University of Groningen

Self-reported health outcomes in patients with obstructive sleep apnoea

Timková, Vladimíra

DOI:
[10.33612/diss.136425533](https://doi.org/10.33612/diss.136425533)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2020

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):
Timková, V. (2020). *Self-reported health outcomes in patients with obstructive sleep apnoea: Unraveling the role of bio-psycho-social factors*. [Thesis fully internal (DIV), University of Groningen]. University of Groningen. <https://doi.org/10.33612/diss.136425533>

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Self-reported health outcomes in patients with obstructive sleep apnoea

Unraveling the role of bio-psycho-social factors

Vladimira Timkova

Copyright
© Vladimira Timkova

Thesis for the University of Groningen, the Netherlands – with summaries in Dutch and Slovak.

All rights reserved. No parts of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any means electronic, mechanical, photocopying, recording or otherwise, without prior written permission of the author.

Correspondence:
Vladimira Timkova
vladimira.timkova@upjs.sk

This work was supported by the Slovak Research and Development Agency under contracts APVV-15-0719 (80%); and by the Agency of the Ministry for Education of the Slovak Republic for the Structural Funds of the European Union, Operational Programme Research and Development (Contract No. 034/2009/2.1/OPRandD) (20%).

The printing of this thesis was supported by the Graduate School for Health Research (SHARE), the Graduate School Kosice Institute for Society and Health (KISH), the University Medical Center Groningen (UMCG) and the University of Groningen (RUG).

Design and layout: Diana Matláková
Book cover: Diana Matláková
Artwork: Armando Bravo
Language corrections: David L. McLean
Press: Equilibria Košice, s.r.o.
Printed in Slovakia

ISBN: 978-80-8143-277-4

university of
 groningen

Self-reported health outcomes in patients with obstructive sleep apnoea

Unraveling the role of bio-psycho-social factors

PhD thesis

to obtain the degree of PhD at the
University of Groningen
on the authority of the
Rector Magnificus Prof. C. Wijmenga
and in accordance with
the decision by the College of Deans.

This thesis will be defended in public on
Wednesday 11 November 2020 at 11.00 hours

by

Vladimira Timkova

born on 15 November 1987
in Kosice, Slovakia

Contents

Supervisors

Prof. U. Bültmann

Prof. R. Tkacova

Dr. J. P. van Dijk

Co-supervisor

Dr. I. Nagyova

Assessment Committee

Prof. R. Ptacek

Prof. G. J. Navis

Prof. P. J. Wijkstra

Chapter 1	
Introduction	9
Chapter 2	
Design of the study and data sources	43
Chapter 3	
Quality of life of obstructive sleep apnoea patients receiving continuous positive airway pressure treatment: a systematic review and meta-analysis	57
Chapter 4	
Are disease severity, sleep-related problems and anxiety associated with work functioning in patients with obstructive sleep apnoea?	91
Chapter 5	
Psychological distress in patients with obstructive sleep apnoea: the role of hostility and coping self-efficacy	117
Chapter 6	
Suicidal ideation in patients with obstructive sleep apnoea and its relationship with disease severity, sleep-related problems and social support	143
Chapter 7	
Social support, mastery, sleep-related problems and their association with functional status in untreated obstructive sleep apnoea patients	163
Chapter 8	
General discussion, implications, and conclusions	187
Summary	223
Sammenvattig	227
Zhrnutie	231
Acknowledgements	235
About the author	237
Supplements	239
Graduate School Kosice Institute for Society and Health (KISH) and previous dissertations	251
Groningen Graduate School of Medical Sciences - Research Institute SHARE and previous dissertations	257

List of abbreviations

AHI	Apnoea-Hypopnoea Index
BAI	Beck Anxiety Inventory
CMHo	Cook Medley Hostility Scale
CPAP	Continuous Positive Airway Pressure
CSE	Coping Self-Efficacy
ESS	Epworth Sleepiness Scale
FOSQ	Functional Outcomes of Sleep Questionnaire
GHQ-28	General Health Questionnaire
MFI	Multidimensional Fatigue Inventory
MLR	Multiple linear regression analyses
MSPSS	Multidimensional Scale of Perceived Social Support
OSA	Obstructive Sleep Apnoea
PMS	Pearlin Mastery Scale
PROMs'	Patients' reported outcome measures
PSC	Polysomnography
PSQI	Pittsburgh Sleep Quality Index
QoL	Quality of Life
RCTs	Randomised Controlled Trials
WRFQ 2.0	Work Role Functioning Questionnaire 2.0

"Sleep is the most
innocent creature there
is and a sleepless man
the most guilty."

Franz KAFKA

Chapter 1

Introduction

Obstructive sleep apnoea (OSA) is a common chronic disorder that often requires lifelong care (Force AOSAT and American Academy of Sleep Medicine, 2009). We aimed to extend current knowledge on the factors which may be closely related to the management of this chronic disease. Therefore, this study on OSA focuses on the bio-psycho-social factors that have been identified as key determinants of health outcomes in various chronic diseases, but for which less is known about their role in OSA. This chapter covers the theoretical background of the study, describes the theoretical model used for the study, presents the aims and the specific research questions, and concludes with the outline of the thesis.

1.1 Obstructive sleep apnoea: definition, symptoms and epidemiology

OSA is defined as a repetitive, intermittent cessation of air flow at the nose and mouth during sleep. The clinical syndrome is characterized by repeated episodes of upper-airway occlusion during sleep, which can be complete (apnoea) or incomplete (hypopnoea) and of varying duration (Leung, 2019). Patients with OSA often snore and report daytime sleepiness (Manarino et al., 2012; Peppard et al., 2013) and fatigue (Manarino et al., 2012).

OSA concerns 2–10% of the adult population (Leger et al., 2012); it is more prevalent in men compared with women and extremely rare in premenopausal women (Krystal et al., 1998). Most population-based studies have identified a gender-specificity in OSA prevalence, i.e. a 2- to 3-fold greater risk for males compared to females (Strohl and Redline, 1996; Quintana-Gallego et al., 2004). OSA prevalence and severity have also been found to rise linearly with age (Bixler et al., 1998; Gabbay and Lavie, 2012). Depending on age, the prevalence of moderate and severe OSA (apnoea-hypopnoea index; AHI ≥ 15) among men is 10–17% and among women 3–9% (Peppard et al., 2013). These estimated prevalence rates represent substantial increases over the last two decades, with relative increases of between 14% and 55% (Peppard et al., 2013).

Furthermore, the majority of people with OSA are typically unaware of apnoea/hypopnoea episodes. Although long-term consequences, such as fatigue, excessive daytime sleepiness, and increased cardiovascular and cerebrovascular risk, may be severe, symptoms often begin subtly and gradually and may remain underestimated for many years, noticed by bed partners only (Schmalzing and Afari, 2000). Previous studies have concluded that OSA affects approximately 20% of US adults (Young et al., 2002; Finkel et al., 2009), about 90% of whom may be undiagnosed (Finkel et al., 2009). Thus, OSA remains a largely underdiagnosed and undertreated problem, although its impact on both morbidity (Macey et al., 2010; Rottapel et al., 2019) and socio-economic costs (Leger et al., 1994; Wittmann and Rodenstein, 2004; Mulgrew et al., 2007; Leger et al., 2012) is enormous.

Sleep-disordered breathing has major socioeconomic consequences for patients and their spouses both years before and after diagnosis (Jennum et al., 2014). Compared to healthy people, individuals suffering from OSA are less productive,

have increased health care utilization, an increased likelihood of accidents (Karimi et al., 2015), reduced work capacity, and work participation (Mulgrew et al., 2007; Leger et al., 2012). Sleep loss among partners of OSA patients also results in frustration, exhaustion, interference with work, and strained relationships (Luyster et al., 2016). It has been shown that untreated OSA patients have up to two-times greater health care costs when compared with controls without OSA (Wittmann and Rodenstein, 2004). Costs of undiagnosed people with OSA include direct costs due to possible consequences, such as driving accidents, as well as the development of comorbidities such as cardiovascular diseases, diabetes, metabolic syndrome, and an increased overall mortality rate (Tkacova and Dorkova, 2010; Leger et al., 2012; Pack et al., 2012; Ayas et al., 2014). Although the exact costs are difficult to calculate, data from 106 countries showed that increased healthcare spending to treat undiagnosed OSA varies between 1,950 and 3,899 dollars per patient per year, which represents approximately a total of 3.4 billion dollars per year (Knauert et al., 2015). These costs are usually caused by more frequent practitioner visits, increased hospitalizations, and the development of comorbidities (Wittmann and Rodenstein, 2004).

OSA-related symptoms such as sleep disruption, snoring, sleep-related choking, insomnia, nocturia, disruption of bedpartner's sleep, morning headaches, impairments in productivity, poor-quality relationships, and daytime fatigue have been shown to have a negative impact on patients' psychological well-being, quality of life (QoL), and functional status (Young et al., 2002; Sharafkhaneh et al., 2005; Mulgrew et al., 2007; Tsara et al., 2009; Antic et al., 2011; Weaver, 2013; Rezaeitalab et al., 2014; Patil et al., 2019). Besides physical impacts, OSA is associated with a higher prevalence of neuropsychiatric comorbidities or symptoms (Sharafkhaneh et al., 2005; Tkacova and Dorkova, 2010; Lin and Winkelmann, 2012; Kang et al., 2012), such as anxiety (Sharafkhaneh et al., 2005; Krakow et al., 2015), depression, posttraumatic stress disorder, psychosis, or dementia (Sharafkhaneh et al., 2005). Choi et al. (2015) reported an increased prevalence of suicidal ideation in OSA patients when compared to the general population. Moreover, psychological distress may reversely influence the progress of OSA-related physical symptoms (e.g. Hall et al., 2004; Krakow et al., 2015).

Another source of concern is that diagnosing OSA may often represent a difficult task for health care professionals because of the patient's unawareness and the variations in presentation (Lurie, 2011; Peppard et al., 2013). Moreover, patients presenting with fatigue or daytime sleepiness may be misdiagnosed with depression or other illness (Lin et al., 2008).

1.2 Measuring self-reported health outcomes in obstructive sleep apnoea

In many areas of medicine, patient-reported outcome measures (PROMs) are gaining substantial attention as priority components to assess when gauging the effect of treatment for all manner of diseases (Tam et al., 2014; Pang et al., 2016; Appleby

et al., 2016). OSA disabling symptoms pose multiple challenges on patients' health outcomes, such as well-being, QoL, and functional status (Antic et al., 2011; Weaver, 2013; Jackson et al., 2018). Therefore, along with an increase of OSA, the assessment of self-reported health outcomes has gained attention and become an important construct in this chronic disease (Kushida et al., 2012; Tam et al., 2014).

The gold standard diagnostic test for OSA is the overnight polysomnography (PSG) (Epstein et al., 2009). During an overnight polysomnogram, the frequency of obstructive events is reported as the apnoea-hypopnoea index (AHI). The severity of OSA is based on the number of apnoea and hypopnoea events per hour (American Academy of Sleep Medicine, 2005). However, there is a discrepancy between the AHI levels used to denote outcomes of therapy and real-world outcomes, such as QoL, functional status, patient perception of disease, cardiovascular measures, or survival (Tam et al., 2014). Some previous studies on continuous positive airway pressure (CPAP) treatment effectiveness (Weaver et al., 2005; Kushida et al., 2012; Tam et al., 2014) also favour the usage of QoL and functional status measures together with AHI; yet in the case of OSA, the AHI remains persistent as the primary, and frequently the only, outcome measure reported in the vast majority of research and clinical practice (Pang et al., 2016).

Therefore, screening PROMs based on self-reported symptoms of OSA is important for gaining information on the prevalence and comorbid conditions of OSA or on CPAP treatment effectiveness (Weaver et al. 2005; Sivertsen et al., 2008; Kushida et al., 2012). Moreover, patients' self-reported outcomes represent any assessment coming directly from patients, without interpretation by a health care professional or others, about how they function or feel in relation to their health condition. Thus, identifying issues faced by patients and their families about living with an illness can generate knowledge that may consequently impact treatment decisions and adherence. In general, the use of PROMs may enhance the understanding of how health-practitioners can affect health outcomes (Krabbe et al., 2017).

1.2.1 Functional status

Recent studies have emphasized the importance of studying patients' functional status in sleep medicine research, because of its ability to provide insights that may go beyond the pathophysiology of commonly investigated OSA-related symptoms (Boccabella and Malouf, 2017). Functional status is defined as an individual's ability to perform normal daily activities or tasks that are essential to meet basic needs and fulfill usual roles (Wilson and Cleary, 1995). The concept of functional status consists of two main domains: capacity and performance. Functional capacity can be defined as a person's maximum ability to perform daily activities in the physical, psychological, and social domains of life, whereas functional performance refers to what people actually do in the course of their daily living (Leidy, 1994). Both domains can be influenced by biological or physiological impairment, symptoms, and mood impairments but also by health perceptions (Krabbe, 2017). There is general consensus that physical function, social function, role function, and psychological

function represent the minimum required to define and measure functional status (Sherbourne et al., 1992).

Previous research has shown an impairment of functional status (Reishtein et al., 2006; Perimenis et al., 2007; Weaver et al., 2007; Tippin et al., 2016), including impairment of work functioning, in OSA patients (Wittmann and Rodenstein, 2004; Mulgrew et al., 2007; Reuveni et al., 2008; Sivertsen et al., 2008; Leger et al., 2012). Furthermore, the current studies show that the treatment response is inadequate to return OSA patients to the functional level of healthy individuals who are asymptomatic of sleep-disordered breathing, and that CPAP treatment may not improve function in a dose-response manner (Weaver, 2013; Tippin et al., 2016; Jackson et al., 2018).

1.2.2 Work functioning

The prevalence of OSA is high; the disease affects 9% of the female and 24% of the male working-age population (Young et al., 2009). While OSA is a non-occupational disease, given its frequency, comorbidities, and potential to impair work functioning, it is inevitable that it may manifest as an important health and safety issue in the workplace (Kales and Czeisler, 2016). Sleep disturbances, excessive daytime sleepiness and frequent awakeness showed to be a risk factors with respect to occupational accidents (Cappuccio et al., 2010). Moreover, the economic costs of OSA on health care systems, as well as on individuals and their households, have also substantial relevance. Previous studies have focused mainly on the economic impact of OSA on public health systems (Wittmann and Rodenstein, 2004; Reuveni et al., 2008) and occupational accidents (e.g. Garbarino et al. 2016), while the assessment of work functioning was not prominent. Some studies have evaluated work performance in patients with OSA, but results have been disputed (Jurado-Gómez et al., 2015). Few previous studies showed a significant impairment of work functioning in patients with OSA (Mulgrew et al., 2007; Sivertsen et al., 2008; Omachi et al., 2009). According to Reishtein, OSA patients have difficulties to complete a task at work, feel a lack of trust from coworkers and report subsequent embarrassment (Reishtein et al., 2006). Working OSA patients were also found to have low productivity levels and a high rate of psychological distress (Jurado-Gómez et al., 2015).

1.2.3 Health related quality of life

The main goal for the treatment of OSA is to prevent complications and comorbidities, while preserving a good quality of life (QoL). Knowledge about the role of biopsychosocial factors and their associations with patients' health outcomes is therefore of great importance (Haslam et al., 2018). The World Health Organisation Quality of Life (WHOQoL) group defined QoL as '*an individual's perception of their position in life, in context of the culture and values in which they live and in relation to their goals, expectations, standards and concerns*' (WHOQoL Group,

1994). QoL has several domains, like functional competence, health-related complaints and psychological and social functioning. Health-related quality of life (HRQoL) is considered to be an integral domain of QoL. When QoL is discussed in relation to health or diseases, it almost always means HRQoL, unless specified otherwise (Dutt et al., 2016). HRQoL is increasingly used as an outcome of treatment effectiveness. In broad terms, HRQoL serves as a restricted definition of QoL in the sense that it was designed to exclude externalities, such as housing, financial situation, living conditions, or spirituality. HRQoL is associated with an expanded concept of health status, one embracing social interaction as well as emotional and psychological well-being (Krabbe, 2017). According to Schipper (1992) QoL in clinical medicine represents the functional effects of illness and its consequent treatment upon patient, as perceived by the patient. Because the concepts of QoL and HRQoL are closely tied to each other (Dutt et al., 2016), we will use them in this paper interchangeably, with omission of external domains such as spirituality, or living conditions.

1.2.4 Psychological distress

Psychological distress is understood as the opposite continuum to psychological well-being (Goldberg and Hillier, 1979; Spiteri et al., 2013). The World Health Organisation (WHO, 2012) states that *‘well-being exists in two dimensions, subjective and objective. It comprises an individual’s experience of their life as well as a comparison of life circumstances with social norms and values’*. Health is projected as an integral component of well-being, while good health represents a necessary condition for attaining the highest possible levels in all other aspects of well-being (Salomon et al., 2003). The relationship between health and well-being is interdependent; health influences well-being and well-being itself influences health. There are a number of associations between psychological well-being and physical health outcomes, such as improved immune system response, higher pain tolerance, increased longevity, improved cardiovascular health, or slower disease progression (Howell et al., 2007; Steptoe et al., 2015).

1.2.4.1 Suicidal ideation

Suicide and attempted suicide are major public health concerns with complex aetiologies which encompass a multifaceted array of risk and protective factors (O’Connor, 2017). Suicide is an important cause of death worldwide. Globally, more than 800,000 people take their life every year, and there are many more suicide attempts (World Health Organization, 2016). Suicidal ideation and suicidal behaviours have been conceptualised to lie on a continuum, whereby those who experience suicidal ideation may progress to make suicide plans and then, subsequently, make an attempt or die by suicide (Tarrier et al., 2013). Indeed, data from a cross-national study of 17 countries estimated that 33.6% of individuals who experience suicidal ideation will subsequently develop a suicide plan, and 56% of those with a plan will make a suicide attempt (Nock et al., 2008). Therefore, identifying

and intervening at the start of this trajectory is imperative for developing effective suicide prevention strategies. Recent approaches have defined suicide as a health behaviour, in the sense that a person makes a decision to take his/her own life, so an appreciation of the psychology of the suicidal mind is crucial to suicide prevention (O’Connor, 2017). One of the key developments in the field of suicide theory and research is the ideation-to-action framework, which stipulates that the development of suicidal ideation and the progression from suicidal ideation to suicidal behaviour are distinct phenomena with distinct explanations and predictors (Klonsky, 2016). Moreover, there is growing recognition that we need to move beyond psychiatric categories to further understand the pathways leading from suicidal ideation to suicidal behaviour (O’Connor, 2017).

Suicidal ideation is a common health concern in primary care (Rückert-Eheberger et al., 2019). The findings of previous studies support the need to screen for suicidality in general medical settings, over and above the use of general depression instruments (Druss and Pincus, 2000; Krakow et al., 2011). A significant association was found between chronic medical conditions and suicidality, and it persisted after adjusting for depressive disorder or alcohol abuse (Druss and Pincus, 2000). A total of 25.2% of individuals with a general medical condition and 35.0% of those with two or more medical illnesses reported lifetime suicidal ideation (Tang and Crane, 2006). The lifetime prevalence of suicide attempts was between 5 and 14% in individuals with chronic pain, and the prevalence of suicidal ideation was 20% (Tang and Crane, 2006).

A growing body of research indicates that sleep disturbances are associated with suicidal ideation and suicidal behaviors. To date, however, the majority of the research has focused on insomnia. Sleep disorders differentially affect functioning, and the relationship between OSA and suicide has yet to be established. OSA, in contrast to insomnia, is characterized by frequent awakenings that disrupt the natural progression of sleep cycles and sleep architecture. Thus, patient with OSA may in fact obtain more total sleep time than the typical insomnia patient; however, the sleep of the OSA patient may be less restorative. Because of this etiologic difference, it is unclear what aspect of generalized sleep disturbance contributes to suicide risk. For example, if the association between sleep and suicide only represents a function of the loss of total sleep time, then sleep disorders such as OSA, that do not significantly reduce total sleep time, should not be associated with increased suicide risk. However, if the association between sleep and suicide is related to other aspects of sleep disturbances (e.g. hypersomnolence, fatigue, or neurophysiologic changes), then OSA and other sleep disorders may emerge as being associated with increased suicide risk (Bishop, et al., 2018).

Recently, an increased suicidal ideation has been observed in patients treated in medical sleep centres (Krakow et al., 2011), including patients with OSA (Choi et al., 2015). Sleep-related problems were found to pose multiple challenges for mental and physical functioning. Poor night-time sleep quality was found to be associated with an increased risk of committing suicide in one decade even when adjusted for depressive symptomatology (Bernert et al., 2014). Krakow et al. (2011)

found an association between sleep-related problems and suicidal ideation in patients treated in medical sleep centres, which remained significant after controlling for depression. In 2015, Choi et al. reported a suicidal ideation prevalence of 20.5% in a Korean population among OSA patients, but information about the prevalence of suicidal ideation in OSA patients in other countries is lacking. Consequently, it is important to understand the associations between sleep-related problems, suicidal ideation, and suicidal behaviour. Another source of concern is that people with sleep problems suffering from psychological distress rarely seek formal mental health care (Weissman et al., 1997; Wojnar et al., 2009). Therefore, the idea of depending solely on the available psychological and psychiatric care to detect individuals at risk of suicidal ideation may be insufficient for early suicide prevention efforts, especially for people with chronic diseases such as OSA.

1.3 Biomedical factors and their associations with self-reported health outcomes

Of all approaches to health, the biomedical approach is unquestionably considered to be the most influential. This approach understands health primarily through the lens of disease, and it attributes the cause of ill health to breakdown in normal biological and physiological functioning. In so doing, it gives a clear direction in how best to manage health – and this is to focus on treating the source of breakdown in the body (Haslam et al., 2018). Relevant and potentially modifiable biological factors in the prediction of health in this study concerned OSA severity (assessed by AHI) and sleep-related problems (including night-time sleep quality, daytime sleepiness, and fatigue). Another biomedical factor in this study concerned CPAP treatment.

1.3.1 OSA severity and sleep-related problems

Since OSA is diagnosed according to a cut-off in the Apnoea-Hypopnoea Index (AHI), a logical assumption is that higher AHI is associated with higher OSA-related symptoms, including sleep-related problems. However, previous research has shown that AHI may not correlate well with the presence or degree of daytime sleepiness (e.g. Bixler et al., 2005; Roure et al., 2008; Macey et al., 2010; Dünder et al., 2015), sleep quality (Macey et al., 2010), anxiety, or depressive symptomatology (Macey et al., 2010; Asghari et al., 2012; Rezaeitalab et al., 2014).

Although excessive daytime sleepiness is considered a cardinal symptom of OSA, the association between daytime sleepiness and OSA severity is unclear (Adams et al., 2016). In the Sleep Heart Health Study and the Wisconsin Sleep Cohort Study, daytime sleepiness was found to be associated with OSA severity (Kapur et al., 2005; Young et al., 2009). On the contrary, some recent studies showed that the presence of daytime sleepiness may represent an unreliable indicator of OSA (Adams et al., 2016; Al Houqani and Arora, 2019). Furthermore, approximately 50% of OSA patients deny daytime sleepiness (Roure et al., 2008). The subjective evaluation of daytime sleepiness is also often complicated by the

fact that patients may report complaints regarding lack of energy or depressive symptomatology (Lin et al., 2008) rather than sleepiness itself (Chervin, 2000). Moreover, the phenomenon of residual sleepiness, e.g. excessive daytime sleepiness in OSA patients treated effectively with CPAP, implies that the underlying pathology of daytime sleepiness may be different from that of OSA per se (More et al., 2019). As this particular area of the associations between OSA severity, sleep-related problems and health-outcomes remains unclear, our studies may be useful in enhancing our understanding of these relationships.

1.3.2 Continuous positive airway pressure treatment

In terms of treatment, CPAP represents the first treatment of choice in most patients with OSA (American Academy of Sleep Medicine, 2008; Patil, 2019). To date, CPAP represents the most effective intervention for managing OSA; however, adherence may be poor (Aloia et al., 2004; Weaver and Grunstein, 2008; Rakel, 2009; Weaver and Sawyer, 2010; Barrata et al., 2018), with rates ranging from 29% to 81% (Weaver and Grunstein, 2008). Approximately, one fourth of all CPAP users discontinue its usage within the first year for reasons that range from discomfort and a feeling of claustrophobia from the mask, to inconvenience and its interference with travel (Aloia et al., 2004). The majority of OSA patients who continue using CPAP do not use it consistently or for the number of recommended hours each night (Aloia et al., 2004). Moreover, some interventions employed to improve CPAP adherence (e.g. education and telephone follow-up calls), were found to have only a limited success (Sawyer et al., 2011).

Some previous studies showed that patients' reports of improvement with CPAP treatment were often found to be discordant with PSG results. Thus, other clinically important health-related outcomes including QoL and functional status, are recommended to be used as complementary part in the evaluation of CPAP treatment response (Weaver et al., 2005). Some studies have concluded that OSA patients, even with a good CPAP compliance level, are not able to achieve their normal functional status and QoL when compared to general population levels of functioning (Perimenis et al., 2007; Weaver et al., 2007; Antic et al., 2011; Weaver, 2013; Tippin et al., 2016; Jackson et al., 2018). Poor CPAP treatment effects on health outcomes were especially profound in patients with psychological symptomatology (Kjelsberg et al. 2005; Hussain et al., 2014; Jackson et al., 2018). Moreover, results on CPAP treatment effectiveness were also found to be inconclusive regarding objective health outcomes, such as a decrease in blood pressure among OSA patients (e.g. Dimsdale et al., 2000; Pepperell et al., 2002; Bazzano et al., 2007; Bratton et al., 2014).

Nevertheless, CPAP therapy represents the gold standard treatment option and should be offered to OSA patients as a first choice treatment. Although improving CPAP treatment to maximize adherence is important, there is also a need for novel strategies which may be helpful in OSA management. Thus, present research and clinical practice should focus not only on the standard treatment of OSA, but

also on ensuring that symptoms such as poor sleep quality, daytime sleepiness, fatigue, or psychological symptoms are managed. To do that, we first need to understand how these biomedical and psycho-social factors relate to health outcomes in untreated OSA patients.

1.4 Psycho-social factors and their associations with self-reported health outcomes

About 40 years ago Engel (1978) authored the bio-psycho-social model and, in so doing, tried to reverse the dehumanization of health sciences and disempowerment of patients (Smith et al. 2013). The bio-psycho-social model considers the need to include not only the characteristics and normative functioning of biological systems (Haslam et al., 2018), but also the consideration of individuals' experience, daily functioning, productivity, emotional stability, performance of social roles, and social determinants (Fava and Sonino, 2007; Haslam et al., 2018).

The psychological and social factors assessed in this thesis have been studied for their positive association with health outcomes in various chronic illnesses, such as multiple sclerosis (Krokavcova et al., 2008a; Mikula et al., 2014; Mikula et al., 2016), chronic obstructive pulmonary disease (Tiemensma et al., 2016), cardiovascular diseases (Silarova et al., 2012; Silarova et al., 2014; Silarova et al., 2016), or insomnia (Troxel et al., 2010), but some of them are less known in OSA. Social factors related to external resources accessed from others were operationalized as perceived social support and coping self-efficacy for the ability to get support from family and friends. Psychological factors included anxiety and hostility together with intra-individual psychological resources such as coping self-efficacy for the ability to stop unpleasant emotions and thoughts, problem-focused coping-self-efficacy, and mastery over one's life and circumstances.

1.4.1 Anxiety

In addition to physical disorders, OSA patients may experience mental impairment. Many OSA patients suffer from anxiety symptoms (Yue et al., 2003; Shapiro et al., 2014; Krakow et al., 2015), but these are rarely systematically studied (Shapiro et al., 2014; Krakow et al., 2015). Anxiety includes a large spectrum of conditions varying from psychiatric diagnoses (e.g. generalised anxiety disorder, social phobia, or obsessive compulsive disorder) to threshold symptoms. Anxiety, especially at severe and panic levels, may have a major impact on sleep and breathing (Shapiro et al., 2014). Anxiety may contribute to poor treatment acceptance and adherence (Aloia et al., 2004) and, consequently, to an overall worsening of OSA symptoms and an increased risk of morbidity (Shapiro et al., 2014). Furthermore, comorbid anxiety in OSA patients has been found to have pathophysiological implications; i.e. permanent neurological alterations in brain areas regulating emotions were noted using magnetic resonance in anxious OSA patients compared to no significant change in non-anxious OSA patients and controls (Kumar et al., 2009). A more nuanced theory suggests that OSA itself may represent a direct cause of anxiety,

because virtually anything that disrupts breathing (e.g. asthma, bronchitis, chronic obstructive pulmonary disease) easily causes or aggravates symptoms of anxiety (Krakow et al., 2015).

1.4.2 Hostility

Previous research has shown that various chronic diseases and an increased risk of illness were associated with hostility (Nabi et al., 2008), with strong evidence for cardiovascular diseases (Nabi et al., 2008; Silarova et al., 2014; Silarova et al., 2016). Affective consequences of OSA were also found to include elevated rates of hostility (Yue et al., 2003). Hostility is defined as a negative cynical attitude toward others, with a propensity for anger, aggression (Cook and Medley, 1954), mistrust, and cynicism (Barefoot et al., 1989). Previous research has identified hostility to be a risk factor for impaired psychological QoL in patients with cardiovascular diseases (Nabi et al., 2008; Silarova et al., 2014; Silarova et al., 2016). Hostility may be linked to increased negative emotionality (Brissette and Cohen, 2002) and psychological symptoms, such as sleep disruption (Brissette and Cohen, 2002; Tsuchiyama et al., 2013), depression (Heponiemi et al., 2006), suicidal ideation, and suicidal attempts (Brezo et al., 2006; Lemogne et al., 2011). In their review, Baglioni et al. (2010) concluded that hostility correlates with poor sleep quality, both in subclinical and clinical samples. Recently, Xiao et al. (2016) reported a strong association between hostility and decreased night-time sleep quality in patients with OSA. Moreover, hostility was found to be related to an attenuated decline in night-time blood pressure (Hall et al., 2004), which may potentiate the negative health consequences of OSA-related cardiovascular symptomatology. Individuals with high hostility may have a delayed onset of sleep due to rumination or elevated arousal following their daily interactions (Hall et al., 1997). Thus, negative experiences during the day may hinder physiological recovery at night, resulting in difficulties initiating sleep and a blunted decline in blood pressure (Hall et al., 2004).

