Journal of Gastroenterology and Hepatology
JGHF
doi:10.1111/jgh.13650

GASTROENTEROLOGY

The association between gastroesophageal reflux disease with sleep quality, depression, and anxiety in a cohort study of Australian men

Zhi Xiang On,*,† Janet Grant,† Zumin Shi,*,† Anne W Taylor,*,† Gary A Wittert,* Phillip J Tully,* Amie C Hayley‡,§ and Sean Martin*

*Freemasons Foundation Centre for Men's Health, Faculty of Health Sciences, †Population Research and Outcome Studies, The University of Adelaide, Adelaide, South Australia, ‡IMPACT SRC, School of Medicine, Barwon Health, Deakin University, Geelong, and §Centre for Human Psychopharmacology, Swinburne University of Technology, Melbourne, Victoria, Australia

Key words
anxiety, depression, gastroesophageal reflux disease, sleep quality.

Accepted for publication 8 November 2016.

Correspondence
Sean Martin, Freemasons Foundation Centre for Men's Health, Faculty of Health Sciences, The University of Adelaide, PO Box 11060, Adelaide, SA 5001, Australia,
Email: sean.martin@adelaide.edu.au

Declaration of conflict of interest: All authors declare no conflict of interest.
Financial support: This work was supported by the National Health and Medical Research Council of Australia (NHMRC Project grant no. 627227 and NHMRC Clinical Overseas Fellowship no. 1053578).
Disclosure statement: The funding body had no role in the design and conduct of the study; in the collection, analysis, and interpretation of the data; or in the preparation, review, or approval of the manuscript.

Abstract

Background and Aim: Previous clinical studies have demonstrated a relationship between gastroesophageal reflux disease (GERD) with anxiety and depression; however, few population-based studies have controlled for sleep disorders. The current study aimed to assess the relationship between GERD and anxiety, depression, and sleep disorders in a community-based sample of Australian men.
Methods: Participants comprised a subset of 1612 men (mean age: 60.7 years, range: 35–80) who participated in the Men Androgen Inflammation Lifestyle Environment and Stress Study during the years 2001–2012, who had complete GERD measures (Gastresophageal Reflux Disease Questionnaire), and were not taking medications known to impact gastrointestinal function (excluding drugs taken for acid-related disorders). Current depression and anxiety were defined by (i) physician diagnosis, (ii) symptoms of depression (Beck Depression Inventory and Centre for Epidemiological Studies Depression Scale) or anxiety (Generalized Anxiety Disorder-7), and/or current depressive or anxiolytic medication use. Previous depression was indicated by past depressive diagnoses/medication use. Data on sleep quality, daytime sleepiness, and obstructive sleep apnea were collected along with several health, lifestyle, and medical factors, and these were systematically evaluated in both univariate and multivariable analyses.
Results: Overall, 13.7% (n = 221) men had clinically significant GERD symptoms. In the adjusted models, an association between GERD and anxiety (odds ratio [OR] 2.7; 95% confidence interval [CI] 1.0–6.8) and poor sleep quality (OR 1.8; 95% CI 1.2–2.9) was observed; however, no effect was observed for current depression (OR 1.5; 95% CI 0.8–2.7). After removing poor sleep quality from the model, an independent association between current depression (OR 2.6; 95% CI 1.7–3.8) and current anxiety (OR 3.2; 95% CI 1.8–6.0) and GERD was observed, but not for previous depression (OR 1.4; 95% CI 0.7–2.8).
Conclusion: In this sample of urban-dwelling men, we observed a strong independent association between GERD, anxiety, and current depression, the latter appearing to be partly mediated by poor sleep quality. Patients presenting with GERD should have concurrent mental health assessments in order to identify potential confounders to the successful management of their symptoms.

Introduction

Gastresophageal reflux disease (GERD) is a chronic condition arising from the reflux of gastric contents through the lower esophageal sphincter, resulting in troublesome symptoms or complications.[1] Acid regurgitation and heartburn are the most common symptoms of this condition.[1,2] The reported prevalence GERD ranges from 10% to 20% among adults in the USA, Australia, and the UK.[3–5] The prevalence of GERD is increasing in Asian countries, with recent estimates that it affects 5% of adults in China and Korea.[6] Although GERD has been extensively studied in clinical settings, there are limited population-based data relating

to the risk factors for, and other health conditions associated with, GERD.[7,8] GERD has been found to be negatively associated with lower health-related quality of life[9] and poorer health outcomes.

Previous studies of affective disorders on GERD have been inconsistent, with some showing no effect,[10] while others have shown a positive and even a negative effect on GERD.[11,12] Furthermore, most previous research on GERD and affective disorders have been conducted in clinical settings in patients with a high-degree of comorbidity and consequent limited applicability to the general population.[13–15]

Sleep disorders are common in the general population.[16,17] Previous research has similarly demonstrated an association between GERD and sleep disturbances, such as obstructive sleep apnea, daytime sleepiness, and insomnia.[18] However, sleep disorders are often more closely associated with other GERD-related morbidities,[16] including lung disorders,[19] high blood pressure,[18] cardiovascular disease (CVD),[18] migraine,[18] cognitive impairment,[16] and psychological disorders.[17] It is unclear whether sleep disorders have an independent effect on GERD, or whether this effect is associated with other factors, such as depression and anxiety.

