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Research paper

Relationship between sedentary behavior and depression: A mediation analysis of influential factors across the lifespan among 42,469 people in low- and middle-income countries

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ABSTRACT

Background: Sedentary behavior (SB) is associated with diabetes, cardiovascular disease and low mood. There is a paucity of multi-national research investigating SB and depression, particularly among low- and middle-income countries. This study investigated the association between SB and depression, and factors which influence this.

Methods: Cross-sectional data were analyzed from the World Health Organization's Study on Global Ageing and Adult Health. Depression was based on the Composite International Diagnostic Interview. The association between depression and SB (self-report) was estimated by multivariable linear and logistic regression analyses. Mediation analysis was used to identify influential factors.

Results: A total of 42,469 individuals (50.1% female, mean 43.8 years) were included. People with depression spent 25.6 (95%CI8.5–42.7) more daily minutes in SB than non-depressed participants. This discrepancy was most notable in adults aged ≥ 65 y (35.6 min more in those with depression). Overall, adjusting for socio-demographics and country, depression was associated with a 1.94 (95%CI1.31–2.85) times higher odds for high SB (i.e., ≥ 8 h/day). The largest proportion of the SB-depression relationship was explained by mobility limitations (49.9%), followed by impairments in sleep/energy (43.4%), pain/discomfort (31.1%), anxiety (30.0%), disability (25.6%), cognition (16.1%), and problems with vision (11.0%). Other health behaviors (physical

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activity, alcohol consumption, smoking), body mass index, and social cohesion did not influence the SB-depression relationship.
Conclusion: People with depression are at increased risk of engaging in high levels of SB. This first multi-national study offers potentially valuable insight for a number of hypotheses which may influence this relationship, although testing with longitudinal studies is needed.

1. Introduction

Depression is a leading cause of global years lived with disability (Whiteford et al., 2015). Whilst depression is associated with elevated mortality due to suicide (Hawton et al., 2013), cardio-metabolic diseases are the leading cause of premature death (Correll et al., 2017). It is known that people with depression have a double increased risk for diabetes and cardiovascular diseases compared to the general population (Vancampfort et al., 2015, 2016; Stubbs et al., 2017b, c, d).

There is established evidence that physical activity (PA) is good for health and confers comparable benefits to pharmacological interventions for preventing cardiovascular mortality (Naci and Ioannidis, 2013). People with established depression are known to engage in low levels of moderate-vigorous PA and are less likely than age-sex matched controls to meet recommended PA guidelines (Schuch et al., 2016a, b). Recent research has demonstrated that low levels of physical activity (PA) are consistently associated with an elevated risk for depression (Mammen and Faulkner, 2013; Stubbs et al., 2016b, c, d). Furthermore, engaging in structured physical activity ("exercise") has been demonstrated to be an effective treatment for depression (Schuch et al., 2016a, b).

There is also increasing evidence in the general population demonstrating that sedentary behavior (SB) is associated with a range of deleterious outcomes such as diabetes, cancer, cardiovascular disease and associated premature mortality (Biswas et al., 2015). SB refers to any waking behavior characterized by an energy expenditure ≤ 1.5 metabolic equivalents (METs), while in a sitting, reclining or lying posture (Sedentary Behaviour Research, 2012; Tremblay et al., 2017). Much like depression, SB is highly prevalent and pervasive in societies across the world (Bennie et al., 2013; Ekelund et al., 2016a, 2016b; Loyen et al., 2016). Within the past five years, there has been growing interest in the potential relationship between SB and depression. A recent meta-analysis, almost exclusively among high-income countries, found that among 110,152 individuals, higher levels of SB were associated with depression (relative risk 1.31 (95%CI 1.16–1.48)) (Zhai et al., 2015). Whilst recent advances in the literature have shone light on this neglected issue, a number of biases and gaps exist in the literature exploring the relationship between SB and depression to date. First, there is a paucity of multinational studies exploring the association between depression and SB. The current focus of micro-populations within specific countries may have limited utility beyond their immediate setting. Second, there is notably limited data on this association in low- and middle-income countries (LMICs), despite the increasing rates of non-communicable diseases and sedentary lifestyles (Christensen et al., 2009) in LMICs. Exploring associations between depression and SB in LMICs is also important given the high levels of depression (Guerra et al., 2016) and the low levels of knowledge regarding the risks associated with SB in LMICs (Pengpid et al., 2015), and compared with HICs, different occupational and socio-cultural structures, methods of transportation, and environmental factors (e.g., safety, climate) (Atkinson et al., 2016). The continuing dearth of studies from LMICs also highlights the gap between where research is conducted and where the largest public health impacts of physical inactivity (defined as not meeting recommended physical activity guidelines) occur (Sallis et al., 2016). Third, many studies investigating the association between SB and depression have relied upon screening tools such as the Patient Health Questionnaire (Adamson et al., 2016), which have limited sensitivity and specificity for identifying "true" depression (Mitchell et al., 2016). Finally, despite the association between depression and SB reported in previous high-income populations, a paucity of research has considered what variables might influence the relationship. Clearly, understanding the influential factors in this relationship, such as sociodemographic (e.g. age, sex, employment status), mental/physical health (e.g. physical comorbidities) and health behaviors (e.g. smoking, alcohol use, mobility), may prove useful for developing effective interventions in the future.

