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Complete List of Authors:	Currow, David ; University of Technology Sydney Chang, Sungwon ; University of Technology Sydney Faculty of Health, Improving Palliative, Aged and Chronic Care through Clinical Research and Translation (IMPACCT) Ferreira, Diana; Flinders University, Department of Palliative and Supportive Services Eckert, Danny; Flinders University, College of Medicine and Public Health Gonzalez-Chica, David; University of Adelaide, Discipline of General Practice, Adelaide Medical School Stocks, Nigel; University of Adelaide, Discipline of General Practice Ekström, Magnus; Lunds Universitet,
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Chronic breathlessness and sleep problems: A population-based survey.

David Currow [1,2]
Sungwon Chang [1]
Diana Ferreira [3]
Danny J. Eckert [3]
David Gonzalez-Chica [4]
Nigel Stocks [4]
Magnus Ekström [5]

[1] IMPACCT, Faculty of Health, University of Technology Sydney, Ultimo, New South Wales, Australia. 2007
[2] Wolfson Palliative Care Research Centre, University of Hull, England. HU6 7RX
[3] College of Medicine and Public Health, Flinders University, Bedford Park, South Australia, Australia. 5042
[4] University of Adelaide, Adelaide, South Australia. Australia.
[5] Department of Clinical Sciences, Division of Respiratory Medicine & Allergology, Lund University, Lund, Sweden.

Corresponding author:
Professor David Currow FAHMS
IMPACCT, Faculty of Health, University of Technology Sydney,
P O Box 123
Ultimo, New South Wales, Australia. 2007
david.currow@uts.edu.au

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Chronic breathlessness, sleep problems, insomnia, population survey, symptom prevalence.

Abstract

Objectives:
This study aimed to explore the relationship (presence and severity) between chronic breathlessness and sleep problems, independently of diagnoses and health service contact by surveying a large, representative sample of the general population.

Setting:
Analysis of the 2017 South Australian Health Omnibus Survey, an annual, cross-sectional, face-to-face, multi-stage, clustered area systematic sampling survey carried out in Spring, 2017.

Chronic breathlessness was self-reported using the ordinal modified Medical Research Council (mMRC; scores 0 (none) to 4 (housebound)) where breathlessness has been present for more than three of the previous six months. '*Sleep problems – ever*' and '*sleep problem – current*' were assessed dichotomously. Regression models were adjusted for age; sex; and BMI.

Results:
2,900 responses were available (mean age 48.2 (sd=18.6); 51% were female; mean BMI 27. 1 (sd=5.9)). Prevalence was: 9.5% (n=276) *sleep problems – ever*; 6.8% (n=197) *sleep problems – current*; breathlessness (mMRC 1-4) was 8.8% (n=254). Respondents with *sleep problems* were more likely to be breathless, female, older with higher BMI.
After adjusting for age, sex and BMI, respondents with chronic breathlessness had 2.3 (95% CI = 1.7, 3.2) times the odds of *sleep problems - ever* similarly to *sleep problems – current* (AOR=2.3; 95% CI = 1.6, 3.3).

Conclusions:
A strong relationship for the prevalence of these two conditions co-existing. Future work will be needed to understand if there is a causal relationship, and whether better managing one condition will improve the other.

Strengths and limitations of this study

Strengths
- This was a large, random survey of the population using trained interviewers in face-to-face interviews, irrespective of health service contact
- The survey used tools that were designed for population survey use.

Limitations
- This study can only reflect associations, not cause and effect
- The data on chronic breathlessness and sleep problems were based on self-report, not clinical assessments.
- The data are cross-sectional, not longitudinal.

Introduction

Chronic breathlessness is highly prevalent. It affects between 9 and 27% of the population,[1-3] is associated with impaired physical and mental quality of life,[4] increased levels of anxiety and depression,[5] decreased levels of sexual activity in the elderly,[6] increased social isolation[7,8] and poorer prognosis.[9,10] Unlike many symptoms, chronic breathlessness often worsens late in life.[11]

Similarly, impaired sleep quality and insomnia are prevalent across the community, even in the absence of obstructive sleep apnoea (OSA).[12 - 14] Up to 40% of people with OSA will also have symptomatic insomnia.[15] Poor sleep quality and insomnia are associated with worse physical and mental quality of life,[16] anxiety and depression,[17-19] less satisfaction with sexual function in post-menopausal women[19,20] and poorer life expectancy.[21] Both chronic breathlessness and poor sleep quality are more common in the elderly.[4,13]

To date, most studies relating to sleep quality pertain to people with specific clinical conditions.[12,22] Associations in the general population, without relying on contact with health services, between chronic breathlessness (irrespective of the underlying aetiologies) and sleep problems have not been defined. Understanding this relationship is important given the high burden of these conditions, the complex relationship between them, and the ability to explore changing the symptomatic course of both by ameliorating either one of them.

By asking a broad sample of randomly selected members of the public about their chronic breathlessness and sleep problems, key clinical and demographic factors can be defined for the first time. Further, if there is a relationship between worsening chronic breathlessness and the presence of sleep problems, intervention studies to improve sleep may be beneficial in the management of chronic breathlessness and *vice versa*.

The aim of this study was to evaluate the association between the presence and severity of chronic breathlessness and self-reported sleep problems.

Methods

Survey Design

This was an analysis of the 2017 South Australian Health Omnibus Survey (HOS),[3, 23] an annual, cross-sectional, face-to-face, multi-stage, clustered area systematic sampling survey. It was run by a commercial research organisation, providing de-identified data for user-pays researchers. Approximately 200 questions (including different questions on symptoms, self-reported conditions and health service utilisation) were asked annually. Each year, demographic questions remained relatively unchanged.

Patient and Public Involvement

Data were collected through interviews in participants' homes by trained interviewers, lasting 60-90 minutes. Members of the public were therefore engaged, independently of health service contact. The methodology has been described previously in detail.[23,24]

Setting and Participants

South Australia is the second smallest state by population in Australia, with a population of approximately 1.73 million people (6.9% of the Australian population), mostly living in Adelaide, the state's capital.[25] The survey was carried out between September and December each year having been piloted with 50 residents from the general community annually. A stratified sampling method identified a representative cohort from metropolitan and rural towns with populations of more than 1000. More than 5000 properties were approached annually.

Two randomisations occurred during the sampling process: (1) by census collector districts (CCD) and (2) starting points within each randomly selected CCDs. From the starting point in each CCD, a skip pattern of every tenth property was used to select the next property. Properties approached included houses, businesses, properties with other uses or vacant land. Hotels, hospitals, caravan parks and aged care facilities were not sampled. When houses were identified, interviewers would return up to six times if contact could not be made with the household initially. Participation rates were calculated on the number of potential participants with whom any contact was made.