The purpose of this study was to examine the relationship between GERD and anxiety and depression, and disordered sleep in a community-dwelling representative cohort of middle aged and older men.

Methods

Study participants. Participants from the present study were drawn from the Men Androgen Inflammation Lifestyle Environment and Stress (MAILES) Study, a randomly-selected group of urban, community-dwelling men aged 35–80 years at recruitment over from two representative, concurrent cohorts: the Florey Adelaide Male Ageing Study[15] and the North West Adelaide Health Study.[20] Details of the study have been published previously.[19] For the current study, data from 2001–2012 (MAILES 1 to 4) were used. Ethics approval was granted by the Human Research Ethics Committee of The Queen Elizabeth and Lyell McEwin Hospitals, and written informed consent was obtained from all participants. Figure 1 shows the selection of participants included in the current analysis.

Gastresophageal reflux disease. The Gastroesophageal Reflux Disease Questionnaire (GerdQ) comprises 12 items using a Likert-type scale measuring the severity and frequency of symptoms, including burning or painful feeling behind the breastbone (upper stomach), acid taste in mouth, and unpleasant movement of material upwards from the stomach.[21] The GerdQ has previously been used to diagnose GERD and was developed as part of an international multicenter study.[22] A validation study in 8065 persons found that the GerdQ was effective at discriminating patients with reflux esophagitis and GERD from those without the condition.[21]

Depression and anxiety. For the present study, depression was categorized into three groups: (i) current depression, (ii) previous depression, and (iii) no depression. Current depression was defined as men who had incident and existing cases of either antidepressant usage and depression symptomology (a score of >14 on the Beck Depression Inventory[23] [for Florey Adelaide Male Ageing Study participants], or a score of $a \geq 21$ on the Centre for Epidemiological Studies Depression Scale[24] [for North West Adelaide Health Study participants]), in addition to a previous diagnosis of depression by a physician. Previous depression was defined as those men who had previous antidepressant usage and depression symptomology. Men who had no history of depression diagnosis, antidepressant usage, or depression symptomology were categorized as having no depression.

Current anxiety was defined as men who had incident and existing cases of anxiolytic usage and current anxiety symptomology (answering "more than half a day" to the question "Over the last 2 weeks, how often have you felt anxious?", and also a score of >10 from questions 2 to 7 comprising a range of anxiety symptoms on the Generalized Anxiety Disorder-7 scale[25]), in addition to a previous diagnosis of anxiety by a physician. Men who had no history of anxiety diagnosis, anxiolytic usage, or anxiety symptomology were categorized as no anxiety.

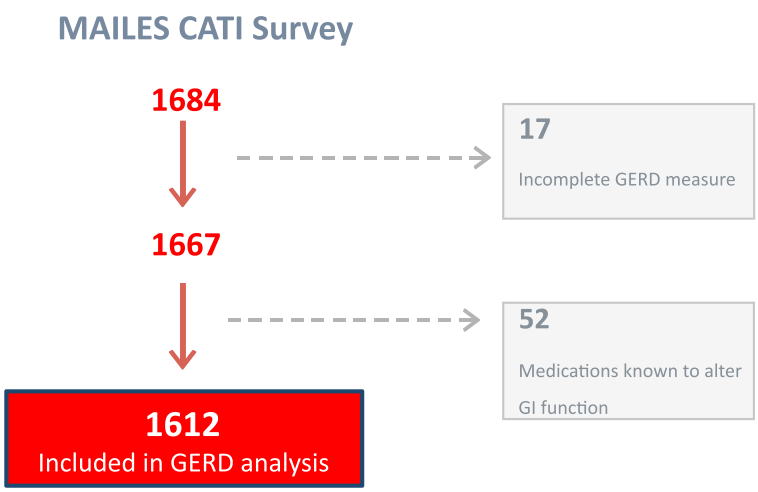

Figure 1 Flow diagram of study participants. CATI, computer-assisted telephone interview; GERD, gastroesophageal reflux disease; GI, gastrointestinal; MAILES, Men Androgen Inflammation Lifestyle Environment and Stress. [Color figure can be viewed at wileyonlinelibrary.com]

Sleep measures. Obstructive sleep apnea was defined as an Apnea–Hypopnea Index (AHI) of at least 10 events per hour of sleep recorded by an eight-channel in-home polysomnography unit (Embletta X100, Embla Systems, Broomfield, Colorado, USA) study from August 2010 to February 2011. The Epworth Sleepiness Scale (ESS)[26] was administered (ranges 0–24), and scores of ≥10 were used to indicate instances of daytime sleepiness. The Pittsburgh Sleep Quality Index was administered to participants to determine self-report sleep quality for the past month. It comprised 10 questions with 9 subquestions, and higher scores indicated lower sleep quality.[27]

Other covariate data. Anthropometric measures (body mass index [BMI] and waist circumference), blood pressure, grip strength, and body composition (by dual energy X-ray absorptiometry) were obtained during one hour clinic visits during MAILES 2. Information on age, education, income, marital, occupational, smoking, alcohol consumption, and other disease status was obtained by self-report questionnaire sent 2 weeks prior to this clinic visit.[19] Medication use was determined by self-report and data linkage with the national medication registry.