The current study used a large, multi-national sample and sought to investigate (1) the association between depression and SB across 6 LMICs; and (2) to investigate the factors that may explain the relation between depression and SB.

2. Methods

2.1. The survey

Data from the Study on Global Ageing and Adult Health (SAGE) survey was analyzed. The survey was conducted between 2007 and 2010 in China, Ghana, India, Mexico, Russia, and South Africa, which were all LMICs at the time of the survey according to the World Bank classification. Details of the survey methodology are provided elsewhere (Kowal et al., 2012). Briefly, in order to obtain nationally representative samples, a multi-stage clustered sampling design method was used. The sample consisted of adults aged ≥ 18 years with oversampling of those aged ≥ 50 years. Trained interviewers conducted face-to-face interviews using a standard questionnaire across countries to collect information. Standard translation procedures for the questionnaires were undertaken to ensure comparability between countries. Sampling weights were calculated to adjust for the population structure as reported by the United Nations Statistical Division. Ethical approval was obtained from the WHO Ethical Review Committee and local ethics research review boards. Written informed consent was obtained from all participants. The survey response rate ranged from 51% (Mexico) to 93% (China). Full details of the sampling strategy are displayed in supplementary file 1.

2.2. Variables

2.2.1. Sedentary behavior (Outcome variable)

In order to assess SB, participants were asked to state the total time they usually spent (expressed in minutes per day) sitting or reclining including at work, at home, getting to and from places, or with friends (e.g., sitting at a desk, sitting with friends, travelling in car, bus, train, reading, playing cards or watching television). This did not include time spent sleeping. The variable on SB was used in the analysis as a continuous variable (minutes per day) and also as a categorical [< 8 or ≥ 8 h per day (high SB)] variable in line with recent publications (Vancampfort et al., 2017a, b). The eight-hour cut-off was chosen as previous research indicated that being sedentary for ≥ 8 h/day in the general population is associated with a higher risk for premature mortality (Ekelund et al., 2016a, b).

2.2.2. Depression (Exposure variable)

Questions based on the World Mental Health Survey version of the Composite International Diagnostic Interview (Kessler and Ustun, 2004) were used for the endorsement of past 12-month DSM-IV depression using the same algorithm used in previous studies using the same dataset (Koyanagi et al., 2014; Garin et al., 2016) (Details provided in eTable 1).

2.2.3. Potential mediators

2.2.3.1. Health status. was evaluated with 10 health-related questions pertaining to five health domains including: (a) mobility; (b) pain and discomfort; (c) cognition; (d) vision; (e) sleep and energy. Each of the five domains corresponds to those in common health related quality of life outcome measures such as the Short Form-12 (SF-12) (Ware et al., 1996), the Health Utilities Index Mark-3 (HUI) (Feeny et al., 1995) and the EUROQOL-5D (Kind, 1996). Each domain consists of two questions that assessed health function in the past 30 days. The actual questions can be found in supplementary eTable 2. Each item was scored on a five-point scale ranging from 'none' to 'extreme/cannot do'. For each separate domain, we used factor analysis with polychoric correlations to obtain a factor score which was later converted to scores ranging from 0 to 100 with higher values representing worse health function (Stubbs et al., 2016b, c, d).

2.2.3.2. Anxiety. In accordance with previous publications using a dataset with the identical question, those who claimed to have severe/extreme problems with worry or anxiety in the past 30 days were considered to have anxiety (Stubbs et al., 2017a; Vancampfort et al., 2017a).

2.2.3.3. Disability. was assessed with six questions on the level of difficulty in conducting standard basic activities of daily living (ADL) in the past 30 days (washing whole body, getting dressed, moving around inside home, eating, getting up from lying down, and using the toilet) (Katz et al., 1963). Those who answered severe or extreme/cannot do to any of the six questions were considered to have disability (Koyanagi et al., 2015).

2.2.3.4. Physical activity. Levels of physical activity was assessed with the Global Physical Activity Questionnaire (Bull et al., 2009). The total amount (min) of moderate-to-vigorous physical activity in a typical week was calculated.

2.2.3.5. Alcohol consumption and smoking. referred to current smoking (Y/N) and alcohol use in the past 30 days (Y/N) respectively.

