiratory, HIV, acute).

4. Discussion

To our knowledge, our study is the first to report on the prospective relationship of sleep problems with mortality in a large population-based sample of older adults from Southern Africa. Our study provides novel evidence on sex-specific associations of sleep problems with mortality among older adults from a low-resource setting in rural South Africa.

Specifically, both men and women who reported severe or extreme nocturnal sleep problems had a significantly greater risk for all-cause mortality in reduced models only adjusted for sociodemographic variables; however, these associations were nonsignificant after further adjustment for measures of QoL and functional ability. By contrast, severe or extreme problems with feeling unrested or unrefreshed during the day were significantly associated with a 2-fold increased risk for all-cause mortality among men, independent of sociodemographic variables, measures of QoL, and functional ability. No significant association was found in women.

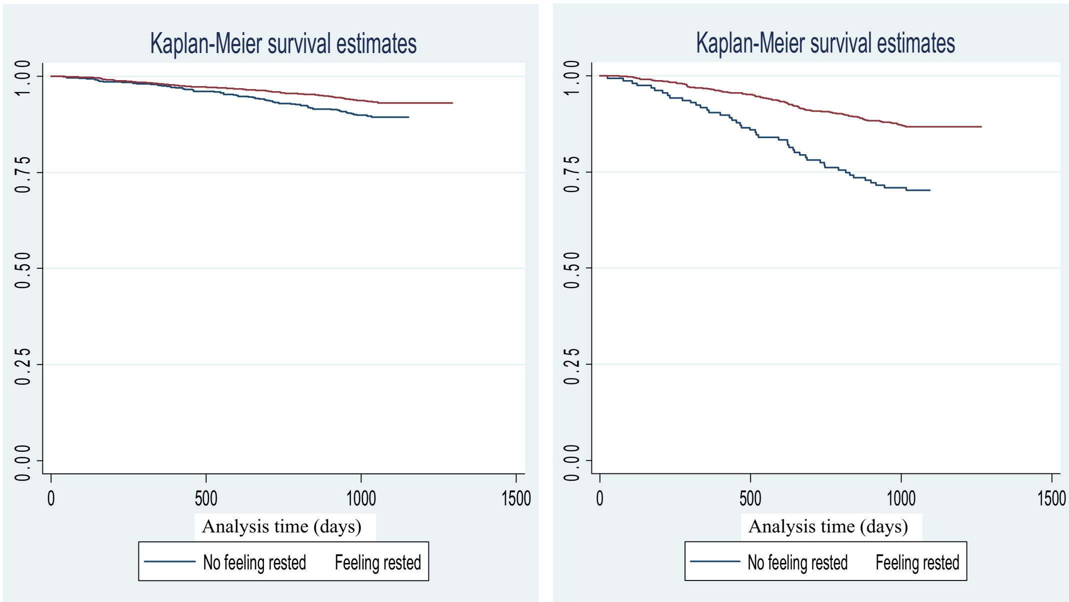
There is a large body of published literature on the association of sleep problems, mostly based on a specific aspect of sleep such as self-reported sleep duration with mortality outcomes among Western populations [8–14]. However, fewer studies have examined the association between sleep disturbances and mortality risk among older adults. Most of these studies were conducted in selected or small samples from high-income countries [15,16,35–40], with a lack of evidence on the potential association of sleep problems with mortality outcomes in low-resource settings.

In previous studies, little attention has been given to the potential impact of different dimensions of sleep quality and insomnia symptoms on survival, especially in aging populations. For example, daytime sleepiness was associated with increased risks for all-cause mortality and CVD among 5888 older adults from four US communities in the Cardiovascular Health Study; however, associations were stronger in women than in men and were somewhat attenuated after multivariate adjustment [15]. Likewise, nighttime insomnia, daytime sleepiness, and sleep-onset delay were significantly associated with a higher mortality risk over a 2-year follow-up in a selected sample of 272 elderly patients who were institutionalized in a geriatric hospital in Japan over a long-term period [35]. Moreover, prospective findings from the large Canadian Study of Health and Aging, among 9008 community-dwelling individuals aged 65 and older showed a significant increased risk for mortality from daytime sleepiness (HR, 1.89 [95% CI, 1.44–2.46]) in unadjusted analyses; however, this association did not persist in multivariate analyses adjusted for age, depression, cognition, comorbid illness, and function [36].