One interview was conducted in each household with the person aged ≥15 years who most recently had a birthday. If that person was unwilling to participate another member of the household was unable to replace them and that household was classified as declining participation.

Data quality

All data were double entered, with a supervisor following up missing responses by telephone. Additionally, 10% of each interviewer's respondents were re-contacted to confirm their eligibility and ensure consistency of responses by re-answering a selection of questions. Data were anonymised and then released to researchers for analysis.

An initial total of 2,977 people were engaged with the interviews with an overall participation rate of 65.3%, of whom 2900 were 18 years or older and were included in the analysis. For the purposes of this study, analyses were restricted to participants 18 years and older who answered questions related to breathlessness and sleep problems (n = 2900). As the rate of missing data was low for all variables, (BMI had the highest at 5.9% (171/2900)) no data were imputed.

Exposure variable

Breathlessness was self-reported using the modified Medical Research Council (mMRC)[26] scale to the question 'thinking back over the last 6 months, have you had an episode of breathlessness that has lasted more than 3 months'. Response categories included 0 = None; 1 = 'I get short of breath when hurrying on the level or up a slight hill'; 2 = 'I have to stop for breath when walking at my own pace on the level'; 3 = 'I stop for breath after walking 100 meters or after a few minutes on the level'; or 4 = 'I am too breathless to leave the house'. mMRC is reliable, valid and the most commonly used scale for categorising the functional

impact and disability from breathlessness in daily life.[27,28] For the purpose of analysis, breathlessness was defined as a mMRC ≥ 1. Additional analyses were undertaken to examine the severity of breathlessness using all mMRC categories (0-4) as an ordinal scale.

Outcome

'Sleep problems – ever' was assessed with the item (yes/no) "Has a doctor ever told you that you had insomnia or some sleep problem?". Two questions "Are you currently taking medication for insomnia or some sleep problem?" and "Have you seen a doctor in the last six months for insomnia or some sleep problem?" were combined to assess 'Sleep problems - current' with 'yes' to either coding as a positive response.

Measures

Sociodemographic data were collected on age, sex, rurality (metropoltan, non-metropolitan), country of birth (Australia, UK/Ireland, Other), marital status (married / *de facto*, separated/divorced, widowed, never married), highest level of educational attainment (secondary, trade/apprenticeship/certificate/diploma, degree or higher) and postcode. The postcodes were linked to the Socio-Economic Index for Areas (SEIFA). SEIFA is used to rank areas according to socio-economic advantage / disadvantage (e.g., wealth, occupation, and education) derived from Australian national census data.[29] For the purpose of this study, SEIFA was based on ranking derived from 2016 Census data and was categorised into a quintiles. Body mass index (BMI; kg/m2) was calculated from self-reported height and weight. In addition to including BMI as a continuous measure, it was categorised according to international criteria – underweight/ normal: ≤24.9, overweight: 25.0-29.9, and obese: ≥30.0.[30]

To examine the association between breathlessness and sleep problems, the analyses were adjusted for potential confounders associated with both variables: age; sex; and BMI.

Statistical analysis

Data were weighted to the 2016 Estimated Residential Population for South Australia by five year age groups, sex, rurality, and household size derived from the Australian census conducted that year.

Data analyses were conducted using SPSS for Windows Version 26.0. (SPSS Chicago, Il. USA. 2011) Respondents' demographic characteristics were tabulated by *sleep problems - ever*. Bivariate associations of *'sleep prolems – ever'* with sociodemographic factors were analysed using Pearson's chi-square tests for categorical variables and for continuous data independent sample t-tests.

The association between chronic breathlessness and sleep problem indicators were analysed using multiple logistic regression, adjusted for age, sex and BMI. Age and BMI were included as continuous variables and the assumption of linearity in their logits were assessed using Box Tidwell test.[31] The 2 way interaction terms were also assessed for

significance.The goodness of fit was evaluated using the Hosmer-Lemeshow test. Associations were expressed as odds ratio (OR) with 95% confidence interval (CI). The Mantel-Haenszel linear-by linear association chi-sqaure test was used to detect the linear trend between severity of breathlessness (mMRC 0-4) and sleep problem indicators. P≤0.05 was considered statistically significant. A sensitivity analysis using unweighted data was performed to evaluate the robustness of the findings.

Ethics approval and consent

The study was approved annually by the Human Research Ethics Committee of the South Australian Department of Health and the University of Adelaide Human Research Ethics Committee (H-097-2010). Informed verbal consent was obtained from each participant and continued participation accepted as ongoing consent.

Results

An initial 2,977 people were engaged with the interviews with an overall participation rate of 65.3%, of whom 2,900 were 18 years or older and answered the key questions on breathlessness and sleep. In the total respondent sample, the mean age was 48.2 (sd=18.6) and 51% (n=1480) were females. Mean BMI was 27. 1 (sd=5.9). The prevalence was 9.5% (n=276) for *sleep problems – ever* and 6.8% (n=197) for *sleep problems – current*. The overall prevalence of breathlessness (mMRC 1-4) was 8.8% (n=254). Respondents with *sleep problems – ever* or *– current* were more likely to be breathless, female, older with higher BMI (Table 1)

Table 1: Demographic and clinical baseline data for respondents to the 2017 South Australian Health Omnibus Survey by response to *sleep problems - ever* or *sleep problems - current*. (weighted total = 2,900)

	Sleep problems - ever			Sleep problems – current		
	Yes (n=276)	No (n=2,674)	p-value	Yes (n=198)	No (n=2,702)	p-value
Age* *Mean(SD)*	52.1 (17.9)	47.8 (18.6)	<0.001	51.5 (18.5)	48.0 (18.6)	0.01
Sex*			0.007			0.001
Male	114 (8.0)	1306 (92.0)		73 (5.1)	1346 (94.9)	
Female	162 (10.9)	1318 (89.1)		124 (8.4)	1356 (91.6)	
Breathlessness			<0.001			<0.001
mMRC = 0	225 (8.5)	2421 (91.5)		160 (6)	2485 (94)	
mMRC ≥ 1	51 (20.1)	203 (79.9)		37 (14.6)	217 (85.4)	
Body Mass Index (BMI)* categories			<0.001			0.001
< 25	90 (8.2)	1001 (91.8)		60 (5.5)	1031 (94.5)	
25-30	83 (8.6)	887 (91.4)		62 (6.4)	908 (93.6)	
> 30	92 (13.8)	575 (86.2)		66 (9.9)	601 (90.1)	
BMI (kg/m²); *Mean (SD)*	28.3 (6.7)	27.0 (5.8)	0.002	28.6 (6.9)	27.0 (5.8)	0.003
Rurality			0.2			0.4
Metropolitan	214 (9.9)	1941 (90.1)		152 (7.1)	2003 (92.9)	