2.2.3.6. Body mass index (BMI). A stadiometer and a routinely calibrated electronic weighting scale were used to measure height and weight respectively. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared, and categorized as < 18.5 (underweight), 18.5–24.9 (normal), 25.0–29.9 (overweight), and ≥ 30 (obese) kg/m^2.

2.2.3.7. Social cohesion. In accordance with a previous SAGE publication (Zamora-Macorra et al., 2017), a social cohesion index was created based on nine questions on the participant's involvement in community activities in the past 12 months (e.g., attended religious services, club, society, union etc) with answer options 'never (coded = 0)', 'once or twice per year (coded = 1)', 'once or twice per month (coded = 2)', 'once or twice per week (coded = 3)', and 'daily (coded = 4)'. The answers to these questions were summed (range 0–36) with higher scores indicating higher levels of social cohesion.

2.2.4. Control variables

These included sociodemographic variables such as sex, age, wealth, highest level of education achieved (≤ primary, secondary, ≥ tertiary), marital status (married/cohabiting or never married/separated/divorced/widowed), setting (urban or rural), and employment status (engaged in paid work ≥ 2 days in last 7 days: Y/N). Wealth quintiles were created based on country-specific income. These variables were not considered as potential mediators as sociodemographic variables are generally considered to be non-modifiable.

2.3. Statistical analysis

The statistical analysis was done with Stata 14.1 (Stata Corp LP, College station, Texas). The difference in sample characteristics between those with and without depression or high SB was tested by Student's *t*-tests and Chi-squared tests for continuous and categorical variables, respectively. Multivariable logistic and linear regression analyses were used to assess the association between depression (exposure) and SB (outcome). The main analysis consisted of the logistic regression analysis using the binary SB variable (i.e., < 8 or ≥ 8 h/day) as the outcome. This analysis was intended to assess the specific association between depression and high levels of SB. A secondary analysis using linear regression with the continuous variable (min/day of SB) as the outcome was also conducted to assess increasing or decreasing levels of SB associated with depression. A base model was constructed adjusting for the sociodemographic variables (i.e., sex, age, wealth, education, marital status, setting, employment status), and country.

Next, in order to gain an understanding of the extent to which various factors may explain the relation between depression and high SB, we conducted mediation analysis. Specifically, we focused on mobility, pain and discomfort, cognition, sleep and energy, vision, anxiety, and disability, physical activity, alcohol consumption, smoking, BMI, and social cohesion for their previously reported association with the exposure (depression) and the outcome (high SB) (Stubbs et al., 2014; Biswas et al., 2015; O'Donoghue et al., 2016; Lakerveld et al., 2017; Prince et al., 2017; Wirth et al., 2017). We used the *khb* (Karlson Holm Breen) command in Stata (Breen et al., 2013) for this purpose. This method can be applied in logistic regression models and decomposes the total effect (i.e., unadjusted for the mediator) of a variable into direct (i.e., the effect of depression on SB adjusted for the mediator) and indirect effects (i.e., the mediational effect). Using this method, the percentage of the main association explained by the mediator can also be calculated (mediated percentage). Each potential mediator was included in the model individually. The mediation analysis controlled for the sociodemographic variables and country.

For the regression analyses, we conducted analysis using the overall sample and by age groups (age 18–49, 50–64, ≥ 65 years). All regression analyses were adjusted for country by including dummy variables for each country. All variables were included in the models as categorical variables with the exception of the variable on age, min/day of SB, social cohesion, health status (mobility, pain and discomfort, cognition, sleep and energy, vision), and physical activity (continuous variables). Under 3% of the data were missing for the variables used in the current analysis with the exception of BMI (5.8%). Complete case analysis was done. The sample weighting and the complex study design were taken into account in all analyses. Results from the regression analyses are presented as odds ratios (ORs) or b-coefficients with 95% confidence intervals (CIs). The level of statistical significance was set at $P < 0.05$.

3. Results

A total of 42,469 (China n = 14,811; Ghana n = 5108; India n = 11,230; Mexico n = 2742; Russia n = 4355; South Africa n = 4223) individuals (50.1% female) with a mean (SD) age of 43.8 (14.4) years were included in the analysis. The overall prevalence (95%CI) of high SB (i.e., ≥ 8 h/day of SB) was 8.3% (7.1–9.7%), while the mean (SD) minutes/day spent sedentary across the whole sample was 207 (149). The overall prevalence (95%CI) of depression was 4.1% (3.6–4.6%). The prevalence of depression was particularly high among those with ≥ 8 h hours/day of SB, with 9.36% of those spending ≥ 11 h/day sedentary having depression (see Fig. 1). The sample characteristics are provided in Table 1. Factors such as older age, not being married/cohabiting, unemployment, mobility limitations, sleep/energy disruption,