Statistical analysis. Descriptive differences among selected variables for men with and without GERD were initially examined using chi-squared and *t*-tests for categorical and continuous variables, respectively. A dichotomous GERD variable was applied as the outcome variable and differences among those with and without GERD in regard to anxiety, depression, and quality of sleep were tested using multistep regression models. Models were adjusted for gross annual household income, highest education status achieved, BMI, smoking status, cardiovascular conditions, and cancer. Where appropriate, all potential confounders and interaction terms were checked in the statistical models. A sensitivity analysis of the influence of sleep quality was performed by selectively removing both sleep quality and depression/anxiety from the final multi-adjusted model and observing the effect on the association between GERD, sleep quality, depression, and anxiety. All analyses were conducted using SPSS V.22 for Windows, and all tests were two-tailed with conventional $P < 0.05$ applied as the significance threshold.

Results

The characteristics of the men with and without GERD are presented in Table 1. The overall prevalence of GERD was 13.7% of men aged 35–80 years (interquartile range: 17). No age difference was observed between men with and without GERD. When comparing men with GERD symptoms and those without, participants with GERD were found to have significantly higher levels of current smoking, CVD, cancer in the previous 5 years, and poorer sleep quality. No differences were found between groups with regard to marital status, household income, work and education status, BMI, waist circumference, abdominal fat mass, physical activity, smoking, alcohol, systolic and diastolic blood pressure, diabetes, AHI, number of medications used, and medications for acid-related disorders.

The multivariable logistic regression is shown in Table 2. In the unadjusted logistic regressions, there were significant associations between current anxiety (odds ratio [OR] 3.1; 95% confidence interval [CI] 1.9–5.1), previous depression (OR 1.9; 95% CI 1.0–3.5), current depression (OR 2.8; 95% CI 2.0–3.9), and self-reported poor sleep quality (OR 2.1; 95% CI 1.4–3.2) and self-reported daytime sleepiness on the ESS (OR 2.4; 95% CI 1.5–3.9), but not the AHI (OR 0.9; 95% CI 0.5–1.6) and instances of GERD. After adjusting for household income, education status, BMI, smoking status, cardiovascular conditions, cancer, and work status, the association between GERD and current anxiety (OR 2.7; 95% CI 1.0–6.8) and self-reported poor quality of sleep (OR 1.8; 95% CI 1.2–2.9) remained, but was not observed for the other sleep measures (ESS and AHI). No effect was observed for current depression (OR 1.5; 95% CI 0.8–2.7) following adjustment for these covariates.

To assess for possible mediating effects of poor sleep quality, this measure was removed from the final model (model 2). In model 2, a multi-adjusted effect of current depression on GERD was observed (OR 2.6; 95% CI 1.7–3.8), with an increase in the effect of current anxiety (OR 3.2; 95% CI 1.8–6.0), but not previous depression (OR 1.4; 95% CI 0.7–2.8).

In models 3 and 4, when poor sleep quality was reintroduced in the model and removing anxiety and depression, respectively, it was found that previous and current depression on GERD remained insignificant (OR 1.7; 95% CI 0.7–4.2; OR 1.6; 95% CI 0.9–2.9, respectively), while the association between current anxiety and GERD was retained (OR 2.8; 95% CI 1.1–6.7). This suggested that poor sleep quality significant drives the association between GERD and depression, but not anxiety.

Figures 2 and 3 show the multi-adjusted regression coefficients of the individual components from the combined depression and anxiety variables on the presence of GERD. For people who currently suffered from depression, the effect of symptoms, specifically somatic-type symptoms, appeared to drive the observed association with GERD (OR: 4.0; 95% CI: 1.7–9.1). For people who currently suffered from anxiety, the effect of symptoms, specifically somatic-type symptoms, appeared to drive the observed association with GERD (OR: 6.5; 95% CI: 1.3–32.9). No effect on GERD was observed for the previous diagnosis of and/or medication usage for either depression or anxiety.

Discussion

This study of community-based middle-aged to elderly men demonstrated a high prevalence of GERD, with around one in six men reporting these symptoms. Further, multivariable logistic regression analyses demonstrated a strong independent association between GERD and anxiety, while suggesting that the previously reported association between depression and GERD may be mediated through poorer sleep quality.