However, evidence for a relationship between hostility and sleep-related problems is still scarce (Granö et al., 2008; Sadeh et al., 2011). Some studies and clinical observations hypothesize that sleep loss reduces affective stability and increases emotional reactivity (Anderson and Platten, 2011), aggression, and hostility (Kamphuis et al., 2012). Booth et al. (2006) found a correlation between daytime sleepiness and anger, as measured by the Bussy-Perry subscale, in sex-offenders with diagnosed OSA. Following CPAP treatment, OSA patients reported a lower level of hostility. Other authors define the role of hostility as the main cause of sleep problems; for example, Granö et al. (2008) in their longitudinal study concluded that transient, but not trait hostility may predispose for a shorter duration of sleep in the general population even when adjusted for psychiatric disorders.

1.4.3 Coping self-efficacy

Coping may be a determinant of both recovery and adaptation to disability (Lo Buono et al., 2017). Effective coping strategies may be beneficial in handling chronic

diseases, including OSA (Bardwell et al., 2001; Cassara et al., 2017). In general terms, coping can be defined as an effort to manage a situation and involves various cognitive and behavioural strategies to overcome external or internal demands which are appraised as either taxing or exceeding the person's resources (Folkman et al., 1986). The terms coping and coping self-efficacy are closely linked to each other (Park and Folkman, 1997; Bandura et al. 1999; Chesney et al., 2006; Mikula et al., 2014; Mikula et al., 2016). The concept of coping self-efficacy is based on an integration of two well established theories within health research: the self-efficacy theory of Bandura (1999) and the coping theory of Lazarus and Folkman (1984). In the framework of these theories, coping-self efficacy addresses the second phase of coping, which represents how a person reacts to a stressful situation and most importantly which coping strategy he or she will apply based on the perceived self-efficacy. The choice and level of coping self-efficacy in a particular circumstance reflects prior relevant experiences (Bandura et al., 1977). During the process of secondary appraisal, the individual judges that an outcome is controllable through coping and addresses the question of whether person believes that he or she can carry out the requisite coping strategy (Lazarus and Folkman, 1984). Coping self-efficacy contributes to this judgment, which is an important prerequisite to coping behaviour (Park and Folkman, 1997). The ability to regulate emotions is crucial in diminishing psychological distress; however, healthy emotion-regulation may not merely be about using the "right" strategies (Haines et al. 2016).

According to the strategy-situation-fit hypothesis, emotion-regulation strategies are able to diminish psychological distress only when used in appropriate contexts (Bonanno and Burton, 2013; Haines et al. 2016). When dealing with their health conditions, patients use various coping strategies which may have different effects on their psychological well-being. When people obtain a 'fit' between stressful events and their coping strategies, they experience less psychological distress than when there is a lack of such a fit (Park et al., 2001). As such, greater levels of coping self-efficacy are associated with more effective regulation of emotional distress (Luberto et al., 2014). Previous research has focused on the effect of coping self-efficacy and coping behaviour on patients' self-reported health outcomes in various diseases, such as heart failure (Graven and Grant, 2013), multiple sclerosis (Mikula et al., 2016), or chronic obstructive pulmonary disease (Tiemensma et al., 2016). A higher level of coping self-efficacy was associated with a better adjustment to various chronic diseases (Chesney et al. 2006; Benka et al., 2014; Mikula et al., 2014; Mikula et al., 2016). Only a few studies have so far addressed this concept, but those that have showed that coping self-efficacy was associated with lower level of psychological distress (Chesney et al., 2006; Benka et al., 2014) and better QoL (Mikula et al., 2014; Mikula et al., 2016) in the context of chronic diseases. Overall, these results suggest that coping self-efficacy has direct effects on distress/well-being outcomes, beyond the impact of clinical and personality variables.

Some studies indicate that problem-focused coping was the most beneficial in handling disease (Scharloo et al., 2000; Graven and Grant, 2013; Tiemensma et al., 2016), especially in the mental health domain (Scharloo et al., 2000). In

other studies, problem-focused coping was generally unrelated to illness adjustment (Bombardier et al., 1990). The emotion-focused coping triad, consisting of wishful thinking, self blame, and avoidance, was also found to be a maladaptive strategy when coping with chronic medical conditions (Bombardier et al., 1990). Nevertheless, in some studies, avoidance coping or more passive coping strategies, such as coping self-efficacy for stopping unpleasant emotions and thoughts, were defined as most effective (Mackay et al., 2012; Harmell et al., 2011; Mikula et al., 2016). Recent studies have concluded that the more active and less passive coping strategies reported by OSA patients, the lower the level of depressive symptoms experienced by patients (Bardwell et al., 2001; Cassara et al., 2017).

1.4.4 Mastery over one's life and circumstances

As patients with OSA have very little control over the symptoms of their disease and have to learn how to live with it, mastery may help them to reduce the stress that breathing difficulties and sleep-related symptoms bring about and may thus improve their health outcomes. Mastery is defined as a general sense of control over one's life and circumstances (Pearlin and Schooler, 1978). A higher level of mastery has been found to be associated with better health in people with chronic disease or disability (Cott et al., 1999). A diminished sense of mastery was associated with a decrease in physical, mental, and social functioning and with increased mortality rates in patients with chronic conditions (Surtees et al., 2006; Krokavcova et al., 2008a; Sloan et al., 2009). In OSA patients with comorbid insomnia, the positive associations between mastery and both physical and mental QoL remained significant even after adjustment for age, obesity, chronic diseases, erectile dysfunction, sleepiness, mood, and financial strain (Lang et al., 2016). Mastery as a part of patient empowerment (Aujoulat et al., 2008) was also found to be associated with individuals' capacity to make decisions about their health behaviour and to have or to take control over aspects of their lives that are related to health (McAllister et al., 2012). Research has also shown that people with a higher level of mastery are more likely to seek treatment at an early stage of disease, and to use health care services more efficiently (Menec and Chipperfield, 1997).

1.4.5 Social support

Social support is a very important aspect in the treatment of chronic and incapacitating diseases (Günbey and Karabulut, 2014). There is some evidence that having adequate psychosocial support may lead to an improvement of perceived QoL and reduced morbidity (Barefoot et al., 2005), while the absence of positive relationships was found to be a significant risk factor for morbidity and mortality (Cacioppo and Cacioppo, 2014). Lack of social support has a significant impact on health-related behaviour and risk for illness (Alemi et al., 2003); i.e. poor social support was associated with poorer self-rated health in patients with acute myocardial infarction (Bucholz et al., 2014), higher levels of blood pressure (Piferi et al., 2006), chronic arthritis pain (Lee et al., 2016), and multiple sclerosis (Krokavcova et al.,

2008b). Social support also had a positive influence on sleep in people with insomnia (Troxel et al., 2010).

Therefore, social support may be an important, though under-investigated, protective factor associated with healthier sleep, better QoL, and daytime functioning also in OSA patients. There are several plausible pathways that may link social support with sleep, including attenuating stress responses, encouraging healthy sleep behaviours, and entraining circadian rhythms (Troxel et al., 2010). OSA patients may experience lower levels of social support compared to other populations with chronic diseases. Some previous studies explained that OSA-related symptoms can negatively impact the partners' sleep and daytime functioning (Luyster, 2017) or engagement in social activities (Luyster et al. 2016). Recently, a significant negative impact of perceived OSA symptoms on marital satisfaction was described (Tramonti et al., 2017). Another indication for lower levels of social support in patients with OSA may be the association between poor social support and sleep disordered breathing symptoms (Glenn et al., 2015). Moreover, a low level of social support was independently associated with short sleep duration when controlled for sociodemographic variables (Glenn et al., 2015).

With a few exceptions (e.g. Troxel et al., 2010; Choi et al., 2015), previous research on sleep disorders has focused mainly on the association between social support and self-reported sleep disturbances (Troxel et al., 2010). Furthermore, very little is known about the role of social support in OSA. To our knowledge, only one study by Choi et al. (2015) focused on social support in OSA patients (i.e. in the association with suicidal ideation). Recently, supportive relationships were found to be associated with CPAP treatment adherence in female patients with OSA (Baron et al., 2017). Insufficient emotional (e.g., encouragement) and instrumental (e.g. help with putting on mask, verbal reminders) support from partners of OSA patients was further identified as a barrier for CPAP adherence (Broström et al., 2010; Luyster et al., 2016). There are two dimensions of social support, namely perceived social support and received social support (Dunkel-Schetter and Bennett, 1990). Perceived social support is defined as 'the perception of an individual about the amount and quality of support received from his/her social network', while received social support is defined as 'the objective quantification of the help and aid the person receives from his/her social network' (Kim et al., 2017). Perceived social support was identified as a stronger predictor of individual well-being than received social support. Furthermore, perceived social support was found to be more strongly associated with personality traits such as self-esteem (Goodwin et al., 2004).

1.5 Health model

In the context of the bio-psycho-social approach (Engel, 1978), our study design is partially based on the model proposed by Wilson and Cleary (1995) (Figure 1.1). The proposed model represents a taxonomy or classification scheme for different measures of health outcomes. These outcomes are divided into four levels:

symptoms, functional status, general health perceptions, and overall quality of life (QoL) (Wilson and Cleary 1995; Krabbe, 2017). In addition to classifying these outcome measures, the authors proposed specific causal relationships between them that link traditional clinical variables to measures of HRQoL. "As one moves from left to the right in the model, one moves outward from the cell to the individual and to the interaction of the individual as a member of society" (Wilson and Cleary, 1995). The model captures the factors affecting health as experienced by individuals (Wilson and Cleary, 1995; Krabbe, 2017). The main purpose of the proposed model was to distinguish between conceptually distinct measures of health-related QoL outcomes and to make the dominant relationships explicit. Therefore, the displayed direction of the arrows do not imply that reciprocal relationships are absent. Neither does the absence of arrows between non-adjacent levels imply that the associations are completely missing (Krabbe, 2017).

Figure 1.1: Relationships among measures of patient outcome in a health-related quality of life. Conceptual model by Wilson and Cleary 1995. Linking clinical variables with health-related quality of life: a conceptual model of patient outcomes. The Journal of the American Medical Association 273 (1): 59-65.

1.6 Aim of the thesis and research questions

This thesis aims to provide insights in the associations between biomedical, psychological, and social factors and self-reported health outcomes in patients with OSA. It builds on previous studies describing populations with various chronic diseases and adds knowledge to previous research by focusing on OSA patients. Figure 1.2 provides a visual overview of the associations examined in this thesis.

Figure 1.2 Conceptual model of the associations examined in the thesis

Research question 1 (Chapter 3)

Does Continuous Positive Airway Pressure (CPAP) treatment have a positive effect on quality of life in OSA patients when compared to sham CPAP, placebo pills, and conservative treatment?

Research question 2 (Chapter 4)

Are OSA-severity, sleep-related problems, and anxiety associated with work functioning in OSA patients when controlled for age, gender, and type of occupation?

Research question 2a (Chapter 4)

Does anxiety moderate the association between sleep-related problems and work functioning?

Research question 3 (Chapter 5)

Are hostility and coping self-efficacy dimensions associated with psychological distress in OSA patients when controlled for sociodemographic, clinical, and sleep-related variables?

Research question 3a (Chapter 5)

Do coping self-efficacy dimensions mediate the association between hostility and psychological distress?

Research question 4 (Chapter 6)

What is the prevalence of suicidal ideation in OSA patients? Are OSA severity, sleep-related problems, and social support related to suicidal ideation in OSA patients?

Research question 5 (Chapter 7)

Is there an association between social support, mastery, sleep-related problems and functional status in OSA patients when controlled for sociodemographic and clinical variables?

Research question 5a (Chapter 7)

Do social support and mastery mediate the association between sleep-related problems and functional status?

1.7 Outline of the thesis

This thesis contains eight chapters.

Chapter 1: “*Introduction*” provides a general introduction into the associations between the key theoretical constructs of the thesis: OSA, CPAP treatment, self-reported health-related outcomes (functional status, work functioning, QoL and psychological distress, including suicidal ideation), sleep-related problems, anxiety,

hostility, coping self-efficacy, mastery, and social support. It also introduces the conceptual framework and research questions.

Chapter 2: “*Design of the study and data sources*” presents information about the study design. It describes the sample and procedure of the data collection and the study design and setting used in the thesis. It also provides a description of the measures and statistical analyses used.

Chapter 3: “*Quality of life of obstructive sleep apnoea patients receiving continuous positive airway pressure treatment: a systematic review and meta-analysis*” investigates the question of the effect of real CPAP treatment on QoL when compared to placebo pills, sham CPAP, and conservative treatment.

Chapter 4: “*Are disease severity, sleep-related problems and anxiety associated with work functioning in patients with obstructive sleep apnoea?*” examines whether OSA-severity, sleep-related problems, and anxiety are associated with work functioning in OSA patients. It also investigates whether anxiety moderates the associations between sleep-related problems and work functioning.

Chapter 5: “*Psychological distress in patients with obstructive sleep apnoea. The role of hostility and coping self-efficacy*” examines whether hostility and coping self-efficacy dimensions are associated with psychological distress in OSA patients. Additionally, it explores whether coping self-efficacy dimensions mediate the association between hostility and psychological distress.

Chapter 6: “*Suicidal ideation in patients with obstructive sleep apnoea and its relationship with disease severity, sleep-related problems and social support*” presents the prevalence of suicidal ideation in OSA patients and examines the relationships between OSA severity, sleep-related problems, social support and suicidal ideation in OSA patients.

Chapter 7: “*Social support, mastery, sleep-related problems and their association with functional status in untreated obstructive sleep apnoea patients*” examines the associations between social support, mastery, sleep-related problems and functional status in OSA patients. It also explores the mediating role of social support and mastery in the association between sleep-related problems and functional status.

Chapter 8: “*General discussion, implications, and conclusions*” summarizes and discusses the main findings of the thesis, its strengths, limitations and implications for practice and future research. At last, conclusions are drawn in the final section.

References

- Adams RJ, Appleton SL, Vakulin A, et al. (2016) Association of daytime sleepiness with obstructive sleep apnoea and comorbidities varies by sleepiness definition in a population cohort of men. *Respirology* 21(7): 1314-1321.
- Alemi F, Stephens R, Llorens S, et al. (2003) The orientation of social support measure. *Addictive Behaviors* 28(7): 1285-1298.
- Al Houqani M and Arora T (2019) Comparison of Commonly Used Questionnaires to Identify Obstructive Sleep Apnea in Pilots. *Sleep* 42 (1) DOI: <https://doi.org/10.1093/sleep/zsz067.443>.
- Aloia MS, Arnedt JT, Riggs RL, et al. (2004) Clinical management of poor adherence to CPAP: Motivational enhancement. *Behavioral Sleep Medicine* 2(4): 205-222.
- American Academy of Sleep Medicine (2005) International Classification of Sleep Disorders: Diagnostic and Coding Manual. 2nd ed. Sleep Disorders Association, Rochester, MN (ICSD-2).
- American Academy of Sleep Medicine (2008) Obstructive sleep apnea. 2510 North Frontage Road Darien, IL 60561.
- Anderson C and Platten CR (2011) Sleep deprivation lowers inhibition and enhances impulsivity to negative stimuli. *Behavioural Brain Research* 217(2): 463-466.
- Antic NA, Catcheside P, Buchan C, et al. (2011) The effect of CPAP in normalizing daytime sleepiness, quality of life, and neurocognitive function in patients with moderate to severe OSA. *Sleep* 34(1): 111-119.
- Appleby J, Devlin N, Parkin D (2016) Using Patient Reported Outcomes to Improve Health Care. John Wiley & Son, Chichester. 978-111-894859-0. 109 pgs.
- Asghari A, Mohammadi F, Kamrava SK, et al. (2012) Severity of depression and anxiety in obstructive sleep apnea syndrome. *European Archives of Oto-Rhino-Laryngology* 269(12): 2549-2553.
- Ajoulat I, Marcolongo R, Bonadiman L, et al. (2008) Reconsidering patient empowerment in chronic illness: A critique of models of self-efficacy and bodily control. *Social Science & Medicine* 66(5): 1228-12239.
- Ayas NT, Hirsch AA, Laher I, et al. (2014) New frontiers in obstructive sleep apnoea. *Clinical Science* 127(4): 209-216.

- Baglioni C, Spiegelhalter K, Lombardo C, et al. (2010) Sleep and emotions: a focus on insomnia. *Sleep Medicine Reviews* 14(4): 227-238.
- Bandura A, Adams NE, Beyer J (1977) Cognitive processes mediating behavioral change. *Journal of Personality and Social Psychology* 35(3): 125-139.
- Bandura A, Freeman WH, Lightsey R (1999) Self-efficacy: The exercise of control. *Journal of Cognitive Psychotherapy* 13(2): 158-166.
- Baratta F, Pastori D, Bucci T, et al (2018) Long-term prediction of adherence to continuous positive air pressure therapy for the treatment of moderate/severe obstructive sleep apnea syndrome. *Sleep Medicine* 43: 66-70.
- Bardwell WA, Ancoli-Israel S, Dimsdale JE (2001) Types of coping strategies are associated with increased depressive symptoms in patients with obstructive sleep apnea. *Sleep* 24(8): 905-909.
- Barefoot JC, Dodge KA, Peterson BL, et al. (1989) The Cook-Medley hostility scale: item content and ability to predict survival. *Psychosomatic Medicine* 51(1): 46-57.
- Barefoot JC, Gronbaek M, Jensen G, et al. (2005) Social network diversity and risks of ischemic heart disease and total mortality: findings from the Copenhagen city heart study. *American Journal of Epidemiology* 161(10): 960-967.
- Baron KG, Gunn HE, Wolfe, LF, et al. (2017) Relationships and CPAP adherence among women with obstructive sleep apnea. *Sleep Science and Practice* 1(1): 10-18.
- Bazzano LA, Khan Z, Reynolds K, et al. (2007) Effect of nocturnal nasal continuous positive airway pressure on blood pressure in obstructive sleep apnea. *Hypertension* 50(2): 417-423.
- Benka J, Nagyova I, Rosenberger J, et al. (2014) Is coping self-efficacy related to psychological distress in early and established rheumatoid arthritis patients?. *Journal of Developmental and Physical Disabilities* 26(3): 285-297.
- Bernert RA, Turvey CL, Conwell Y, et al. (2014) Association of poor subjective sleep quality with risk for death by suicide during a 10-year period: a longitudinal, population-based study of late life. *JAMA Psychiatry* 71(10): 1129-1137.
- Bishop TM, Ashrafioun L, Pigeon WR (2018) The association between sleep apnea and suicidal thought and behavior: an analysis of national survey data. *Journal of Clinical Psychiatry* 79(1): 17m1480.
- Bixler EO, Vgontzas AN, Lin HM, et al. (2005) Excessive daytime sleepiness in a general population sample: the role of sleep apnea, age, obesity, diabetes, and depression. *The Journal of Clinical Endocrinology & Metabolism* 90(8): 4510-4515.
- Bixler EO, Vgontzas AN, Ten Have T, et al. (1998) Effects of age on sleep apnea in men: I. Prevalence and severity. *American Journal of Respiratory and Critical Care Medicine* 157(1): 144-148.
- Boccabella A and Malouf J (2017) How do sleep-related health problems affect functional status according to sex?. *Journal of Clinical Sleep Medicine* 13(5): 685-692.
- Bombardier CH, D'Amico C, Jordan JS (1990) The relationship of appraisal and coping to chronic illness adjustment. *Behavior Research and Therapy* 28(4): 297-304.
- Bonanno GA and Burton CL (2013) Regulatory flexibility: An individual differences perspective on coping and emotion regulation. *Perspectives on Psychological Science* 8(6): 591-612.
- Booth BD, Paul Fedoroff J, Curry SD, et al. (2006) Sleep Apnea as a Possible Factor Contributing to Aggression in Sex Offenders. *Journal of Forensic Sciences* 51(5): 1178-1181.
- Bratton DJ, Stradling JR, Barbe F, et al. (2014) Effect of CPAP on blood pressure in patients with minimally symptomatic obstructive sleep apnoea: a meta-analysis using individual patient data from four randomized controlled trials. *Thorax* 69(12): 1128-1135.
- Brezo J, Paris J, Turecki G (2006) Personality traits as correlates of suicidal ideation, suicide attempts, and suicide completions: a systematic review. *Acta Psychiatrica Scandinavica* 113(3): 180-206.
- Brisette I and Cohen S (2002) The contribution of individual differences in hostility to the associations between daily interpersonal conflict, affect, and sleep. *Personality and Social Psychology Bulletin* 28(9): 1265-1274.
- Broström A, Nilsen P, Johansson P, et al. (2010) Putative facilitators and barriers for adherence to CPAP treatment in patients with obstructive sleep apnea syndrome: a qualitative content analysis. *Sleep Medicine* 11(2): 126-30.
- Bucholz EM, Strait KM, Dreyer RP, et al. (2014) Effect of low perceived social support on health outcomes in young patients with acute myocardial infarction: results from the variation in recovery: role of gender on outcomes of young AMI patients (VIRGO) study. *Journal of the American Heart Association* 3(5): 1-11.

- Cacioppo JT and Cacioppo S (2014) Social relationships and health: The toxic effects of perceived social isolation. *Social and Personality Psychology Compass* 8(2): 58-72.
- Cappuccio F, Miller MA and Lockley SW (Eds.) (2010) *Sleep, health, and society: From aetiology to public health*. Oxford University Press, USA. ISBN 978-0-19-956659-4.
- Chervin RD (2000) Sleepiness, fatigue, tiredness, and lack of energy in obstructive sleep apnea. *Chest* 118(2): 372-379.
- Chesney M, Neilands TB, Chambers DB (2006) A validity and reliability study of the coping self-efficacy scale. *British Journal of Health Psychology* 11(3): 421-437.
- Choi SJ, Joo EY, Lee YJ, et al. (2015) Suicidal ideation and insomnia symptoms in subjects with obstructive sleep apnea syndrome. *Sleep Medicine* 16(9): 1146-1150.
- Cook WW and Medley DM (1954) Proposed hostility and pharisaic-virtue scales for the MMPI. *Journal of Applied Psychology* 38(6): 414-418.
- Cott CA, Gignac MA, Badley EM (1999) Determinants of self rated health for Canadians with chronic disease and disability. *Journal of Epidemiology & Community Health* 53(11): 731-736.
- Dimsdale JE, Lored JS, Profant J (2000) Effect of continuous positive airway pressure on blood pressure. *Hypertension* 35(1): 144-147.
- Druss B and Pincus H (2000) Suicidal ideation and suicide attempts in general medical illnesses. *Archives of Internal Medicine* 160(10): 1522-1526.
- Dunkel-Schetter C and Bennett TL (1990) Differentiating the cognitive and behavioral aspects of social support. In IG Sarason, Sarason BR, and Pierce GR (Eds.) *Social support: an interactional view* (pp. 267-296). New York: Wiley.
- Dünder Y, Saylam G, Tatar EÇ, et al. (2015) Does AHI Value Enough for Evaluating the Obstructive Sleep Apnea Severity? *Indian Journal of Otolaryngology and Head & Neck Surgery* 67(1): 16-20.
- Dutt N, Chaudhry K, Chauhan NK, et al. (2016) Health related quality of life in adult obstructive sleep apnea. *Journal of Sleep Disorders Therapy* 5(2): 2-7.
- Engel GL (1978) The biopsychosocial model and the education of health professionals. *Annals of the New York Academy of Sciences* 310(1): 169-181.
- Epstein LJ, Kristo D, Strollo PJ Jr, et al. (2009) Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. *Journal of Clinical Sleep Medicine* 5(3): 263-276.
- Fava GA and Sonino N (2007) The biopsychosocial model thirty years later. *Psychotherapy and Psychosomatics* 77(1):1.
- Finkel KJ, Scarleman AC, Tymkew H, et al. (2009) Prevalence of undiagnosed obstructive sleep apnea among adult surgical patients in an academic medical center. *Sleep Medicine* 10(7): 753-758.
- Folkman S, Lazarus RS, Dunkel-Schetter C, et al. (1986) Dynamics of a stressful encounter: Cognitive appraisal, coping, and encounter outcomes. *Journal of Personality and Social Psychology* 50(5): 992-1003.
- Force AOSAT and American Academy of Sleep Medicine (2009) Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. *Journal of Clinical Sleep Medicine: official publication of the American Academy of Sleep Medicine* 5(3): 263-276.
- Gabbay IE and Lavie P (2012) Age-and gender-related characteristics of obstructive sleep apnea. *Sleep and Breathing* 16(2): 453-460.
- Garbarino S, Guglielmi O, Sanna A, et al. (2016) Risk of occupational accidents in workers with obstructive sleep apnea: systematic review and meta-analysis. *Sleep* 39(6): 1211-1218.
- Gassara I, Thabet JB, Msaad S, et al. (2017) Impact of coping strategies on emotional status in patients with obstructive sleep apnea syndrome. *European Psychiatry* DOI: <https://doi.org/10.1016/j.eurpsy.2017.01.602>.
- Glenn C, Enwerem N, Odeyemi Y, et al. (2015) Social support and sleep symptoms in US adults. *Journal of Clinical Sleep Medicine* 11(8): 957-957.
- Goodwin R, Costa P, Adonu, J (2004) Social support and its consequences: 'Positive' and 'deficiency' values and their implications for support and self-esteem. *British Journal of Social Psychology* 43(3): 465-474.
- Goldberg DP and Hillier VF (1979) A scaled version of the General Health Questionnaire. *Psychological Medicine* 9(1): 139-145.
- Granö N, Vahtera J, Virtanen M, et al. (2008) Association of hostility with sleep duration and sleep disturbances in an employee population. *International Journal of Behavioral Medicine* 15(2): 73-80.

Graven LJ and Grant JS (2013) Coping and health-related quality of life in individuals with heart failure: An integrative review. *Heart & Lung: The Journal of Acute and Critical Care* 42(3): 183-194.

Günbey E and Karabulut H (2014) Multidimensional scale of perceived social support in patients with obstructive sleep apnea syndrome. *European Archives of Oto-Rhino-Laryngology* 271(11): 3067-3071.

Haslam C, Jetten J, Cruwys T, et al. (2018) *The New Psychology of Health: Unlocking the Social Cure*, 1st Edition London Routledge: 510 pages, ISBN-13: 978-1138123885.

Haines SJ, Gleeson J, Kuppens P, et al. (2016) The wisdom to know the difference: Strategy-situation fit in emotion regulation in daily life is associated with well-being. *Psychological Science* 27(12): 1651-1659.

Hall GCN and Barongan C (1997) Prevention of sexual aggression: Sociocultural risk and protective factors. *American Psychologist* 52(1): 5-14.

Hall M, Vasko R, Buysse DJ, et al. (2004) Acute stress affects heart rate variability during sleep. *Psychosomatic Medicine* 66(1): 56-62.

Harmell AL, Mausbach BT, Roepke SK, et al. (2011) The relationship between self-efficacy and resting blood pressure in spousal Alzheimer's caregivers. *British Journal of Health Psychology* 16(2): 317-328.

Heponiemi T, Elovainio M, Pekkarinen L, et al. (2006) The moderating effect of employee hostility on the association of long-term elderly care unit's negative resident characteristics to employee stress and well-being. *Journal of Occupational Health Psychology* 11(2): 157-168.

Howell RT, Kern ML, Lyubomirsky S (2007) Health benefits: Meta-analytically determining the impact of well-being on objective health outcomes. *Health Psychology Review* 1(1): 83-136.

Hussain SF, Irfan M, Waheed Z, et al. (2014) Compliance with continuous positive airway pressure (CPAP) therapy for obstructive sleep apnea among privately paying patients-a cross sectional study. *BioMed Central Pulmonary Medicine* 14(1): 188.

Jackson ML, McEvoy RD, Banks S (2018) Neurobehavioral impairment and CPAP treatment response in mild-moderate obstructive sleep apnea. *Journal of Clinical Sleep Medicine* 14(1): 47-56.

Jennum P, Ibsen R, Kjellberg J (2014) Social consequences of sleep disordered

breathing on patients and their partners: a controlled national study. *European Respiratory Journal* 43(1): 134-144.

Kales SN and Czeisler CA (2016) Obstructive sleep apnea and work accidents: time for action. *Sleep* 39(6): 1171-1173.

Kamphuis J, Meerlo P, Koolhaas JM, et al. (2012) Poor sleep as a potential causal factor in aggression and violence. *Sleep Medicine* 13(4): 327-334.

Kang EW, Abdel-Kader K, Yabes J, et al. (2012) Association of sleep disorder breathing with cognitive dysfunction in CKD stages 4-5. *American Journal of Kidney Disease* 60(6): 949-958.

Kapur VK, Baldwin CM, Resnick HE, et al. (2005) Sleepiness in patients with moderate to severe sleep-disordered breathing. *Sleep* 28(4): 472-478.

Karimi M, Hedner J, Zou D, et al. (2015) Attention deficits detected in cognitive tests differentiate between sleep apnea patients with or without a motor vehicle accident. *Sleep Medicine* 16(4): 528-533.

Kim GM, Lim JY, Kim EJ, et al. (2018) A model of adaptation for families of elderly patients with dementia: focusing on family resilience. *Aging & Mental Health* 22(10): 1295-1303.

Kjelsberg FN, Ruud EA, Stavem K (2005) Predictors of symptoms of anxiety and depression in obstructive sleep apnea. *Sleep Medicine* 6(4): 341-346.

Klonsky ED, May AM, Saffer BY (2016) Suicide, suicide attempts, and suicidal ideation. *Annual Review of Clinical Psychology* 12: 307-330.

Knauert M, Naik S, Gillespie MB, et al. (2015) Clinical consequences and economic costs of untreated obstructive sleep apnea syndrome. *World Journal of Otorhinolaryngology-Head and Neck Surgery* 1(1): 17-27.

Krabbe PFM (2017) *The Measurement of Health and Health Status. Concepts, Methods and Applications from a Multidisciplinary Perspective*. Academic Press. 9780128017203. 380 pgs.

Krakov B, Ribeiro JD, Ulibarri VA, et al. (2011) Sleep disturbances and suicidal ideation in sleep medical center patients. *Journal of Affective Disorders* 131(1): 422-427.