Non-metropolitan	62 (8.3)	682 (91.7)		46 (6.2)	699 (93.8)	
Socio-Economic Indexes for Area (SEIFA) Quintile			0.6			0.2
1 - Most disadvantaged	69 (9.4)	662 (90.6)		56 (7.7)	675 (92.3)	
2	42 (9.8)	386 (90.2)		31 (7.3)	396 (92.7)	
3	55 (10.1)	487 (89.9)		37 (6.8)	505 (93.2)	
4	68 (10.3)	595 (89.7)		49 (7.4)	614 (92.6)	
5 – Most advantaged	42 (7.8)	494 (92.2)		24 (4.5)	512 (95.5)	
Country of Birth			0.001			0.03
Australia	204 (9.8)	1887 (90.2)		143 (6.8)	1948 (93.2)	
UK/Ireland	37 (14.4)	220 (85.6)		26 (10.2)	230 (89.8)	
Other	35 (6.3)	517 (93.7)		28 (5.1)	523 (94.9)	
Highest level of Educational attainment*#			0.01			0.01
Up to a secondary	107 (10.3)	932 (89.7)		80 (7.7)	959 (92.3)	
Trade, Apprenticeship, Certificate, Diploma	118 (10.6)	990 (89.4)		84 (7.6)	1024 (92.4)	
Degree or higher	51 (6.8)	699 (93.2)		34 (4.5)	716 (95.5)	
Marital Status*			<0.001			<0.001
Married / *de facto*	136 (7.4)	1701 (92.6)		92 (5)	1745 (95.0)	
Separated, divorced	56 (21.3)	207 (78.7)		42 (15.9)	222 (84.1)	
Widowed	26 (16.1)	135 (83.9)		18 (11.3)	142 (88.8)	
Never married	58 (9.1)	577 (90.9)		45 (7.1)	590 (92.9)	

*Missing values; ^mMRC – modified Medical Research Council breathlessness scale

After adjusting for age, sex and BMI, breathlessness was strongly associated *with sleep problems - ever* and also *sleep problems - current*. Respondents with chronic breathlessness had 2.3 (95% CI = 1.7, 3.2; Table 2) times the odds of *sleep problems - ever* than those without breathlessness. Association between breathlessness and *sleep problems – current* was of similar magnitude (AOR=2.3; 95% CI = 1.6, 3.3; Table 2). No interaction terms were significant in the adjusted analysis.

Table 2. Odds ratio and adjusted odds ratio of *sleep problems - ever* and *sleep problems - current* by level of chronic breathlessness (mMRC; 0 - 4) in an unweighted population (n=2,900).

Self-reported exertion before breathlessness supervenes	Sleep problems	
	OR (95% CI)	AOR* (95% CI)
	- Ever	
mMRC = 0	Reference	
mMRC ≥1	2.8 (2.1, 3.8)	2.3 (1.7, 3.2)
	- Current	
mMRC = 0	Reference	
mMRC ≥1	2.7 (1.9, 3.8)	2.3 (1.6, 3.3)

OR - odds ratio; AOR - adjusted odds ratio; mMRC - modified Medical Research Council breathlessness scale

* having adjusted for age (years), sex and body mass index (BMI; kg/m2).

Mantel–Haenszel chi-square tests demonstrated significant linear-by-linear associations between chronic breathlessness (mMRC 0-4) and *sleep problems – ever* ($p<0.001$) and sleep problems - current ($p<0.001$). The prevalence of both sleep problems – ever or current - generally increased with severity of breathlessness as measured with mMRC (0-4). (Figure 1).

The sensitivity analysis of the unweighted data demonstrated similar associations between breathlessness and sleep problems, supporting the robustness of the models.

Discussion

In a random adult population sample, this study found a strong association between the presence of chronic breathlessness and insomnia or sleep problems. These findings complement previous findings that have sampled specific disease states that may be associated with chronic breathlessness such as chronic obstructive pulmonary disease (COPD), interstitial lung disease or cardiac failure.[32]

Two in three people responding to Omnibus surveys who identified symptomatic chronic breathlessness identified respiratory causes for their chronic breathlessness.[32] Sleep problems and breathlessness are both prevalent in people with COPD, with both problems impacting on quality of life.[33 - 38] One study of 51 patients with COPD found no relationship between sleep measures (Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS)) polygraphic sleep studies and mMRC breathlessness scales.[35] Another study of 130 people with COPD sought to generate symptom clusters, one of which was sleep disturbance and fatigue.[36] In another case series of 60 patients with COPD, poor sleep quality and impaired health-related quality of life were highly correlated and in the regression analysis, sleep quality was the strongest predictor of quality of life.[39]

Other causes of chronic breathlessness include malignancy. In 128 people with advanced lung cancer, there was a strong correlation between the severity of respiratory symptoms and the likelihood of sleep disturbance (measured with the PSQI) and poor quality of life (measured with Functional Assessment of Cancer Therapy – Lung (FACT-Lung).[35] In another series of 115 people with lung cancer undergoing chemotherapy, sleep disturbance was strongly associated with poorer functional status and poorer cognition.[39]

Strengths

This is a survey of a random selection of the general population not limited by contact with health services. The dataset was standardised to a census-defined national population. The study builds on previous work defining rates of self-reported levels of exertion limited by breathlessness.[3, 10, 40] These rates are surprisingly stable across the population.

Limitations

There is an association between breathlessness and sleep problems, but the dynamics of this relationship (which comes first, which problem is dominant) cannot be defined from this study. Having found this strong signal, this will be the subject of future studies. More detailed clinical histories related to sleep are required as are laboratory sleep studies to understand the interaction between chronic breathlessness and specific sleep problems including insomnia. For example, the current study questions cannot distinguish between common sleep disorders such as insomnia and sleep apnoea. This preliminary exploration would strongly justify more in-depth population analyses comprising clinical and physiological data. The mMRC only provides a broad-brush picture of the level of exertion required before breathlessness supervenes. Multi-dimensional tools such as the Dyspnoea-12 or Multi-dimensional Dyspnea Profile would allow a more detailed exploration of the aspects of breathlessness that most strongly impact insomnia and sleep disturbances.[41] Given that these are observational data, findings can only be interpreted as associations and not cause and effect.

The relationship between the more severe levels of breathlessness and sleep problems is not statistically significant and almost certainly relates to the power achieved in the study because of low prevalence of severe and very severe breathlessness.

Implications for future research

Understanding whether people had long term sleep problems and developed breathlessness with worsening COPD in later life, *vice versa* or a mixture of both will be important.