Overall, due to lack of definitive evidence on a direct causal link between sleep problems and health outcomes, it is plausible that self-reported poor sleep quality and generic sleep disturbances may represent a risk marker for poor health, chronic comorbidities, overall tiredness, and functional deficits, conditions which are all associated with reduced survival in aging populations [18].

Our previous findings [19] among older adults from a low-resource setting in rural South Africa add to this body of evidence. Although self-reported nocturnal sleep problems were significantly associated with a greater mortality risk in analyses adjusted for socio-demographics only, these associations did not persist once analyses were adjusted for QoL, functional ability, and psychologic co-morbidities. By contrast, severe or extreme problems with not feeling rested or refreshed during the day were significantly associated with a 2-fold increased mortality risk, which persisted after multivariate adjustment; however, this association was only observed in men.

Potential explanations for the sex differences in the association of sleep problems with mortality, as observed in our study, can only be speculative at the present time. These differences may reflect a



Log rank test *P*<.001

Log rank test *P*<.001.

Fig. 2. Kaplan–Meir survival curves by difficulty related to daytime function in women (left) and men (right).

larger burden of undiagnosed chronic disease in men than in women in these settings [20–22], whereby sleep problems such as difficulty related to daytime function may be a proxy for other morbid conditions, and therefore for overall tiredness. However, the prevalence of HIV, a common condition in this setting, was not substantially different between sexes in this older age group [22].

Our study highlights the public health importance of sleep problems in low-resource settings, especially in aging populations [19]. The proportion of participants (approximately 30%) who reported severe/extreme nocturnal sleep problems in our study population was higher than the proportion reporting sleep problems (9.1%) in a recent national survey of older South Africans including both urban and rural areas [41].

Our study has several strengths, primarily the large community-wide population and prospective study design. However, some limitations should be noted. First, data on comorbidities and lifestyle behaviors were not collected, preventing any analysis adjusting for these variables. Although information on comorbidities such as obstructive sleep apnea and other chronic conditions was not available, we used measures of self-reported QoL and disability as well as psychologic conditions, such as depression and anxiety as a proxy for comorbidities. However, it also is possible that these comorbidities might mediate the associations between sleep and mortality, despite the lack of significant interactions in our analyses. Second, information about sleep problems and daytime symptoms was self-reported, which could produce misclassification of true sleep patterns [42–45]. In addition, our sleep questions were not ideal. For example, one particular problem was that individuals who felt fatigued due to health problems not related to sleep may have endorsed the second question [43]. Additionally, these questions might have been interpreted differently by individuals in different cultures [46], which could account for the inconsistency of our findings with some previous work from high-income and Western populations. However, self-reports of problems related to sleep quality or insomnia symptoms may be less prone to misclassification than self-reported sleep duration [47]. Moreover, we only included those reporting severe and extreme sleep problems to increase the specificity of our tool, excluding those with mild and moderate sleep problems. In addition, sleep quality may represent a more comprehensive measure of sleep patterns than sleep duration and is strongly associated with measures of general well-being and QoL [47].

In conclusion, our study provides novel evidence on the association of sleep problems with mortality in a rural population of older adults from a poor setting in a middle-income country where environmental and lifestyle factors as well as chronic conditions known to influence sleep might substantially differ from developed Western societies [48]. Nevertheless, our findings also support the potential adverse impact of sleep problems on survival in low-resource settings.

Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2013.10.003.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.sleep.2013.10.003.

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