Krakov BJ, Ulibarri VA, Moore BA, et al. (2015) Posttraumatic stress disorder and sleep-disordered breathing: a review of comorbidity research. *Sleep Medicine Reviews* 24: 37-45.

Krokavcova M, Nagyova I, van Dijk JP, et al. (2008a) Mastery, functional disability and perceived health status in patients with multiple sclerosis. *European Journal of Neurology* 15(11): 1237-1244.

Krokavcova M, van Dijk JP, Nagyova I, et al. (2008b) Social support as a predictor of perceived health status in patients with multiple sclerosis. *Patient Education and Counselling* 73(1): 159-165.

Krystal AD, Edinger J, Wohlgemuth W, et al. (1998) Sleep in peri-menopausal and post-menopausal women. *Sleep Medicine Reviews* 2(4): 243-253.

Kumar R, Macey PM, Cross RL, et al. (2009) Neural alterations associated with anxiety symptoms in obstructive sleep apnea syndrome. *Depression and Anxiety* 26(5): 480-491.

Kushida CA, Nichols DA, Holmes TH, et al. (2012) Effects of continuous positive airway pressure on neurocognitive function in obstructive sleep apnea patients: The Apnea Positive Pressure Long-term Efficacy Study. *Sleep* 35(12): 1593-602.

Lang CJ, Appleton S, Vakulin A, et al. (2016) Psychological and quality of life factors in men with comorbid Obstructive Sleep Apnea (OSA) and insomnia (Ins): a population study. In: *Sleep DownUnder 2016: 28th ASM of Australasian Sleep Association and Australasian Sleep Technologists Association* (20 October - 22 October 2016: Adelaide, Australia). *Journal of Sleep Research* 25(2): 14.

Lazarus R and Folkman S (1984) Stress, Appraisal and coping. Springer Publishing Company. ISBN 0-8261-4191-9. 456 pgs.

Lee JE, Kahana B, Kahana E (2016) Social support and cognitive functioning as resources for elderly persons with chronic arthritis pain. *Aging & Mental Health* 20(4): 370-379.

Leger D (1994) The cost of sleep-related accidents: a report for the National Commission on Sleep Disorders Research. *Sleep* 17(1): 84-93.

Leger D, Bayon V, Laaban JP, et al. (2012) Impact of sleep apnea on economics. *Sleep Medicine Reviews* 16(5): 455-462.

Leidy NK (1994) Using functional status to assess treatment outcomes. *CHEST Journal* 106(6): 1645-1646.

Lemogne C, Fossati P, Limosin F, et al. (2011) Cognitive hostility and suicide. *Acta Psychiatrica Scandinavica* 124(1): 62-69.

Leung RS (2019) Arousability in Obstructive Sleep Apnea: Friend or Foe?. *American Journal of Respiratory and Critical Care Medicine* 199(7): 821-822.

Lin CM, Davidson TM, Ancoli-Israel S (2008) Gender differences in obstructive sleep apnea and treatment implications. *Sleep Medicine Reviews* 12(6): 481-496.

Lin WC and Winkelman JW (2012) Obstructive sleep apnea and severe mental illness: evolution and consequences. *Current Psychiatry Reports* 14(5): 503-510.

Lo Buono V, Corallo F, Bramanti P, et al. (2017) Coping strategies and health-related quality of life after stroke. *Journal of Health Psychology* 22(1): 16-28.

Luberto CM, Cotton S, McLeish AC, et al. (2014) Mindfulness skills and emotion regulation: The mediating role of coping self-efficacy. *Mindfulness* 5(4): 373-380.

Lurie A (2011) Obstructive sleep apnea in adults: epidemiology, clinical presentation, and treatment options. *Advances in Cardiology* 46: 1-42.

Luyster FS (2017) Impact of obstructive sleep apnea and its treatments on partners: a literature review. *Journal of Clinical Sleep Medicine* 13(3): 467-477.

Luyster FS, Dunbar-Jacob J, Aloia MS, et al. (2016) Patient and partner experiences with obstructive sleep apnea and CPAP treatment: a qualitative analysis. *Behavioral Sleep Medicine* 14(1): 67-84.

Macey PM, Woo MA, Kumar R, et al. (2010) Relationship between obstructive sleep apnea severity and sleep, depression and anxiety symptoms in newly-diagnosed patients. *Public Library of Science One* 5(4): e10211.

Mackay C and Pakenham KI (2012) A stress and coping model of adjustment to caring for an adult with mental illness. *Community Mental Health Journal* 48(4): 450-462.

Manarino MR, Fillipo FD, Piro M (2012) Obstructive sleep apnea syndrome. *European Journal of Internal Medicine* 23(7): 586-593.

McAllister M, Dunn G, Payne K, et al. (2012) Patient empowerment: the need to consider it as a measurable patient-reported outcome for chronic conditions. *BMC Health Services Research* 12(1): 157.

Menec VH and Chipperfield JG (1997) The interactive effect of perceived control and functional status on health and mortality among young-old and old-old adults. *Journals of Gerontology. Series B: Psychological Sciences and Social Sciences* 52(3): 118-126.

Mikula P, Nagyova I, Krokavcova M, et al. (2014) Coping and its importance for quality of life in patients with multiple sclerosis. *Disability and Rehabilitation* 36(9): 732-736.

Mikula P, Nagyova I, Krokavcova M, et al. (2018) Do coping strategies mediate the association between Type D personality and quality of life among people with multiple sclerosis? *Journal of Health Psychology* 23(12): 1557-1565.

More CE, Papp C, Harsanyi S, et al. (2019) Altered irisin/BDNF axis parallels excessive daytime sleepiness in obstructive sleep apnea patients. *Respiratory Research* 20(1):67. <https://doi.org/10.1186/s12931-019-1033-y>.

Mulgrew AT, Ryan CF, Fleetham JA, et al. (2007) The impact of obstructive sleep apnea and daytime sleepiness on work limitation. *Sleep Medicine* 9(1): 42-53.

Nabi H, Kivimäki M, Zins M, et al. (2008) Does personality predict mortality? Results from the GAZEL French prospective cohort study. *International Journal of Epidemiology* 37(2): 386-396.

National Mental Health Information Center. Suicide warning signs [online] Substance Abuse and Mental Health Services Administration (SAMHSA); 2005. [Accessed 31 January 2018]. URL: <http://www.mentalhealth.samhsa.gov/publications/allpubs/walletcard/engwal-letcard.asp>.

Nock MK, Borges G, Bromet EJ, et al. (2008) Suicide and suicidal behavior. *Epidemiologic Reviews* 30(1): 133-154.

O'Connor R (2017) Suicide as (health) behaviour: towards a psychological understanding of suicidal behaviour. *European Health Psychologist* 19(4): 333-334.

Omachi TA, Claman DM, Blanc PD (2009) Obstructive sleep apnea: a risk factor for work disability. *Sleep* 32(6): 791-798.

Pang KP, Pang KA, Pang EB, et al. (2016) Current Concepts in Assessing Outcomes for OSA Surgery. *Current Otorhinolaryngology Reports* 4(1): 26-34.

Park CL and Folkman S (1997) Meaning in the context of stress and coping. *Review of General Psychology* 1(2): 115-144.

Park CL, Folkman S, Bostrom A (2001) Appraisals of controllability and coping in caregivers and HIV+ men: Testing the goodness-of-fit hypothesis. *Journal of Consulting and Clinical Psychology* 69(3): 481-488.

Patil SP, Ayappa IA, Caples SM (2019) Treatment of adult obstructive sleep apnea with positive airway pressure: an American Academy of Sleep Medicine Clinical Practice Guideline. *Journal of Clinical Sleep Medicine* 15(2): 335-343.

Pearlin LI and Schooler C (1978) The structure of coping. *Journal of Health and Social Behavior* 19(1): 2-21.

Peppard PE, Young T, Barnett JH, et al. (2013) Increased prevalence of sleep-disordered breathing in adults. *American Journal of Epidemiology* 177(9): 1006-1014.

Pepperell JC, Ramdassingh-Dow S, Crosthwaite N, et al. (2002) Ambulatory blood pressure after therapeutic and subtherapeutic nasal continuous positive airway pressure for obstructive sleep apnoea: a randomised parallel trial. *The Lancet* 359(9302): 204-210.

Perimenis P, Karkoulas K, Konstantinopoulos A, et al. (2007) Sildenafil versus continuous positive airway pressure for erectile dysfunction in men with obstructive sleep apnea: a comparative study of their efficacy and safety and the patient's satisfaction with treatment. *Asian Journal of Andrology* 9(2): 259-264.

Piferi RL and Lawler KA (2006) Social support and ambulatory blood pressure: An examination of both receiving and giving. *International Journal of Psychophysiology* 62(2): 328-336.

Quintana-Callejo E, Carmona-Bernal C, Capote F, et al. (2004) Gender differences in obstructive sleep apnea syndrome: a clinical study of 1166 patients. *Respiratory Medicine* 98(10): 984-989.

Rakel RE (2009) Clinical and societal consequences of obstructive sleep apnea and excessive daytime sleepiness. *Postgraduate Medicine* 121(1): 86-95.

Reishtein JL, Pack AI, Maislin G, et al. (2006) Sleepiness and relationships in obstructive sleep apnea. *Issues in Mental Health Nursing* 27(3): 319-330.

Reuveni H, Greenberg-Dotan S, Simon-Tuval T, et al. (2008) Elevated health-care utilisation in young adult males with obstructive sleep apnoea. *European Respiratory Journal* 31(2): 273-279.

Rezacitalab F, Moharrari F, Saberi S, et al. (2014) The correlation of anxiety and depression with obstructive sleep apnea syndrome. *Journal of Research in Medical Sciences: The Official Journal of Isfahan University of Medical Sciences* 19(3): 205-210.

Rottapel R, Reid M, Bertisch S, et al. (2019) Prevalence and Morbidity of Sleepiness in an Online Sleep Apnea Patient Cohort. *Sleep* 42(1): 195-195.

Roure N, Gomez S, Mediano O, et al. (2008) Daytime sleepiness and polysomnography in obstructive sleep apnea patients. *Sleep Medicine* 9(7): 727-731.

Rückert-Eheberg IM, Lukaschek K, Brenk-Franz K, et al. (2019) Association of adult attachment and suicidal ideation in primary care patients with multiple chronic conditions. *Journal of Affective Disorders* 246: 121-125.

Sadeh N, Javdani S, Finy MS, et al. (2011) Gender differences in emotional risk for self-and other-directed violence among externalizing adults. *Journal of Consulting and Clinical Psychology* 79(1): 106-117.

Salomon JA, Mathers CD, Chatterji S, et al. (2003) Quantifying individual levels of health: definitions, concepts and measurement issues. In Salomon JA, Joshua A, Mathers CD, Colin D (Eds.) *Health Systems Performance Assessment: Debate, Methods, and Empiricism* 301-318. World Health Organisation. ISBN 92 4 156245 5: 900 pgs.

Sawyer AM, Gooneratne NS, Marcus CL, et al. (2011) A systematic review of CPAP adherence across age groups: Clinical and empiric insights for developing CPAP adherence interventions. *Sleep Medicine Reviews* 15(6): 343-356.

Scharloo M, Kaptein AA, Weinman JA, et al. (2000) Physical and psychological correlates of functioning in patients with chronic obstructive pulmonary disease. *Journal of Asthma* 37(1): 17-29.

Schipper H (1992) Quality of life: the final common pathway. *Journal of Palliative Care* 8(3): 5-7.

Schmalting KB and Afari N (2000) Couples coping with respiratory illness. In Schmalting KA, Goldman ST, Turk DC (Eds.) *The psychology of couples and illness: Theory, research, and practice* (71-104). Washington, DC: *American Psychological Association*. ISBN 978-1-55798-649-8. 407 pgs.

Shapiro AL, Culp S, Azulay Chertok IR (2014) OSA symptoms associated with and predictive of anxiety in middle-aged men: secondary analysis of NHANES data. *Archives of Psychiatric Nursing* 28(3): 200-205.

Sharafkhan A, Giray N, Richardson P, et al. (2005) Association of psychiatric disorders and sleep apnea in a large cohort. *Sleep* 28(11): 1405-1411.

Sherbourne CD, Allen HM, Kamberg CJ, et al. (1992) Physical/Psychophysiologic Symptoms Measure. In: Stewart A, Ware JE. *Measuring Functioning and*

Well-Being: The Medical Outcomes Study Approach, Durham, N.C.: Duke University Press, 1992), 260-275.

Silarova B, Nagyova I, Rosenberger J, et al (2016) Sense of coherence as a mediator between hostility and health-related quality of life among coronary heart disease patients. *Heart & Lung: The Journal of Acute and Critical Care* 45(2): 126-131.

Silarova B, Nagyova I, Rosenberger J, et al. (2012) Sense of coherence as an independent predictor of health-related quality of life among coronary heart disease patients. *Quality of Life Research* 21(10): 1863-1871.

Silarova B, van Dijk JP, Nagyova I, et al. (2014) Differences in health-related quality of life between Roma and non-Roma coronary heart disease patients: the role of hostility. *International Journal of Public Health* 59(2): 271-277.

Sivertsen B, Øverland S, Glozier N, et al. (2008) The effect of OSAS on sick leave and work disability. *European Respiratory Journal* 32(6): 1497-1503.

Sloan FA, Padrón NA, Platt AC (2009) Preferences, Beliefs, and Self-Management of Diabetes. *Health Services Research* 44(3): 1068-1087.

Smith RC, Fortin AH, Dwamena et al. (2013) An evidence-based patient-centered method makes the biopsychosocial model scientific. *Patient Education and Counseling* 91(3): 265-270.

Spiteri MC, Jomeen J, Martin CR (2013) Reimagining the General Health Questionnaire as a measure of emotional wellbeing: a study of postpartum women in Malta. *Women and Birth* 26(4): 105-111.

Stephoe A, Deaton A, Stone, AA (2015) Subjective wellbeing, health, and ageing. *The Lancet* 385(9968): 640-648.

Strohl K and Redline S (1996) Recognition of obstructive sleep apnea. *American Journal of Respiratory and Critical Care Medicine* 154(2): 274-289.

Surtees PG, Wainwright NW, Luben R, et al. (2006) Mastery, sense of coherence, and mortality: evidence of independent associations from the EPIC-Norfolk Prospective Cohort Study. *Health Psychology* 25(1): 102-110.

Tam S, Woodson BT, Rotenberg B (2014) Outcome measurements in obstructive sleep apnea: Beyond the apnea-hypopnea index. *The Laryngoscope* 124(1): 337-343.

Tang NK and Crane C (2006) Suicidality in chronic pain: a review of the prevalence, risk factors and psychological links. *Psychological Medicine* 36(5): 575-586.

- Tarrier N, Gooding P, Pratt D, et al. (2013) *Cognitive behavioural prevention of suicide in psychosis: a treatment manual*. Routledge.
- Tiemensma J, Gaab E, Voorhaar M, et al. (2016) Illness perceptions and coping determine quality of life in COPD patients. *International Journal of Chronic Obstructive Pulmonary Disease* 11: 2001.
- Tippin J, Aksan N, Dawson J, et al. (2016) Sleep remains disturbed in patients with obstructive sleep apnea treated with positive airway pressure: a three-month cohort study using continuous actigraphy. *Sleep Medicine* 24: 24-31.
- Tkacova R and Dorkova Z (2010) Clinical presentations of OSA in adults. *European Respiratory Society Monograph* 50: 86-103.
- Tramonti F, Maestri M, Carnicelli L, et al. (2017) Relationship quality of persons with obstructive sleep apnoea syndrome. *Psychology, Health & Medicine* 22(8): 896-901.
- Troxel WM, Buysse DJ, Monk TH, et al. (2010) Does social support differentially affect sleep in older adults with versus without insomnia? *Journal of Psychosomatic Research* 69(5): 459-466.
- Tsara V, Kaimakamis E, Serasli E, et al. (2009) Health related quality of life in Greek patients with sleep apnea-hypopnea syndrome treated with continuous positive airway pressure. *Sleep Medicine* 10(2): 217-225.
- Tsuchiyama K, Terao T, Wang Y, et al. (2013) Relationship between hostility and subjective sleep quality. *Psychiatry Research* 209(3): 545-548.
- Weaver EM, Woodson BT, Steward DL (2005) Polysomnography indexes are discordant with quality of life, symptoms, and reaction times in sleep apnea patients. *Otolaryngology-Head and Neck Surgery* 132(2): 255-262.
- Weaver TE and Grunstein RR (2008) Adherence to continuous positive airway pressure therapy: the challenge to effective treatment. *Proceedings of the American Thoracic Society* 5(2): 173-178.
- Weaver TE and Sawyer AM (2010) Adherence to continuous positive airway pressure treatment for obstructive sleep apnea: implications for future interventions. *The Indian Journal of Medical Research* 131: 245-258.
- Weaver TE, Maislin G, Dinges DF, et al. (2007) Relationship between hours of CPAP use and achieving normal levels of sleepiness and daily functioning. *Sleep* 30(6): 711-719.
- Weaver TE (2013) Don't Start Celebrating—CPAP Adherence Remains a Problem. *Journal of Clinical Sleep Medicine: JCSM: Official Publication of the American Academy of Sleep Medicine* 9(6): 551-552.
- Weissman MM, Greenwald S, Niño-Murcia G, et al. (1997) The morbidity of insomnia uncomplicated by psychiatric disorders. *General Hospital Psychiatry* 19(4): 245-250.
- WHOQOL Group (1994) Development of the WHOQOL: Rationale and current status. *International Journal of Mental Health* 23(3): 24-56.
- Wilson IB and Cleary PD (1995) Linking clinical variables with health-related quality of life: a conceptual model of patient outcomes. *Journal of the American Medical Association* 273(1): 59-65.
- Wittmann V and Rodenstein D (2004) Health care costs and sleep apnea syndrome. *Sleep Medicine Reviews* 8(4): 269-279.
- Wojnar M, Ilgen MA, Wojnar J, et al. (2009) Sleep problems and suicidality in the National Comorbidity Survey Replication. *Journal of Psychiatric Research* 43(5): 526-531.
- World Health Organization (2012) Public Health Action for the Prevention of Suicide: A Framework. Available at: <http://apps.who.int/iris/bitstream/10665/75166/1/9789241503570eng.pdf> (accessed 4 January 2017).
- World Health Organization (2016) Suicide. Fact Sheet no. 398. Available at: <http://www.who.int/mediacentre/factsheets/fs398/en/> (accessed 2 August 2016).
- Xiao Y, Han D, Zang H, Wang D (2016) The effectiveness of nasal surgery on psychological symptoms in patients with obstructive sleep apnea and nasal obstruction. *Acta Oto-laryngologica* 136(6): 626-632.
- Young T, Palta M, Dempsey J, et al. (2009) Burden of sleep apnea: Rationale, design, and major findings of the Wisconsin Sleep Cohort study. *Wisconsin Medical Journal* 108(5): 246-249.
- Young T, Peppard PE, Gottlieb DJ (2002) Epidemiology of obstructive sleep apnea: a population health perspective. *American Journal of Respiratory and Critical Care Medicine* 165(9): 1217-1239.
- Yue W, Hao W, Liu P, et al. (2003) A case-control study on psychological symptoms in sleep apnea-hypopnea syndrome. *Canadian Journal of Psychiatry* 48(5): 318-323.

Design of the study and data sources

A sun of rubber
was convulsed and set;
A blood black: nothingness.
A system of cells.
Within cells interlinked.
Within one stem.
And dreadfully distinct.
Against the dark.
A tall white fountain played.

John Francis SHAD
and Vladimir NABOKOV

This chapter provides a general overview of the study design, the origin of the data sources, and the statistical analyses used in this study.

2.1 Study design and setting

This cross-sectional study was conducted at the Department of Pneumology and Phtiseology, L. Pasteur University Hospital, and the Medical Faculty of PJ Safarik University in Kosice, Slovak Republic. All patients who visited the Department for a one-night polysomnography (PSG) between July 2013 and June 2016 and underwent PSG were eligible for the study. In line with ethical principles, we explained the purpose of the study to all participants and guaranteed confidentiality. We also explained that the collected data would only be used for the purposes of this study. All patients completed and signed an informed consent form prior to their participation in the study, which was fully voluntary and included no incentives for participation. The study was approved by the Ethics Committee of PJ Safarik University (approval no. 115/2011).

2.2 Sample and procedure

The Indication for a PSG was based on a general practitioner referral form. OSA was diagnosed based on an overnight sleep examination. Only OSA patients between 18 and 65 years of age were included due to possible functional changes, increased vulnerability and a decline in abilities and performance related to age. The study sample comprised patients with an Apnoea Hypopnoea Index (AHI; number of apnoeas+ hypopnoeas per hour of sleep) score of 5 or more, (American Academy of Sleep Medicine, 2005) who had no previous continuous positive airway pressure (CPAP) therapy or other OSA treatment, were Slovak-speaking and had no major comorbidities. Out of 263 eligible patients, 41 patients who underwent PSG refused to participate in the study, yielding a total response rate of 84.0%. Another 72 patients were excluded because of major comorbidities. The final study population comprised N=150 patients. The reasons for exclusion were major comorbidities related to sleep (a coexisting sleep disorder, such as insomnia, narcolepsy or circadian rhythm sleep disorder), major cardiovascular diseases (e.g. myocardial infarction, angina pectoris, primary pulmonary hypertension); pulmonary conditions (e.g. chronic obstructive pulmonary disease, Pickwick syndrome) and a history of cancer in the past twelve months. Neurological and psychological comorbidities included a neurological condition (e.g. stroke, epilepsy), a major psychiatric diagnosis (e.g. psychotic disorders, major depression) in the medical record, and/or current usage of psychiatric medications which may affect cognitive functions (e.g. benzodiazepines, antipsychotics, or antidepressants), drug abuse in the past six months and regular shift work in the past six months. Due to the assessment of health outcomes related to intimate relationships and sexual functioning, we excluded patients with diabetes and those using hypotensive medication, which may affect sexual function (following Hoekema et al., 2007). The screening for comorbidities was based on medical data and an initial clinical

interview prior to data collection. The clinical diagnoses were established according to the standard International Classification of Diseases-10 revision Codes. Medical examinations of patients were conducted by a pulmonologist specialized in sleep-disordered breathing. Patients with non-respiratory sleep-related complaints (e.g. narcolepsy, insomnia) were routinely referred to another group of clinical specialists. The invitation letter, the informed consent and the questionnaire was sent to participants by postal mail three weeks before the medical examination. One week before the medical examination, patients were reminded about the questionnaire by a phone call. Patients completed the self-report questionnaire at home.

The final study sample comprised 150 OSA patients (AHI $\geq$ 5). The sample had a mean age of 48.9 $\pm$ 9.5 years and consisted of 68% men. More detailed information on each particular sample is described in the separate Chapters 3-7. The process of sample formation is depicted in Figure 2.1.

Figure 2.1 Process of sample formation

2.3 Measures

The Work Role Functioning Questionnaire (WRFQ 2.0) and the Functional Outcomes of Sleep Questionnaire (FOSQ) were systematically translated from the original language. A forward-backward translation was conducted to ensure that no original meaning was lost in the translation. Final changes in the translated versions were made accordingly. The measures used in the Chapters 3–7 are described below.

Functional status

Functional status was assessed using the Functional Outcomes of Sleep Questionnaire (FOSQ) (Weaver et al., 1997; Weaver et al., 2007). The FOSQ is a 30-item self-report, disease-specific measure designed to assess the impact of sleep disorders of excessive daytime sleepiness on multiple activities of functional outcomes relevant to daily behaviour and QoL. Functional status, as a measure of QoL, assesses those activities performed routinely in meeting basic needs and fulfilling essential roles (Leidy, 1994). The FOSQ has five subscales: activity level, vigilance, intimacy and sexual relationships, general productivity, and social outcomes. Patients have to rate the difficulty of performing a given activity on a 4-point scale (no difficulty to extreme difficulty). Responses were averaged (excluding missing responses) to create a subscale score of 1 to 4, and then the subscale scores were summed for the total score (5–20), with higher scores indicating less effect of sleepiness on daily life (Billings et al., 2014). In our sample, the Cronbach's alphas were 0.90 for the total scale, 0.90 for the activity level, 0.84 for vigilance, 0.95 for intimacy and sexual relationships, 0.90 for the general productivity, and 0.82 for the social outcomes subscale, respectively.

Work functioning

Work functioning was assessed using the Work Role Functioning Questionnaire (WRFQ 2.0) (Abma et al., 2013). The WRFQ measures the perceived difficulties in performing work demands among workers, given their emotional or physical health problems. The WRFQ consists of 27 items divided into subscales: work scheduling demands and output demands, physical demands, mental and social demands, and flexibility demands. In addition, a total score can be calculated. Items are answered on a five-point scale: 0 = difficult all the time (100%), 1 = difficult most of the time (75%), 2 = difficult half of the time (50%), 3 = difficult some of the time (25%), 4 = difficult none of the time (0%). The scores on 'Does not apply to my job' are transformed into missing values (Abma et al., 2013). The total score is calculated by adding all the answers and dividing by the number of items and then multiplying by 25 to obtain percentages between 0 and 100. Higher scores indicate better work functioning. To identify the prevalence of impaired work functioning, we used the cut-off value (<90) according Amick et al. (2004). In our sample, the Cronbach's alphas were 0.93 for the total scale, 0.97 for the work scheduling and output demands, 0.90 for the physical demands, 0.90 for the flexibility demands, and 0.94 for the mental and social demands subscale, respectively.

Psychological distress

Psychological distress was assessed using the General Health Questionnaire (GHQ-28) (Goldberg and Hillier, 1979). The GHQ-28 is a 28-item measure of psychological distress in the general population and within community or non-psychiatric clinical settings, such as among primary care or general medical out-patients. The GHQ-28 was developed as a screening tool to detect those likely to be at risk of developing psychiatric disorders. The questionnaire is divided into four subscales: somatic symptoms (items 1–7); anxiety/insomnia (items 8–14); social dysfunction (items 15–21) and severe depression (items 22–28) (Goldberg and Hillier, 1979). The items were assessed on a continuous scale (0–3), with the total score ranging from 0 to 84. Higher scores indicated a higher level of psychological distress. A total score of 23/24 represents the threshold for the presence of psychological distress (Goldberg and Hillier, 1979). In our sample the Cronbach's alpha for the total GHQ-28 scale was 0.83.

Suicidal ideation

Suicidal ideation was assessed using the General Health Questionnaire (GHQ-28) (Goldberg and Hillier, 1979). Four items directly dealing with suicidal ideation were used: "Have you thought about the possibility of killing yourself?"; "Do you wish to be dead and far away from everything?"; "Do you have continual thoughts about ending your life?"; and "Do you have the impression that life is not worth of living?" The validated four-item suicidal ideation subscale of the GHQ-28 has been previously used to assess suicidal ideation (Gili-Planas et al., 2001; Watson et al., 2001). In some previous studies the threshold of $SI \geq 1$ was used to assess the presence of suicidal ideation (Gili-Planas et al., 2001; Biddle et al., 2004). The GHQ threshold is partly determined by the prevalence of multiple diagnoses, with higher thresholds being associated by higher rates of both single and multiple diagnosis (Goldberg, et al. 1998). Thus, we assessed suicidal ideation in a binary manner to determine the prevalence of suicidal ideation, with a cut off of $SI \geq 2$, with the negative responses, given a score of zero, and the positive responses a score of one. The sum-score of the four items of suicidal ideation ranged from 0 to 4. Suicidal ideation was also used as continuous variable (1–4) in structural equation modelling, with a range from 4 to 16. Higher scores indicated a higher level of suicidal ideation. In our sample the Cronbach's alpha was 0.83.

Anxiety

Anxiety was measured using the 21-item Beck Anxiety Inventory (BAI), defining the most common anxiety symptoms (Beck and Steer, 1990). The BAI is a brief measure of anxiety with a focus on somatic symptoms. It was developed as an efficient measure to discriminate between anxiety and depression (Beck et al., 1988). Scores range from 0 to 63, with higher scores indicating a higher anxiety level. The following categories were defined: no anxiety symptoms (score 0–9), mild anxiety (score 10–18), severe anxiety (score 19–29), and very severe anxiety (score 30–63) (Beck and Steer, 1990). The Cronbach's alpha in our sample was 0.90.

Hostility

Hostility was measured by the abbreviated 27-item version of the Cook-Medley Hostility Scale (CMHo) (Cook and Medley, 1954). The CMHo scale is a widely used self-report measure of the trait hostility. The scale primarily assesses the cognitive aspects of hostility, cynicism and mistrust. Cynicism items are defined as statements of belief; aggressive response items reflect behaviour, and hostile affect items reflect emotional experiences. Each item was rated on a dichotomised scale (1=“true”, 0=“false”). The score ranges from 0 to 27, with a higher score indicating a higher level of symptoms (Cook and Medley, 1954). The Cronbach’s alpha for the total scale in our sample was 0.85.

Coping self-efficacy

Coping self-efficacy (CSE) was measured using the 26-item CSE Scale developed specifically for people suffering from chronic disease (Chesney et al., 2006). The CSE scale represents a measure of an individual’s confidence in performing coping behaviours when faced with life challenges. The term CSE relates to the tendency to make certain attributions about control not in one context but many (Lazarus and Folkman, 1984). The CSE scale advances our ability to explore the theoretical links between the secondary appraisal of stress, which asks ‘what can I do?’, and the major coping functions postulated by stress and coping theory – the regulation of distress and the management of underlying problems (Chesney et al., 2006). Coping self-efficacy and coping behaviour are closely linked to each other (Park and Folkman, 1997; Bandura, 1999; Chesney et al., 2006; Mikula et al., 2014; Mikula et al., 2018). The term coping self-efficacy is understood as a prerequisite for using actual coping strategies, as people need to be sure that they can perform coping actions before they act upon them (Chesney et al., 2006). Patients were asked to respond to the following question: ‘When things are not going well for you, or when you are having problems, how confident or certain are you that you can do the following’: ‘sort out what can be changed, and what cannot be changed’, ‘break an upsetting problem down into smaller parts’, ‘look for something good in a negative situation’, and ‘get emotional support from friends and family’, or ‘take your mind off unpleasant thoughts’. The CSE consists of three subscales representing self-efficacy for the use of ‘problem-focused coping’ strategies (ranging from 0 to 120), ‘ability to get support from friends and family’ (ranging from 0 to 50) and the ‘ability to stop unpleasant emotions and thoughts’ (ranging from 0 to 90). Coping self-efficacy for the use of ‘problem-focused coping’ consists of items that measure an individual’s self-efficacy with respect to overcoming problems by analysing the nature of the problem and employing cognitive strategies to make the respondent’s perception of the problem less severe (e.g. ‘break an upsetting problem down into smaller parts’). Coping self-efficacy for the ‘ability to stop unpleasant emotions and thoughts’ measures a respondent’s self-efficacy with respect to trying not to dwell on negative feelings and altering the emotional response to an unsettling event or problem rather than addressing the characteristics of the problem itself (e.g. ‘take your mind off negative thoughts’). The ‘ability to get support from friends and family’ represents a set of items that captures a social dimension by tapping the

respondent’s perception of their ability to seek help from friends and family to cope with problems (e.g. ‘get emotional support from friends and family’) (Chesney et al., 2006). The three factors in the CSE scale are consistent with the three major aspects of coping – problem-focused coping, emotion-focused coping, and social support. Although the scales are correlated, the results of the concurrent validity analyses indicate that the scales assess self-efficacy with respect to different types of coping and lend support to using the factors separately (Chesney et al., 2006). Respondents answered on an 11-point scale. A higher score indicates a higher ability to cope with a particular situation (Chesney et al., 2006). In our sample, the Cronbach’s alphas were 0.94 for self-efficacy for the use of problem-focused coping strategies, 0.86 for coping self-efficacy focused on getting support, and 0.93 for stopping unpleasant emotions and thoughts, respectively.