A before-and-after study of pulmonary rehabilitation in people with COPD demonstrated improvements in sleep quality measured on the PSQI and in breathlessness after 8 weeks of outpatient pulmonary rehabilitation.[42] Such findings suggest that improving one symptom may have measurable collateral benefits with other long-standing symptoms. Future studies focusing on improving sleep may provide insights into better symptom control and the mechanisms of sleep disturbance.

Conversely, at least one double-blind, placebo controlled cross over randomised trial has shown that when symptomatic breathlessness is reduced successfully, perceived sleep improves.[43] This observation needs to be explored in a much larger study with individuals participating in the study for longer than the eight days reported in the study by Martins *et al.* Such work should include formal sleep studies at least in a sub-group of participants.

Implications for clinical care

Notwithstanding the further research that needs to be done, these data suggest that clinicians should enquire about sleep health when they identify someone with chronic breathlessness and *vice versa*. This is especially the case for people with more severe chronic breathlessness.

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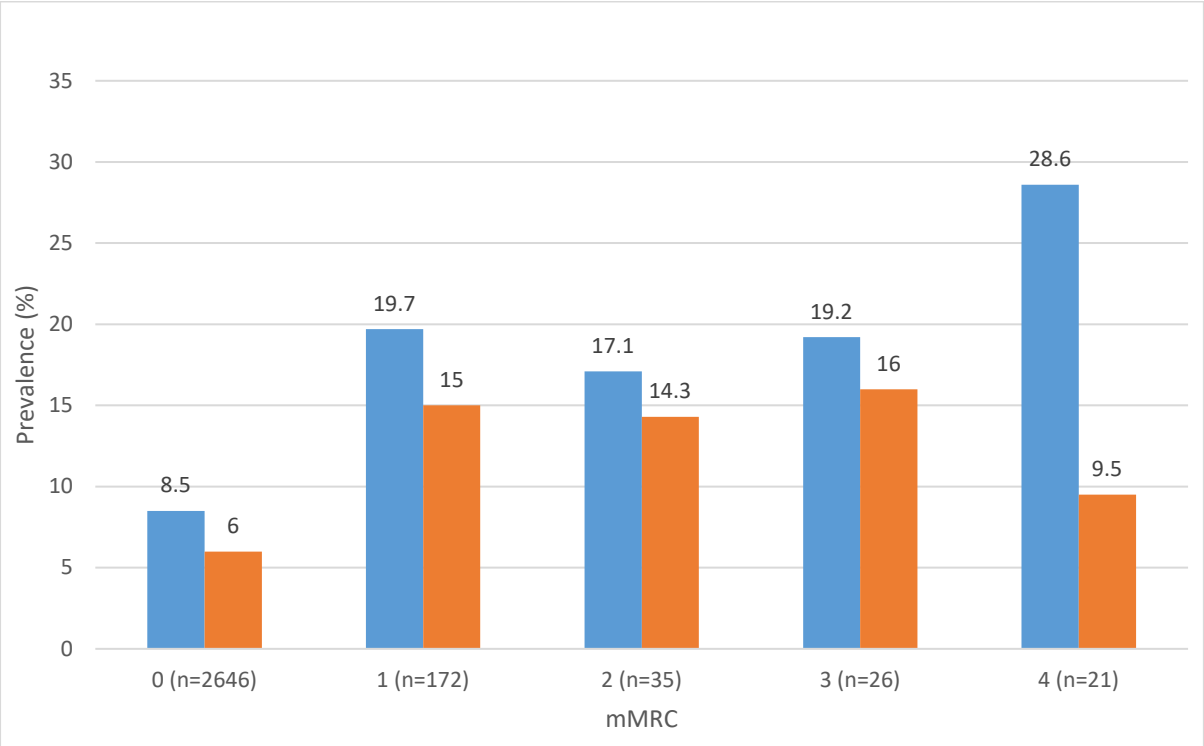
Figure 1. Relationship between *chronic breathlessness* (modified Medical Research Council mMRC breathlessness scale (0-4) and *sleep problems – ever* and *sleep problems – current* in a random sample of the general population in the 2017 South Australian Health Omnibus Survey. (n=2,900)



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Chronic breathlessness and sleep problems: a population-based survey.

David Currow [1,2]
Sungwon Chang [1]
Diana Ferreira [3]
Danny J. Eckert [3]
David Gonzalez-Chica [4]
Nigel Stocks [4]
Magnus Ekström [5]

[1] IMPACCT, Faculty of Health, University of Technology Sydney, Ultimo, New South Wales, Australia. 2007
[2] Wolfson Palliative Care Research Centre, University of Hull, England. HU6 7RX
[3] College of Medicine and Public Health, Flinders University, Bedford Park, South Australia, Australia. 5042
[4] University of Adelaide, Adelaide, South Australia. Australia.
[5] Department of Clinical Sciences, Division of Respiratory Medicine & Allergology, Lund University, Lund, Sweden.

Corresponding author:
Professor David Currow FAHMS
IMPACCT, Faculty of Health, University of Technology Sydney,
P O Box 123
Ultimo, New South Wales, Australia. 2007
david.currow@uts.edu.au

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Chronic breathlessness, sleep problems, insomnia, population survey, symptom prevalence.

Abstract

Objectives:
This study aimed to explore the relationship (presence and severity) between chronic breathlessness and sleep problems, independently of diagnoses and health service contact by surveying a large, representative sample of the general population.

Setting:
Analysis of the 2017 South Australian Health Omnibus Survey, an annual, cross-sectional, face-to-face, multi-stage, clustered area systematic sampling survey carried out in Spring, 2017.

Chronic breathlessness was self-reported using the ordinal modified Medical Research Council (mMRC; scores 0 (none) to 4 (housebound)) where breathlessness has been present for more than three of the previous six months. '*Sleep problems – ever*' and '*sleep problem – current*' were assessed dichotomously. Regression models were adjusted for age; sex; and body mass index (BMI).

Results:
2,900 responses were available (mean age 48.2 (sd=18.6); 51% were female; mean BMI 27. 1 (sd=5.9)). Prevalence was: 2.7% (n=78) *sleep problems – past*; 6.8% (n=198) *sleep problems – current*; breathlessness (mMRC 1-4) was 8.8% (n=254). Respondents with *sleep problems - past* were more likely to be breathless, older with a higher BMI and *present* also included a higher likelihood of being female.
After adjusting for age, sex and BMI, respondents with chronic breathlessness had 1.9 (95% CI = 1.0, 3.5) times the odds of *sleep problems - past* and *sleep problems – current* (aOR=2.3; 95% CI = 1.6, 3.3).

Conclusions:
There is a strong association between the two prevalent conditions. Future work will seek to understand if there is a causal relationship using validated sleep assessment tools, and whether better managing one condition improves the other.