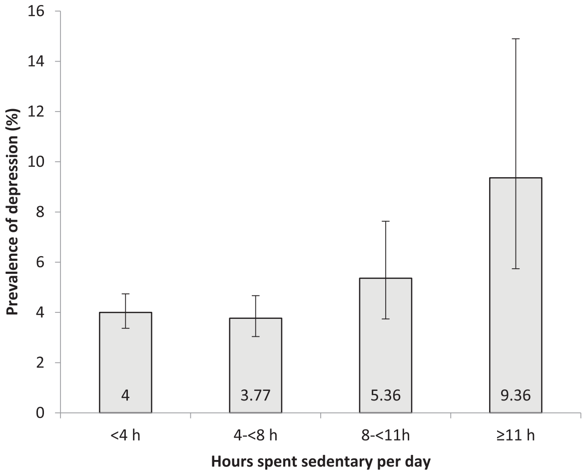

Fig. 1. Prevalence of depression by hours of sedentary behavior per day, Estimates are based on weighted sample. Bars denote 95% confidence intervals.

Table 2
Association between depression and sedentary behavior assessed by multivariable logistic and linear regression (overall and by age groups).

	Logistic regression Outcome (high SB[a])		Linear regression Outcome (min/day of SB)	
Sample	OR	95%CI	b-coefficient	95%CI
Overall[b]	1.94***	[1.31,2.85]	25.57**	[8.46,42.69]
Age 18–49 years[b]	2.19*	[1.06,4.52]	26.33*	[1.36,51.31]
Age 50–64 years[b]	1.66*	[1.11,2.49]	22.84*	[0.77,44.92]
Age ≥ 65 years[b]	1.72**	[1.21,2.45]	35.55**	[8.59,62.52]

Abbreviation: SB Sedentary behavior; OR Odds ratio; CI Confidence interval.
[a] Those reporting ≥ 8 h per day spent sedentary were considered to be highly sedentary.
[b] Adjusted for sex, age, wealth, education, marital status, setting, employment status, and country.
* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.

and disability were strongly associated with both depression and high SB.

In models adjusted for sociodemographics and country, depression was associated with a 1.94 (95%CI = 1.31–2.85) times higher odds for high SB, while the mean time spent sedentary was 26 (95%CI = 9–43) minutes longer per day among depressed individuals (Table 2). Estimates across age groups were similar. The results of the mediation analysis that assessed the degree to which the association between depression and high SB can be explained by various factors are

Table 1
Characteristics of the study sample.

				Depression			Highly sedentary behavior[a]		
Characteristic		Unweighted N	Overall	No	Yes	P-value[b]	No	Yes	P-value[b]
Sex	Female	24,137	50.1	49.7	59.9	< 0.001	50.1	50.6	0.853
Age (years)	18–49	8340	72.7	73.3	59.5	< 0.001	73.5	64.7	< 0.001
	50–64	19,544	17.0	16.7	24.1		17.1	15.8	
	≥ 65	14,585	10.3	10.0	16.4		9.4	19.6	
	Mean (SD)		43.8 (14.4)	43.6 (14.3)	48.0 (16.7)	< 0.001	43.6 (14.0)	46.6 (17.7)	0.022
Wealth	Poorest	7954	14.9	14.5	24.8	< 0.001	15.1	13.2	0.099
	Poorer	8292	17.8	17.6	24.2		18.0	16.3	
	Middle	8259	18.8	18.7	20.4		18.7	21.4	
	Richer	8758	21.1	21.4	14.4		21.7	15.9	
	Richest	9026	27.3	27.8	16.2		26.6	33.2	
Education	≤ Primary	25,451	43.1	42.2	63.1	< 0.001	44.1	33.2	0.001
	Secondary	13,231	46.5	47.2	31.7		45.9	51.5	
	≥ Tertiary	2935	10.4	10.6	5.2		10.0	15.2	
Marital status	Married/cohabiting	11,774	80.8	81.4	69.6	< 0.001	82.0	72.1	< 0.001
Setting	Rural	22,182	55.6	55.4	64.4	0.016	57.5	37.0	< 0.001
Unemployed	Yes	23,778	38.5	37.9	51.6	< 0.001	37.5	49.4	< 0.001
Physical activity (min)[c]	Mean (SD)		1440 (1500)	1443 (1498)	1380 (1529)	0.464	1480 (1517)	1001 (1237)	< 0.001
Alcohol consumption	Yes	7805	21.9	22.3	9.7	< 0.001	21.7	21.2	0.865
Smoking	Yes	11,275	35.2	35.0	39.2	0.130	34.9	36.6	0.617
Body mass index (kg/m^2)	Underweight	5343	16.8	16.1	35.4	< 0.001	17.3	13.3	0.005
	Normal	19,817	55.3	55.7	46.6		55.7	53.1	
	Overweight	9625	20.9	21.2	13.5		20.5	22.9	
	Obese	5229	7.0	7.0	4.6		6.6	10.7	
Social cohesion[d]	Mean (SD)		8.6 (4.9)	8.6 (4.8)	8.7 (6.0)	0.760	8.7 (4.9)	7.3 (4.3)	< 0.001
Mobility[e]	Mean (SD)		18.0 (23.8)	16.8 (22.8)	46.5 (29.7)	< 0.001	17.4 (23.1)	25.3 (29.0)	< 0.001
Pain and discomfort[e]	Mean (SD)		19.6 (24.4)	18.4 (23.5)	47.8 (27.8)	< 0.001	19.4 (24.1)	23.2 (26.9)	0.021
Cognition[e]	Mean (SD)		16.8 (23.6)	15.8 (22.7)	41.8 (30.9)	< 0.001	16.7 (23.2)	19.6 (27.3)	0.056
Sleep and energy[e]	Mean (SD)		17.1 (23.4)	16.0 (22.3)	43.9 (31.4)	< 0.001	16.4 (23.0)	24.4 (26.0)	< 0.001
Vision[e]	Mean (SD)		14.6 (22.4)	13.9 (21.8)	31.3 (31.1)	< 0.001	14.3 (22.0)	18.3 (25.6)	0.006
Anxiety	Yes	2630	5.7	4.2	42.1	< 0.001	5.6	7.6	0.037
Disability	Yes	2440	3.1	2.5	18.0	< 0.001	2.6	8.4	< 0.001