Our study reports a higher prevalence of GERD than previous Australian studies,[3,4] but is consistent with the prevalence data reported in recent clinical studies.[5,13] This discrepancy may relate to the use of a different GERD measure administered by general practitioners and the inclusion of younger men and women.[3] It may also reflect recent observations of secular increases in upper gastrointestinal chronic conditions.[5] A recent meta-analysis of 15 studies found an approximate prevalence of 10–20% prevalence in Western nations and less than 5% prevalence in Asian countries.[5] Discrepancies in prevalence reported in the various studies

Table 1 Descriptive characteristics of study participants with and without GERD in a population of middle-aged and elderly men

Variable	GERD				*P*
	No GERD (*n* = 1391)		GERD (*n* = 221)		
	%/*x*	*N*/SD	%/*x*	*N*/SD	
Anxiety					
No	90.6	1159	79.3	161	
Current	9.5	121	20.7	42	<0.001
Depression					
No	81.2	1079	62.9	132	
Previous	4.6	61	6.7	14	
Current	14.2	189	30.5	64	<0.001
Age (groups)					
35–44 years	6.5	88	6	13	
45–54 years	25.7	348	26.9	58	
55–64 years	31.3	423	31.9	69	
65–74 years	23.5	317	14.4	45	
75+ years	13	176	12.4	31	0.91
Marital status					
Married/defacto	78.4	1057	78.6	169	
Divorced/separated	11.7	157	10.2	22	
Widowed	4	54	5.6	12	
Never married	5.9	80	5.6	12	0.69
Household income					
Up to 20 000	12.9	164	14.6	30	
20 001–40 000	23	292	26.8	55	
40 001–60 000	19.8	252	23.4	48	
60 000+	44.3	563	35.1	72	0.11
Work status					
Employed	61.2	775	55.3	110	
Unemployed	38.8	492	44.7	89	0.11
Education status					
Up to high school	27.7	372	25.2	54	
Trade/apprenticeship	25.1	337	22.9	49	
Certificate/diploma	32.3	433	41.1	88	
Bachelor+	14.8	199	10.8	23	0.06
BMI (kg/m) groups					
Normal 18.5–24.9	18.6	246	21.9	47	
Overweight 25.0–29.9	47.2	624	43.7	94	
Obese 30.0+	34.1	451	34.4	74	0.17
Waist circumference[†]					
<99.9 cm	50.3	664	53	114	
≥100.0 cm)	49.7	656	47	101	0.46
Abdominal fat mass [Δ] (%; DEXA)	36.7	8.3	37.6	7.7	0.10
Physical activity (Active Australia)[‡]					
No activity or activity but insufficient to confer benefit	28.8	320	30.9	55	
Sufficient activity to confer benefit	71.2	790	69.1	123	0.57
Smoking					
Non-smoker	42.1	563	34	73	
Ex-smoker	43.9	587	48.4	104	
Current smoker	14	187	17.7	38	0.06
Alcohol[§]					
Does not drink alcohol	13.3	180	15.7	34	
No risk	49.3	665	48.2	104	
Lifetime risk of alcohol-related harm	37.4	504	36.1	78	0.63
Systolic BP (mmHg)	134.3	17.6	134.0	16.8	0.82
Diastolic BP (mmHg)	81.9	9.2	82.7	9.7	0.24
Cardiovascular disease[¶]					
No	89.4	1204	84.3	182	

(Continues)

Table 1. (Continued)

Variable	GERD				*P*
	No GERD (*n* = 1391)		GERD (*n* = 221)		
	%/*x*	*N*/SD	%/*x*	*N*/SD	
Yes	10.6	143	15.7	34	0.03
Diabetes					
No	81.4	1101	80.6	174	
Yes	18.6	251	19.4	42	0.76
Cancer in the past 5 years					
No	93.9	1270	88.9	192	
Yes	6.1	82	11.1	24	0.01
Chronic diseases[††]					
No	41.4	518	39.6	80	
1+	58.6	734	60.4	122	0.64
Total number of medications[‡‡]					
None	64.9	759	65.8	121	
1	11	129	9.2	17	
2+	24	281	25	46	0.76
Drugs for acid-related disorders					
None	90.3	1055	86.4	159	
1+	9.8	114	13.6	25	0.11
PSQI sleep quality					
Good	55.3	383	37.1	43	
Poor	44.7	310	62.9	73	<0.001
Daytime sleepiness ESS					
No	88.7	630	76.5	91	
Yes	11.3	80	23.5	28	<0.001
AHI					
None to mild OSA	73.9	519	78	92	
Mild OSA	14.1	99	11	13	
Moderate to severe OSA	12	84	11	13	0.61

Data presented are mean ± SD (continuous) or *N* (%) (categorical) for participants with and without GERD, cancer, diabetes, chronic beryllium disease, rheumatoid or osteoarthritis, and high cholesterol).

[†]Waist circumference—mean of three measurements (cm).

[‡]Physical activity is measured by duration and frequency of walk, gardening, household, etc.

[§]Participants were asked about their alcohol consumption in the previous week and 12 months, with responses used to estimate lifetime alcohol risk and categorized into (i) does not drink alcohol, (ii) low lifetime alcohol-related risk, and (iii) high lifetime risk of alcohol-related risk.

[¶]Cardiovascular disease included heart attack, stroke, angina, TIA, and other heart conditions.

[††]Chronic diseases are based on self-reported cases of physician-diagnosed conditions.

[‡‡]Total number of medications was based on self-report.

AHI, Apnea–Hypopnea Index; BMI, body mass index; BP, blood pressure; DEXA, X-ray absorptiometry; ESS, Epworth Sleepiness Scale; GERD, gastroesophageal reflux disease; OSA, obstructive sleep apnea; PSQI, Pittsburgh Sleep Quality Index; TIA, transient ischemic attack.

may be attributable to varying diagnostic criteria, highlighting the need for a global consensus on a symptom-based definition of GERD.