Strengths and limitations of this study

Strengths
- This was a large, random survey of the population using trained interviewers in face-to-face interviews, irrespective of health service contact
- The survey used tools that were designed for population survey use.

Limitations
- This study can only reflect associations, not cause and effect
- The data on chronic breathlessness and sleep problems were based on self-report, not clinical assessments.
- The data are cross-sectional, not longitudinal.

Introduction

Chronic breathlessness is highly prevalent. It affects up to 8% of the adult population in high income countries, [1-3] is associated with impaired physical and mental quality of life,[4] increased levels of anxiety and depression,[5] decreased levels of sexual activity in the elderly,[6] increased social isolation[7,8] and poorer prognosis.[9,10] Unlike many symptoms, chronic breathlessness often worsens late in life.[11]

Similarly, impaired sleep quality and insomnia are prevalent across the community, even in the absence of obstructive sleep apnoea (OSA).[12 - 14] Up to 40% of people with OSA will also have symptomatic insomnia.[15] Poor sleep quality and insomnia are associated with worse physical and mental quality of life,[16] anxiety and depression,[17-19] less satisfaction with sexual function in post-menopausal women[19,20] and poorer life expectancy.[21] Both chronic breathlessness and poor sleep quality are more common in the elderly.[4,13]

Associations in the general population, without relying on contact with health services, between chronic breathlessness (irrespective of the underlying aetiologies) and sleep problems have not been defined. Understanding this relationship is important given the high burden of these conditions, the complex relationship between them, and the ability to explore changing the symptomatic course of both by ameliorating either one of them.

By asking a broad sample of randomly selected members of the public about their chronic breathlessness and sleep problems, key clinical and demographic factors can be defined for the first time. Further, if there is a relationship between worsening chronic breathlessness and the presence of sleep problems, intervention studies to improve sleep may be beneficial in the management of chronic breathlessness and *vice versa*.

The aim of this study was to evaluate the association between the presence and severity of chronic breathlessness and self-reported sleep problems.

Methods

Survey Design

This was an analysis of the 2017 South Australian Health Omnibus Survey (HOS),[3, 22] (Appendix 1) an annual, cross-sectional, face-to-face, multi-stage, clustered area systematic sampling survey. It was run by a commercial research organisation, providing de-identified data for user-pays researchers. Approximately 200 questions (including different questions on symptoms, self-reported conditions and health service utilisation) were asked annually. Each year, demographic questions remained relatively unchanged.

Data were collected through interviews in participants' homes by trained interviewers, lasting 60-90 minutes. Members of the public were therefore engaged, independently of health service contact. The methodology has been described previously in detail.[22,23]

Setting and Participants

South Australia is the second smallest state by population in Australia, with a population of approximately 1.73 million people (6.9% of the Australian population), mostly living in Adelaide, the state's capital.[24] The survey was carried out between September and December each year having been piloted with 50 residents from the general community annually. A stratified sampling method identified a representative cohort from metropolitan and rural towns with populations of more than 1000. More than 5000 properties were approached annually.

Two randomisations occurred during the sampling process: (1) by census collector districts (CCD) and (2) starting points within each randomly selected CCDs. From the starting point in each CCD, a skip pattern of every tenth property was used to select the next property. Properties approached included houses, businesses, properties with other uses or vacant land. Hotels, hospitals, caravan parks and aged care facilities were not sampled. When houses were identified, interviewers would return up to six times if contact could not be made with the household initially. Participation rates were calculated on the number of potential participants with whom any contact was made.

One interview was conducted in each household with the person aged ≥15 years who most recently had a birthday. If that person was unwilling to participate and another member of the household was unable to replace them then that household was classified as declining participation.

Data quality

All data were double entered, with a supervisor following up missing responses by telephone. Additionally, 10% of each interviewer's respondents were re-contacted to confirm their eligibility and ensure consistency of responses by re-answering a selection of questions. Data were anonymised and then released to researchers for analysis.

An initial total of 2,977 people were engaged with the interviews with an overall participation rate of 65.3%, of whom 2900 were 18 years or older and were included in the analysis. All eligible respondents were included to maximise power and minimise bias. For the purposes of this study, analyses were restricted to participants 18 years and older who answered questions related to breathlessness and sleep problems (n = 2900). As the rate of missing data was low for all variables except BMI (5.9%), no data were imputed.

Exposure variable

Breathlessness was self-reported using the modified Medical Research Council (mMRC)[25] scale to the question 'thinking back over the last 6 months, have you had an episode of breathlessness that has lasted more than 3 months'. This timeframe was an arbitrary period used in previous population studies to assess a degree of chronicity. [11] Response categories included 0 = None; 1 = 'I get short of breath when hurrying on the level or up a slight hill'; 2 = 'I have to stop for breath when walking at my own pace on the level'; 3 = 'I stop for breath after walking 100 meters or after a few minutes on the level'; or 4 = 'I am too breathless to leave the house'. mMRC is reliable, valid and the most commonly used scale for categorising

the functional impact and disability from breathlessness in daily life.[26,27] For the purpose of analysis, breathlessness was defined as a mMRC ≥ 1. Additional analyses were undertaken to examine the severity of breathlessness using all mMRC categories (0-4) as an ordinal scale.

Outcome

'Sleep problems – ever' was assessed with the item (yes/no) "Has a doctor ever told you that you had insomnia or some sleep problem?". Two questions "Are you currently taking medication for insomnia or some sleep problem?" and "Have you seen a doctor in the last six months for insomnia or some sleep problem?" were combined to assess 'Sleep problems - current' with 'yes' to either coding as a positive response. The study reports *sleep problems – past* by subtracting *sleep-problems – current* from *sleep problems – ever*.

Measures

Sociodemographic data were collected on age, sex, rurality (metropoltan, non-metropolitan), country of birth (Australia, UK/Ireland, Other), marital status (married / *de facto*, separated/divorced, widowed, never married), highest level of educational attainment (secondary, trade/apprenticeship/certificate/diploma, degree or higher) and postcode. The postcodes were linked to the Socio-Economic Index for Areas (SEIFA). SEIFA is used to rank areas according to socio-economic advantage / disadvantage (e.g., wealth, occupation, and education) derived from Australian national census data.[28] For the purpose of this study, SEIFA was based on ranking derived from 2016 Census data and was categorised into a quintiles. Body mass index (BMI; kg/m2) was calculated from self-reported height and weight. In addition to including BMI as a continuous measure, it was categorised according to international criteria – underweight/ normal: ≤24.9, overweight: 25.0-29.9, and obese: ≥30.0.[29]

Statistical analysis

Data were weighted to the 2016 Estimated Residential Population for South Australia by five year age groups, sex, rurality, and household size derived from the Australian census conducted that year.