Mastery

Mastery was measured using the Pearlin Mastery Scale (PMS) (Pearlin and Schooler, 1978). The PMS measures an individual’s level of mastery, a psychological resource that has been defined as “the extent to which one regards one’s life-chances as being under one’s own control in contrast to being fatalistically ruled” (Pearlin and Schooler, 1978). The scale includes 7 items (five negatively worded items and two positively worded items), e.g. “You have little control over the things that happen to you”, and “What happens to you in the future mostly depends upon you”. The negatively worded items require reverse coding prior to scoring, resulting in a score range of 7 to 35, with higher scores indicating higher levels of mastery (Pearlin and Schooler, 1978). The Cronbach’s alpha of the scale was 0.85.

Social support

The Multidimensional Scale of Perceived Social Support (MSPSS) is a 12-item self-report measure of social support (Zimet et al., 1988). It uses a seven-point Likert-type scale, with scores ranging from ‘very strongly disagree’ (1) to ‘very strongly agree’ (7), so the total score ranges from 12 to 84, with higher scores indicating greater social support (Zimet et al., 1988). The MSPSS has three subscales: significant others, family, and friends. In our sample, the Cronbach’s alpha was 0.90 for all three separate subscales, and 0.94 for the total scale, respectively.

Sleep-related problems

Sleep-related problems concerned night-time sleep quality, daytime sleepiness and fatigue. *Night-time sleep quality* was measured using the Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989). The PSQI is a self-rated questionnaire to assess sleep quality and disturbances over a one-month time interval. The PSQI consists of 19 self-report questions covering seven domains: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction. The score ranges from 0 to 21, with higher scores reflecting poor night-time sleep quality. A cut-off score of 5 separates good from poor sleepers (Buysse et al., 1989). Results of some previous studies suggested that the seven PSQI domains are best represented by three latent factors (e.g.

Cole et al., 2006; Casement et al., 2012). The empirical examination of the factor structure of the PSQI identified distinct factors for perceived sleep quality, sleep efficiency, and daily disturbances (Cole et al., 2006). The PSQI subscales subjective sleep quality, sleep medications, and sleep latency loaded on the latent variable *perceived sleep quality*; the PSQI subscales sleep duration and habitual sleep efficiency loaded on the latent variable *sleep efficiency*; and the PSQI subscales sleep disturbances and daytime dysfunction loaded on the latent variable *daily disturbances* (Cole et al., 2006). *Sleep efficiency* is closely related to sleep quantity (Casement et al., 2012), while *daily disturbances* reflect sleep-related daytime impairment (i.e., trouble performing daytime activities) and interruptions in sleep due to physical or psychological symptoms (Casement et al., 2012). In our sample, the Cronbach's alpha was 0.85 for the total PSQI scale.

Daytime sleepiness was measured using the self-report Epworth Sleepiness Scale (ESS), an eight-item questionnaire assessing the tendency to fall asleep in various daytime scenarios (Miletin and Hanly, 2003). The score ranges from 0 to 24, with higher scores indicating greater daytime sleepiness. An ESS total score greater than 10 indicates excessive daytime sleepiness (Miletin and Hanly, 2003). The Cronbach's alpha in our sample was 0.86.

Fatigue was measured using the Multidimensional Fatigue Inventory (MFI-20) (Smets et al., 1995). It consists of 20 items that measure five dimensions of fatigue: general fatigue, physical fatigue, reduced activity, reduced motivation, and mental fatigue. Each dimension contains four items with a five-point response format; the total score in each dimension ranges from 4 (no fatigue) to 20 (highest possible fatigue). The Cronbach's alphas were 0.80 for general fatigue, 0.89 for physical fatigue, 0.75 for reduced activity, 0.81 for reduced motivation, and 0.83 for mental fatigue, respectively.

Sociodemographic and clinical data

Information on age, gender, and marital status was obtained from patient records. Patients were asked to identify the one industry that best characterized their current employment (over the last 24 months) from a list of International Standard Classification of Occupations (International Labour Office, 1990). Patients were also asked to specify their occupation to reduce incorrect or inconsistent information. OSA patients in the following industries were classified as blue-collar workers: primary resource industry, construction industry, manufacturing industry, warehousing, transportation, and trade. Patients employed in public administration, armed forces, government and the service sector (including tourism, business services, education, healthcare, legislators, managerial occupations, professional and utilities) were classified as white-collar workers. Body Mass Index (BMI; height and weight) was assessed by a physician. BMI was categorized into: underweight (<18.50), normal (18.50–24.99), overweight (25.00–29.99) and obese (≥ 30.00). PSG was used to determine whether the diagnosis of OSA was present and to identify the severity of the disorder. OSA severity was determined based on the AHI (American Academy of Sleep Medicine, 2005) score, with three categories: mild OSA (AHI ≥ 5 and ≤ 15), moderate OSA (AHI > 15 and ≤ 30) and severe OSA (AHI

> 30). OSA severity was used as a continuous variable measured by AHI. OSA severity was determined using PSG and was based on an AHI (number of apnoeas + hypopnoeas per hour of sleep) score of 5 or more, according to standard criteria (American Academy of Sleep Medicine, 2005). An obstructive apnoea or hypopnoea can be defined as an event that lasts for ≥ 10 s and is characterized by an absence or a decrease from baseline in the amplitude of a valid measure of breathing during sleep that either reaches $> 50\%$ with an oxygen desaturation of 3% or an arousal (alternatively a 30% reduction with 4% desaturation) (American Academy of Sleep Medicine, 2005). PSG consisted of the overnight recording of left and right electrooculograms, standard central and occipital electroencephalogram, submental electromyogram (EMG), bilateral tibialis EMG, nasal and oral airflow using a thermistor and thoracic, and abdominal excursions using respiratory inductive plethysmography, which directly monitor and quantify the number of respiratory events, related hypoxemia and arousals.

2.4 Statistical analyses

Several statistical methods were used for data analyses. The majority of the analyses were performed using the Statistical Package for the Social Sciences (IBM SPSS 23), MedGraph, and ModGraph. Data management in the meta-analyses was conducted as proposed by Neyeloff et al. (2012). Additionally, Structural Equation Modelling (SEM) was performed (Chapter 6) with Mplus 7.1 (Muthén and Muthén, 2015). We described the background characteristics of the sample and calculated means and standard deviations (SD) for the total sample for continuous variables (Chapter 4–7) and stratified by variables under study, including gender (Chapter 7) and suicidal ideation (Chapter 6). Descriptive procedures included frequencies and percentages for categorical variables. T-tests were conducted to assess differences in the continuous variables. Differences in the categorical variables were analysed using Chi-square tests. Before we proceeded with more complex analyses, we investigated the bivariate correlations between the variables under study (Chapter 4, 5, 7). Partial correlations were used to control for sociodemographic variables (Chapter 6, Chapter 7). We applied an enter method in linear regression in Chapters 4, 5, and 7. We used G*Power 3 (Faul et al., 2009) to analyse different types of power in different statistical tests with medium effect size at $\alpha = 0.05$. Multicollinearity was assessed using the variance inflation factor ($VIF < 2.0$). Missing data were expressed as percentage of total number of patients for each variable. A p-value of < 0.05 was considered statistically significant. Finally, we performed mediation (Chapter 5 and Chapter 7) and moderation analyses (Chapter 4). The proportion of the effect which is mediated was calculated as the indirect effect divided by the total effect and multiplied by 100, while the as-advised standardized total effect was at least ± 0.2 (Kenny, 2016). Sobel z-tests were used to examine the mediating effects in Chapters 5 and 7. To test the moderation effects (Chapter 4), the interaction terms between independent variables were added into the equation (Baron and Kenny, 1986). Detailed information about statistical analyses performed can be found in the “Statistical analyses” section of each chapter.

References

- Abma FI, van der Klink JJ, Bültmann U (2013) The work role functioning questionnaire 2.0 (Dutch version): examination of its reliability, validity and responsiveness in the general working population. *Journal of Occupational Rehabilitation* 23(1): 135-147.
- American Academy of Sleep Medicine (2005) International Classification of Sleep Disorders: Diagnostic and Coding Manual. 2nd ed. Sleep Disorders Association, Rochester, MN (ICSD-2).
- Amick III BC, Habeck RV, Ossmann J, et al. (2004) Predictors of successful work role functioning after carpal tunnel release surgery. *Occupational and Environmental Medicine* 46(5): 490-500.
- Bandura A (1999) Social cognitive theory: an agentic perspective. *Asian Journal of Social Psychology* 2(1): 21-41.
- Baron RM and Kenny DA (1986) The moderator-mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. *Journal of Personality and Social Psychology* 51(6): 1173-1182.
- Beck AT and Steer RA (1991) Relationship between the Beck Anxiety Inventory and the Hamilton Anxiety Rating Scale with anxious outpatients. *Journal of Anxiety Disorders* 5(3): 213-223.
- Beck AT, Epstein N, Brown G, et al. (1988) An inventory for measuring clinical anxiety: psychometric properties. *Journal of Consulting and Clinical Psychology* 56(5): 893-897.
- Beck AT, Steer RA. Beck Anxiety Inventory Manual. (1990) San Antonio: The Psychological Corporation Harcourt Brace Jovanovich Inc.
- Biddle L, Gunnell D, Sharp D, et al. (2004) Factors influencing help seeking in mentally distressed young adults: a cross-sectional survey. *British Journal of General Practice* 54(501): 248-253.
- Billings ME, Rosen CL, Auckley D, et al. (2014) Psychometric performance and responsiveness of the Functional Outcomes of Sleep Questionnaire and Sleep Apnea Quality of Life Index in a randomized trial: the HomePAP study. *Sleep* 37(12): 2017-2024.
- Buysse DJ, Reynolds CF, Monk TH, et al. (1989) The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Research* 28(2): 193-213.
- Casement MD, Harrington KM, Miller MW, et al. (2012) Associations between Pittsburgh Sleep Quality Index factors and health outcomes in women with post-traumatic stress disorder. *Sleep Medicine* 13(6): 752-758.
- Chesney M, Neilands TB, Chambers DB, et al. (2006) A validity and reliability study of the coping self-efficacy scale. *British Journal of Health Psychology* 11(3): 421-437.
- Cole JC, Motivala SJ, Buysse DJ, et al. (2006) Validation of a 3-factor scoring model for the Pittsburgh sleep quality index in older adults. *Sleep* 29(1): 112-116.
- Cook WW and Medley DM (1954) Proposed hostility and pharisaic-virtue scales for the MMPI. *Journal of Applied Psychology* 38(6): 414-418.
- Faul F, Erdfelder E, Buchner A, et al. (2009) Statistical power analyses using G*Power 3.1: Tests for correlation and regression analyses. *Behavioral Research Methods* 41(4): 1149-1160.
- Gili-Planas M, Roca-Bennasar M, Ferrer-Perez V, et al. (2001) Suicidal ideation, psychiatric disorder, and medical illness in a community epidemiological study. *Suicide Life-Threatening Behavior* 31(2): 207-213.
- Goldberg DP and Hillier VF (1979) A scaled version of the General Health Questionnaire. *Psychological Medicine* 9(1): 139-145.
- Goldberg DP, Oldehinkel T, Ormel J (1998) Why GHQ threshold varies from one place to another. *Psychological Medicine* 28(4): 915-921.
- Hoekema A, Stel AL, Stegenga B, et al. (2007) Sexual function and obstructive sleep apnea-hypopnea: A randomized clinical trial evaluating the effects of oral-appliance and continuous positive airway pressure therapy. *The Journal of Sexual Medicine* 4(4): 1153-1162.
- International Labour Office. International standard classification of occupations: ISCO-88. Geneva: International Labour Office; 1990.
- Kenny DA (2016) Mediation. Available at: <http://www.davidakenny.net/cm/mediate.htm> (accessed 7 April 2017).
- Lazarus R and Folkman S (1984) Stress, Appraisal and coping. Springer Publishing Company. ISBN 0-8261-4191-9. 456 pgs.
- Leidy NK (1994) Using functional status to assess treatment outcomes. *Chest* 106(6): 1645-1646.

Mikula P, Nagyova I, Krokavcova M, et al. (2018) Do coping strategies mediate the association between Type D personality and quality of life among people with multiple sclerosis?. *Journal of Health Psychology* 23(12): 1557-1565.

Mikula P, Nagyova I, Krokavcova M, et al. (2014) Coping and its importance for quality of life in patients with multiple sclerosis. *Disability and Rehabilitation* 36(9): 732-736.

Miletin MS and Hanly PJ (2003) Measurement properties of the Epworth sleepiness scale. *Sleep Medicine* 4(3): 195-199.

Muthén LK and Muthén BO (2015) Mplus User's Guide (7.4). Los Angeles, CA: Muthén & Muthén 16(1): 1-27.

Neyeloff JL, Fuchs SC, Moreira LB (2012) Meta-analyses and Forest plots using a microsoft excel spreadsheet: step-by-step guide focusing on descriptive data analysis. *BMC Research Notes* 5(1): 52-56.

Park CL and Folkman S (1997) Meaning in the context of stress and coping. *Review of General Psychology* 1(2): 115-144.

Pearlin LI and Schooler C (1978) The structure of coping. *Journal of Health and Social Behavior* 19(1): 2-21.

Smets EMA, Garssen B, Bonke BD, et al. (1995) The Multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. *Journal of Psychosomatic Research* 39(3): 315-325.

Spiteri MC, Jomeen J, Martin CR (2013) Reimagining the General Health Questionnaire as a measure of emotional wellbeing: a study of postpartum women in Malta. *Women and Birth* 26(4): 105-111.

Watson D, Goldney R, Fisher L, et al. (2001) The measurement of suicidal ideation. *Crisis* 22(1): 12-14.

Weaver TE, Laizner AM, Evans LK, et al. (1997) An instrument to measure functional status outcomes for disorders of excessive sleepiness. *Sleep* 20(10): 835-843.

Weaver TE, Maislin G, Dinges DF, et al. (2007) Relationship between hours of CPAP use and achieving normal levels of sleepiness and daily functioning. *Sleep* 30(6): 711-719.

Zimet, GD, Dahlem, NW, Zimet SG, et al. (1988) The multidimensional scale of perceived social support. *Journal of Personality Assessment* 52(1): 30-41.

And now you're mine.
Rest with your dream
in my dream.
Love and pain and work
should all sleep, now.
The night turns on its
invisible wheels,
and you are pure beside me
as a sleeping ember.

Pablo NERUDA

Chapter 3

Quality of life of obstructive sleep apnoea patients receiving continuous positive airway pressure treatment: a systematic review and meta-analysis

Vladimira Timkova, Iveta Nagyova, Sijmen A. Reijneveld,
Ruzena Tkacova, Jitse P. van Dijk, Ute Bültmann

Heart & Lung: The Journal of Acute and Critical Care.
2020; 49(1): 10-24.

Abstract

Background

Previous studies have shown conflicting results on the effect of continuous positive airway pressure (CPAP) on quality of life (QoL) in obstructive sleep apnoea (OSA) patients.

Objectives

To systematically evaluate the effect of CPAP on QoL in OSA patients compared to sham CPAP, placebo pills, and conservative treatment.

Methods

Studies were identified via Web of Knowledge, PubMed, PsychInfo, CINAHL, EMBASE, OpenGrey, and the Cochrane Library. Effect sizes and effect summaries were used for estimation of CPAP treatment effect. Subgroup analyses and sensitivity analyses were conducted to assess the robustness of the findings.

Results

Meta-analysis of 13 randomised controlled trials showed no significant differences in overall and psychological QoL comparing values of CPAP treated patients with controls; however, physical QoL improved. CPAP significantly affected the overall QoL in studies with controls receiving sham CPAP, parallel design, low risk of bias, and mild OSA patients.

Conclusion

Medical treatment of OSA may help to improve physical symptoms of OSA, whereas impaired psychological QoL still cannot be successfully alleviated with CPAP treatment.

Introduction

Obstructive sleep apnoea (OSA) is an incapacitating chronic disease characterized by repetitive sleep-related episodes of complete (apnoea) or partial (hypopnoea) breathing pauses. It is a prevalent disorder associated with a multitude of adverse outcomes (Aurora et al., 2015). Symptoms of OSA include snoring, sleepiness, and fatigue (Manarino et al., 2012). Most studies have found that OSA concerns 2–10% of the adult population (Stradling and Davies, 2004; Leger et al., 2012). The prevalence of undiagnosed OSA syndrome in Western countries is up to 5% (Young et al., 2002). The impact of OSA on both morbidity and socioeconomic costs is enormous. Costs concern, in particular, health care expenditures and reduced work capacity and work participation (Stradling and Davies, 2004; Mulgrew et al., 2007). Although the exact costs are difficult to calculate, data from 106 countries showed that increased healthcare spending to treat undiagnosed OSA varies between 1,950 and 3,899 dollars per patient per year (Knauert et al., 2015).

OSA is associated with poor quality of life (QoL) (Sharafkhaneh et al., 2005; Mulgrew et al., 2007; Weaver, 2013) and has been linked to severe public health issues, such as obesity, diabetes, metabolic syndrome, cardio-vascular diseases (Stradling and Davies, 2004; Tkacova and Dorkova, 2010), and neuropsychiatric problems (Tkacova and Dorkova, 2010). The occurrence of an impairment in cognitive functioning, reduced vigilance (Kang et al., 2012), microsleeps or accidents is typical in people with OSA (Tregear et al., 2009). Sharafkhaneh et al. (2005) showed a significantly higher prevalence of mood disorders, posttraumatic stress disorder, psychosis and dementia among OSA patients. Some studies report an increased prevalence of suicidal ideation in OSA patients (Choi et al., 2015) when compared to the general population.

In terms of treatment, continuous positive airway pressure (CPAP) is the first treatment of choice in most OSA patients (American Academy of Sleep Medicine, 2008). CPAP has been reported to be effective in reducing OSA symptoms, cardiovascular morbidity and mortality, neurocognitive consequences and sleepiness, and in improving QoL (Moyer et al., 2001; Giles et al., 2006; Ye et al., 2009; Kuhn et al., 2017). Krahn et al. (2008) described a decrease in depression and suicidal ideation in untreated OSA patients immediately after the initiation of CPAP treatment. In recent years, increasing attention has been paid to the effectiveness of CPAP treatment on QoL improvement. The efficiency of OSA treatment has typically been judged based on polysomnography (PSG) outcomes. However, patients' reports of improvement were often found to be discordant with PSG results. Thus, other clinically important outcomes, including QoL and functional status, have been recommended as complementary outcomes in the evaluation of treatment response (Weaver et al., 2005).

Previous systematic reviews (Moyer et al., 2001; Merino et al., 2017) and meta-analyses (Jing et al., 2008; Kuhn et al., 2017; Patil et al., 2019) have shown conflicting results on the effect of CPAP treatment on QoL in OSA patients. The findings vary from improvement of QoL after receiving CPAP treatment (Moyer et al., 2001;

Merino et al., 2017) to improvement in the physical QoL domain only (Jing et al. 2008), or overall QoL improvement only when disease specific QoL measures (Patil et al., 2019), and also when all prospective studies, i.e. not only randomised controlled trials (RCTs) (Kuhn et al., 2017), were included.

Furthermore, earlier meta-analyses of RCTs included only one type of QoL measure (Kuhn et al., 2017); analysed studies focusing exclusively on elderly OSA patients (Jing et al., 2008; Kuhn et al., 2017; Merino et al., 2017) and included studies where the whole sample of OSA patients suffered from major comorbidities, such as stroke or heart failure (Jing et al., 2008; Kuhn et al., 2017; Patil et al., 2019), or studies of a combination of CPAP treatment with conservative treatment (Jing et al., 2008; Patil et al., 2019). We therefore aimed to systematically evaluate the effect of CPAP treatment on QoL in OSA patients compared to sham CPAP, placebo pills, and conservative treatment. Our systematic review and meta-analysis was restricted to RCTs only, with the exclusion of studies having a clear focus on major comorbidities, populations of children or elderly OSA patients, and studies that combined CPAP treatment with conservative treatment.

Methods

A systematic literature review was conducted in accordance with the current guidelines for systematic reviews and meta-analyses (Higgins and Green, 2011). The multidisciplinary systematic review team consisted of six reviewers (VT, IN, SAR, RT, JPvD, and UB). Two authors had expertise in psychology (VT, IN), one in pulmonology, tuberculosis and respiratory diseases (RT), and three authors were trained in epidemiological methods and public health (SAR, JPvD, and UB).

Formulation of the research question

The research question was formulated according to the PICO method (Higgins and Green, 2011), i.e.: ‘In obstructive sleep apnoea patients, what is the effect of CPAP treatment on QoL compared to placebo pills, sham CPAP, and conservative treatment?’ The anticipated *outcome* was improved overall QoL as well as the improvement in psychological and physical QoL after CPAP treatment.

Search strategy and study identification

Studies were identified via Web of Knowledge, PubMed, PsychInfo, CINAHL, EMBASE, and the Cochrane Library from the inception date of the databases to March 2019. OpenGrey database was searched for any resources that might have been missed. Previous systematic reviews, meta-analyses, and guidelines were sought, and their reference lists were scanned. We did not include dissertations, economical evaluations, technical reports, conference abstracts, case studies, and letters. We did not use any language restrictions. Titles and abstracts were screened to identify potentially relevant studies. If the suitability of an article was uncertain, the full text was reviewed. We used keywords (Table 3.1) according to the PICO method (Higgins and Green, 2011). The detailed literature search strings for each

of the databases can be found in Supplement 3.1 (Table S3.2). Inclusion criteria were: RCTs examining the effect of CPAP treatment on QoL in OSA patients compared to controls using placebo pills, sham CPAP, or conservative treatment.

Table 3.1 Description of used keywords according to the PICO method

P=population/patients/problem	‘sleep apnea’, ‘sleep apnoea’, ‘OSA’
I=intervention	‘continuous positive airway pressure’, ‘CPAP’
C= comparison/control	‘placebo pills’, ‘sham CPAP’, ‘conservative treatment’
O=outcome	‘quality of life’, ‘health status’, ‘self-rated health’, ‘self-perceived health’, ‘functional status’

Exclusion criteria

We excluded reviews, meta-analyses, studies focusing only on compliance with CPAP treatment or side effects of CPAP and different healthcare services, studies including only baseline comparison without a control group, and studies focusing on other types of treatment, or a combination of CPAP treatment with conservative treatment, such as lifestyle interventions. Studies including children, adolescents (<18), and elderly OSA patients (≥65 years of age) only were also excluded because of a possible increased vulnerability, functional changes, and a decline in abilities and/or performance related to age. Since major comorbidities may influence QoL, sleep, and affective symptomatology (Macey et al., 2010), studies including a primary study sample with an acute or severe comorbid medical illness, such as stroke, neurological disorders, heart failure, myocardial infarction, cognitive decline, or psychiatric diagnoses, were also excluded. The verification of the presence of major comorbidities in the full sample of OSA patients was based on Title, Abstract, and full-text screening.

We developed a form to standardize the first selection of relevant studies, based on the following criteria: 1) the study is an RCT, quantitative, and interventional; 2) the study population consists of adult OSA patients diagnosed by a medical professional; 3) the intervention is CPAP, and a control condition is present; and 4) generic or disease-specific QoL is measured. The title, abstract, and full-text screening were conducted independently by VT and IN. Disagreements were resolved by reaching a consensus of opinion. A third author (UB) was invited if consensus could not be achieved. Full-text screening was conducted by VT.

Types of studies

We included RCTs with parallel (Jenkinson et al., 1999; Barbé et al., 2001; Montserrat et al., 2001; Chakravorty et al., 2002; Siccoli et al., 2008; Weaver et al., 2012; Batool-Anwar et al., 2016) and crossover design (Engleman et al., 1997; Engleman et al., 1998; Engleman et al., 1999; Faccenda et al., 2001; Barnes et al., 2004; Marshall et al., 2005).

Type of participants

Included were OSA patients newly diagnosed by a medical professional using nocturnal, laboratory-based PSG or oximetry. The standard criterion of five or more apnoeas/hypopnoeas per hour of sleep was used to diagnose OSA by PSG. OSA patients were diagnosed as mild, moderate and severe, with an AHI greater than 5/hr, 15/hr, and 30/hr, respectively (Iber et al., 2007). In oximetry, an apnoea was defined as a minimum of 10 seconds of airflow cessation, and a hypopnoea was determined by a 30% reduction in airflow preceding a period of normal breathing for a minimum of 10 seconds and oxyhemoglobin desaturation (decrease in SpO₂ $\geq$ 4%) (Berry et al., 2012). Severity of OSA was measured by the number of falls in arterial oxygen saturation (SaO₂) of more than 4% in each hour of study (Jenkinson et al., 1999). All participants were treatment naïve at the start of the research. Controls/comparisons were defined as placebo pills, sham CPAP, and conservative treatment.

The intervention

The intervention was defined as CPAP treatment with a duration of at least two weeks. CPAP devices were titrated to an effective pressure to overcome respiratory disturbances.

Concept of quality of life and health-related quality of life

The World Health Organization Quality of Life (WHOQoL) group defined QoL as ‘an individual’s perception of their position in life, in the context of the culture and values in which they live and in relation to their goals, expectations, standards and concerns’ (WHOQoL Group, 1994). QoL has several domains, such as functional competence, health-related complaints, and psycho-social functioning. Health-related QoL (HRQoL) is understood as an integral QoL domain and is increasingly used as an outcome of treatment effectiveness. In broad terms, HRQoL serves as a restricted QoL definition, as it was designed to exclude external domains, such as housing, financial situation, living conditions or spirituality. HRQoL is associated with an expanded concept of health status, embracing social interaction as well as emotional and psychological well-being (Krabbe, 2017). The concepts of QoL and HRQoL are closely tied to each other (Dutt et al., 2016). When QoL is discussed in relation to health or diseases, it almost always means HRQoL, unless specified otherwise (Dutt et al., 2016). According to Schipper (1992), QoL in clinical medicine represents the functional effect of disease and its consequent treatment upon patient, as perceived by the patient. It is concluded that the concept of HRQoL as used now is confusing as most of the definitions fail to distinguish between HRQoL and health or between HRQoL and QoL (Carlozzi and Tulskey, 2013; Karimi and Brazier, 2016). Perhaps more reasonable is the variant of the definition, where HRQoL is the aspects of QoL the most significantly affected by ill health. However, in practice, this definition may not eliminate the number of QoL domains much because it is problematic to define ‘most’ (Karimi and Brazier, 2016). Furthermore, most of the previous systematic reviews and meta-analyses (Moyer et al., 2001; Jing et al., 2008; Schwartz et al., 2018; Patil et al., 2019) as well as all RCTs included in

our meta-analysis used the term QoL, while one RCT used both terms interchangeably (Chakravorty et al., 2002). Thus, we will use in this paper the term QoL, with omission of external domains, such as spirituality or living conditions.

Main comparisons

Based on the type of QoL scales we aimed to conduct the following comparisons: a) the effect of CPAP treatment on overall QoL (using general QoL scales); b) the effect of CPAP treatment on psychological QoL (using psychological QoL subscales); c) the effect of CPAP treatment on physical QoL (using physical QoL subscales).

Sensitivity analyses

We conducted sensitivity analyses to reveal the potential sources of heterogeneity, such as the number of participants in analysed studies, the duration of CPAP treatment, the level of compliance with CPAP treatment, and risk of bias (RoB). We repeated the analyses with restrictions regarding: a) *number of participants* $N > 100$ (the effect of CPAP treatment on overall/psychological/physical QoL in RCTs involving participants of $N > 100$ (following Dechartres, 2013; Grainge, 2015)); b) *duration of CPAP treatment* > 6 weeks (the effect of CPAP treatment on overall/psychological/physical QoL in RCTs with duration of CPAP treatment of more than 6 weeks); c) *compliance level* ≥ 4 h/night (the effect of CPAP treatment on overall/psychological/physical QoL in RCTs involving participants with CPAP compliance level of ≥ 4 h/night); and d) *low RoB* (the effect of CPAP treatment on overall/psychological/physical QoL restricted to RCTs with low RoB).

Subgroup analyses

We analysed how the CPAP treatment effect varies across different subgroups of patients or trials. The covariates included type of control group, OSA severity, study design, and type of QoL measures. The following subgroup comparisons were conducted based on: a) *type of control group* (the separate analyses of the effect of CPAP treatment on overall/psychological/physical QoL in RCTs involving controls using placebo pills, sham CPAP, and conservative treatment); b) *OSA severity* (the separate analyses of the effect of CPAP treatment on overall/psychological/physical QoL in RCTs involving patients with mild OSA and moderate to severe OSA); c) *study design* (the separate analyses of the effect of CPAP treatment on overall/psychological/physical QoL in RCTs with a crossover design and parallel design); d) *type of QoL measures* (the separate analyses of the effect of CPAP treatment on overall/psychological/physical QoL in RCTs using generic QoL measures and disease-specific measures).