In contrast to previous studies, we defined both depression and anxiety by current symptomology, self-reports of a physician-diagnosis, and the use of relevant medications. Our sensitivity analyses demonstrated that it was primarily somatic symptoms that drove the association between GERD and both depression and anxiety. Previous studies have highlighted an overlap in depressive symptoms and reflux disease (e.g. heartburn, regurgitation, and dysphagia in patients with reflux disease) in patients with irritable bowel disease.[2] We have extended these findings to a group of community-based men, suggesting that any patient who reports such symptoms should also be screened for depression and especially somatic symptoms. Indeed, the full PHQ battery contains modules for depression, anxiety, and somatization that might be especially useful. The strong effect we observed for anxiety on GERD symptoms was similar to that recently observed in a large community-based study of otherwise healthy Norwegian men and women.[28] While this study also demonstrated a strong association between a range of somatic symptoms (including heartburn) and anxiety in men, our study extends these findings to all GERD symptoms and controls for the presence of other comorbidities that also produce somatic symptoms (e.g. CVD, cancer, and alcohol consumption). However, considering that increased sensitivity underlies many anxiety disorders and subclinical symptoms, we cannot rule out that anxious participants were more hypervigilant to somatic symptoms including gastroesophageal reflux.

Table 2 Odds ratios (95% CI) for GERD according to sociodemographic factors, depression, anxiety, and sleep quality in a community-based cohort of South Australian men

Variables	Unadjusted			Model 1			Model 2			Model 3			Model 4		
	OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI	*P*
Income	0.87	(0.76–0.99)	0.11	1.45	(0.52–4.04)	0.48	1.05	(0.56–1.99)	0.88	1.34	(0.49–3.65)	0.57	1.35	(0.49–3.71)	0.57
Education	1.76	(1.08–2.87)	0.02	0.94	(0.42–2.14)	0.89	1	(0.55–1.81)	0.99	0.94	(0.42–2.13)	0.89	1.05	(0.48–2.32)	0.91
BMI	1.00	(0.97–1.03)	0.17	0.56	(0.31–1.03)	0.06	0.67	(0.42–1.05)	0.08	0.55	(0.30–1.01)	0.06	0.57	(0.31–1.05)	0.07
Work status	0.79	(0.58–1.06)	0.11	1.19	(0.63–2.26)	0.59	1.09	(0.70–1.69)	0.72	1.15	(0.61–2.16)	0.66	1.19	(0.63–2.23)	1.19
Current smoker	1.58	(1.02–2.40)	0.04	2.23	(1.16–4.28)	0.01	1.59	(0.97–2.59)	0.07	2.20	(1.15–4.20)	0.02	2.31	(1.22–4.37)	0.01
Cardiovascular conditions	1.57	(1.05–2.36)	0.03	1.08	(0.47–2.45)	0.86	1.51	(0.94–2.42)	0.09	1.05	(0.46–2.38)	0.92	1.17	(0.53–2.59)	0.79
Cancer in the past 5 years	1.94	(1.20–3.12)	0.01	2.15	(0.96–4.82)	0.06	1.85	(1.06–3.25)	0.03	1.98	(0.89–4.41)	0.09	1.99	(0.90–4.43)	0.09
Current anxiety	3.06	(1.85–5.08)	<0.001	2.65	(1.03–6.80)	0.04	3.23	(1.77–5.97)	<0.001	—	—	—	2.76	(1.14–6.68)	0.03
Current depression	2.77	(1.98–3.87)	<0.001	1.47	(0.81–2.69)	0.21	2.56	(1.72–3.80)	<0.001	1.74	(0.73–4.16)	0.21	—	—	—
Previous depression	1.88	(1.02–3.45)	0.04	1.72	(0.72–4.14)	0.23	1.43	(0.73–2.83)	0.3	1.62	(0.90–2.93)	0.11	—	—	—
Poor sleep quality	2.10	(1.40–3.15)	<0.001	1.83	(1.15–2.89)	0.01	—	—	—	1.93	(1.23–3.03)	<0.01	1.93	(1.23–3.02)	<0.01

†Model 1 is adjusted for income, education, BMI, work status, smoking status, cardiovascular conditions, and cancer status.

‡Model 2 (sleep quality omitted) is adjusted for income, education, BMI, work status, smoking status, cardiovascular conditions, and cancer status.

§Model 3 (anxiety omitted) is adjusted for income, education, BMI, work status, smoking status, cardiovascular conditions, and cancer status

¶Model 4 (depression omitted) is adjusted for income, education, BMI, work status, smoking status, cardiovascular conditions, and cancer status.

CI, confidence interval; BMI, body mass index; GERD, gastroesophageal reflux disease; OR, odds ratio.