Data analyses were conducted using SPSS for Windows Version 26.0. (SPSS Chicago, Il. USA. 2011) Respondents' demographic characteristics were tabulated by *sleep problems - ever*. Bivariate associations of *'sleep prolems – ever'* with sociodemographic factors were analysed using Pearson's chi-square tests for categorical variables and for continuous data independent sample t-tests.

The association between chronic breathlessness and sleep problem indicators were analysed using multiple logistic regression, adjusted for the potential confounders age, sex and BMI. Variables to adjust for were selected based on subject matter knowledge and the literature. [30] Age and BMI were included as continuous variables and the assumption of linearity in their logits were assessed using Box Tidwell test.[31] The two way interaction terms were also assessed for significance.The goodness of fit was evaluated using the Hosmer-Lemeshow test. Associations were expressed as odds ratio (OR) with 95% confidence

interval (CI). The Mantel-Haenszel linear-by-linear association chi-square test was used to detect the linear trend between severity of breathlessness (mMRC 0-4) and sleep problem indicators. P≤0.05 was considered statistically significant. A sensitivity analysis using unweighted data was performed to evaluate the robustness of the findings.

Ethics approval, consent and reporting

The study was approved annually by the Human Research Ethics Committee of the South Australian Department of Health and the University of Adelaide Human Research Ethics Committee (H-097-2010). Informed verbal consent was obtained from each participant and continued participation accepted as ongoing consent. The study is reported in compliance with the STROBE checklist for cross-sectional studies.[32]

Results

An initial 2,977 people were engaged with the interviews with an overall participation rate of 65.3%, of whom 2,900 were 18 years or older and answered the key questions on breathlessness and sleep. In the total respondent sample, the mean age was 48.2 (sd=18.6) and 51% (n=1480) were females. Mean BMI was 27. 1 (sd=5.9). The prevalence was 2.7% (n=78) for *sleep problems – past* and 6.8% (n=198) for *sleep problems – current*. The overall prevalence of breathlessness (mMRC 1-4) was 8.8% (n=254). Respondents with *sleep problems – past* were more likely to be breathless, older and with a higher BMI. Respondents with *sleep problems – current* were also more likely to be female. These factors were taken into the regression models. (Table 1)

Table 1: Demographic and clinical baseline data for respondents to the 2017 South Australian Health Omnibus Survey by response to past and current *sleep problems* (weighted total = 2,900).

	Sleep problems - past			**Sleep problems – current**		
	Yes (n=78)	No (n=2,822)	p-value	Yes (n=198)	No (n=2,702)	p-value
Age* *Mean(SD)*	54.3 (16.6)	48.1 (18.6)	0.002	51.5 (18.5)	48.0 (18.6)	0.01
Sex*			0.7			0.001
Male	40 (51.3)	1380 (48.9)		74 (37.4)	1346 (49.8)	
Female	38 (48.7)	1442 (51.1)		124 (62.6)	1356 (50.2)	
Breathlessness			0.008			<0.001
mMRC = 0	65 (83.3)	2581 (91.5)		160 (81.2)	2485 (92)	
mMRC ≥ 1	13 (16.7)	241 (8.5)		37 (18.8)	217 (8)	
Body Mass Index (BMI)* categories			0.09			0.001
< 25	30 (39.5)	1061 (40)		60 (31.6)	1031 (40.6)	
25-30	20 (26.3)	951 (35.8)		62 (32.6)	908 (35.7)	
> 30	26 (34.2)	642 (24.2)		67 (35.3)	601 (23.7)	
BMI (kg/m^2); *Mean (SD)*	27.8 (6.1)	27.1 (5.9)	0.3	28.6 (6.9)	27.0 (5.8)	0.003
Rurality			0.4			0.4
Metropolitan	61 (78.2)	2094 (74.2)		152 (76.8)	2003 (74.1)	

Non-metropolitan	17 (21.8)	728 (25.8)		46 (23.2)	699 (25.9)	
Socio-Economic Indexes for Area (SEIFA) Quintile			0.4			0.2
1 - Most disadvantaged	13 (16.7)	718 (25.4)		56 (28.3)	675 (25)	
2	11 (14.1)	416 (14.7)		31 (15.7)	396 (14.7)	
3	18 (23.1)	524 (18.6)		37 (18.7)	505 (18.7)	
4	18 (23.1)	645 (22.9)		49 (24.7)	614 (22.7)	
5 – Most advantaged	18 (23.1)	519 (18.4)		25 (12.6)	512 (18.9)	
Country of Birth			0.03			0.03
Australia	61 (78.2)	2030 (71.9)		143 (72.2)	1948 (72.1)	
UK/Ireland	10 (12.8)	247 (8.8)		27 (13.6)	230 (8.5)	
Other	7 (9)	545 (19.3)		28 (14.1)	523 (19.4)	
Highest level of Educational attainment*#			0.7			0.01
Up to a secondary	27 (34.6)	1012 (35.9)		80 (40.4)	959 (35.5)	
Trade, Apprenticeship, Certificate, Diploma	33 (42.3)	1075 (38.1)		84 (42.4)	1024 (37.9)	
Degree or higher	18 (23.1)	732 (25.9)		34 (17.2)	716 (26.5)	
Marital Status*			0.01			<0.001
Married / *de facto*	43 (55.1)	1794 (63.6)		92 (46.5)	1745 (64.6)	
Separated, divorced	14 (17.9)	249 (8.8)		42 (21.2)	222 (8.2)	
Widowed	8 (10.3)	154 (5.5)		19 (9.6)	143 (5.3)	
Never married	13 (16.7)	622 (22.1)		45 (22.7)	590 (21.9)	

*Missing values; ^mMRC – modified Medical Research Council breathlessness scale

After adjusting for age, sex and BMI, breathlessness was strongly associated with *sleep problems - past* and also *sleep problems - current*. Respondents with chronic breathlessness had 1.9 (95% CI = 1.0, 3.5; Table 2) times the odds of *sleep problems - past* than those without breathlessness. The association between breathlessness and *sleep problems – current* was similar (aOR=2.3; 95% CI = 1.6, 3.3; Table 2). No interaction terms were significant in the adjusted analysis.

Table 2. Odds ratio and adjusted odds ratio of *sleep problems - ever* and *sleep problems - current* by level of chronic breathlessness (mMRC; 0 - 4) in an unweighted population (n=2,900).