Abbreviation: SD Standard deviation.
Data are column percentage unless otherwise stated.
Estimates are based on weighted sample apart from the unweighted N.
[a] Those spending ≥ 8 h per day sedentary were considered to be highly sedentary.
[b] The difference in sample characteristics by depression and sedentary behavior was tested by Chi-squared tests and Student's *t*-tests for categorical and continuous variables respectively.
[c] The total amount of moderate-to-vigorous physical activity in a typical week.
[d] Scores ranged from 0 to 36 with higher scores representing higher levels of social cohesion.
[e] Scores ranged from 0 to 100 with higher scores representing worse health status.

illustrated in Tables 3, 4. Based on the overall sample, the largest proportion of the total effect was explained by mobility limitations (49.9%), followed by impairments in sleep/energy (43.4%), pain/discomfort (31.1%), anxiety (30.0%), disability (25.6%), cognition (16.1%), and problems with vision (11.0%) (Table 3). Mobility and pain/discomfort explained more than 50% of the association in individuals aged ≥ 65 years. Cognition and anxiety were important mediators mainly among older adults. Health behaviors (physical activity, alcohol consumption, smoking), BMI, and social cohesions were not significant mediators (i.e., no significant indirect effects) in the overall sample or any of the age groups (Table 4).

4. Discussion

To the best of our knowledge, ours is the first multi-national study to investigate the relationship between depression and SB and its influential factors. Our data suggest that higher levels of SB (particularly over 11 h) are associated with an elevated prevalence of depression. The relationship between high levels of SB and depression held across the lifespan, and depression across the entire sample was associated with a 26-min increase in SB per day. Previous research has found that such differences in SB are associated with worse cardiometabolic health (Katzmarzyk, 2010; Katzmarzyk and Lee, 2012), increased inflammation and worse mood profile (Endrighi et al., 2015). Interestingly, we found evidence that mobility limitations, disability and sleep problems explained the relationship between depression and SB across all age ranges. Moreover, smoking, alcohol consumption, BMI, physical activity and social cohesion had little influence in the association between depression and SB. Given the high levels of SB among those with depression previously reported (Schuch et al., 2016a, b), and the deleterious outcomes of high levels of SB in the general population (Biswas et al., 2015), our data provide important insights that might help shape future interventions.