It is also well known that acute, reflux symptoms are frequently reported with certain types of depression medication (e.g. selective serotonin reuptake inhibitors).[12,29] Furthermore, previous studies have demonstrated that GERD is more likely to be reported in patients with depression who are taking antidepressants, than those without.[12] However, there is also some suggestion that low doses of antidepressants may be used in the treatment of GERD through their effects on visceral hypersensitivity.[30] Our study demonstrated that antidepressant usage was not associated with likelihood of patients reporting GERD symptoms. However, subsequent analysis suggests there was a modest effect on GERD for higher doses of antidepressants (data not shown). In the case of anxiety, we also did not find that anxiety medications increased the likelihood of GERD. While some studies suggest that anxiolytics may help with GERD through relaxation of lower esophageal tone,[14] others have demonstrated side effects, including reflux, associated with the commencement of anxiolytics for anxiety disorders.[11] Further work is required to understand the nature of the association between GERD and depression and anxiety medications.

Our data suggest the previously reported association between GERD and depression maybe mediated by poorer sleep quality. Poor sleep quality results in lower mood and an increased susceptibility to depressive symptoms.[14] It is known that individuals with either undiagnosed or diagnosed depression are more likely to report a higher degree of severity for various conditions and more likely to endorse negative symptom rating indices.[31] Not only is GERD directly likely to result in increased sleep fragmentation and disturbance, sleep deprivation has also been shown to induce hyperalgesia of the esophageal mucosa in response to acid.[32] Of note, we observed positive associations with GERD and self-reported (poor overall sleep quality and excessive daytime sleepiness) but not objectively measured (AHI) sleep dysfunction.

The strong association between smoking and GERD symptoms is consistent with previous research.[33–36] Acid reflux is often promoted by smoking, as it impairs lower esophageal sphincter function,[33] slowing esophageal acid clearance[34] or increasing the frequency of acid reflux episodes.[35] Of note however, our data showed that there was no association between use of drugs for acid related disorders and GERD. This may be due to the high usage of over-the-counter agents for such conditions in Australia.[37] Unlike many previous studies, we did not observe an association between alcohol consumption and GERD symptoms.[36,38,39] This discrepancy could be to the use of a randomly selected population, with a varying, but mostly modest, range of alcohol consumption and the dominant effect of other covariates.

A notable strength of the present study was the inclusion of community-based men and the use of an extensive dataset to help better understand some of the relationships between mental health, sleep, and GERD. It is acknowledged, however, that inferences regarding the strength of the reported associations are limited by some methodological constraints. Specifically, the use of self-report data for some measures may underestimate the true effect of these observed relationships. As the study assessed a sample of men only, we are unable to generalize to the broader population. Moreover, different depression measures have been adopted in this study. While we were able to examine the effect of both current

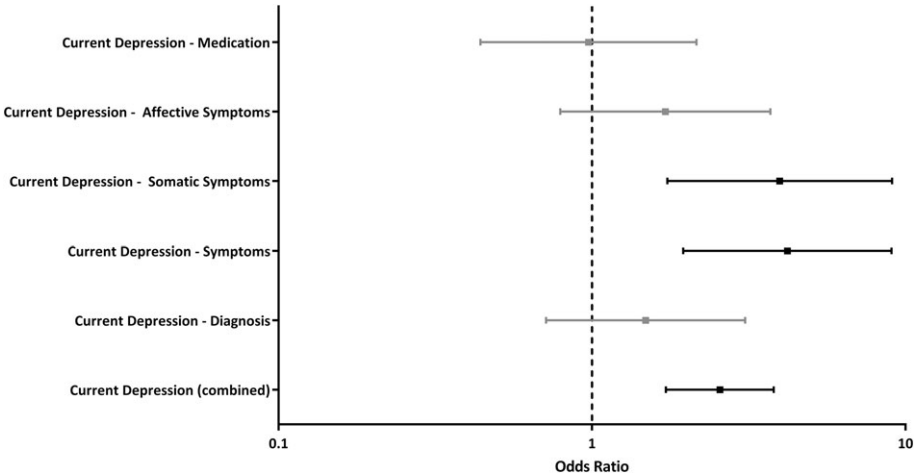

Figure 2 Odds ratio (95% confidence interval) for the effect of individual depressions items (medication, symptoms [somatic and cognitive], and physician diagnosis) for gastroesophageal reflux disease in a community-based cohort of South Australian men with current depression. Data presented are odds ratio (95% confidence interval) from binary logistic regression. Models also adjusted for income, education level, body mass index, smoking status, cardiovascular conditions, cancer in the past 5 years, and working status.