Data extraction and management

Two authors (VT, IN) extracted the following information from each study: a) *general*: title, country, language of publication, year of publication; b) *methods*: study design, setting, inclusion and exclusion criteria, follow-up, standardized QoL instruments, QoL domains; c) *participants*: OSA diagnosis, adult population (age of

the whole group > 18 years, ≤ 65 years), no focus on major comorbidid diseases other than OSA (such as stroke, myocardial infarction, neuropsychiatric disorder), age, sex distribution; *d) intervention per treatment group*: use of CPAP treatment, duration of CPAP treatment; compliance with CPAP treatment; *e) controls/comparisons*: placebo pills, sham CPAP, conservative treatment; *f) outcomes*: QoL improvement, overall QoL scores, and psychological/physical QoL; *g) results*: CPAP treatment effect on QoL improvement in OSA patients. In case of disagreement in data extraction, consensus was achieved by discussion between the two review authors (VT, IN). If needed, a third author (UB) was invited to resolve disputes. Mean differences between the groups for the continuous outcomes, and standard deviations/standard errors of the group differences were extracted for the meta-analysis.

Dealing with missing data

When information for the meta-analysis was missing, we asked the author to provide the information. If the author did not reply, or the information was no longer available, the study was not included in the meta-analysis.

Assessment of risk of bias

The risk of bias (RoB) was assessed by two authors (VT, UB) using the Cochrane Collaboration tool for assessing RoB, as described in the *Cochrane Handbook for the Systematic Review of Interventions*, version 5.1.0 (Higgins and Green, 2011). The following nine criteria were assessed: Random sequence generation, Allocation concealment, Blinding of participants, Blinding of personnel, Blinding of outcome assessment, Co-interventions avoided, Treatment fidelity, Incomplete outcome data and Selective outcome reporting. We scored the criteria as ‘low RoB’, ‘high RoB’, or ‘unclear RoB’ (Higgins and Green, 2011). When the two independent authors disagreed about the RoB, they tried to reach a consensus. If consensus could not be achieved, a third author (IN) was invited in. Key domains for summary RoB assessment were identified, such as random sequence generation, allocation concealment, and incomplete outcome data (Nieuwenhuijsen et al, 2014). We judged studies to have a high RoB when one or more key domains were rated as high RoB. We judged studies to have an unclear RoB when one or more key domains were rated as “unclear”. We judged studies to have a low RoB when all the key domains were rated as low RoB (Higgins and Green, 2011; Nieuwenhuijsen et al, 2014). Subsequently, we calculated the proportion of items that were scored as having low, unclear, or high RoB.

Assessment of heterogeneity

Heterogeneity was investigated using Cochrane’s Q statistic and I^2 statistics. Due to differences in sample sizes of the included studies, we used random-effects models, as study weights were defined to be more balanced under the random-effects model than under the fixed-effects model (Borenstein et al., 2009). Furthermore, when studies are gathered from the published literature, the random-effects model is found to be generally a more plausible match (Borenstein et al., 2009). As

Cochrane’s Q is considered to be vulnerable to small sample sizes, the I^2 provided an estimate of the proportion of real variance caused by extraneous study variables. I^2 thresholds have been proposed (Higgins et al., 2003), with 25, 50, and 75% representing low, moderate, and high variance, respectively.

Assessment of reporting biases

Visual inspection with funnel plots and the Egger test (Egger et al., 1997) were used to evaluate publication bias in the reviewed studies.

Quality of the evidence

We applied GRADE criteria (Ryan and Hill, 2016) to assess the confidence in the estimated effects within the studies. Two reviewers (VT, IN) worked independently to assess the quality of the evidence and resolve disagreements. At the start of the GRADE assessment we assumed the presence of high quality for all included studies. We downgraded a starting rating of “high quality” evidence by one level (or by two levels for very serious concerns) for RoB, inconsistency, indirectness, imprecision, and publication bias (Ryan and Hill, 2016).

We considered random sequence generation, allocation concealment, and incomplete outcome data as prerequisites for high quality (following Nieuwenhuijsen et al., 2014). We only considered studies with low risks on these items to have a low RoB. To assess the RoB for a comparison, we considered the RoB for each study included in that comparison (following Ryan and Hill, 2016). For each comparison we downgraded the quality due to the RoB (-1) if most of the outcome information was from studies at low or unclear RoB, as this could seriously alter the results. We applied a -2 downgrade in case of a high RoB for one criterion, or multiple criteria, that were considered as likely to very seriously alter the results. For inconsistency, we considered an I^2 value of 50% to 75% downgrade (-1). Indirectness of the evidence was not an issue in our review, as all comparisons in the included studies directly addressed the comparison. For imprecision of results, we judged serious imprecision leading to downgrading (-1) if a comparison either included less than 400 participants or a wide CI around the effect estimate. For a non-significant effect, we considered a CI to be wide if it included an effect size of both 0 and a moderate effect size (>0.5 or <-0.5). For a significant effect, we considered a CI to be wide if it included both a small and large effect size (small=0.2 or -0.2; large=0.8 or -0.8). We applied a -2 downgrade in case of imprecision based on the both assessed points.

In the GRADE system, the quality of evidence for each outcome is scored as high, moderate, low, or very low. In high quality studies, further research is very unlikely to change our confidence in the estimate of effect. In studies with moderate quality, further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. Low quality of evidence means that further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. In studies with very low quality of the evidence any estimate of effect is very uncertain (Ryan and Hill, 2016).

Measures of treatment effect and data synthesis

A total of 13 RCTs were included in the MA. The analyses were performed using the Statistical Package for the Social Sciences (IBM SPSS 23) and Microsoft Office Excel, following Neyeloff et al. (2012). We used random-effects models by calculating the Cohen's d effect sizes (ES) with their standard errors (SE) as the standardized outcome of the CPAP treatment effect (Hedges and Olkin 2014). ES was calculated for each QoL outcome for which a complete assessment was possible. ESs were calculated from means and standard deviations (SD). When the SD was not available it was calculated from the SE of the mean using the following formula: $SD = SE \sqrt{N}$. Cohen's d ES was calculated according to the following formula:

$$ES = \frac{\text{mean controls} - \text{mean CPAP}}{\text{pooled SD}}$$

ES was positive, if the mean difference was in the predicted direction and favoured real CPAP treatment (where 0.20–0.40 means a small ES; 0.50–0.70 a medium ES; and 0.80 or higher a large ES). The comparison of CPAP treatment effect vs. the control group was described as: 'negative direction of ES' for differences favouring the control group; and 'positive direction of ES' for differences favouring the real CPAP treatment group. Finally, the effect summary ($\overline{ES}_v$) was computed using a random effects model by calculating a new weight (w_v) for each QoL outcome adjusted with the constant (v). $\overline{ES}_v$ was calculated using the following formula: $\overline{ES}_v = \frac{\sum (w_v * ES)}{\sum w_v}$.

Additionally, the confidence intervals (CIs) for the ES of each study and ($\overline{ES}_v$) were computed with the 95% confidence coefficient used as the default, following Hedges and Olkin (2014). CIs were calculated with the formula $CI = ES \pm 1.96 * SE$. Forest plots were used for graphical representations of the MA.

Results

Results of the search process

After title, abstract, and full-text screening, 13 RCTs describing the effectiveness of CPAP treatment met the inclusion criteria (see flowchart Figure 3.1). One of the eligible studies (Campos-Rodrigues et al., 2016) was excluded from our MA, as we did not receive the missing, additional information.

Figure 3.1 Flow diagram of study selection process (Moher et al., 2009)

Description of included studies

All studies included in our meta-analysis investigated whether real CPAP treatment affected QoL more significantly compared to the control condition. Seven RCTs had a parallel design and six RCTs had a crossover design. As the study by Montserrat et al. (2001) combined a partial crossover and parallel design, we analysed the parallel comparisons only. The duration of CPAP treatment ranged between 3 and 24 weeks. Most of the studies used only one treatment centre, two studies were multi-centre studies (Barbé et al., 2001; Batool-Anwar et al., 2016). Data in all the studies were collected during the patients' clinical visits.

A total of 678 participants formed the control group and 795 participants received real CPAP treatment. The number of participants in the reviewed studies varied between 8 (Engleman et al., 1997) and 409 (Batool-Anwar et al., 2016). The reported ages of the patients ranged from 25 to 72 years. The number of female patients varied from 0 to 103. Two studies (Jenkinson et al., 1999; Siccoli et al., 2008) included only male OSA patients. In all included RCTs, all subjects underwent a baseline assessment with PSG first and were then randomised to CPAP, treatment with placebo pills, sham CPAP, or conservative treatment (Table 3.3). Oximetry was used to diagnose OSA in one study by Jenkinson et al. (1999). Patients suffered from mild to severe OSA.

Five crossover studies (Engleman et al., 1997; Engleman et al., 1998; Engleman et al., 1999; Faccenda et al., 2001; Barnes et al., 2004) compared CPAP treatment with placebo pills. With the permission of local ethic committee, patients were informed that the oral placebo tablet (Glaxo pills, UK) may improve their daytime function in total of three studies (Engleman et al., 1997; Engleman et al., 1998; Engleman et al., 1999). In two studies (Faccenda et al., 2001; Barnes et al., 2004) no specific information on placebo pills was provided.

Six parallel (Jenkinson et al., 1999; Montserrat et al., 2001; Siccoli et al., 2008; Barbé et al., 2001; Weaver et al., 2012; Batool-Anwar, 2016) and one crossover study (Marshall et al., 2005) used a machine set at subtherapeutic pressure, connected to a mask with holes to produce a leak as placebo (sham CPAP). Chakravorty et al. (2002) conducted a study with parallel design and used conservative treatment, including weight loss and sleep hygiene, to compare with CPAP treatment.

When a repeated measures design was used (Batool-Anwar et al., 2016), the longer duration of CPAP treatment on QoL was analysed. If possible, we also included groups of participants with a higher compliance level (≥ 4 hours/night) (Engleman et al., 1997; Batool-Anwar et al., 2016) and a longer treatment duration (Batool-Anwar et al., 2016) in the final meta-analysis. If more than one similar QoL estimator was used (Chakravorty et al., 2002; Siccoli et al., 2008), we used the estimator that could provide us with the most comprehensive information related to QoL. More detailed information about the study design, number of included participants, disease severity, type of control group, duration of the intervention, and instruments used to measure QoL is provided in Table 3.3. The criteria for inclusion and exclusion of the participants in the particular study type, sociodemographic data, clinical data, and mean values of CPAP compliance are presented in Supplement 3.2, Table S3.4.

Table 3.3 Overview of the included studies

Study	Design	N	OSA severity	Intervention, type of control group, treatment duration	d; 95%CI	QoL instruments
Engleman et al., 1997* Scotland	-RCT, crossover	-8 patients with compliance ≥ 5 -8 CPAP 8 controls	mild	-CPAP patients/ placebo pills -1 month	1.07; 95%CI (-0.72; 2.14)	NHP
Engleman et al., 1998* Scotland	-RCT, crossover -single blind	-23 CPAP -23 controls	moderate to severe	-CPAP patients/ placebo pills -1 month	0.09; 95%CI (-0.73; 0.91)	NHP
Engleman et al., 1999* Scotland	-RCT, crossover	-34 CPAP -34 controls	mild	-CPAP patients/ placebo pills -1 month	0.24; 95%CI (-0.43; 0.92)	NHP
Jenkinson et al., 1999 UK	-RCT, parallel -double blind	-52 CPAP -49 controls	moderate to severe	-CPAP patients/ sham CPAP -1 month	1.00; 95%CI (0.46; 1.25) 0.38; 95%CI (0.01; 0.76)	SF-36 mental component SF-36 physical component
Barbé et al., 2001 Spain	-RCT, parallel -double blind	-29 CPAP -25 controls	severe	-CPAP patients/ sham CPAP -1.5 month	-0.10; 95%CI (-0.63; 0.44) 0.19; 95%CI (-0.34; 0.73) -0.27; 95%CI (-0.73; 0.54)	SF-36 mental component SF-36 physical component FOSQ
Faccenda et al., 2001 UK	-RCT, crossover	-68 CPAP -68 controls	moderate and severe	-CPAP patients/ placebo pills -1 month	0.16; 95%CI (-0.30; 0.60)	FOSQ

Table 3.3 Overview of the included studies - continued

Study	Design	N	OSA severity	Intervention, type of control group, treatment duration	d; 95%CI	QoL instruments
Montserrat et al., 2001 Spain	-RCT, parallel, (partial crossover) -double blind	-23 CPAP -22 controls	moderate and severe	-CPAP patients/ sham CPAP -1.5 month	0.52; 95%CI (-0.08; 1.11) -0.30; 95%CI (-0.89; 0.29) 0.21; 95%CI (-0.38; 0.79)	FOSQ SF-36 mental component SF-36 physical component
Chakravorty et al., 2002 UK	-RCT, parallel	-32 CPAP -21 CT controls	moderate to severe	-CPAP patients/ CT controls -3 months	0.00; 95%CI (-0.07; 0.07)	EuroQoL (Usq)
Barnes et al., 2004 Australia	-RCT, crossover	-80 CPAP -80 controls	mild to moderate	-CPAP patients/ placebo pills -3 months	0.00; 95%CI (-0.48; 0.48)	FOSQ
Marshall et al., 2005 New Zealand	-RCT, crossover	-29 CPAP -29 controls	mild	-CPAP patients/ sham CPAP -3 weeks	0.30; 95%CI (-0.50; 1.10)	FOSQ
Siccoli et al., 2008 UK	-RCT, parallel -double blind	-50 CPAP -49 controls	moderate to severe	-CPAP patients/ sham CPAP -1 month	0.42; 95%CI (-0.14; 0.97) 0.04; 95%CI (-0.35; 0.44) 0.44; 95%CI (-0.12; 0.99)	SF-36 mental component SF-36 physical component SAQLI
Weaver et al., 2012 USA	-RCT, parallel -double blind	-113 CPAP -110 controls	mild to moderate	-CPAP patients/ sham CPAP/ -2 months	0.41; 95%CI (0.14; 0.67)	FOSQ

Table 3.3 Overview of the included studies - continued

Study	Design	N	OSA severity	Intervention, type of control group, treatment duration	d; 95%CI	QoL instruments
Batool-Anwar et al., 2016 USA	-RCT, parallel -double blind	-249 CPAP -160 controls with compliance >4	mild to severe	-CPAP patients/ sham CPAP/ -6 months	0.14; 95%CI (-0.06; 0.34)	SAQLI
Subgroup analyses						
		-mild OSA -16 controls -37 patients with compliance >4		-6 months	-0.13; 95%CI (-0.72; 0.46)	
		-moderate to severe OSA -98 controls -146 OSA patients with compliance >4		-6 months	0.27; 95%CI (0.01; 0.53)	

CPAP: continuous positive air pressure; QoL: quality of life; RCT: randomised control trial; d: effect sizes for subscales comparison of CPAP effect vs. control group; (d - a statistically significant difference favouring the control group; d + a statistically significant difference favouring the treatment group); 0.20-0.40 -small effect size; 0.50-0.70 -medium effect size; 0.80>large effect size. CI: confidence interval, CT: conservative treatment; * all participants in the studies by Engleman et al. (1997; 1998; 1999) were recruited from the new attenders at the sleep clinic (Engleman et al., 1999).

Quality of life measures

QoL was measured using generic questionnaires – the Short Form 36 Health Survey – (SF-36), the Nottingham Health Profile (NHP), the European Quality of Life Questionnaire (EuroQoL) and disease specific QoL questionnaires – the Calgary Sleep Apnea Quality of Life Index (SAQLI) and the Functional Outcomes of Sleep Questionnaire (FOSQ). Out of the 13 analysed RCTs, 12 studies measured overall QoL and four studies assessed the level of psychological and physical QoL.

Risk of bias in the included studies

As shown in Table 3.4, we considered the overall RoB to be high in three studies (Chakravorty et al., 2002; Barnes et al., 2004; Siccoli et al., 2008). These studies had either unclear (Chakravorty et al., 2002; Barnes et al., 2004) or inadequate (Siccoli et al., 2008) allocation concealment. Two (Chakravorty et al., 2002; Barnes et al., 2004) of these three studies also had incomplete outcome data. We considered seven studies to have an overall unclear RoB (Engleman et al., 1997; Engleman et al., 1998; Jenkinson et al., 1999; Barbé et al., 2001; Montserrat et al., 2001; Weaver et al., 2012; Batool-Anwar et al., 2016). We judged three studies to have low RoB (Engleman et al., 1999; Faccenda et al., 2001; Marshall et al., 2005). Figure 3.2 shows the proportion of items that were scored as low, unclear, or high RoB.

Table 3.4 Risk of bias assessment

Study ID	Level of RoB*	a	b	c	d	e	f	g	h	i
Engleman et al., 1997	unclear	?	?	-	-	?	+	+	+	+
Engleman et al., 1998	unclear	+	?	+	-	-	+	+	+	+
Engleman et al., 1999	low	+	+	-	-	?	+	+	+	+
Jenkinson et al., 1999	unclear	+	?	+	+	?	+	?	+	+
Barbé et al., 2001	unclear	+	?	+	+	+	+	+	+	+
Faccenda et al., 2001	low	+	+	-	?	+	+	?	+	+
Montserrat et al., 2001	unclear	+	?	+	?	+	-	+	+	+
Chakravorty et al., 2002	high	+	?	-	-	?	+	?	-	+
Barnes et al., 2004	high	+	?	-	-	?	+	+	-	+
Marshall et al., 2005	low	+	+	-	+	?	+	+	+	+
Siccoli et al., 2008	high	+	-	+	+	-	+	+	+	+
Weaver et al., 2012	unclear	?	?	+	+	+	?	+	?	+
Batool-Anwar et al., 2016	unclear	+	?	+	+	?	+	+	+	+

+ Low risk of bias; - High risk of bias; ? Unclear risk of bias; a. Random sequence generation, b. Allocation concealment, c. Blinding of participants; d. Blinding of personnel; e. Blinding of outcome assessment; f. Co-interventions avoided; g. Treatment fidelity; h. Incomplete outcome data; i. Selective outcome reporting; *Level of RoB per study based on a, b, and h.

Figure 3.2 Flow chart of the risk of bias graph: judgements about each risk of bias item presented as percentages across all the included studies

Assessment of reporting biases

A total of three estimators favoured the control group, and two estimators showed no difference in CPAP treatment effects when compared to controls (Figure 3.3 a, b, c). In general, the funnel plots showed a low possibility of publication bias. The results of the Egger tests for publication bias were not significant for the overall QoL ($p=0.59$), the psychological QoL domain ($p=0.44$), and the physical QoL domain ($p=0.29$).

Figure 3.3 a Funnel plot of publication bias for overall QoL

Figure 3.3 b Funnel plot of publication bias for psychological QoL

Figure 3.3 c Funnel plot of publication bias for physical QoL

Meta-analyses

Meta-analyses were conducted with 13 RCTs. ESs were computed for overall QoL and the physical and psychological domains. $\overline{ES}_v$ was used as the standardized outcome of the CPAP treatment effect. The forest plots show the ESs with CIs for scales and subscales and the final $\overline{ES}_v$ obtained by using a random effects model.

Overall QoL score

The effect of CPAP treatment compared to placebo pills, sham CPAP treatment, and conservative treatment was examined in 12 RCTs. The meta-analysis demonstrated a negligible improvement in overall QoL score with CPAP treatment (0.18; 95%CI=0.10, 0.26) in OSA patients compared to controls. A moderate I^2 (68%) was found (Figure 3.4 a).

Figure 3.4 a Meta-analysis of CPAP treatment effect on improvement in overall QoL score; effect sizes and 95% confidence intervals

Psychological QoL score

CPAP did not show significant superiority to controls in terms of psychological QoL (0.25; 95%CI=-0.23; 0.72). A low I^2 (31%) was found (Figure 3.4 b).

Figure 3.4 b Meta-analysis of CPAP treatment effect on improvement in psychological QoL score; effect sizes and 95% confidence intervals

Physical QoL score

The meta-analysis demonstrated a small, but significant improvement in physical QoL (0.20; 95%CI=0.04, 0.35) with CPAP treatment in OSA patients compared to controls. A low I² (26%) was observed (Figure 3.4 c).

Figure 3.4 c Meta-analysis of CPAP treatment effect on improvement in physical QoL score; effect sizes and 95% confidence intervals

Sensitivity analyses

We performed sensitivity analyses to assess the effect of CPAP treatment on overall QoL when controlled for the number of included participants, duration of intervention, level of compliance with CPAP treatment, and RoB. As the studies measuring psychological and physical QoL (Jenkinson et al., 1999; Barbé et al., 2001; Montserrat et al., 2001; Siccoli et al., 2008) were homogenous in terms of the number of included participants (N≤100), duration of intervention (≤ 6 weeks),

compliance level (≥4 hours/night), and RoB, not enough data were available to conduct sensitivity analyses for psychological and physical QoL.

The effect of CPAP treatment on overall QoL controlled for number of participants (N>100)

Sensitivity analysis of four studies (Faccenda et al., 2001; Barnes et al., 2004; Weaver et al., 2012; Batool-Anwar et al., 2016), controlled for the number of participants (N>100), showed small, non-significant improvement in overall QoL score with CPAP treatment (0.19; 95%CI =-0.01; 0.38; I²=4%).

The effect of CPAP treatment on overall QoL controlled for duration of CPAP (>6 weeks)

CPAP did not show superiority to controls in terms of effect on overall QoL score (0.13; 95%CI =0.03; 0.22; I²=31%) in the four studies (Chakravorty et al., 2002; Barnes et al., 2004; Weaver et al., 2012; Batool-Anwar et al., 2016) with a treatment duration of more than 6 weeks.

The effect of CPAP treatment on overall QoL controlled for compliance with CPAP treatment (≥4.0 hrs/night)

We found no significant difference in overall QoL comparing CPAP treated patients with controls (0.32; 95%CI =-0.20; 0.79; I²=10%) in four studies with a CPAP compliance level of at least 4 hours per night (Engleman et al., 1997; Barbé et al., 2001; Marshall et al., 2005; Siccoli et al., 2008).

The effect of CPAP treatment on overall QoL controlled for risk of bias

CPAP showed superiority to controls in terms of the effect on overall QoL score (0.20; 95%CI= 0.12; 0.27; I²=13%) in three studies with low RoB (Engleman et al., 1999; Faccenda et al., 2001; Marshall et al., 2005).

Subgroup analyses

We performed subgroup analyses to investigate whether the effect of CPAP treatment on overall QoL varies across different subgroups of patients or trials. We analysed subgroups based on the type of control group, OSA severity, study design, and type of QoL measures. As studies measuring psychological and physical QoL (Jenkinson et al., 1999; Barbé et al., 2001; Montserrat et al., 2001; Siccoli et al., 2008) were homogenous in terms of the type of the control group (sham CPAP), OSA severity (moderate to severe), study design (parallel), and type of QoL measures (generic), not enough data were available for the predefined subgroup comparisons.

The effect of CPAP treatment on overall QoL controlled for type of control group

We found a small but significant improvement in overall QoL in subgroup analyses of six studies (Barbé et al., 2001; Montserrat et al., 2001; Marshall et al., 2005; Siccoli et al., 2008; Weaver et al., 2012; Batool-Anwar et al., 2016) using sham

CPAP as a control condition (0.25; 95%CI=0.04; 0.46). A value of 32% indicated moderate heterogeneity. CPAP led to negligible improvement in overall QoL in the subgroup analyses of five studies (Engleman et al., 1997; Engleman et al., 1998; Engleman et al., 1999; Faccenda et al., 2001; Barnes et al., 2004) using placebo pills (0.14; 95%CI=0.03; 0.25). A value of 52% indicated moderate heterogeneity. CPAP did not show superiority to controls receiving conservative treatment in terms of effect on overall QoL score (0.00; 95%CI=-0.07; 0.07) in a single study by Chakravorty et al. (2002).

The effect of CPAP treatment on overall QoL controlled for OSA severity

Subgroup analyses of mild OSA patients showed small CPAP treatment effect on overall QoL (0.31; 95%CI=0.13; 0.50; $I^2=27\%$) in four studies (Engleman et al. 1997; Engleman et al. 1999; Marshall et al., 2005; Batool-Anwar et al., 2016). A negligible improvement in overall QoL was found in subgroup analyses of six studies (Engleman et al. 1998; Barbé et al., 2001; Faccenda et al., 2001; Montserrat et al., 2001; Sicoli et al., 2008; Batool-Anwar et al., 2016) with participants suffering from moderate to severe OSA (0.19; 95%CI=0.03; 0.34; $I^2=53\%$).

The effect of CPAP treatment on overall QoL controlled for study design

CPAP led to a small but significant improvement in overall QoL score (0.22; 95%CI=0.07, 0.38; $I^2=70\%$) in six studies with a parallel design (Montserrat et al. 2001; Barbé et al., 2001; Chakravorty et al., 2002; Siccoli et al., 2008; Weaver et al., 2012; Batool-Anwar et al., 2016). CPAP did not show superiority to controls in terms of the effect on overall QoL (0.16; 95%CI=0.10, 0.26; $I^2=35\%$) in subgroup analyses of six studies with a crossover design (Engleman et al. 1997; Engleman et al. 1998; Engleman et al. 1999; Faccenda et al., 2001; Barnes et al., 2004; Marshall et al., 2005).

The effect of CPAP treatment on overall QoL score controlled for the type of QoL measures

A total of four studies (Engleman et al. 1997; Engleman et al. 1998; Engleman et al. 1999; Chakravorty et al., 2002) using generic QoL questionnaires showed non-significant improvement in overall QoL with CPAP treatment (0.13; 95%CI=-0.001; 0.28; $I^2=53\%$). A negligible improvement in overall QoL score was found in eight studies (Barbé et al., 2001; Faccenda et al., 2001; Montserrat et al., 2001; Barnes et al., 2004; Marshall et al., 2005; Siccoli et al., 2008; Weaver et al., 2012; Batool-Anwar et al., 2016) using OSA-specific QoL questionnaires (0.14; 95%CI=0.04, 0.24; $I^2=64\%$).

Summary of the quality of the findings

The quality of the evidence within the studies was assessed based on levels of RoB, inconsistency, indirectness, and imprecision (Ryan and Hill, 2016). The evidence for improvement in overall QoL was of low quality and was downgraded by one level, as most of the studies had an unclear selection bias. For inconsistency, we considered an I^2 value of 68% to downgrade by one level.

The meta-analysis of psychological QoL provided very low quality of evidence. The evidence for psychological QoL was downgraded by one level due to a small number of included studies, and an unclear allocation concealment in most of the included studies. We also downrated the quality of evidence by two levels for imprecision due to a small sample size ($N<400$) and a wide CI around effect estimate that included an effect size of 0 and moderate effect size.

The evidence for physical QoL provided low quality of evidence. The evidence for improvement in physical QoL was downgraded by one level due to a small number of included studies and an unclear allocation concealment in most of the included studies. We also downrated the quality of evidence by one level for imprecision due to a small sample size ($N<400$).

Discussion

The aim of this study was to systematically evaluate the effect of continuous positive airway pressure (CPAP) treatment on quality of life (QoL) in patients with obstructive sleep apnoea (OSA) compared to sham CPAP, placebo pills, and conservative treatment. We found no significant differences in overall and psychological QoL between CPAP treated patients and controls. However, physical QoL improved in CPAP treated patients compared with control treatments. Furthermore, subgroup analyses and sensitivity analyses showed that the type of control group, the study design, OSA severity, and risk of bias (RoB) may be relevant in capturing the effect of CPAP on QoL.

We found that patients undergoing CPAP treatment reported significantly higher physical QoL compared to controls. This result provided additional support for the effect of CPAP on physical QoL revealed in an earlier meta-analysis by Jing et al. (2008). These findings may be of clinical importance, as physical QoL was found to be related to nocturnal parameters indicating sleep disruption (Sforza et al., 2003; Jing et al., 2008). However, no treatment effect of CPAP compared to controls was found for psychological QoL. This finding may be explained by the low severity of psychological symptoms at baseline. As we excluded studies with focus on major comorbidities, it is possible that the occurrence or severity of some confounders related to comorbid medical illnesses that could negatively affect psychological QoL in OSA patients may have been low. Furthermore, meta-analysis by Huang et al. (2017) demonstrated the significant alterations of brain structural and functional response in OSA patients possibly explaining psychic disorders. Patients with OSA showed both decreased grey matter volume and functional response in orbital frontal cortex compared to healthy controls, while the cerebellum VI bilateral anterior (para)cingulate gyri and the amygdala/hipocampus exhibited atrophy of grey matter volume but increased activity. These changes suggest that early diagnosis and treatment are crucial (Huang et al., 2019). However, recent histopathological investigations of autopsy of brain tissue from OSA patients further indicate that myelin in OSA patients is impacted and not protected by CPAP treatment (Owen et al., 2018). Therefore, the suboptimal effect of CPAP treatment on psychological

QoL may also be explained by the irreversible OSA-related brain injuries, that may further contribute to the development of the psychological symptomatology in OSA patients (Owen et al., 2018; Huang et al., 2019).

Subgroup analyses showed non-significant improvements in overall QoL with CPAP treatment when controlled for type of QoL measures. The results of the subgroup comparisons are not particularly surprising given the fact that disease-specific and generic QoL measures in OSA patients were found to be highly correlated (Flemons and Reimer, 2002; Silva et al., 2016). However, recent meta-analysis by Patil et al. (2019) identified significant effect of CPAP treatment on QoL using disease specific measures. The explanation for this inconsistency in results may be that Patil et al. (2019) included only studies with longer duration of CPAP treatment (6 weeks), while we used cut-off of 2 weeks.

We found a significant improvement in overall QoL when controlled for OSA severity. This result may be surprising as self-reported health outcomes are usually discordant with polysomnography (PSG) measures of OSA severity (Weaver et al., 2005). Issues such as abbreviated PSG monitoring, night-to-night variability, or the “first-night effect” of the PSG may partly explain the variability of OSA severity across different studies (Punjabi, 2008). Nevertheless, the significant effect of CPAP treatment on QoL in patients with mild OSA may also be caused by the low RoB in two (Engelman et al., 1999; Marshall et al., 2005) of the four studies included in subgroup analysis.