In addition to extending the literature on being the first multinational study to explore the association between depression and SB, our study provides some indication of factors that may influence this relationship. Perhaps unsurprisingly, we found evidence across all age groups that mobility limitations mediated 49% of the association between SB and depression. Mobility limitations can arise from a multitude of problems, and have previously been associated with SB (Stubbs et al., 2014) and an increased risk of developing depression (Veronese et al., 2017). Importantly, increasing PA among people with mobility limitations can reduce the risk of developing activities of daily living difficulties (Tak et al., 2013) and promote healthy ageing (Daskalopoulou et al., 2017). When one considers that low PA is associated with depression (Mammen and Faulkner, 2013) and depression reduces with participation in PA (Schuch et al., 2016a, b), strategies such as sitting reduction interventions tailored to those with mobility limitations may play a pivotal role in this population. We also observed that pain, particularly among older adults explained a considerable proportion of the association between SB and depression. Pain is known to be highly comorbid with depression (Stubbs et al., 2016b, c, d, 2017b, c, d), particularly among older adults (Abdulla et al., 2013) and is associated with low PA (Stubbs et al., 2013) and SB (Stubbs et al., 2014). Interestingly, we also found a relationship between sleep and energy problems as an important influential factor across all age ranges. Sleep and energy issues are known to be a core feature of depression and are closely linked to energy expenditure (Luca et al., 2013). Prolonged periods of SB are known to increase tiredness and predispose people to "napping" which has been associated with depression (Luca et al., 2013) and other deleterious outcomes such as a poor cardiometabolic profile (Yamada et al., 2015). Future interventions that address sleep and in particular daytime napping may play an important role in preventing high levels of SB and depression.

Whilst in the overall sample, anxiety mediated 30% of the association between SB and depression, this relationship was only evident in working and older age adults. Depression and anxiety are often comorbid (Rebar et al., 2017) and anxiety has been associated with SB

Table 3
Health status, anxiety, and disability as mediators in the association between depression and highly sedentary behavior (overall and by age groups).

Mediator	Sample	Total effect	P-value	Direct effect	P-value	Indirect effect	P-value	% Mediated
Mobility	Overall	1.95 [1.32,2.89]	0.001	1.40 [0.94,2.09]	0.100	1.40 [1.25,1.56]	< 0.001	49.9
	Age 18–49 years	2.20 [1.06,4.57]	0.034	1.64 [0.77,3.50]	0.200	1.34 [1.08,1.67]	0.008	37.2
	Age 50–64 years	1.65 [1.09,2.48]	0.017	1.29 [0.85,1.96]	0.225	1.27 [1.17,1.38]	< 0.001	48.2
	Age ≥ 65 years	1.77 [1.23,2.55]	0.002	1.29 [0.91,1.84]	0.156	1.37 [1.23,1.53]	< 0.001	55.2
Pain and discomfort	Overall	1.93 [1.32,2.83]	0.001	1.58 [1.07,2.32]	0.021	1.23 [1.12,1.34]	< 0.001	31.1
	Age 18–49 years	2.18 [1.07,4.44]	0.032	1.88 [0.91,3.86]	0.087	1.16 [0.99,1.37]	0.075	NA
	Age 50–64 years	1.67 [1.11,2.52]	0.014	1.38 [0.92,2.07]	0.121	1.21 [1.12,1.31]	< 0.001	37.3
	Age ≥ 65 years	1.75 [1.23,2.50]	0.002	1.30 [0.92,1.86]	0.140	1.34 [1.22,1.48]	< 0.001	52.7
Cognition	Overall	1.93 [1.30,2.85]	0.001	1.73 [1.16,2.59]	0.007	1.11 [1.03,1.20]	0.005	16.1
	Age 18–49 years	2.20 [1.06,4.55]	0.034	2.43 [1.14,5.18]	0.022	0.90 [0.75,1.09]	0.281	NA
	Age 50–64 years	1.67 [1.11,2.52]	0.014	1.38 [0.92,2.09]	0.124	1.21 [1.12,1.30]	< 0.001	37.0
	Age ≥ 65 years	1.75 [1.21,2.53]	0.003	1.48 [1.02,2.15]	0.038	1.18 [1.10,1.26]	< 0.001	29.7
Sleep and energy	Overall	1.89 [1.27,2.82]	0.002	1.43 [0.95,2.17]	0.088	1.32 [1.17,1.48]	< 0.001	43.4
	Age 18–49 years	2.11 [0.99,4.49]	0.053	1.53 [0.70,3.34]	0.284	1.38 [1.13,1.68]	0.002	42.8
	Age 50–64 years	1.66 [1.10,2.51]	0.015	1.35 [0.89,2.04]	0.154	1.23 [1.12,1.35]	< 0.001	40.9
	Age ≥ 65 years	1.75 [1.22,2.50]	0.002	1.47 [1.02,2.13]	0.039	1.19 [1.10,1.28]	< 0.001	30.5
Vision	Overall	1.91 [1.29,2.82]	0.001	1.78 [1.21,2.62]	0.004	1.07 [1.02,1.13]	0.003	11.0
	Age 18–49 years	2.14 [1.04,4.41]	0.039	2.02 [0.99,4.16]	0.055	1.06 [0.97,1.15]	0.180	NA
	Age 50–64 years	1.68 [1.12,2.52]	0.012	1.60 [1.07,2.39]	0.023	1.05 [1.00,1.11]	0.033	10.0
	Age ≥ 65 years	1.73 [1.21,2.49]	0.003	1.62 [1.13,2.30]	0.008	1.07 [1.02,1.13]	0.005	12.9
Anxiety	Overall	1.89 [1.26,2.83]	0.002	1.56 [1.01,2.42]	0.047	1.21 [1.08,1.35]	< 0.001	30.0
	Age 18–49 years	2.17 [1.03,4.56]	0.042	1.95 [0.86,4.43]	0.109	1.11 [0.90,1.38]	0.341	NA
	Age 50–64 years	1.63 [1.08,2.45]	0.019	1.31 [0.86,1.97]	0.205	1.25 [1.11,1.41]	< 0.001	45.4
	Age ≥ 65 years	1.71 [1.19,2.44]	0.004	1.42 [0.97,2.06]	0.068	1.20 [1.08,1.34]	< 0.001	34.9
Disability	Overall	1.85 [1.23,2.78]	0.003	1.58 [1.04,2.39]	0.031	1.17 [1.10,1.25]	< 0.001	25.6
	Age 18–49 years	2.12 [0.99,4.50]	0.052	1.81 [0.83,3.94]	0.133	1.17 [1.04,1.31]	0.011	20.5
	Age 50–64 years	1.64 [1.09,2.47]	0.018	1.53 [1.00,2.32]	0.048	1.07 [1.02,1.13]	0.007	14.5
	Age ≥ 65 years	1.68 [1.14,2.45]	0.008	1.37 [0.94,2.00]	0.097	1.22 [1.12,1.32]	< 0.001	38.4