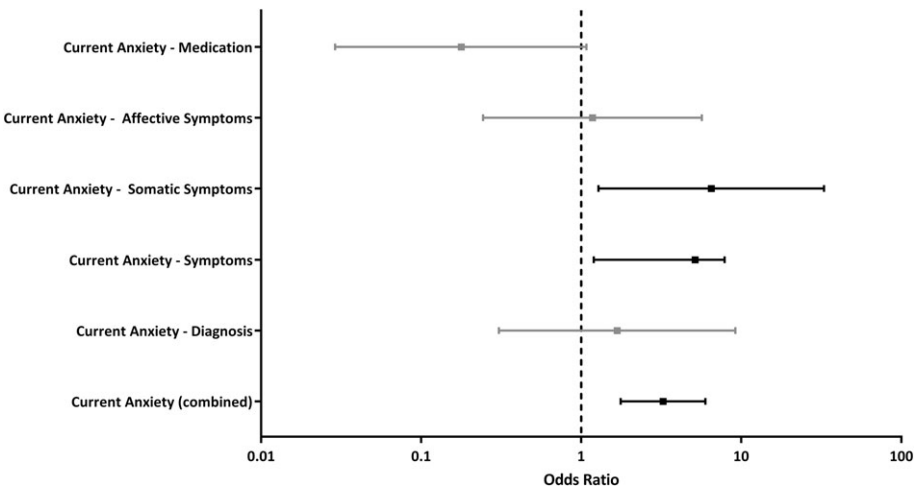

Figure 3 Odds ratio (95% confidence interval) for the effect of individual anxiety items (medication, symptoms [somatic and cognitive], and physician diagnosis) for gastroesophageal reflux disease in a community-based cohort of South Australian men with current anxiety. Data presented are odds ratio (95% confidence interval) from binary logistic regression. Models also adjusted for income, education level, body mass index, smoking status, cardiovascular conditions, cancer in the past 5 years, and working status.

and previous depression on GERD, we were not able to test for exposure length with anxiety given a symptomatic measure for anxiety was unavailable at baseline. Lastly, the use of cross-sectional data only precludes any inferences regarding the direction of the observed relationship. Further research should employ longitudinal design in order to assess the natural course of these associations.

In conclusion, our data support the strong association between depression and anxiety, particularly somatic symptoms, and GERD in community-based men. In the case of depression, it appears this association may, in part, be mediated by poorer sleep quality. Good sleep health is pivotal for optimal functional outcomes and perceived health status, particularly among populations with poor mental health. Therefore, health practitioners treating GERD symptoms should perform concomitant assessments of their patients' mental state in order to identify real or perceived confounders to the successful management of their gastrointestinal symptoms.

Acknowledgments

The authors thank the MAILES investigators for their role in the study.