In line with the meta-analysis by Jing et al. (2008) we found only a negligible CPAP treatment effect on overall QoL scores in studies with a crossover design compared to a small but significant effect revealed in studies with a parallel design. This result is consistent with previous research, as long-term parallel-group trials were found to be more efficient at capturing the important information regarding the benefits of CPAP treatment (Richens, 2001; Jing et al., 2008). Furthermore, the crossover study design was found to be less effective in assessment of CPAP treatment effects, as the washout period is usually too short to eliminate the effects of first treatment (Richens, 2001). The washout period in crossover studies included in our meta-analysis ranged from 0 to 2 weeks (Engleman et al., 1997; Engleman et al., 1998; Engleman et al., 1999; Faccenda et al., 1999; Barnes et al., 2004; Marshall et al., 2005). Consequently, it is understandable that these short washout periods could not eliminate CPAP treatment effects.

Subgroup analyses also showed that CPAP led to a small but significant improvement in overall QoL in studies with controls receiving sham CPAP compared to the negligible improvement revealed in controls using placebo pills. This result is surprising, as sham CPAP is supposed to worsen both sleep and gas exchange (Sanner et al., 2000; Engleman et al., 1999). An explanation may be that most of the studies that used placebo pills as a control condition also had a very low number of participants (Engleman et al. 1997; Engleman et al. 1998; Engleman et al. 1999). Furthermore, all studies with placebo pills as a control condition had a crossover design, identified as less sensitive in capturing the effect of CPAP treatment (Richens et al., 2001).

Sensitivity analyses that controlled for the number of included participants, duration of intervention, and compliance level showed only small, non-significant effects of CPAP treatment on overall QoL scores. The results of our meta-analysis may be explained by the relatively small sample sizes, the short durations of the interventions, and the relatively low CPAP compliance level (with the highest value of 5.0 hours per night) in the included studies. For example, a compliance of ≥ 4 hours per night has been considered acceptable (e.g. Masa and Corral-Peñafiel, 2014). However, the adequate use of CPAP treatment may vary for different outcomes. For instance, to obtain an improvement in daytime sleepiness, at least 4 hours per night of compliance with CPAP are required (Weaver et al., 2007); 6 hours per night are needed for memory improvement (Zimmerman et al., 2006) and 7.5 hours per night is considered to be adequate for improvement in sleep-related quality of life (Weaver et al., 2007). But, there are individuals who are not able to achieve normal functional status or remain excessively sleepy despite optimal CPAP treatment of more than 7 hours per night (Weaver et al., 2007; Antic et al., 2011; Jackson et al., 2018). As adherence with CPAP treatment appears to be associated with positive changes in QoL (Lynch et al., 2019), future research and clinical practice should examine strategies for its improvement. More attention should be given to educational and behavioural intervention strategies that were found to be efficient in improving adherence with CPAP (Sawyer et al., 2011), while device improvements were found to have only modest impact on adherence with CPAP treatment (Smith et al., 2009).

Finally, we found a small, non-significant effect of CPAP treatment when controlled for the number of included participants. This result is not surprising as cut-offs based on study size introduce an extra element of subjectivity and thus may not ameliorate bias if the large studies are insufficiently critiqued (Turner et al., 2009). Although we stated the cut-off value of 100 participants following previous recommendations (Dechartres, 2013; Grainge, 2015), the concept of single threshold to distinguish small trials from large trials in the area of medical interventions is not straightforward. A solution may therefore be to make a separate exclusion of studies with high and unclear RoB. In line with this assumption, we found a small but significant CPAP treatment effect on QoL in studies with low RoB (Engleman et al., 1999; Faccenda et al., 2001; Marshall et al., 2005).

Strengths and limitations

The strength of this review and meta-analysis is that randomised controlled trials (RCTs) were conducted in different countries, which adds to the generalizability of our results. The results of our study are applicable to adult patients of both genders with mild to severe OSA. We tried to avoid meta-bias by searching in multiple databases. As most of the participants in the included studies were diagnosed by PSG in the same way, misclassification based on differences in sensitivity and specificity of diagnostic measures can be excluded. All studies included in our review and meta-analysis used the SF-36 to measure psychological and physical QoL. Despite some limitations, the mental health component of the SF-36, and in particular the

“vitality” domain, is still considered to be the most suitable generic health-related QoL measure for OSA patients (Abma et al., 2016). However, a potential drawback may be that the questions of the SF-36 related to daily activities or social functioning are assessed by asking about limitations due to “emotional problems” or “physical health”. Moreover, neither of these categories is considered to clearly cover the main reasons for impaired functioning that OSA patients experience (i.e., fatigue, sleepiness, or poor sleep quality) (Abma et al., 2016). One of the eligible studies was excluded from our MA, as we did not receive the missing, additional information. However, the results of the excluded study were consistent with our findings, i.e. QoL improvement was found only in the physical QoL domain and not in the psychological QoL domain (Campos-Rodriguez et al., 2016). We also have to be careful in the interpretation of the results, as many studies had a high or unclear RoB. Next, the studies in our review consistently rated poorly on allocation concealment and blinding. Because inadequately concealed trials and lack of proper blinding may show even more favourable treatment effects than adequately blinded and concealed studies (Wood et al., 2008; Higgins and Green, 2011), careful attention must be paid when interpreting CPAP treatment effect on QoL in OSA patients. We also tried to avoid biases in the assessment of CPAP treatment effect on QoL by exclusion of studies with full samples of OSA patients with major comorbidities that may affect QoL; i.e. heart failure, stroke, or comorbid sleep disorders. However, the limitation of our study may be that comorbidities may not be fully eliminated as the exclusion criteria in analysed studies varied from not specified (Barnes et al., 2004), to less strict (Engleman et al., 1997; Engleman et al., 1998; Engleman et al., 1999; Jenkinson et al., 1999; Faccenda et al., 2001; Montserrat et al., 2001; Chakravorty et al., 2002; Siccoli et al., 2008); or led to exclusion of all chronic conditions (Barbé et al., 2001; Weaver et al., 2012; Batool-Anwar et al., 2016). Finally, since the reported treatment duration ranged from three weeks to six months, this review cannot conclude on the long-term effects of CPAP treatment.

Implications and recommendations for practice and future research

More high-quality RCTs with larger samples are needed to learn more about the effectiveness of CPAP treatment on QoL improvement. Most of the studies included in our review had a moderate duration of CPAP treatment; thus, repetitions with longer treatment duration is recommended. Future RCTs should also consider evaluating secondary outcome measures, such as sleep-related problems.

Conclusion

In conclusion, when comparing CPAP with control treatment, our meta-analysis showed no significant impact of CPAP on overall and psychological QOL. However, CPAP was found to improve physical QoL compared with control treatments. Moreover, we found that CPAP may significantly affect overall QoL in studies with sham CPAP controls, parallel design, low risk of bias, and mild OSA patients. More high-quality trials are needed for further investigation of the effects of CPAP treatment on QoL improvement.

References

- Abma IL, van der Wees PJ, Veer V, et al. (2016) Measurement properties of patient-reported outcome measures (PROMs) in adults with obstructive sleep apnea (OSA): A systematic review. *Sleep Medicine Reviews* 28: 18–31.
- American Academy of Sleep Medicine (2008) Obstructive sleep apnea. 2510 North Frontage Road Darien, IL 60561.
- Antic NA, Catcheside P, Buchan C, et al. (2011) The effect of CPAP in normalizing daytime sleepiness, quality of life, and neurocognitive function in patients with moderate to severe OSA. *Sleep* 34(1): 111–119.
- Aurora RN, Collop NA, Jacobowitz O, et al. (2015) Quality measures for the care of adult patients with obstructive sleep apnea. *Journal of Clinical Sleep Medicine* 11(03): 357–383.
- Barbé F, Mayoralas LR, Duran J, et al. (2001) Treatment with continuous positive airway pressure is not effective in patients with sleep apnea but no daytime sleepiness: a randomized, controlled trial. *Annals of Internal Medicine* 134(11): 1015–1023.
- Barnes M, McEvoy RD, Banks S, et al. (2004) Efficacy of positive airway pressure and oral appliance in mild to moderate obstructive sleep apnea. *American Journal of Respiratory and Critical Care Medicine* 170(6): 656–664.
- Batool-Anwar S, Goodwin JL, Kushida CA, et al. (2016) Impact of continuous positive airway pressure (CPAP) on quality of life in patients with obstructive sleep apnea (OSA). *Journal of Sleep Research* 25(6): 731–738.
- Berry RB, Budhiraja R, Gottlieb DJ, et al. (2012) Rules for scoring respiratory events in sleep: update of the 2007 AASM Manual for the Scoring of Sleep and Associated Events. Deliberations of the Sleep Apnea Definitions Task Force of the American Academy of Sleep Medicine. American Academy of Sleep Medicine. *Journal of Clinical Sleep Medicine* 8(5): 597–619.
- Borenstein M, Hedges LV, Higgins J, et al. (2009) John Wiley & Sons, Ltd. ISBN: 978-0-470-05724-7.
- Campos-Rodriguez F, Queipo-Corona C, Carmona-Bernal C, et al. (2016) Continuous positive airway pressure improves quality of life in women with obstructive sleep apnea. A randomized controlled trial. *American Journal of Respiratory and Critical Care Medicine* 194(10): 1286–1294.
- Carlozzi NE and Tulskey DS (2013) Identification of health-related quality of life (HRQOL) issues relevant to individuals with Huntington disease. *Journal of Health Psychology* 18(2): 212–225.

Dechartres A, Trinquart L, Boutron I, et al. (2013) Influence of trial sample size on treatment effect estimates: meta-epidemiological study. *Biomedical Journal* 346: 2304.

Dutt N, Chaudhry K, Chauhan NK, et al. (2016) Health related quality of life in adult obstructive sleep apnea. *Journal of Sleep Disorders Therapy* 5(2): 2-7.

Egger M, Davey Smith G, Schneider M, Minder C (1997) Bias in meta-analysis detected by a simple, graphical test. *Bio Medical Journal* 315: 629-634.

Engleman HM, Kingshott RN, Wraith PK, et al. (1999) Randomized placebo-controlled crossover trial of continuous positive airway pressure for mild sleep apnea/hypopnea syndrome. *American Journal of Respiratory and Critical Care Medicine* 159(2): 461-467.

Engleman HM, Martin SE, Deary IJ, et al. (1997) Effect of CPAP therapy on daytime function in patients with mild sleep apnoea/hypopnoea syndrome. *Thorax* 52(2): 114-119.

Engleman HM, Martin SE, Kingshott RN, Mackay, et al. (1998) Randomised placebo controlled trial of daytime function after continuous positive airway pressure (CPAP) therapy for the sleep apnoea/hypopnoea syndrome. *Thorax* 53: 341-345.

Faccenda JF, Mackay TW, Boon NA, Douglas, et al. (2001) Randomized placebo-controlled trial of continuous positive airway pressure on blood pressure in the sleep apnea-hypopnea syndrome. *American Journal of Respiratory and Critical Care Medicine* 163(2): 344-348.

Flemons WW and Reimer MA (2002) Measurement properties of the calgary sleep apnea quality of life index. *American Journal of Respiratory and Critical Care Medicine* 165(2): 159-164.

Giles TL, Lasserson TJ, Smith B, et al. (2006) Continuous positive airways pressure for obstructive sleep apnoea in adults. *Cochrane Database of Systematic Reviews* 19(3): 1-113.

Grainge M (2015) Excluding small studies from a systematic review or meta-analysis. In *CSG Annual Meeting*, pp. 12-18.

Hedges LV and Olkin I (2014) *Statistical methods for meta-analysis*. Academic Press. ISBN 0-12-336380-2.

Higgins J, Thompson SG, Deeks JJ, et al. (2003) Measuring inconsistency in meta-analyses [journal article as teaching resource, deposited by John Flynn]. *British Medical Journal* 327: 557-560.

Higgins JPT, and Green S (2011) *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0* [updated March 2011]. The Cochrane Collaboration. Available from <http://handbook.cochrane.org>.

Huang X, Tang S, Lyu X, et al. (2019) Structural and functional brain alterations in obstructive sleep apnea: a multimodal meta-analysis. *Sleep Medicine* 54: 195-204.

Chakravorty I, Cayton RM, Szczepura A (2002) Health utilities in evaluating intervention in the sleep apnoea/hypopnoea syndrome. *European Respiratory Journal* 20(5): 1233-1238.

Choi SJ, Joo EY, Lee YJ, et al. (2015) Suicidal ideation and insomnia symptoms in subjects with obstructive sleep apnea syndrome. *Sleep Medicine*, 16(9): 1146-1150.

Iber C, Ancoli-Israel S, Chesson ALJ, Quan SF (2007) The AASM manual for the scoring sleep and associated events: rules, terminology and technical specifications, 1st ed. Westchester, Illinois: American Academy of Sleep Medicine.

Jackson ML, McEvoy RD, Banks S, et al. (2018) Neurobehavioral impairment and CPAP treatment response in mild-moderate obstructive sleep apnea. *Journal of Clinical Sleep Medicine* 14(01): 47-56.

Jenkinson C, Davies RJ, Mullins R, et al. (1999) Comparison of therapeutic and subtherapeutic nasal continuous positive airway pressure for obstructive sleep apnoea: a randomised prospective parallel trial. *Lancet* 353: 2100-2105.

Jing J, Huang T, Cui W, et al. (2008) Effect on quality of life of continuous positive airway pressure in patients with obstructive sleep apnea syndrome: a meta-analysis. *Lung* 186(3): 131-144.

Kang EW, Abdel-Kader K, Yabes J, et al. (2012) Association of sleep disorder breathing with cognitive dysfunction in CKD stages 4-5. *American Journal of Kidney Diseases* 60(6): 949-958.

Karimi M and Brazier J (2016) Health, health-related quality of life, and quality of life: what is the difference?. *Pharmacoeconomics* 34(7): 645-649.

Knauert M, Naik S, Gillespie MB, et al. (2015) Clinical consequences and economic costs of untreated obstructive sleep apnea syndrome. *World Journal of Otorhinolaryngology-Head and Neck Surgery* 1(1): 17-27.

Krabbe PFM (2017) The Measurement of Health and Health Status. Concepts, Methods and Applications from a Multidisciplinary Perspective. Academic Press. 9780128017203. 380 pgs.

Krahn LE, Miller BW, Bergstrom LR (2008) Rapid resolution of intense suicidal ideation after treatment of severe obstructive sleep apnea. *Journal of Clinical Sleep Medicine* 4: 64–65.

Kuhn E, Schwarz EI, Bratton DJ, et al. (2017) Effects of CPAP and MADs on health-related quality of life in OSA: a systematic review and meta-analysis. *Chest* 151(4): 786–794.

Leger D, Bayon V, Laaban JP, et al. (2012) Impact of sleep apnea on economics. *Sleep Medicine Reviews* 16: 455–462.

Lynch MK, Elliott LC, Avis KT, et al. (2019) Quality of life in youth with obstructive sleep apnea syndrome (OSAS) treated with continuous positive airway pressure (CPAP) therapy. *Behavioral Sleep Medicine* 17(3): 238–245.

Macey PM, Woo MA, Kumar R, et al. (2010) Relationship between obstructive sleep apnea severity and sleep, depression and anxiety symptoms in newly-diagnosed patients. *Public Library of Science One* 5.4: e10211.

Manarino MR, Fillipo FD, Piro M (2012) Obstructive sleep apnea syndrome. *European Journal of Internal Medicine* 23(7): 586–593.

Marshall NS, Neill AM, Campbell AJ, et al. (2005) Randomised controlled crossover trial of humidified continuous positive airway pressure in mild obstructive sleep apnoea. *Thorax* 60(5): 427–432.

Masa JF and Corral-Peñafiel J (2014) “Should use of 4 hours continuous positive airway pressure per night be considered acceptable compliance?.” *European Respiratory Society* 44: 1119–1120.

Merino JS, de Torres LAP, Gómez RM, et al. (2017) Impact of CPAP therapy on health-related quality of life in elderly patients with apnoea–hypopnea syndrome: a systematic review of randomised clinical trials. *European Respiratory Journal* 49(1): 1601644.

Moher D, Liberati A, Tetzlaff J, Altman, et al. (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Medicine* 6(7): e1000097.

Montserrat JM, Ferrer M, Hernandez L, et al. (2001) Effectiveness of CPAP treatment in daytime function in sleep apnea syndrome: a randomized controlled study with an optimized placebo. *American Journal of Respiratory Critical Care Medicine* 164(4): 608–613.

Moyer CA, Sonnad SS, Garetz SL, et al. (2001) Quality of life in obstructive sleep apnea: a systematic review of the literature. *Sleep Medicine* 2(6): 477–491.

Mulgrew AT, Ryan CF, Fleetham JA, et al. (2007) The impact of obstructive sleep apnea and daytime sleepiness on work limitation. *Sleep Medicine* 9(1): 42–53.

Neyeloff JL, Fuchs SC, Moreira LB (2012) Meta-analyses and forest plots using a microsoft excel spreadsheet: step-by-step guide focusing on descriptive data analysis. *BioMed Central Research Notes* 5(1): 52.

Nieuwenhuijsen K, Faber B, Verbeek JH, et al. (2014). Interventions to improve return to work in depressed people. *The Cochrane Library*.

Owen JE, Benediktsdóttir B, Gislason T, et al. (2018) Neuropathological investigation of cell layer thickness and myelination in the hippocampus of people with obstructive sleep apnea. *Sleep* 42(1):199.

Patil SP, Ayappa IA, Caples SM, et al. (2019) Treatment of adult obstructive sleep apnea with positive airway pressure: an American Academy of Sleep Medicine systematic review, meta-analysis, and GRADE assessment. *Journal of Clinical Sleep Medicine* 15(02): 301–334.

Punjabi NM (2008) The epidemiology of adult obstructive sleep apnea. *Proceedings of the American Thoracic Society* 5(2): 136–143.

Richens A (2001) Proof of efficacy trials: cross-over versus parallel-group. *Epilepsy Research* 45 (1-3): 43–47.

Ryan R and Hill S (2016) How to GRADE the quality of the evidence. *Cochrane consumers and communication group, available at <http://ccerg.cochrane.org/author-resources>. Version, 3.*

Sanner BM, Klewer J, Trumm A et al. (2000) Long-term treatment with continuous positive airway pressure improves quality of life in obstructive sleep apnoea syndrome. *European Respiratory Journal* 16(1): 118–122.

Sawyer AM, Gooneratne NS, Marcus CL, et al. (2011) A systematic review of CPAP adherence across age groups: clinical and empiric insights for developing CPAP adherence interventions. *Sleep Medicine Reviews* 15(6): 343–356.

Sforza E, Janssens JP, Rochat T, et al. (2003) Determinants of altered quality of life in patients with sleep-related breathing disorders. *European Respiratory Journal* 21: 682–687

Sharafkhan A, Giray N, Richardson P, et al. (2005) Association of Psychiatric Disorders and Sleep Apnea in a Large Cohort. *Sleep* 28(11): 1405-1411.

Schipper H (1992) Quality of life: the final common pathway. *Journal of Palliative Care* 8(3): 5-7.

Schwartz M, Acosta L, Hung YL, et al. (2018) Effects of CPAP and mandibular advancement device treatment in obstructive sleep apnea patients: a systematic review and meta-analysis. *Sleep and Breathing* 22(3): 555-568.

Siccoli MM, Pepperell JC, Kohler M, et al. (2008) Effects of continuous positive airway pressure on quality of life in patients with moderate to severe obstructive sleep apnea: data from a randomized controlled trial. *Sleep* 31(11): 1551-1558.

Silva, GE, Goodwin JL, Vana KD, et al. (2016) Obstructive sleep apnea and quality of life: comparison of the SAQLI, FOSQ, and SF-36 questionnaires. *Southwest Journal of Pulmonary & Critical Care* 13(3): 137-149.

Smith I, Lasserson TJ (2009) Pressure modification for improving usage of continuous positive airway pressure machines in adults with obstructive sleep apnoea. *Cochrane Database Systematic Reviews*;a (4):CD003531.

Stradling JR, Davies RJO (2004) Sleep 1: Obstructive sleep apnoea/hypopnoea syndrome: definitions, epidemiology, and natural history. *Thorax* 59(1): 73-78.

Tkacova R, Dorkova Z. (2010) Clinical presentations of OSA in adults. *European Respiratory Society Monograph* 50: 86-103.

Tregear S, Reston J, Schoelles K, et al. (2009) Obstructive sleep apnea and risk of motor vehicle crash: systematic review and meta-analysis. *Journal of Clinical Sleep Medicine* 5(6): 573-581.

Turner RM, Spiegelhalter DJ, Smith GC, et al. (2009) Bias modelling in evidence synthesis. *Journal of the Royal Statistical Society: Series A (Statistics in Society)*: 172(1): 21-47.

Weaver EM, Woodson BT, Steward DL (2005) Polysomnography indexes are discordant with quality of life, symptoms, and reaction times in sleep apnea patients. *Otolaryngology - Head & Neck Surgery* 132: 255-262.

Weaver TE (2013) Don't Start Celebrating—CPAP Adherence Remains a Problem. *Journal of Clinical Sleep Medicine: JCSM: Official Publication of the American Academy of Sleep Medicine* 9(6): 551-552.

Weaver TE, Mancini C, Maislin G, Cater, et al. (2012) Continuous positive airway pressure treatment of sleepy patients with milder obstructive sleep apnea: results of the CPAP Apnea Trial North American Program (CATNAP) randomized clinical trial. *American Journal of Respiratory and Critical Care Medicine* 186(7): 677-683.

Weaver TE, Maislin G, Dinges DF, et al. (2007) Relationship between hours of CPAP use and achieving normal levels of sleepiness and daily functioning. *Sleep* 30(6): 711-719.

WHOQOL Group (1994) Development of the WHOQOL: Rationale and current status. *International Journal of Mental Health* 23(3): 24-56.

Wood L, Egger M, Gluud LL, et al. (2008) Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: meta-epidemiological study. *British Medical Journal* 336(7644): 601-605.

Ye L, Pien GW, Ratcliffe SJ, et al. (2009) Gender differences in obstructive sleep apnea and treatment response to continuous positive airway pressure. *Journal of Clinical Sleep Medicine* 5(6): 512-518.

Young T, Peppard P, Gottlieb D (2002) Epidemiology of obstructive sleep apnea: a population health perspective. *American Journal of Respiratory and Critical Care Medicine* 165: 1217-1239.

Zimmerman ME, Arnedt JT, Stanchina M, et al. (2006) Normalization of memory performance and positive airway pressure adherence in memory-impaired patients with obstructive sleep apnea. *Chest* 130(6): 1772-1778.

Are disease severity, sleep-related problems and anxiety associated with work: functioning in patients with obstructive sleep apnoea?

Vladimira Timkova, Iveta Nagyova, Sijmen A. Reijneveld,
Ruzena Tkacova, Jitse P. van Dijk, Ute Bültmann

Disability and Rehabilitation. 2019; 41(18): 2164-2174.

"Under-slept employees are not, therefore,
going to drive your business forward
with productive innovation.
Like a group of people riding stationary
exercise bikes,
everyone looks like they are pedaling,
but the scenery never changes."

Matthew WALKER

Abstract

Background and aim

Obstructive Sleep Apnoea (OSA) has a substantial economic impact on healthcare systems as well as on individuals. We aimed to examine whether OSA severity, sleep-related problems, and anxiety are associated with work functioning in OSA patients when controlled for age, gender, and type of occupation. We also aimed to investigate whether anxiety moderates the associations between sleep-related problems and work functioning

Methods

We included 105 OSA patients (70% male; mean age 46.62 ± 9.79 years). All patients completed the Pittsburgh Sleep Quality Index, the Epworth Sleepiness Scale, the Beck Anxiety Inventory, and the Work Role Functioning Questionnaire-2.0.

Results

OSA severity, poor night-time sleep quality, and anxiety were univariately associated with impaired work functioning. Multivariate analyses revealed that poor perceived sleep quality was more strongly associated with work functioning than sleep efficiency and daily disturbances. Anxiety was strongly associated with impaired work functioning. After adding anxiety, the explained variance in work functioning increased from 20% to 25%. Anxiety moderated the association between low and medium level of night-time sleep quality problems and work functioning.

Conclusion

Poor perceived sleep quality and anxiety were strongly associated with impaired work functioning in OSA patients. These findings may help to optimize management, standard treatment and work functioning in people with OSA when confirmed in longitudinal studies.

Introduction

Obstructive Sleep Apnoea (OSA) is an incapacitating chronic disease caused by pharyngeal collapse during sleep (Manarino et al., 2012). OSA is considered to be one of the most prevalent sleep disorders (Manarino et al., 2012), with an estimated prevalence of 2–10% among the adult population (Leger et al., 2012). The disease is characterized by repeated breathing pauses which cause frequent awakenings, fragmented sleep and, consequently, excessive sleepiness and fatigue (Tippin et al., 2016). Besides physical disorders, OSA patients may also have substantial mental health problems, such as depression, anxiety (Borak et al., 1996; Sharafkhaneh et al., 2005; Kang et al., 2012; Lin and Winkelman, 2012; Krakow et al., 2015), post-traumatic stress syndrome (Sharafkhaneh et al., 2005) or panic attacks (Su et al., 2015). OSA has a substantial economic impact on healthcare systems as well as on individuals and their households. Studies show a significant impairment of functional status, including work functioning, in these patients; i.e. undiagnosed OSA is associated with notable increases in healthcare costs (Wittmann and Rodenstein, 2004; Reuveni et al., 2008) but also with reduced work capacity and work disability (Leger et al., 2012; Mulgrew et al., 2007; Sivertsen et al., 2008).

Earlier studies report an impairment of work functioning in OSA patients (Mulgrew et al., 2007; Sivertsen et al., 2008; Omachi et al., 2009). Tregear et al. (2009) described the occurrence of microsleeps and accidents, while Sivertsen et al. (2008) showed that self-reported OSA symptoms were an independent risk factor for subsequent long-term sick leave and permanent work disability. The association between OSA severity and the individual experience of work limitations was dependent on job type (Mulgrew et al., 2007); i.e. OSA severity did not affect work performance (time management, physical, mental-interpersonal, and output demands) in white-collar workers, while it did in blue-collar workers. Most of the previous research on work correlates in OSA patients has quantified the outcomes using objective variables, such as absenteeism (Sivertsen et al., 2008) or occupational accidents (Noda et al., 1998; Pizza et al., 2009), which may be lower-incidence events when compared to work functioning impairment. Others have assessed the economic impact of OSA on public health systems (Wittman and Rodenstein, 2004; Reuveni et al., 2008). Furthermore, some older studies on work functioning in OSA patients did not use polysomnography (PSC) to diagnose OSA (Sivertsen et al. 2008; Ulfberg et al; 1996), nor did they use validated measures of work role performance (Ulfberg et al; 1996; Grunstein et al., 1995). Thus, more studies are needed in which OSA is diagnosed with reliable methods and occupational variables are assessed with standardized and validated questionnaires (Guglielmi et al., 2015).

Moreover, despite the acceptance of continuous positive airway pressure as the standard OSA treatment, there is a lack of consensus regarding the positive evidence of continuous positive airway pressure treatment effect on functional status (Tippin et al., 2016; Weaver et al., 2007; Weaver et al., 2013). Furthermore, a large proportion of the population is at risk of experiencing a sleep disorder (Hiestand et

al., 2005); thus, it is important to quantify work-related outcomes in these persons. Sleep-related OSA symptoms were also found to contribute to decreased employee productivity (Rosekind et al., 2010; Nena et al., 2010) and are related to high costs for employers (Rosekind et al., 2010). According to Swanson et al. (2011), sleep disorders adversely affect work performance, while mood and affective symptoms impact relationships with co-workers and presenteeism.

Many OSA patients suffer from anxiety symptoms (Borak et al., 1996; Krakow et al., 2015; Yue et al., 2003; Li et al. 2004; Shapiro et al., 2014), but these are rarely studied systematically (Krakow et al., 2015; Shapiro et al., 2014). The omission of anxiety associated with OSA symptomatology may contribute to poor treatment acceptance and adherence (Aloia et al., 2004), and consequently, to an overall worsening of OSA symptoms and increased risk of morbidity (Shapiro et al., 2014). Although previous research on OSA patients suggests that there may be a considerable association between sleep-related problems and anxiety (Borak et al., 1996), these may also occur separately from each other (Krakow et al., 2015). Anxiety can have a major impact on functional status and may interfere with work productivity (Erickson et al., 2009). However, the findings are inconclusive; e.g. Mughal et al. (1996) found that employees with high trait anxiety exerted greater work effort than those with low trait anxiety, which resulted in better work performance.

We sought to address several gaps in the existing literature, because to the best of our knowledge, no studies have investigated the associations between night-time sleep quality, anxiety and work functioning in OSA patients. Increased awareness of the associations between OSA and affective problems might improve diagnostic accuracy as well as treatment outcomes (Krakow et al., 2015; Schroder and O'Hara, 2005). Insight into which specific OSA symptomatology, such as sleep-related and mental health problems, are associated with impaired work functioning, may provide opportunities for preventive strategies for productivity-loss among workers with OSA. Therefore, the present research and clinical practice should focus not only on the standard treatment of OSA, but also on ensuring that symptoms such as sleep-related problems or mental health impairment are managed. To do that, we first need to understand how these symptoms relate to functioning in OSA untreated patients. Thus, the aims of this study were 1) to examine whether OSA severity, sleep-related problems and anxiety are associated with work functioning in OSA patients, and 2) to investigate whether anxiety moderates the associations between sleep-related problems and work functioning.

Materials and methods

Sample and procedure

This cross-sectional study was conducted at the Department of Pneumology and Phthisiology, L. Pasteur University Hospital and the Medical Faculty of PJ Safarik University in Kosice, Slovak Republic. All patients who visited the Department for one-night polysomnography (PSG) from July 2013 to April 2016 and underwent PSG were eligible for the study. Indication for PSG was based on a general practitioner

referral form. OSA was diagnosed based on an overnight sleep examination. PSG was used to determine whether the diagnosis of OSA was present and to identify the severity of the disorder. PSG consists of a simultaneous recording of multiple physiological parameters related to sleep and wakefulness, which directly monitor and quantify the number of respiratory events, related hypoxemia and arousals. PSG comprised the overnight recording of left and right electrooculograms, standard central and occipital electroencephalogram, submental electromyogram (EMG), bilateral tibialis EMG, nasal and oral airflow using a thermistor and thoracic and abdominal excursions using respiratory inductive plethysmography.