Self-reported exertion before breathlessness supervenes	Sleep problems	
	OR (95% CI)	AOR* (95% CI)
	- Past	
mMRC = 0	Reference	
mMRC ≥1	2.3 (1.3, 4.1)	1.9 (1.0, 3.5)
	- Current	
mMRC = 0	Reference	
mMRC ≥1	2.7 (1.9, 3.8)	2.3 (1.6, 3.3)

OR - odds ratio; AOR - adjusted odds ratio; mMRC - modified Medical Research Council breathlessness scale
* having adjusted for age (years), sex and body mass index (BMI; kg/m2).

Mantel–Haenszel chi-square tests demonstrated significant linear-by-linear associations between chronic breathlessness (mMRC 0-4) and *sleep problems – past* ($p<0.001$) and sleep problems - current ($p<0.001$). The prevalence of *sleep problems – ever or current* - generally increased with severity of breathlessness as measured with mMRC (0-4; Figure 1).

The sensitivity analysis of the unweighted data demonstrated similar associations between breathlessness and sleep problems, supporting the robustness of the models.

Discussion

In a random adult population sample, this study found a strong association between the presence of chronic breathlessness and insomnia or sleep problems. These findings complement previous findings that have sampled specific disease states that may be associated with chronic breathlessness such as chronic obstructive pulmonary disease (COPD), interstitial lung disease or cardiac failure.[33]

Two in three people responding to Omnibus surveys who identified symptomatic chronic breathlessness identified respiratory causes for their chronic breathlessness.[33] Sleep problems and breathlessness are both prevalent in people with COPD, with both problems impacting on quality of life.[34 - 39] One study of 51 patients with COPD found no relationship between sleep measures (Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS)) polygraphic sleep studies and mMRC breathlessness scales.[36] Another study of 130 people with COPD sought to generate symptom clusters, one of which was sleep disturbance and fatigue.[37] In another case series of 60 patients with COPD, poor sleep quality and impaired health-related quality of life were highly correlated and in the regression analysis, sleep quality was the strongest predictor of quality of life.[40]

Other causes of chronic breathlessness include malignancy. In 128 people with advanced lung cancer, there was a strong correlation between the severity of respiratory symptoms and the likelihood of sleep disturbance (measured with the PSQI) and poor quality of life (measured with Functional Assessment of Cancer Therapy – Lung (FACT-Lung).[36] In another series of 115 people with lung cancer undergoing chemotherapy, sleep disturbance was strongly associated with poorer functional status and poorer cognition.[40]

Strengths

This is a survey of a random selection of the general population not limited by contact with health services. The dataset was standardised to a census-defined national population. The study builds on previous work defining rates of self-reported levels of exertion limited by breathlessness.[3, 10, 41] These rates are surprisingly stable across the population.

Limitations

There is an association between breathlessness and sleep problems, but the dynamics of this relationship (which comes first, which problem is dominant) cannot be defined from this study. Having found this strong signal, this will be the subject of future studies. More detailed clinical histories related to sleep are required as are laboratory sleep studies to understand the interaction between chronic breathlessness and specific sleep problems including insomnia. For example, the current study questions cannot distinguish between common sleep disorders such as insomnia and sleep apnoea. This preliminary exploration would strongly justify more in-depth population analyses comprising clinical and physiological data. The mMRC only provides a broad-brush picture of the level of exertion required before breathlessness supervenes. Multi-dimensional tools such as the Dyspnoea-12 or the Multidimensional Dyspnea Profile would allow a more detailed exploration of the aspects of breathlessness that most strongly impact insomnia and sleep disturbances.[42] This preliminary study seeking to explore the relationship between sleep problems and chronic breathlessness in face-to-face interviews covering a very wide range of health topics has shown a relationship in univariate and multivariate analyses that now justifies progressing to a population study using validated tools for the assessment of sleep and chronic breathlessness. Validated and standardised tools such as the Pittsburgh Sleep Quality Index can now be justified in future study design and funding applications [43] in order to reliably categorise individuals with sleep problems. Given that these are observational data, findings can only be interpreted as associations and not cause and effect. Future work could include seeking permission to contact respondents' treating clinicians or even extend to formal sleep studies for a sub-group of respondents that identify current sleep problems.

The relationship between the more severe levels of breathlessness and sleep problems is not statistically significant and almost certainly relates to the power achieved in the study because of low prevalence of severe and very severe breathlessness.

Implications for future research

Understanding whether people had long term sleep problems and developed breathlessness with worsening COPD in later life, *vice versa* or a mixture of both will be important.

A before-and-after study of pulmonary rehabilitation in people with COPD demonstrated improvements in sleep quality measured on the PSQI and in breathlessness after 8 weeks of outpatient pulmonary rehabilitation.[44] Such findings suggest that improving one symptom may have measurable collateral benefits with other long-standing symptoms. Future studies focusing on improving sleep may provide insights into better symptom control and the mechanisms of sleep disturbance.

Conversely, at least one double-blind, placebo controlled cross over randomised trial has shown that when symptomatic breathlessness is reduced successfully, perceived sleep improves.[45] This observation needs to be explored in a much larger study with individuals participating in the study for longer than the eight days reported in the study by Martins *et al.* Such work should include formal sleep studies at least in a sub-group of participants.

Implications for clinical care

Notwithstanding the further research that needs to be done, these data suggest that clinicians should enquire about sleep health when they identify someone with chronic breathlessness and *vice versa*. This is especially the case for people with more severe chronic breathlessness.

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Authors' Contributions: DC, ME conceptualised the study and planned the data analysis and drafted the manuscript. DC, ME, DE acquired the data, offered intellectual input and provided critical revision. SC performed the data analysis with input from DC. DC, SC, DF, DE, DGC, NS, ME all contributed to the drafts and approved the final version of the manuscript for publication.