Data are odds ratio [95% confidence interval].
Models are adjusted for sex, age, wealth, education, marital status, setting, employment status, and country.
The mediated percentage was calculated only when the indirect effect was significant ($P < 0.05$).

Table 4
Physical activity, alcohol consumption, smoking, body mass index, and social cohesion as mediators in the association between depression and highly sedentary behavior.

Mediator	Sample	Total effect	P-value	Direct effect	P-value	Indirect effect	P-value
Physical activity	Overall	1.98 [1.33,2.95]	0.001	1.93 [1.30,2.87]	0.001	1.03 [0.99,1.07]	0.649
	Age 18–49 years	2.23 [1.07,4.68]	0.033	2.20 [1.05,4.59]	0.036	1.02 [0.97,1.07]	0.512
	Age 50–64 years	1.66 [1.10,2.51]	0.016	1.63 [1.08,2.47]	0.020	1.02 [0.98,1.05]	0.311
	Age ≥ 65 years	1.77 [1.22,2.55]	0.003	1.71 [1.17,2.50]	0.006	1.04 [0.98,1.10]	0.212
Alcohol consumption	Overall	1.94 [1.32,2.86]	0.001	1.94 [1.31,2.85]	0.001	1.00 [0.99,1.01]	0.734
	Age 18–49 years	2.20 [1.08,4.50]	0.030	2.18 [1.07,4.43]	0.031	1.01 [0.98,1.04]	0.448
	Age 50–64 years	1.66 [1.10,2.50]	0.015	1.66 [1.10,2.50]	0.016	1.00 [0.99,1.01]	0.550
	Age ≥ 65 years	1.72 [1.20,2.46]	0.003	1.72 [1.20,2.46]	0.003	1.00 [0.99,1.01]	0.932
Smoking	Overall	1.93 [1.31,2.84]	0.001	1.91 [1.30,2.81]	0.001	1.01 [0.99,1.03]	0.276
	Age 18–49 years	2.18 [1.06,4.46]	0.033	2.18 [1.07,4.47]	0.033	1.00 [0.97,1.03]	0.910
	Age 50–64 years	1.66 [1.11,2.50]	0.015	1.66 [1.10,2.49]	0.015	1.00 [0.99,1.01]	0.491
	Age ≥ 65 years	1.73 [1.21,2.47]	0.003	1.71 [1.19,2.45]	0.003	1.01 [0.99,1.03]	0.201
Body mass index (kg/m^2)	Overall	1.97 [1.31,2.96]	0.001	1.97 [1.31,2.96]	0.001	1.00 [0.99,1.02]	0.901
	Age 18–49 years	2.23 [1.09,4.58]	0.028	2.26 [1.10,4.64]	0.026	0.99 [0.96,1.02]	0.472
	Age 50–64 years	1.63 [1.05,2.54]	0.031	1.61 [1.03,2.54]	0.037	1.01 [0.98,1.04]	0.494
	Age ≥ 65 years	1.76 [1.19,2.59]	0.004	1.78 [1.21,2.62]	0.004	0.99 [0.97,1.01]	0.328
Social cohesion	Overall	1.92 [1.30,2.83]	0.001	1.91 [1.29,2.82]	0.001	1.00 [0.98,1.03]	0.782
	Age 18–49 years	2.17 [1.05,4.48]	0.037	2.17 [1.05,4.48]	0.037	1.00 [0.98,1.02]	0.997
	Age 50–64 years	1.65 [1.09,2.50]	0.018	1.63 [1.08,2.46]	0.021	1.01 [0.98,1.04]	0.361
	Age ≥ 65 years	1.73 [1.22,2.45]	0.002	1.70 [1.20,2.41]	0.003	1.02 [0.98,1.06]	0.315

Data are odds ratio [95% confidence interval].
Models are adjusted for sex, age, wealth, education, marital status, setting, employment status, and country.
The mediated percentage was not calculated as the indirect effect was not significant for any of the mediators.