The study sample consisted of working patients with an Apnoea Hypopnoea Index (AHI; number of apnoeas + hypopnoeas per hour of sleep) score of 5 or more (American Academy of Sleep Medicine, 2005) who had not undergone any continuous positive airway pressure therapy or other OSA treatment, were Slovak-speaking and had no major comorbidities. Patients with non-respiratory sleep-related complaints (e.g. circadian rhythm sleep disorder, insomnia) were routinely referred to another group of clinical specialists and were therefore not represented in our sample. Only OSA patients between 18 and 65 years of age were included due to possible functional changes, increased vulnerability and a decline in abilities and performance related to age.

Out of N=152 eligible OSA patients, a total of N=33 were excluded because of major comorbidities (a coexisting major sleep disorder such as insomnia, narcolepsy, or circadian rhythm sleep disorder; major cardiovascular diseases, primary pulmonary hypertension, chronic obstructive pulmonary disease, diabetes, Pickwick syndrome, a history of cancer in the past twelve months, neurological deficit, a major psychiatric diagnosis in the medical record, and/or current usage of psychiatric medications which may affect cognitive functions (e.g. antipsychotics, benzodiazepines, or antidepressants), or drug abuse in the past six months) and regular shift work in the past six months. Screening for comorbidities was based on medical data and an initial clinical interview prior to data collection. The clinical diagnoses of the comorbidities were established according to the standard International Classification of Diseases, 10 Revision codes. Medical examinations of patients were conducted by a pulmonologist specialized in sleep-disordered breathing. Another N=14 patients refused to participate in the study (response rate 89%). A total of N=105 OSA patients (70% male; mean age 46.62 ± 9.79 years) constituted the final study sample.

The invitation letter, the informed consent and the self-reporting questionnaires were sent to participants by postal mail three weeks before the medical examination. One week before the medical examination, patients were reminded about the questionnaires by a phone call. Patients filled in the questionnaires at home. Each patient completed and signed an informed consent form prior to their participation in the study, which was fully voluntary and included no incentives for participation. The study was approved by the Ethics Committee of PJ Safarik University (approval no. 115/2011).

Measures

Sociodemographic and clinical data

Information on age, gender, and marital status was obtained from patient records. Patients were asked to identify the one industry that best characterized their current employment (over the last 24 months) from a list of International Standard Classification of Occupations (1990). Patients were also asked to specify their occupation to reduce the obtaining of incorrect or inconsistent information. OSA patients in the following industries were classified as blue-collar workers: primary resource industry, construction industry, manufacturing industry, warehousing, trade, and transportation. Patients employed in public administration, armed forces, government and the service sector (including tourism, business services, education, healthcare, legislators, managerial occupations, professional, and utilities) were classified as white-collar workers. Body Mass Index (height and weight) was assessed by a physician. BMI was used to sort patients into categories: underweight (<18.5), normal ($18.5\text{--}24.99$), overweight ($25.0\text{--}29.99$), and obese ($30+$). The diagnosis of OSA was determined using PSG and was based on the Apnoea Hypopnoea Index (AHI; number of apnoeas + hypopnoeas per hour of sleep) starting with a score of 5 or more according to the standard criteria (American Academy of Sleep Medicine, 2005). According to this, OSA severity is mild ($\text{AHI} \geq 5 \leq 15$), moderate ($\text{AHI} > 15 \leq 30$), or severe ($\text{AHI} > 30$). An obstructive apnoea or hypopnoea can be defined as an event that lasts for ≥ 10 seconds and is characterized by an absence or a decrease from baseline in the amplitude of a valid measure of breathing during sleep that either reaches $>50\%$ with an oxygen desaturation of 3% or an arousal (alternatively a 30% reduction with 4% desaturation) (American Academy of Sleep Medicine, 2005).

Sleep-related problems

Sleep-related problems concerned night-time sleep quality and daytime sleepiness. *Night-time sleep quality* was measured using the Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989). The PSQI is a self-rated questionnaire to assess sleep quality and disturbances over a one-month time interval. The PSQI consists of 19 self-reported questions which cover seven domains: sleep latency, subjective sleep quality, sleep duration, sleep disturbances, habitual sleep efficiency, daytime dysfunction, and use of sleep medication. The score ranges from 0 to 21, with higher scores reflecting poor night-time sleep quality. A cut-off score of 5 separates good from poor sleepers (Buysse et al., 1989). The results of some previous studies suggested that the seven PSQI domains are best represented by three latent factors (Cole et al., 2006; Casement et al., 2012). Empirical examination of the factor structure of the PSQI identified three distinct factors: perceived sleep quality, sleep efficiency, and daily disturbances. The PSQI subscales for subjective sleep quality, sleep medications and sleep latency were loaded onto the latent variable *perceived sleep quality*; the PSQI subscales for sleep duration and habitual sleep efficiency were loaded onto the latent variable *sleep efficiency*; and the PSQI subscales for sleep disturbances and daytime dysfunction were loaded onto the latent variable

daily disturbances (Cole et al., 2006). *Sleep efficiency* is defined as closely related to sleep quantity (Casement et al., 2012), while the *daily disturbances* factor reflects sleep-related daytime impairment (i.e., trouble performing daytime activities) and interruptions in sleep due to physical or psychological symptoms (Casement et al., 2012). In our sample, Cronbach's alpha was 0.85 for the total PSQI scale.

Daytime sleepiness was measured using the self-report Epworth Sleepiness Scale (ESS), an eight-item questionnaire assessing the tendency to fall asleep in various daytime scenarios (Miletin and Hanly, 2003). The score ranges from 0 to 24, with higher scores indicating greater daytime sleepiness. An ESS total score greater than 10 indicates excessive daytime sleepiness (Miletin and Hanly, 2003). Cronbach's alpha for ESS in our sample was 0.87.

Anxiety

Anxiety was measured using the Beck Anxiety Inventory (BAI), which consists of 21 items defining the most common anxiety symptoms (Beck and Steer, 1990). The BAI is a brief measure of anxiety with a focus on somatic symptoms and was developed as a measure adept at discriminating between anxiety and depression (Beck et al., 1988). Scores range from 0 to 63, with higher scores indicating a higher anxiety level. The following categories were defined: no anxiety symptoms (score 0–9), mild anxiety (score 10–18), severe anxiety (score 19–29), and very severe anxiety (score 30–63) (Beck and Steer, 1990). Cronbach's alpha in our sample was 0.90.

Work functioning

Work functioning was assessed with the Work Role Functioning Questionnaire (WRFQ 2.0) (Abma et al., 2013). The WRFQ measures the perceived difficulties in performing work demands among workers, given their emotional or physical health problems. The WRFQ consists of 27 items divided into subscales: work scheduling demands and output demands, physical demands, mental and social demands, and flexibility demands. In addition, a total score can be calculated. Items are answered on a five-point scale: 0 = difficult all the time (100%), 1 = difficult most of the time (75%), 2 = difficult half of the time (50%), 3 = difficult some of the time (25%), 4 = difficult none of the time (0%). There is also a response option 'Does not apply to my job'. The total score is calculated by adding all answers and dividing by the number of items and then multiplying by 25 to obtain percentages between 0 and 100. Higher scores indicate better work functioning. The scores on 'Does not apply to my job' are transformed into missing values (Abma et al., 2013). To identify the prevalence of impaired work functioning, we used the cut-off value (<90) for patients with a chronic disease according Amick et al. (2004). In our sample, Cronbach's alpha was 0.93 for the total scale, 0.97 for the work scheduling and output demands, 0.90 for the physical demands, 0.90 for the flexibility demands and 0.94 for the mental and social demands subscale.

Statistical analyses

All analyses were performed using the Statistical Package for the Social Sciences (IBM SPSS 23) and Modgraph. We started with a description of the background characteristics of the sample and determined the prevalence of OSA severity, night-time sleep quality (PSQI), daytime sleepiness (ESS), anxiety (BAI), and impaired work functioning (WRFQ). Descriptive analyses included frequencies and percentages for categorical variables and mean values and standard deviations (SD) for continuous variables. Next, we investigated the correlations between all variables. Then, we examined the associations between OSA severity, night-time sleep quality, daytime sleepiness, anxiety, and work functioning in crude and adjusted linear regression analyses, including interactions between sleep-related problems and anxiety. We applied the enter method in linear regression to identify the factors associated with summary scores of work functioning for the total scale and the subscales. For each factor, unstandardised beta coefficients represent the mean variation of work functioning. The first model of the variables included sociodemographic data (age, gender). The second model included a clinical variable (OSA severity - measured by AHI); the third model included the night-time sleep quality total scale. In addition, each of the three subscales of sleep quality was analysed separately. In the fourth model anxiety was included to assess the increase in the explained amount of total variance in work functioning. Multicollinearity was assessed using the variance inflation factor (VIF<2.0). Finally, we used moderation analyses to examine whether the associations between night-time sleep quality total scale as well as the three subscales and work functioning were moderated by anxiety. A p-value of <0.05 was considered to be statistically significant. Power analysis revealed that the statistical power for multivariate analysis exceed 86% with medium effect size at $\alpha=0.05$. The statistical power for univariate analyses was 93% with medium effect size at $\alpha=0.05$ (Faul et al., 2009).

Results

Patient characteristics

Most of the patients were male (70%) and had secondary education (60%). A total of 55% were obese, with severe OSA (47%). Poor night-time sleep quality was present in 84% of the OSA patients, and the prevalence of daytime sleepiness was 59%. The majority (80%) of OSA patients were anxious and reported mild to very severe anxiety. Impaired work functioning was present among 82% of OSA patients. Participants worked 39.5±7.8 hours and 5.3±1.1 days a week (Table 4.1).

Table 4.1 Baseline characteristics of the OSA patients (AHI ≥5)

Characteristics	N=105
Age in years; mean, sd	46.62±9.79
Gender; N, % male	73 (70%)
Education; N, %	
Elementary	4 (4%)
Secondary	63 (60%)
University	38 (36%)
Occupation type; N, % white-collar	51 (49%)
Marital status; N, % single	21 (20%)
Body Mass Index; N, %	31.27±7.04
Underweight (<18.5)	0 (0%)
Normal (18.5-24.99)	23 (22%)
Overweight (25.0-29.99)	24 (23%)
Obese (30+)	58 (55%)
Apnoea-hypopnoea index; mean, sd	37.03±22.75
OSA severity; N, %	
Mild (AHI≥5≤15)	16 (15%)
Moderate (AHI>15≤30)	40 (38%)
Severe (AHI>30)	49 (47%)
Night-time sleep quality (PSQI); mean, sd (0-21)	10.31±4.31
Perceived sleep quality; mean, sd	4.78±2.36
Sleep efficiency; mean, sd	1.81±1.83
Daily disturbances; mean, sd	3.74±1.32
Prevalence of night-time sleep quality disturbance; N, % (cut-off score >5)	88 (85%)
Excessive daytime sleepiness (ESS); mean, sd (0-24)	11.09±5.29
Prevalence of increased daytime sleepiness; N, % (cut-off score >10)	62 (59%)
Anxiety (BAI); mean, sd (0-63)	32.99±13.03
Prevalence of anxiety; N, % (cut-off score >9)	84 (80%)
Prevalence of mild anxiety (10-18)	31 (30%)
Prevalence of severe anxiety (19-29)	35 (33%)
Prevalence of very severe anxiety (30-63)	18 (17%)
Work functioning (WRFQ) total scale; mean, sd (0-100%)	52.58±28.76
Work Scheduling and Output demands	49.19± 31.69
Physical demands	57.43± 30.57
Mental and Social demands	52.74± 31.15
Flexibility demands	56.25± 30.04
Impaired Work functioning; N, % (cut-off score <90)	82 (82%)
Workdays per week; mean, sd	5.32±1.10
Work hours per week; mean, sd	39.73±7.82

AHI – Apnoea-Hypopnoea Index; OSA – Obstructive Sleep Apnoea; PSQI – Pittsburgh Sleep Quality Index; ESS – Epworth Sleepiness Scale; BAI – Beck Anxiety Inventory; WRFQ – Work Role Functioning Questionnaire; Missing data: Occupation type: 1%; PSQI: 1%; WRFQ: 4%.

Correlations between OSA severity, sleep-related problems, anxiety and work functioning

Table 4.2 displays the correlations between the study variables. High OSA severity, poor overall night-time sleep quality, poor perceived sleep quality, poor sleep efficiency, high level of daily disturbances, and severe anxiety were significantly correlated with impaired work functioning. Daytime sleepiness was not correlated with work functioning.

Table 4.2 Correlation coefficients between OSA severity, night-time sleep quality the total scale and its three subscales, daytime sleepiness, anxiety and work functioning

	OSA severity	Night-time sleep quality	Perceived sleep quality	Sleep efficiency	Daily disturbances	Daytime sleepiness	Anxiety
Night-time sleep quality	0.23*	-	-	-	-	-	-
Perceived sleep quality	0.26*	0.68***	-	-	-	-	-
Sleep efficiency	0.14	0.65***	0.43***	-	-	-	-
Daily disturbances	0.33***	0.62***	0.62***	0.20*	-	-	-
Daytime sleepiness	0.34***	0.20*	0.14	0.04	0.49***	-	-
Anxiety	0.18	0.58***	0.34***	0.32**	0.44***	0.31**	-
Work role functioning	-0.20*	-0.41***	-0.47***	-0.23*	-0.36***	-0.09	-0.45***

OSA – Obstructive Sleep Apnoea; *p<0.05; **p<0.01; ***p<0.001

Associations between OSA severity, sleep-related problems, anxiety and work functioning (total scale)

A crude effect on work functioning was found for all variables, except for age (B: -0.22; 95%CI= -0.79; 0.36; p=0.46), type of occupation (B: -4.03; 95%CI= -15.40; 7.34; p=0.49) and daytime sleepiness (B: -0.61; 95%CI= -1.70; 0.48; p=0.27) (Table 4.3). A weak association between OSA severity (B: -0.27; 95%CI= -0.53; -0.01; p<0.05) and poor work functioning was found in crude analyses but was no longer significant (B: -0.18; 95%CI= -0.45; 0.08; p=0.17) in the subsequent multivariate models (Model 2-Model 5). Poor night-time sleep quality total scale (B: -2.63; 95%CI= -3.85; -1.42; p<0.001) was significantly associated with impaired work functioning (Model 3). The association between poor night-time sleep quality total scale and work functioning attenuated (B: -1.64; 95%CI= -3.07; -0.23; p<0.05) when anxiety (B: -0.61; 95%CI= -1.10; -0.15; p<0.01) was added to the model (Model 4). After adding anxiety (Model 4), the explained variance in work functioning increased from 20% to 25% (Table 4.3).

Table 4.3 Multiple linear regression analysis: associations of OSA severity, night-time sleep quality, daytime sleepiness and anxiety with work functioning

Work functioning (WRFQ)	Crude	Model 1	Model 2	Model 3	Model 4	Model 5
	B (95%CI)	B (95%CI)	B (95%CI)	B (95%CI)	B (95%CI)	B (95%CI)
Age	-0.22 (-0.79; 0.36)	-0.06 (-0.62; 0.51)	-0.01 (-0.56; 0.58)	-0.02 (-0.55; 0.50)	-0.14 (-0.66; 0.39)	-0.17 (-0.68; 0.34)
Gender	14.70 (2.56; 26.84)*	16.11 (3.67; 28.59)*	14.41 (1.76; 27.05)*	9.83 (-2.03; 21.60)	7.20 (-4.54; 18.85)	3.82 (-7.87; 15.44)
Occupation	-4.03 (-15.40; 7.34)	-	-	-	-	-
OSA severity	-0.27 (-0.53; -0.01)*	-	-0.18 (-0.45; 0.08)	-0.08 (-0.33; 0.17)	-0.08 (-0.32; 0.16)	-0.08 (-0.32; 0.15)
Night-time sleep quality	-2.95 (-4.12; -1.79)***	-	-	-2.63 (-3.85; -1.42)***	-1.64 (-3.07; -0.23)*	-6.10 (-9.80; -2.40)**
Daytime sleepiness	-0.61 (-1.70; 0.48)	-	-	-	-	-
Anxiety	-1.02 (-1.40; -0.63)***	-	-	-	-0.61 (-1.10; -0.15)**	-1.93 (-3.05; -0.80)**
Nighttime sleep quality x Anxiety	-0.05 (-0.07; -0.03)***	-	-	-	-	0.12 (0.03; 0.22)*
F Change	-	3.55	1.88	18.45***	6.25*	6.61*
Adjusted R ²	-	0.05	0.06	0.20	0.25	0.29

Crude effects: effect of each variable separately on work functioning; Model 1: effect of age and gender on work functioning; Model 2: effect of age, gender and OSA severity on work functioning; Model 3: effect of age, gender, OSA severity and night-time sleep quality on work functioning; Model 4: effect of age, gender, OSA severity, night-time sleep quality and anxiety on work functioning; Model 5: interaction between night-time sleep quality and anxiety; B: unstandardized regression coefficient; CI – confidence interval; Gender – male gender was set as the reference; Blue-white collar – white collar was set as the reference; OSA – Obstructive Sleep Apnoea; F Change – significance of prediction improvement in the model fit; Adjusted R² – explained variance adjusted for the number of predictors in the model; *p<0.05; **p<0.01; ***p<0.001.

A crude effect on work functioning was found for all of the three night-time sleep quality subscales. Multivariate analyses of the three subscales revealed that perceived sleep quality (B: -5.28; 95%CI= -7.48; -3.08; $p<0.001$) was more strongly associated with work functioning (Model 3, Supplementary Table S4.1, Supplement 4.1) than sleep efficiency and daily disturbances (Model 3, Supplementary Table S4.2, Supplementary Table S4.3, Supplement 4.1). The associations between sleep efficiency (B: -3.31; 95%CI= -6.35; -0.27; $p<0.05$), daily disturbances (B: -6.45; 95%CI= -10.92; -1.99; $p<0.01$) and work functioning (Model 3, Supplementary Table S4.2, Supplementary Table S4.3, Supplement 4.1) were no longer significant when anxiety was added to the model (Model 4, Supplementary Table S4.2, Supplementary Table S4.3, Supplement 4.1). The explained amount of total variance in work functioning varied from 22% for models with sleep efficiency and daily disturbances included to 27% for the model with sleep efficiency included.

Associations between OSA severity, sleep-related problems, anxiety and work functioning by subscale

A crude effect on work functioning subscales was found for all variables, except for age, type of occupation and daytime sleepiness. OSA severity was associated with physical demands only. Overall night-time sleep quality and anxiety were significantly associated with all work functioning subscales. Multivariate analyses showed that night-time sleep quality and anxiety were significantly associated with the work scheduling-output demands and physical demands in the final models (with an explained total variance of 26% for work scheduling and output demands, and 16% for physical demands) (Supplementary Table S4.4).

Moderation analyses

To test the moderation effects, the interaction terms between anxiety and overall night-time sleep quality were added into the equation (Model 5). The interaction of overall night-time sleep quality and anxiety was statistically significant (B: 0.12; 95%CI= 0.03; 0.22; $p<0.05$) (Table 4.3). Anxiety moderated the association between low and medium night-time sleep quality problems and work functioning. The impact of anxiety on the association between night-time sleep quality and work functioning was negligible in the case of high night-time sleep quality problems (Figure 4.1).

Figure 4.1 Anxiety as a moderator of the association between night-time sleep quality and work functioning

PSQI – Pittsburgh Sleep Quality Index; BAI – Beck Anxiety Inventory; WRFQ – Work Role Functioning Questionnaire; Higher WRFQ scores indicated better work functioning.

Separate analyses of the three night-time sleep quality subscales showed that the interactions of perceived sleep quality (B: 0.18; 95%CI= 0.10; 0.35; $p<0.05$) and daily disturbances (B: 0.56; 95%CI= 0.22; 0.90; $p<0.01$) with anxiety were statistically significant (Model 5, Supplementary Table S4.1, Supplementary Table S4.3, Supplement 4.1). The interaction of sleep efficiency and anxiety was not significant (B: 0.09; 95%CI= -0.14; 0.32; $p=0.45$) (Model 5, Supplementary Table S4.2). The moderating effect of anxiety in the association between perceived sleep quality, daily disturbances and work functioning was especially profound in the case of low and medium perceived sleep quality problems and low and medium levels of daily disturbances (Figure 4.2, Figure 4.3).

Figure 4.2 Anxiety as a moderator of the association between perceived sleep quality and work functioning

PSQI – Pittsburgh Sleep Quality Index; BAI – Beck Anxiety Inventory; WRFQ – Work Role Functioning Questionnaire; Higher WRFQ scores indicated better work functioning.

Figure 4.3 Anxiety as a moderator of the association between daily disturbances and work functioning

PSQI – Pittsburgh Sleep Quality Index; BAI – Beck Anxiety Inventory; WRFQ – Work Role Functioning Questionnaire; Higher WRFQ scores indicated better work functioning.

Discussion

The aims of this study were 1) to examine whether OSA severity, sleep-related problems, and anxiety are associated with work functioning in OSA patients when controlled for age, gender, and type of occupation, and 2) to investigate whether anxiety moderates the associations between sleep-related problems and work functioning. Our results provided suggestive evidence that poor night-time sleep quality and increased anxiety were associated with impaired work functioning. Further, the moderating effect of anxiety on the association between night-time sleep quality and work functioning was especially profound in patients with better sleep quality, while the effect of anxiety on the association between work functioning and night-time sleep quality was negligible in the case of high night-time sleep quality problems.

Separate analyses of the three night-time sleep quality subscales showed that perceived sleep quality was more strongly associated with work functioning than sleep efficiency and daily disturbances. The associations between sleep efficiency, daily disturbances and work functioning were weak and no longer significant when anxiety was added to the models. Additionally, the moderating effect of anxiety on the association between perceived sleep quality, daily disturbances and work functioning was especially present in OSA patients with better-perceived sleep quality and a lower level of daily disturbances. No moderating role of anxiety in the association between sleep efficiency and work functioning was found.

We found a weak association between OSA severity and impaired work functioning; only significant in crude analyses. In the study by Mulgrew et al. (2007), patients with the lowest apnoea-hypopnoea index (AHI) scores exhibited an even more significant level of work limitation, and this association was dependent on the type of occupation and particular subscale of the Work Limitation Questionnaire.

In contrast, no association between the type of occupation and work functioning for the total scale, not even for subscales was found in our study. An explanation for the lack of clear association between OSA severity and work functioning could be the use of polysomnography (PSG) to determine the diagnosis of OSA. Although a one-night PSG is sufficient for a diagnosis of OSA (Scholle et al., 2003; Gouveris et al., 2010), current techniques to measure OSA are a matter of some controversy; i.e. PSG-based AHI has been discussed as being inadequate to detect OSA severity (Ryu et al., 2016; Lee et al., 2016). Our findings confirm the suggestion of Macey et al. (2010) that mechanisms other than the AHI may contribute to adverse health effects in OSA patients.

Our study revealed an association between poor night-time sleep quality and impaired work functioning, whereas daytime sleepiness was not related to work functioning. Contrary to this finding, previous studies in patients referred for OSA described an association between excessive sleepiness (measured by ESS) and work limitation (Mulgrew et al., 2007; Ulfberg et al., 1996; Grunstein et al., 1995). There are a variety of potential explanations for the lack of clear association between daytime sleepiness and work functioning. The study of Ulfberg et al. (1996) did not use PSG to diagnose OSA, and measures of work limitation and daytime sleepiness were combined into a single questionnaire, making interpretation difficult. Similarly, Grunstein et al. (1995) did not use validated measures of work role performance. Furthermore, the concepts used by Ulfberg et al. (1996) and Omachi et al. (2009), such as recent work disability and longer-term work duty modification, do not fully capture the scope or nature of subjective work functioning impairment measured in our study. Another possible explanation for these discrepancies could be that daytime sleepiness, measured by ESS, is assessed predominantly in a setting of decreased activity level (e.g. watching TV, sitting, reading etc.) compared with the higher mental or physical activity level usually expected in the working environment. The lack of association between daytime sleepiness and work functioning can be explained based on the hypothesized pathophysiology of insomnia; i.e. the symptoms of poor sleep quality and anxiety might be linked to each other by some form of underlying “hyperarousal” (Perlis et al., 2005). Anxiety in OSA patients may develop into a chronic state of hypervigilance (Krakow et al., 2015), which refers to the predisposition to be on high alert much more than is considered normal. This arousal ultimately leads to a state of chronic anxiety and eventually sleeplessness. All these cases epitomize the related phenomenon of an anxiety process that may obliterate natural sleepiness (Perlis et al., 2005; Krakow et al., 2015). In line with the delineated hyperarousal theory, we found that anxiety was more strongly associated with poor overall night-time sleep quality and its three separate factors than with daytime sleepiness.

The fact that the association between night-time sleep quality and work functioning was greatly attenuated after anxiety was added to the model is not surprising. Sleep disturbances are closely related to anxiety symptoms, as sleep disturbances are both a precursor and a symptom of anxiety (Shanahan et al., 2014). Moreover, we found a moderating effect of anxiety on the association between low and medium

night-time sleep quality problems and work functioning. Based on our results, it can be hypothesized that work functioning in OSA patients may be impacted by anxiety more significantly than by poor night-time sleep quality. However, the moderating role of anxiety in the association between work functioning and sleep quality was weakened in patients with the highest levels of sleep quality problems. Thus, high night-time sleep quality problems may become more significant in the association with poor work functioning than anxiety, while the moderating effect of anxiety on work functioning was especially profound in patients with better sleep quality. In line with the evidence that poor perceived sleep quality is more predictive of negative affectivity and impaired physical health than sleep efficiency, i.e. sleep quantity (Pilcher et al., 1997), we found that perceived sleep quality was more strongly associated with work functioning than sleep efficiency and daily disturbances. The association between sleep efficiency and work functioning was only weak and no longer significant when anxiety was added to the model.

Regarding the role of sociodemographic variables, we identified a higher impairment of work functioning in male when compared with female OSA patients. In contrast to our study, general functional status was found to be more impaired in female OSA patients when compared with males in some previous studies (Chervin 2000; Quintana-Gallego et al., 2004; Silva et al., 2016). A potential explanation for these discrepancies can be that men more often than women work in jobs that are incompatible with increased sleep-related symptoms. Hence, male OSA patients may more often than females face demands in their jobs that cannot be dealt with when sleep-related problems are above a certain level (Bültmann et al., 2013). Furthermore, in our sample, 70% of OSA patients were men; thus, our results may be less generalizable to the female population of OSA patients.

Although, it may be assumed that some OSA symptoms, such as sleep-related problems, may be more difficult to overcome due to the sedentary nature of work in the group of white-collar OSA patients, we found no significant difference regarding work functioning impairment in blue- and white-collar workers. However, the fact that white-collar workers in particular may have modified and more flexible work options or benefits enabling those with more severe OSA symptoms to continue to work without significant impairment should be considered (Mulgrew et al., 2007).

Strengths and limitations

The strengths of this study are that we shed light on several novel aspects of work functioning among OSA patients. Patients in our study were diagnosed using PSG, which is an asset of the study. To our knowledge, this is the first time that the PSQI factor structure has been used in a sample of OSA patients. It is also the first study using the Work Role Functioning Questionnaire in an OSA population. Some limitations should also be noted. Due to the cross-sectional design of the study, causal inferences cannot be made. Next, work functioning has not been objectively evaluated. Nevertheless, the used instrument has been found to be appropriate to measure health-related work functioning in the occupational health care practice or

in the rehabilitation process of disabled workers (Ramada et al., 2014). We can also assume that anxiety symptoms assessed in our study may be associated with panic disorder, rather than with anxiety in general. Although the Beck Anxiety Inventory (BAI) may be used as an indicator of anxiety in primary care patients with different anxiety disorders (Wetherell and Gatz, 2005) it has been disputed for its focus on psychophysiological symptoms linked to panic disorder (Beck and Steer, 1991; Cox et al., 1996), such as a racing heart or dizziness (Julian, 2011). The associations identified in our study may also occur due to latent mental health problems or somatic disease; i.e. sleep disturbances have also been identified to be both a precursor and a consequence of depression (Ford and Cooper-Patric, 2001). Nevertheless, the measure of anxiety used in our study was found to be suitable to distinguish an overlap between anxiety and depressive symptoms (Beck et al., 1988). Furthermore, considering that patients with any major somatic or mental health comorbidity in the medical record were excluded from our study, this bias is rather unlikely. Previous study showed that OSA patients had difficulties to complete the work tasks and they subjectively felt a lack of trust from co-workers, which consequently caused subsequent embarrassment related to this (Reishtein et al., 2006). Thus, it should be considered that increased anxiety may also be work (e.g. working environment, cutting down jobs) and not only OSA-related.

Implications for practice and future research

This study shows that poor night-time sleep quality and anxiety were strongly associated with impaired work functioning in OSA patients. Thus, employee assessment of their work functioning may be an important proxy for the economic burden of OSA (Mulgrew et al., 2007). Although patients with any major somatic or mental health comorbidity in the medical record were excluded, we found that 80% of OSA patients experienced increased symptoms of anxiety, which varied from mild (30%) to severe (17%). Thus, the study suggests that early detection and treatment of OSA and anxiety should be one of the priorities on the stakeholders' agenda. Furthermore, identifying patients with overlapping diagnoses of mental health problems and OSA in clinical care may help to improve their treatment outcomes through careful dosing of pharmacotherapy and use of continuous positive airway pressure treatment (Gupta and Simpson, 2015). Compared with sleep efficiency, perceived sleep quality was more strongly associated with work functioning. These results indicate that health care professionals, in their efforts to understand the role of sleep in the daily life of patients with OSA, should rather focus on sleep quality than on sleep quantity. In clinical and research settings, these qualitative aspects of sleep may be captured by clinical interviews and specific patient-reported outcomes. There is a need for workplace strategies that encourage behaviours and practices that may be helpful in reducing OSA-related symptoms and improve work functioning in OSA patients. Employers can play a role in educating employees about effective management of sleep loss through a variety of proven strategies, including better managed work demands, regular exercise, duty hour considerations, and instructing them on the basics of sleep hygiene (Jansson and Linton, 2006).

Some recent evidence shows that workplace flexibility (allowing more flexible work start and end times) may contribute to positive health-related behaviours and may play an important role in effective workplace health promotion programs (Moen et al., 2011). Previous studies have also shown that enabling “unwinding” time between work and home may improve sleep patterns; as reduced work-to-home interference has the potential to decrease the risk of poor night-time sleep quality (Nylen et al., 2007).