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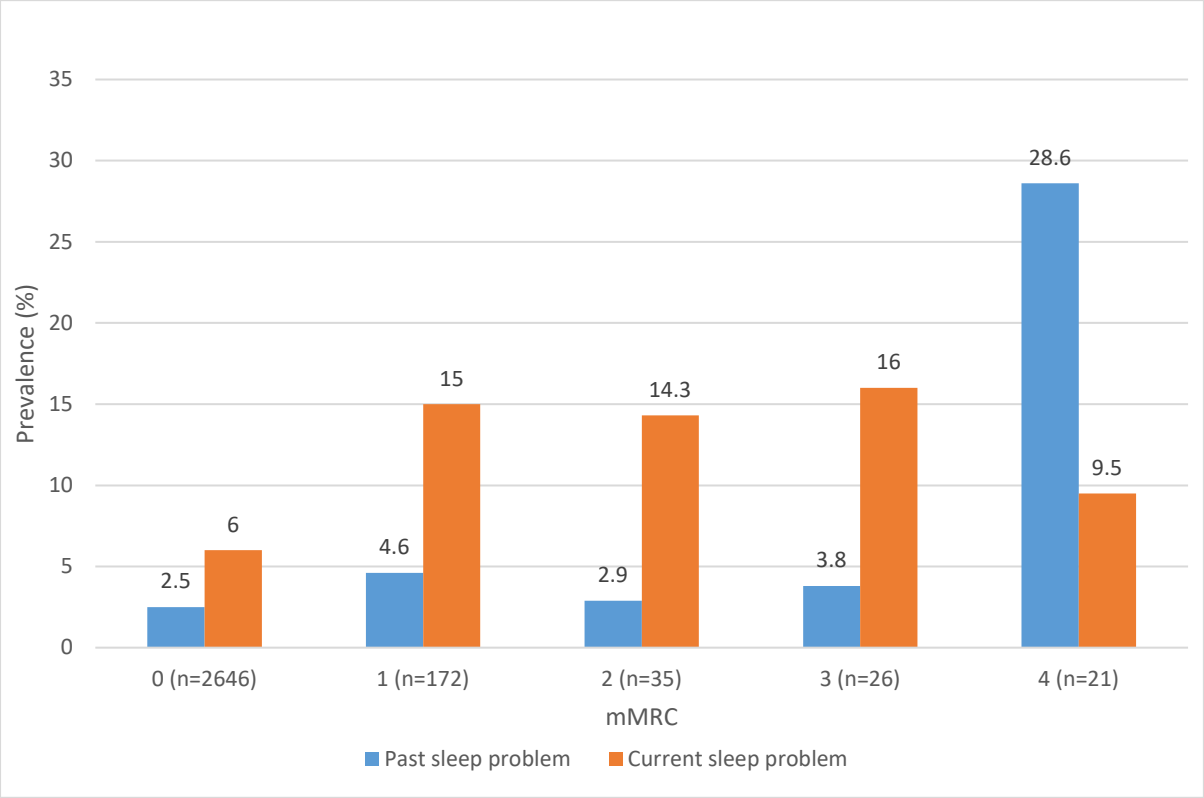
Figure Legend

Figure 1: Prevalence of past nd current sleep problems by level of chronic breathlessness in a random sample of the population of South Australia. (n = 2,898)

Figure 1: Prevalence of past and current sleep problems by level of chronic breathlessness in a random sample of the population of South Australia. (n = 2,898)



*mMRC – modified Medical Research Council breathlessness scale

Appendix 1

SPRING 2017 HEALTH OMNIBUS SURVEY

E. HEIGHT/WEIGHT

Changing the subject.

E1 What is your height without shoes?

☐☐☐ Centimetres *(OR)*

☐:☐☐ Feet/Inches

☐ (D)Don't' know

E2 What is your weight (undressed in the morning)?

☐☐☐ Kilograms *(OR)*

☐☐:☐☐ Stones/Pounds

☐ (D) Don't know

O. BREATHLESSNESS/EQOL

O1 Thinking back over the last 6 months, have you had an episode of breathlessness that has lasted more than 3 months? *(An episode of breathlessness means breathlessness experienced on most days over that period) Show prompt card O1*

1 No *Go to O4*

2 Yes, I got short of breath when hurrying on the level or up a slight hill

3 Yes, I had to stop for breath when walking at my own pace on the level

4 Yes, I stop for breath after walking 100 metres or after a few minutes on the level

5 Yes, I was too breathless to leave the house or breathless when dressing or undressing

6 Refused

O2 About how long have you been this breathless?
Enter years and/or months.

1 Enter years ☐☐

2 Enter months ☐☐

3 Can't remember

4 Refused

O3 What do you understand is causing your shortness of breath? *(Primary condition only)*
Show prompt card O2.

1 **Lungs (e.g. emphysema, smoking, asbestosis, work related, asthma)**

2 **Heart (e.g. ischaemic, heart disease, valve disease, abnormal heart rhythms)**

3 **Disorder of nerves or muscles (e.g. motor neurone disease, multiple sclerosis)**

4 **Other (specify).....**

.....

5 Don't know

6 Refused

O4 Which of the following statements best describes your health TODAY regarding....*Show prompt card O3*

Mobility

1 **I have no problems in walking about**

2 **I have slight problems in walking about**

3 **I have moderate problems in walking about**

4 **I have severe problems in walking about**

5 **I am unable to walk about**

O5 Self-Care? *Show prompt card O3*

1 **I have no problems washing or dressing myself**

2 **I have slight problems washing or dressing myself**

3 **I have moderate problems washing or dressing myself**

4 **I have severe problems washing or dressing myself**

5 **I am unable to wash or dress myself**

O6	**Usual Activities (e.g. work, study, housework, family or leisure activities)?** *Show prompt card O3*
	1 I have no problems doing my usual activities
	2 I have slight problems doing my usual activities
	3 I have moderate problems doing my usual activities
	4 I have severe problems doing my usual activities
	5 I am unable to do my usual activities
O7	**Pain/Discomfort?** *Show prompt card O4*
	1 I have no pain or discomfort
	2 I have slight pain or discomfort
	3 I have moderate pain or discomfort
	4 I have severe pain or discomfort
	5 I have extreme pain or discomfort
O8	**Anxiety/Depression?** *Show prompt card O5*
	1 I am not anxious or depressed
	2 I am slightly anxious or depressed
	3 I am moderately anxious or depressed
	4 I am severely anxious or depressed
	5 I am extremely anxious or depressed

R9	**In the past 3 months have you been using breathing equipment for sleep apnoea?**
	1 Yes
	2 No
	3 Refused/don't know

		R10 Has a doctor <u>ever</u> told you that you have…?	**R11 Are you <u>currently</u> taking medication for…?**	**R12 Have you seen a doctor in the <u>last six months</u> for..?**
		Yes/No/Don't know/Refused	Yes/No/Don't know/Refused	Yes/No/Don't know/Refused
	Show prompt card R2	*Enter Y, N, DK or R in every box below*	*Ask R.11 if Yes, to R.10*	*Ask R.12 if Yes, to R.10*
	Sleep Apnoea			
	Insomnia or some sleep problem			

Z10 What is your postcode?

Enter postcode

Harrison Research. Findings from Spring 2017 Health Omnibus Survey

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page number
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5,6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	6
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	n/a
		(*e*) Describe any sensitivity analyses	7
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5
		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7, 13
		(b) Indicate number of participants with missing data for each variable of interest	13
Outcome data	15*	Report numbers of outcome events or summary measures	13
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7, 14

		(*b*) Report category boundaries when continuous variables were categorized	6, 13
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7
Discussion			
Key results	18	Summarise key results with reference to study objectives	7,8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	8
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8, 9
Generalisability	21	Discuss the generalisability (external validity) of the study results	9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	1

*Give information separately for exposed and unexposed groups.

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