(Teychenne et al., 2015). Whilst PA can reduce anxiety symptoms (Stubbs et al., 2017b, c, d), our data suggest that PA does not per se influence the SB and depression relationship. Whilst our data cannot provide a causal inference, some previous studies can provide some indication of a potentially causal relationship which underpin our assertions. For instance, previous research from randomized controlled trials in Western samples has demonstrated the independent deleterious impact of increasing SB on mood and in particular symptoms of anxiety (Edwards and Loprinzi, 2016), possibly through changes in inflammation (Endrighi et al., 2015). Previous research has also suggested that SB is associated with inflammation, most notably c-reactive protein and interleukin 6 (Henson et al., 2013; Wirth et al., 2017). There is some provisional evidence to suggest that standing and breaking up prolonged periods of SB can improve inflammatory biomarker profiles (Healy et al., 2008, 2011; Owen et al., 2010; Hansen et al., 2012). Thus, future interventions may consider investigating the potential benefits of disrupting SB on mood (depression and anxiety) and underlying mechanisms of potential change, such as inflammation. We also found some evidence that cognition influenced SB and depression, notably among working and older age adults. There is evidence that both depression (Rock et al., 2014) and SB (Falck et al., 2016) are associated with cognitive impairment. Whether or not reducing SB can improve cognition is unclear, although there is robust evidence that PA can improve cognition (Stanmore et al., 2017), however, this did not appear to influence the SB and depression relationship in our data.

Surprisingly, none of the measured health behaviors (alcohol use, PA, smoking), or risk factors (body mass index, social cohesion) influenced the SB-depression relationship. Many of these findings are inconsistent with the wider literature. For example, PA has been shown to have a multitude of benefits for both depression and many of the other potential influencing factors (e.g. disability, mobility, cognition), and so could be expected to influence the impact of SB on depression. Similarly, BMI is known to be associated with SB (Wirth et al., 2017) and depression (Vancampfort et al., 2015, 2016; Fornaro et al., 2017). However, simply being correlated with both SB and depression does not mean that BMI is a potential mediator of this relationship and clearly, future longitudinal research is required to disentangle the relationships we observed and explore potentially modifiable mediators. Future research is also required to consider the type and context of SB (e.g. sitting at home, work) and depression, preferably using a longitudinal design and objective measures of SB.

The current findings should be interpreted in light of some limitations. First, the study is cross-sectional, therefore the directionality of the relationships cannot be deduced with certainty. The aim of the study was only to quantify the degree to which potentially influential factors in the depression-SB relationship may explain this association. Thus, directionality or causality cannot be established and the effect of these influential factors as mediators or confounders cannot be known. Therefore, future longitudinal studies are required to better disentangle the relationships we observed. Second, SB was captured with a self-report measure, the accuracy of which has been questioned (Soundy et al., 2014; Stubbs et al., 2016a). Future research should utilize objective measures of SB. Accelerometers-inclinometers are available that allow for valid and reliable objective measures of SB (Grant et al., 2006). Finally, we have not investigated context specific SB (e.g. TV viewing) which may provide important insights into the underlying relationships we observed. Nonetheless, the strengths of the study include the large sample size (over 42,000) and the multi-national scope. Most of the research in the domain of SB and depression has been conducted in Western countries, and little is known about these experiences and mediators in regions across which there are multiple economic, cultural or social factors or differences in the health systems. The present study was furthermore performed with nationally representative samples of non-institutionalized persons. Moreover, by conducting mediation analyses, we have advanced the understanding of factors influencing SB and depression, which has largely been missing from the literature to date.

In conclusion, our paper provides evidence of a relationship between SB and depression. In fact, across this representative cohort over 6 countries, being depressed was associated with 26 more daily minutes of sedentary time. Mobility limitations, pain and discomfort, cognition problems, sleep and energy issues, anxiety and disability may potentially influence the relationship between SB and depression. If replicated using longitudinal designs to more reliably establish directionality/causality, these findings could offer important new targets and strategies for interventions to tackle the depression-SB relationship.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.jad.2017.12.104.

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