References

1 Lee KJ, Kwon HC, Cheong JY, Cho SW. Demographic, clinical, and psychological characteristics of the heartburn groups classified using the Rome III criteria and factors associated with the responsiveness to proton pump inhibitors in the gastresophageal reflux disease group. *Digestion* 2009; **79**: 131–6.
2 Klauser AG, Schindlbeck NE, Muller-Lissner SA. Symptoms in gastro-esophageal reflux disease. *Lancet* 1990; **335**: 205–8.
3 Knox SA, Harrison CM, Britt HC, Henderson JV. Estimating prevalence of common chronic morbidities in Australia. *Med. J. Aust.* 2008; **189**: 66–70.
4 Kim JI, Kim SG, Kim N *et al.* Changing prevalence of upper gastrointestinal disease in 28 893 Koreans from 1995 to 2005. *Eur. J. Gastroenterol. Hepatol.* 2009; **21**: 787–93.
5 Dent J, El-Serag HB, Wallander MA, Johansson S. Epidemiology of gastro-esophageal reflux disease: a systematic review. *Gut* 2005; **54**: 710–17.
6 Jung HK, Choung RS, Talley NJ. Gastresophageal reflux disease and sleep disorders: evidence for a causal link and therapeutic implications. *J. Neurogastroenterol. Motil.* 2010; **16**: 22–9.
7 Ruigomez A, Garcia Rodriguez LA, Wallander MA, Johansson S, Graffner H, Dent J. Natural history of gastro-esophageal reflux disease diagnosed in general practice. *Aliment. Pharmacol. Ther.* 2004; **20**: 751–60.
8 Corley DA, Kubo A. Body mass index and gastresophageal reflux disease: a systematic review and meta-analysis. *Am. J. Gastroenterol.* 2006; **101**: 2619–28.
9 Ronkainen J, Aro P, Storskrubb T *et al.* Gastro-esophageal reflux symptoms and health-related quality of life in the adult general population—the Kalixanda study. *Aliment. Pharmacol. Ther.* 2006; **23**: 1725–33.
10 Jansson C, Nordenstedt H, Wallander MA *et al.* Severe symptoms of gastro-esophageal reflux disease are associated with cardiovascular disease and other gastrointestinal symptoms, but not diabetes: a population-based study. *Aliment. Pharmacol. Ther.* 2008; **27**: 58–65.
11 Avidan B, Sonnenberg A, Giblovich H, Sontag SJ. Reflux symptoms are associated with psychiatric disease. *Aliment. Pharmacol. Ther.* 2001; **15**: 1907–12.
12 Martin-Merino E, Ruigomez A, Garcia Rodriguez LA, Wallander MA, Johansson S. Depression and treatment with antidepressants are associated with the development of gastro-esophageal reflux disease. *Aliment. Pharmacol. Ther.* 2010; **31**: 1132–40.
13 Sanna L, Stuart AL, Berk M, Pasco JA, Girardi P, Williams LJ. Gastro esophageal reflux disease (GORD)-related symptoms and its association with mood and anxiety disorders and psychological symptomotology: a population-based study in women. *BMC Psychiatry* 2013; **13**: 194.
14 Kamolz T, Velanovich V. Psychological and emotional aspects of gastresophageal reflux disease. *Diseases of the esophagus : official journal of the International Society for Diseases of the Esophagus / ISDE* 2002; **15**: 199–203.
15 Martin SA, Haren MT, Middleton SM, Wittert GA. The Florey Adelaide Male Ageing Study (FAMAS): design, procedures & participants. *BMC Public Health* 2007; **7**: 126.
16 Sivertsen B, Overland S, Neckelmann D *et al.* The long-term effect of insomnia on work disability: the HUNT-2 historical cohort study. *Am. J. Epidemiol.* 2006; **163**: 1018–24.
17 Wallander MA, Johansson S, Ruigomez A, Garcia Rodriguez LA, Jones R. Morbidity associated with sleep disorders in primary care: a longitudinal cohort study. *Primary care companion to the Journal of clinical psychiatry* 2007; **9**: 338–45.
18 Zee PC, Turek FW. Sleep and health: everywhere and in both directions. *Arch. Intern. Med.* 2006; **166**: 1686–8.
19 Grant JF, Martin SA, Taylor AW *et al.* Cohort profile: the Men Androgen Inflammation Lifestyle Environment and Stress (MAILES) Study. *Int. J. Epidemiol.* 2014; **43**: 1040–53.
20 Grant JF, Taylor AW, Ruffin RE *et al.* Cohort profile: the North West Adelaide Health Study (NWAHS). *Int. J. Epidemiol.* 2009; **38**: 1479–86.
21 Bai Y, Du Y, Zou D *et al.* Gastresophageal reflux disease questionnaire (GerdQ) in real-world practice: a national multicenter survey on 8065 patients. *J. Gastroenterol. Hepatol.* 2013; **28**: 626–31.
22 Dent J, Vakil N, Jones R *et al.* Accuracy of the diagnosis of GORD by questionnaire, physicians and a trial of proton pump inhibitor treatment: the Diamond Study. *Gut* 2010; **59**: 714–21.
23 Lasa L, Ayuso-Mateos JL, Vazquez-Barquero JL, Diez-Manrique FJ, Dowrick CF. The use of the Beck Depression Inventory to screen for depression in the general population: a preliminary analysis. *J. Affect. Disord.* 2000; **57**: 261–5.
24 Irwin M, Artin K, Oxman MN. Screening for depression in the older adult: criterion validity of the 10-item Center for Epidemiological Studies Depression Scale (CES-D). *Arch. Intern. Med.* 1999; **159**: 1701–4.
25 Spitzer RL, Kroenke K, Williams JB, Lowe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch. Intern. Med.* 2006; **166**: 1092–7.
26 Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep* 1991; **14**: 540–5.
27 Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res.* 1989; **28**: 193–213.
28 Haug TT, Mykletun A, Dahl AA. The association between anxiety, depression, and somatic symptoms in a large population: the HUNT-II study. *Psychosom. Med.* 2004; **66**: 845–51.
29 Haug TT, Mykletun A, Dahl AA. The prevalence of nausea in the community: psychological, social and somatic factors. *Gen. Hosp. Psychiatry* 2002; **24**: 81–6.
30 Weijenborg PW, de Schepper HS, Smout AJ, Bredenoord AJ. Effects of antidepressants in patients with functional esophageal disorders or gastresophageal reflux disease: a systematic review. *Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association* 2015; **13**: 251–9. e1.
31 Ohayon MM, Caulet M, Lemoine P. Comorbidity of mental and insomnia disorders in the general population. *Compr. Psychiatry* 1998; **39**: 185–97.
32 Fujiwara Y, Arakawa T, Fass R. Gastresophageal reflux disease and sleep. *Gastroenterol. Clin. North Am.* 2013; **42**: 57–70.
33 Dennish GW, Castell DO. Inhibitory effect of smoking on the lower esophageal sphincter. *N. Engl. J. Med.* 1971; **284**: 1136–7.
34 Kjellen G, Tibbling L. Influence of body position, dry and water swallows, smoking, and alcohol on esophageal acid clearing. *Scand. J. Gastroenterol.* 1978; **13**: 283–8.
35 Kahrilas PJ, Gupta RR. The effect of cigarette smoking on salivation and esophageal acid clearance. *J. Lab. Clin. Med.* 1989; **114**: 431–8.
36 Wong WM, Lai KC, Lam KF *et al.* Prevalence, clinical spectrum and health care utilization of gastro-esophageal reflux disease in a Chinese population: a population-based study. *Aliment. Pharmacol. Ther.* 2003; **18**: 595–604.
37 Westbrook JI, Talley NJ. Diagnostic investigation rates and use of prescription and non-prescription medications amongst dyspeptics: a population-based study of 2300 Australians. *Aliment. Pharmacol. Ther.* 2003; **17**: 1171–8.
38 Mohammed I, Nightingale P, Trudgill NJ. Risk factors for gastro-esophageal reflux disease symptoms: a community study. *Aliment. Pharmacol. Ther.* 2005; **21**: 821–7.
39 Vitale GC, Cheadle WG, Patel B, Sadek SA, Michel ME, Cuschieri A. The effect of alcohol on nocturnal gastresophageal reflux. *JAMA* 1987 Oct 16; **258**: 2077–9.