As boundaries between work and private life become more blurry, there is a real need to examine the associations between work habits, sleep and other related aspects, especially in common diseases such as OSA. Further research should identify risk groups of patients with impaired work functioning and increased anxiety levels and tailor the counseling and interventions suitably for these patients. Although PSG is considered to be a gold standard for making a diagnosis of OSA, it is not easily applicable in large population-based studies due to its intrusiveness and high costs (Sivertsen et al., 2008). Therefore, screening instruments based on self-reported symptoms of OSA have been important in order to gain information on the prevalence, comorbid conditions of OSA or continuous positive airway pressure treatment effectiveness, which would be difficult to obtain without using scale surveys (Sivertsen et al., 2008). As BAI does not assess other symptoms of anxiety, such cognitive aspects, further research may be accompanied by additional anxiety measures to distinguish between panic symptoms and other anxiety disorders (e.g. generalized anxiety disorder). Moreover, the possibility that anxiety may mask the certain amount of daytime sleepiness in OSA patients (Krakow et al., 2015) should be examined in the future studies. Further prospective, longitudinal research is needed to elucidate the pathways from OSA, sleep-related problems, and anxiety to impaired work functioning. As perceived sleep quality and sleep efficiency are influenced by a range of factors related to age or health (Foley et al., 2004), there is a need for further studies examining the factor structure of the PSQI in OSA patients. Finally, we studied OSA patients without major comorbidities, as these are assumed to influence sleep and affective OSA symptoms (Macey et al., 2010). As a group with minimal comorbidities and recent diagnosis is not fully representative of the general OSA population, it may be assumed that work functioning and other health-related outcomes would be even more significantly impaired in a sample of OSA patients with comorbid diseases (Macey et al., 2010).

Conclusion

Poor sleep quality and anxiety were significantly associated with impaired work functioning in OSA patients. We also found that perceived sleep quality was more strongly associated with work functioning than sleep efficiency; i.e. sleep quantity. Further, the moderating effect of anxiety on work functioning was especially strong in patients with better sleep quality. The role of anxiety in the association between sleep quality and work functioning was weakened in the case of poor night-time sleep quality. Impaired work functioning in OSA patients may represent a possible

cause of disability, which may be improved by workplace strategies focused on decreasing poor sleep quality and anxiety when confirmed in longitudinal studies. As many people with OSA are undiagnosed, our results demonstrate to employers and health care professionals the need to encourage patients for OSA screening, especially in the situation of impaired work functioning, increased anxiety and poor sleep quality.

References

- Abma FI, van der Klink JJ, Bültmann U (2013) The work role functioning questionnaire 2.0 (Dutch version): examination of its reliability, validity and responsiveness in the general working population. *Journal of Occupational Rehabilitation* 23(1): 135-147.
- Aloia MS, Arnedt JT, Davis JD, et al. (2004) Neuropsychological sequelae of obstructive sleep apnea-hypopnea syndrome: a critical review. *Journal of International Neuropsychological Society* 10(05): 772-785.
- American Academy of Sleep Medicine (2005) International Classification of Sleep Disorders: Diagnostic and Coding Manual (2nd ed). Sleep Disorders Association, Rochester, MN (ICSD-2).
- Amick III BC, Habeck RV, Ossmann J, et al. (2004) Predictors of successful work role functioning after carpal tunnel release surgery. *Occupational and Environmental Medicine* 46(5): 490-500.
- Beck AT, Epstein N, Brown G, et al. (1988) An inventory for measuring clinical anxiety: psychometric properties. *Journal of Consulting and Clinical Psychology* 56(5): 893-7.
- Beck AT, Steer RA (1990) Beck Anxiety Inventory Manual. San Antonio: The Psychological Corporation Harcourt Brace Jovanovich Inc.
- Beck AT, Steer RA (1991) Relationship between the Beck Anxiety Inventory and the Hamilton Anxiety Rating Scale with anxious outpatients. *Journal of Anxiety Disorders* 5(3): 213-223.
- Borak J, Cieslicki JK, Koziej M, et al. (1996) Effects of CPAP treatment on psychological status in patients with severe obstructive sleep apnoea. *Journal of Sleep Research* 5(2): 123-127.
- Bültmann U, Nielsen MBD, Madsen IE, et al. (2013) Sleep disturbances and fatigue: independent predictors of sickness absence? A prospective study among 6538 employees. *European Journal of Public Health* 23(1): 123-128.

Buysse DJ, Reynolds CF, Monk TH, et al. (1989) The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Research* 28(2): 193-213.

Casement MD, Harrington KM, Miller MW, et al. (2012) Associations between Pittsburgh Sleep Quality Index factors and health outcomes in women with post-traumatic stress disorder. *Sleep Medicine* 13(6): 752-758.

Chervin RD (2000) Sleepiness, fatigue, tiredness, and lack of energy in obstructive sleep apnea. *Chest* 118(2): 372-379.

Cole JC, Motivala SJ, Buysse DJ, et al. (2006) Validation of a 3-factor scoring model for the Pittsburgh sleep quality index in older adults. *Sleep* 29(1): 112-116.

Cox BJ, Cohen E, Drenfeld DM, et al. (1996) Does the Beck Anxiety Inventory measure anything beyond panic attack symptoms?. *Behavioral Research and Therapy* 34(11): 949-954.

Erickson SR, Guthrie S, VanEtten-Lee M, et al. (2009) Severity of anxiety and work-related outcomes of patients with anxiety disorders. *Depression and Anxiety* 26(12): 1165-1171.

Faul F, Erdfelder E, Buchner A, et al. (2009) Statistical power analyses using G*Power 3.1: Tests for correlation and regression analyses. *Behavioural Research Methods* 41(4): 1149-1160.

Foley D, Ancoli-Israel S, Britz P, et al. (2004) Sleep disturbances and chronic disease in older adults: results of the 2003 National Sleep Foundation Sleep in America Survey. *Journal of Psychosomatic Research* 56(5): 497-502.

Ford DE, Cooper-Patrick L (2001) Sleep disturbances and mood disorders: an epidemiologic perspective. *Depression and Anxiety* 14(1): 3-6.

Gouveris H, Selivanova O, Bausmer U, et al. (2010) First-night-effect on polysomnographic respiratory sleep parameters in patients with sleep-disordered breathing and upper airway pathology. *European Archives of Otorhinolaryngology* 267(9): 1449-1453.

Grunstein RR, Stenlof K, Hedner JA, et al. (1995) Impact of self-reported sleep-breathing disturbances on psychosocial performance in the Swedish Obese Subjects (SOS) study. *Sleep* 18(8): 635-643.

Guglielmi O, Jurado-Gómez B, Gude, F, et al. (2015) Occupational health of patients with obstructive sleep apnea syndrome: a systematic review. *Sleep and Breathing* 19(1): 35-44.

Gupta MA, Simpson FC (2015) Obstructive sleep apnea and psychiatric disorders: a systematic review. *Journal of Clinical Sleep Medicine* 11(2): 165-175.

Hiestand DM, Britz P, Goldman M, et al. (2006) Prevalence of symptoms and risk of sleep apnea in the US population: results from the national sleep foundation sleep in America 2005 poll. *Chest* 130(3): 780-786.

International Labour Office (1990) International standard classification of occupations: ISCO-88. Geneva: International Labour Office.

Jansson M, Linton SJ (2006) Psychosocial work stressors in the development and maintenance of insomnia: a prospective study. *Journal of Occupational and Health Psychology* 11(3): 241-248.

Julian LJ (2011) Measures of anxiety: State-Trait Anxiety Inventory (STAI), Beck Anxiety Inventory (BAI), and Hospital Anxiety and Depression Scale-Anxiety (HADS-A). *Arthritis Care and Research* 63(11): 467-472.

Kang EW, Abdel-Kader K, Yabes J, et al. (2012) Association of sleep disorder breathing with cognitive dysfunction in CKD stages 4-5. *American Journal of Kidney Diseases* 60(6): 949-958.

Krakov BJ, Ulibarri VA, Moore BA, et al. (2015) Posttraumatic stress disorder and sleep-disordered breathing: a review of comorbidity research. *Sleep Medicine Reviews* 24: 37-45.

Lee W, Lee SA, Ryu HU, et al. (2016) Quality of life in patients with obstructive sleep apnea: Relationship with daytime sleepiness, sleep quality, depression, and apnea severity. *Chronic Respiratory Disorders* 13(1): 33-39.

Leger D, Bayon V, Laaban J, et al. (2012) Impact of sleep apnea on economics. *Sleep Medicine Reviews* 16(5): 455-462.

Li HY, Huang YS, Chen NH, et al. (2004) Mood improvement after surgery for obstructive sleep apnea. *Laryngoscope* 114(6): 1098-1102.

Lin WC, Winkelmann JW. (2012) Obstructive sleep apnea and severe mental illness: evolution and consequences. *Current Psychiatry Reports* 14(5): 503-510.

Macey PM, Woo MA, Kumar R, et al. (2010) Relationship between obstructive sleep apnea severity and sleep, depression and anxiety symptoms in newly-diagnosed patients. Public Library of Science one. 5(4):e10211.

Manarino MR, Fillipo FD, Piro M (2012) Obstructive sleep apnea syndrome. *European Journal of Internal Medicine* 23(7): 586-593.

- Miletin MS, Hanly PJ (2003) Measurement properties of the Epworth sleepiness scale. *Sleep Medicine* 4(3):195-199.
- Moen P, Kelly EL, Tranby E, et al. (2011) Changing work, changing health: can real work-time flexibility promote health behaviors and well-being? *Journal of Health and Social Behavior* 52(4): 404-429.
- Mughal S, Walsh J, Wilding J (1996) Stress and work performance: The role of trait anxiety. *Personality and Individual Differences* 20(6): 685-691.
- Mulgrew AT, Ryan CF, Fleetham JA, et al. (2007) The impact of obstructive sleep apnea and daytime sleepiness on work limitation. *Sleep Medicine* 9(1): 42-53.
- Nena E, Steiropoulos P, Constantinidis TC, et al. (2010) Work productivity in obstructive sleep apnea patients. *Journal of Occupational and Environmental Medicine* 52(6): 622-625.
- Noda A, Yagi T, Yokota M, et al. (1998) Daytime sleepiness and automobile accidents in patients with obstructive sleep apnea syndrome. *Psychiatry Clinical Neuroscience* 52(2): 221-222.
- Nylen L, Melin B, Laflamme L (2007) Interference between work and outside-work demands relative to health: unwinding possibilities among full-time and part-time employees. *International Journal of Behavioral Medicine* 14(4): 229-236.
- Omachi TA, Claman DM, Blanc PD (2009) Obstructive sleep apnea: a risk factor for work disability. *Sleep* 32(6): 791-798.
- Perlis ML, Smith MT, Pigeon WR. Principles and practice of sleep medicine. 4th ed. Philadelphia: Elsevier Saunders; 2005. Chapter 60, *Etiology and Pathophysiology of Insomnia*. 714-725.
- Pilcher JJ, Ginter DR, Sadowsky B. (1997) Sleep quality versus sleep quantity: relationships between sleep and measures of health, well-being and sleepiness in college students. *Journal of Psychosomatic Research* 42: 583-596.
- Pizza F, Contardi S, Mondini S, et al. (2009) Daytime sleepiness and driving performance in patients with obstructive sleep apnea: comparison of the MSLT, the MWT, and a simulated driving task. *Sleep* 32(3): 382-391.
- Quintana-Gallego E, Carmona-Bernal C, Capote F, et al. (2004) Gender differences in obstructive sleep apnea syndrome: a clinical study of 1166 patients. *Respiratory Medicine* 98(10): 984-989.
- Ramada JM, Serra C, Amick III BC, et al. (2014) Reliability and validity of the work role functioning questionnaire (Spanish version). *Journal of Occupational Rehabilitation* 24(4): 640-649.
- Reishtein JL, Pack AI, Maislin G et al. (2006) Sleepiness and relationships in obstructive sleep apnea. *Issues Mental Health Nursing* 27(3): 319-330.
- Reuveni H, Greenberg-Dotan S, Simon-Tuval T, et al. (2008) Elevated health-care utilisation in young adult males with obstructive sleep apnoea. *European Respiratory Journal* 31(2): 273-279.
- Rosekind, MR, Gregory KB, Mallis, MM, et al. (2010) The cost of poor sleep: workplace productivity loss and associated costs. *Journal of Occupational and Environmental Medicine* 52(10): 91-98.
- Ryu HS, Lee SA, Lee GH, et al. (2016) Subjective apnoea symptoms are associated with daytime sleepiness in patients with moderate and severe obstructive sleep apnoea: a retrospective study. *Clinical Otolaryngology* 41(4): 395-401.
- Scholle S, Scholle HC, Kemper A, et al. (2003) First night effect in children and adolescents undergoing polysomnography for sleep-disordered breathing. *Clinical Neurophysiology* 114(11): 2138-2145.
- Schroder CM, O'Hara, R (2005) Depression and obstructive sleep apnea (OSA). *Annals of General Psychiatry* 4(1): 1-8.
- Shanahan L, Copeland WE, Angold A. (2014) Sleep problems predict and are predicted by generalized anxiety/depression and oppositional defiant disorder. *Journal of the American Academy of Child and Adolescent Psychiatry* 53(5): 550-558.
- Shapiro AL, Culp S, Azulay Chertok IR (2014) OSA symptoms associated with and predictive of anxiety in middle-aged men: secondary analysis of NHANES data. *Archives of Psychiatric Nursing* 28(3): 200-205.
- Sharafkhaneh A, Giray N, Richardson P, et al. (2005) Association of Psychiatric Disorders and Sleep Apnea in A Large Cohort. *Sleep* 28(11): 1405-1411.
- Silva GE, Goodwin JL, Vana KD, et al. (2016) Obstructive sleep apnea and quality of life: comparison of the SAQLI, FOSQ, and SF-36 questionnaires. *Southwest Journal of Pulmonary and Critical Care* 13(3): 137.
- Sivertsen B, Øverland, S, Glozier, N, et al. (2008) The effect of OSAS on sick leave and work disability. *European Respiratory Journal* 32(6): 1497-1503.

Su VYF, Chen YT, Lin WC, et al. (2012) Sleep apnea and risk of panic disorder. *The Annals of Family Medicine* 13(4): 325-330.

Swanson LM, Arnedt J, Rosekind MR, et al. (2011) Sleep disorders and work performance: findings from the 2008 National Sleep Foundation Sleep in America poll. *Journal of Sleep Research* 20(3): 487-494.

Tippin J, Aksan N, Dawson J, et al. (2016) Sleep remains disturbed in patients with obstructive sleep apnea treated with positive airway pressure: a three-month cohort study using continuous actigraphy. *Sleep Medicine* 24: 24-31.

Tregear S, Reston J, Schoelles K, et al. (2009) Obstructive sleep apnea and risk of motor vehicle crash: systematic review and meta-analysis. *Journal of Clinical Sleep Medicine* 5(6): 573-581.

Ulfberg J, Carter N, Talbäck M, et al. (1996) Excessive daytime sleepiness at work and subjective work performance in the general population and among heavy snorers and patients with obstructive sleep apnea. *Chest* 110(3): 659-663.

Weaver TE, Maislin G, Dinges DF, et al. (2007) Relationship between hours of CPAP use and achieving normal levels of sleepiness and daily functioning. *Sleep* 30(6): 711-719.

Weaver TE. (2013) “Don’t start celebrating—CPAP adherence remains a problem.” *Journal of Clinical Sleep Medicine* 9(6): 551-552.

Wetherell JL, Gatz M (2005) The Beck Anxiety Inventory in Older Adults With Generalized Anxiety Disorder. *Journal of Psychopathology and Behavioral Assessment* 27(1): 17-24.

Wittmann V, Rodenstein DO (2004) Health care costs and the sleep apnea syndrome. *Sleep Medicine Reviews* 8 (4): 269-279.

Yue W, Hao W, Liu P et al. (2003) A case-control study on psychological symptoms in sleep apnea-hypopnea syndrome. *The Canadian Journal of Psychiatry* 48(5): 318-323.

Psychological distress in patients with obstructive sleep apnoea: the role of hostility and coping self-efficacy

Vladimira Timkova, Iveta Nagyova, Sijmen A. Reijneveld,
Ruzena Tkacova, Jitse P. van Dijk, Ute Bültmann

Journal of Health Psychology. 2018;
Aug 11 DOI: 1359105318792080.

"I have such a desire
to sleep and am so much
behind my sleep.
A good night, one good
night and all this
nonsense will be swept
away."

Jean Paul SARTRE

Abstract

Background and aim

So far, very little is known about the association between hostility, coping self-efficacy and psychological distress in Obstructive Sleep Apnoea (OSA) patients. We aimed to assess whether hostility and coping self-efficacy are associated with psychological distress in OSA patients. Furthermore, we examined whether coping self-efficacy mediates the association between hostility and psychological distress.

Methods

We included 150 OSA patients (Apnoea-Hypopnoea Index–AHI $\geq$ 5; 68% male; mean age 48.9 ± 9.5 years), diagnosed by a full-night polysomnography. Patients completed the General Health Questionnaire-28, the Coping Self-efficacy Scale, the Cook-Medley Hostility Scale, the Pittsburgh Sleep Quality Index and the Epworth Sleepiness Scale. Multiple linear regression and mediation analyses were used to analyse the data.

Results

Regression models showed that hostility and poor coping self-efficacy were strongly associated with psychological distress in OSA patients. All assessed coping self-efficacy dimensions mediated the association between hostility and psychological distress. Coping self-efficacy for stopping unpleasant emotions and thoughts showed the strongest association with a lower level of psychological distress.

Conclusion

This study has led us to conclude that the presence of psychological distress in OSA patients may not be solely due to the effect of OSA itself. Rather, hostility and the choice of coping strategies may play a key role in examining which OSA patients will experience higher level of psychological distress.

Introduction

Obstructive Sleep Apnoea (OSA) is considered one of the most prevalent sleep disorders (Manarino et al., 2012), affecting 2–10% of the adult population (Leger et al., 2012). OSA leaves patients exhausted due to sleep disruption (Tkacova and Dorkova, 2010; Manarino et al., 2012; Rezaeitalab et al., 2014). Besides physical symptoms, OSA patients may experience psychological distress (Kang et al., 2012; Rezaeitalab et al., 2014; Su et al., 2015), irritability and hostility (Yue et al., 2003; Booth et al., 2006; Lau and Lee, 2014; Unal et al., 2017). Sleep-related OSA symptoms, such as poor night-time sleep quality and daytime sleepiness, have been shown to have a negative impact on patients' psychological well-being and overall quality of life (Tsara et al., 2009; Antic et al., 2011).

Hostility has previously been found to be associated with the presence of OSA, the degree of daytime sleepiness (Yue et al., 2003) and poor night-time sleep quality (Xiao et al., 2016; Freitag et al., 2017) but not with severity of the apnoea-hypopnoea index (AHI) or oxygen desaturation (Yue et al., 2003). Hostility is conceptualized as a negative cynical attitude toward others, with a propensity for anger, aggression (Cook and Medley, 1954; Ireland and Culpin, 2006), distrust or cynicism (Barefoot et al., 1989). Hostility may represent a risk factor for all-cause mortality (Nabi et al., 2008) and impaired mental health outcomes, with evidence being especially strong in patients with cardiovascular diseases (Silarova et al., 2016). Furthermore, hostility may be linked to increased negative emotionality (Brisette and Cohen, 2002), depression (Heponiemi et al., 2006), suicidal ideation and attempts (Brezo et al., 2006; Lemogne et al., 2011), sleep disruption (Brisette and Cohen, 2002) and poor sleep quality (Freitag et al., 2017). This symptomatic sleep disruption often causes serious decreases in blood oxygen levels, with potentially life-threatening cardiovascular consequences (Bardwell et al., 2001; Leger et al., 2012), while these mechanisms may be even more strongly aggravated by hostility (Hall et al., 2004; Mezick et al., 2010). Several mechanisms explaining the link between hostility and health consequences have been proposed. For instance, hostile persons exhibit increased sympathetic reactivity in some situations, experience more interpersonal conflicts and may display more unhealthy behaviours (Smith, 1992; Vandervoort, 2006).

Effective coping strategies may be beneficial in handling chronic diseases, including OSA (Bardwell et al., 2001; Cassara et al., 2017). Coping can be defined as an effort to manage a situation and involves various cognitive and behavioural strategies to overcome external or internal demands, which are appraised as either taxing or exceeding the person's resources (Folkman et al., 1986). The terms coping and coping self-efficacy are closely linked (Park and Folkman, 1997; Bandura et al., 1999; Chesnay et al., 2006). The concept of coping self-efficacy is based on the integration of two well established theories within health research: the self-efficacy theory of Bandura (1999) and the coping theory of Lazarus and Folkman (1984). In the framework of these theories, coping-self efficacy addresses which coping strategy a person will apply based on the perceived self-efficacy, and thus, it represents an important prerequisite to coping behaviour (Park and Folkman, 1997).

The choice and level of coping self-efficacy in a particular circumstance reflects prior relevant experiences (Bandura et al., 1977). As such, greater levels of coping self-efficacy were found to be associated with more effective regulation of emotional distress (Luberto et al., 2014). The ability to regulate emotions is crucial in diminishing psychological distress; however, healthy emotion-regulation may not merely be about using the “right” strategies (Haines et al. 2016). According to the strategy-situation-fit hypothesis, emotion-regulation strategies are able to diminish psychological distress only when used in appropriate contexts (Bonanno and Burton, 2013; Haines et al. 2016).

Previous research has focused on the effect of coping self-efficacy and coping behaviour on patients’ self-reported health outcomes in various diseases, such as heart failure (Graven and Grant, 2013), multiple sclerosis (Mikula et al., 2016) or chronic obstructive pulmonary disease (Tiemensma et al., 2016; Vaske et al., 2017). Previous studies have shown that a higher level of coping self-efficacy was associated with a better adjustment to various chronic diseases (Chesney et al., 2006; Benka et al., 2014; Mikula et al., 2016). Only a few studies have thus far addressed this concept, but these have shown an association between coping self-efficacy and psychological distress (Chesney et al. 2006; Benka et al., 2014) and better quality of life (Mikula et al., 2016) in the context of various chronic diseases. Overall, these results suggest that coping self-efficacy has direct effects on distress/well-being outcomes, beyond the impact of clinical and personality variables. Some studies indicate that problem-focused coping was the most beneficial in handling disease (Graven and Grant, 2013; Tiemensma et al., 2016), especially in the mental health domain (Scharloo et al., 2000). Nevertheless, in some studies, avoidance-oriented coping, such as coping self-efficacy for the ability to stop unpleasant emotions and thoughts, were defined as most effective in dealing with the disease (Mackay et al., 2012; Harmell et al., 2011). Recent studies have concluded that the more active and less passive coping strategies reported by OSA patients, the lower the level of depressive symptoms experienced by patients (Bardwell et al., 2001; Gassara et al., 2017). Moreover, a mediating role of coping self-efficacy in the association between personality traits and psychological health was identified in patients with multiple sclerosis (Mikula et al., 2016). Coping strategies were found to play a mediating role in the relationship between hostility and self-rated health outcomes in a sample of healthy individuals (Vandervoort, 2006). Unfortunately, the nature of coping styles utilized by hostility-prone individuals has received scant empirical attention.

So far, very little is known about the association between hostility, coping self-efficacy and psychological distress in OSA patients. To our knowledge, only two studies have directly focused on the association between coping and self-rated health outcomes, i.e. depression, in OSA patients (Bardwell et al., 2001; Gassara et al., 2017). Due to a lack of general consensus regarding the continuous positive airway pressure treatment effect on self-reported (Weaver, 2013; Tippin et al., 2016) and objective (Dimsdale et al., 2000) health outcomes, the present research and clinical practice should also focus on the identification of adequate internal resources which may diminish psychological distress in OSA patients. Thus, the

aims of this study were 1) to assess whether hostility and coping self-efficacy are associated with psychological distress in OSA patients when controlled for sociodemographic, clinical and sleep-related variables, and 2) to examine whether coping self-efficacy mediates the association between hostility and psychological distress.

Methods

Sample and procedure

This cross-sectional study was conducted at the Department of Pneumology and Phthisiology, L. Pasteur University Hospital and the Medical Faculty of PJ Safarik University in Kosice, Slovak Republic. All patients who visited the department for one-night polysomnography (PSG) from July 2013 to June 2016 were eligible for the study. The indication for PSG was based on a general practitioner referral form. OSA was diagnosed based on an overnight sleep examination.

Only OSA patients between 18 and 65 years of age were included due to possible increased vulnerability, functional changes and a decline in abilities and/or performance related to age. The study sample consisted of patients with an Apnoea Hypopnoea Index (AHI; number of apnoeas + hypopnoeas per hour of sleep) score of 5 or more (American Academy of Sleep Medicine, 2005), who had not undergone any previous continuous positive airway pressure (CPAP) treatment or other OSA treatment, had no regular shift work in the past six months, were Slovak-speaking and had no major comorbidities.

Out of N=263 patients, N=41 refused to participate in the study (response rate 84.0%). Another N=72 patients were excluded because of major comorbidities. The reasons for exclusion were major comorbidities related to sleep (a coexisting sleep disorder such as insomnia, narcolepsy, or circadian rhythm sleep disorder), major cardiovascular diseases (e.g. angina pectoris, myocardial infarction, primary pulmonary hypertension), pulmonary conditions (e.g. Pickwick syndrome, chronic obstructive pulmonary disease) and a history of cancer in the past twelve months. Neurological and psychological comorbidities included a neurological condition (e.g. epilepsy, stroke), a major psychiatric diagnosis (e.g. major depression, psychotic disorders) in the medical record and/or current usage of psychiatric medications which may affect cognitive functions (e.g. benzodiazepines, antidepressants or antipsychotics), drug abuse in the past six months, and regular shift work in the past six months. The clinical diagnoses of the comorbid diseases were established according to the standard International Classification of Diseases to revision Codes. Screening for comorbidities was based on medical data and an initial clinical interview prior to data collection. Medical examinations of patients were conducted by a pulmonologist specialized in sleep-disordered breathing. Patients with non-respiratory sleep-related complaints (e.g. narcolepsy, insomnia) were routinely referred to another group of clinical specialists.

The invitation letter, informed consent and questionnaires were sent to participants by postal mail three weeks before the medical examination. One week before the medical examination, patients were reminded about the questionnaires by

telephone. Patients filled in self-report questionnaires at home. All patients' signed the informed consent form prior to study participation. Participation in the study was fully voluntary, with no incentives offered to participate in the research. The study was approved by the Ethics Committee of PJ Safarik University in Kosice (approval no. 115/2011).

Measures

Psychological distress

Psychological distress was assessed using the General Health Questionnaire (GHQ-28) (Goldberg and Hillier, 1979). The GHQ-28 is a 28-item measure of psychological distress in the general population and within community or non-psychiatric clinical settings, such as among primary care or general medical out-patients. The GHQ-28 was developed as a screening tool to detect those likely to be at risk of developing psychiatric disorders. The questionnaire is divided into four subscales: somatic symptoms (items 1–7); anxiety/insomnia (items 8–14); social dysfunction (items 15–21) and severe depression (items 22–28) (Goldberg and Hillier, 1979). Psychological distress was defined as a continuous variable (0–3), ranging from 0 to 84. A total score of 23/24 represents the threshold for the presence of psychological distress (Goldberg and Hillier, 1979). Psychological distress is understood as the opposite continuum to psychological well-being (Goldberg and Hillier, 1979; Spiteri et al., 2013). Higher scores indicated a higher level of psychological distress. In our sample the Cronbach's alpha for the total GHQ-28 scale was 0.83.

Hostility

Hostility was measured by the abbreviated 27-item version of the Cook-Medley Hostility Scale (CMHo) (Cook and Medley, 1954). The CMHo scale is a widely used self-report measure of trait hostility. The scale primarily assesses the cognitive aspects of hostility, cynicism and distrust. Cynicism items are defined as statements of belief; aggressive response items reflect behaviour and hostile affect items reflect emotional experiences. Each item is rated on a dichotomised scale (1="true", 0="false"). The score ranges from 0 to 27, with a higher score indicating more hostility (Cook and Medley, 1954). Cronbach's alpha for the total scale in our sample was 0.85.

Coping self-efficacy

Coping self-efficacy (CSE) was measured using the 26-item CSE Scale developed specifically for people suffering from chronic disease (Chesney et al., 2006). The CSE scale represents a measure of an individual's confidence in performing coping behaviours when faced with life challenges. The term CSE relates to the tendency to make certain attributions about control not in one context but in many (Lazarus and Folkman, 1984). The CSE scale advances our ability to explore the theoretical links between the secondary appraisal of stress, which asks 'what can I do?', and the major coping functions postulated by stress and coping theory – the regulation of distress and the management of underlying problems (Chesney et al., 2006). The term coping self-efficacy is understood as a prerequisite for using

actual coping strategies, as people need to be sure that they can perform coping actions before they act upon them (Chesney et al., 2006). Patients were asked to respond to the following question: 'When things are not going well for you, or when you are having problems, how confident or certain are you that you can do the following': 'sort out what can be changed, and what cannot be changed', 'break an upsetting problem down into smaller parts', 'look for something good in a negative situation', and 'get emotional support from friends and family', or 'take your mind off unpleasant thoughts'. The CSE consists of three subscales representing self-efficacy for the use of 'problem-focused coping' strategies (ranging from 0 to 120), 'ability to get support from friends and family' (ranging from 0 to 50) and the 'ability to stop unpleasant emotions and thoughts' (ranging from 0 to 90). Coping self-efficacy for the use of 'problem-focused coping' consists of items that measure an individual's self-efficacy with respect to overcoming problems by analysing the nature of the problem and employing cognitive strategies to make the respondent's perception of the problem less severe (e.g. 'break an upsetting problem down into smaller parts'). Coping self-efficacy for the 'ability to stop unpleasant emotions and thoughts' measures a respondent's self-efficacy with respect to trying not to dwell on negative feelings and altering the emotional response to an unsettling event or problem rather than addressing the characteristics of the problem itself (e.g. 'take your mind off negative thoughts'). The 'ability to get support from friends and family' represents a set of items that captures the social dimension by tapping the respondent's perception of their ability to seek help from friends and family to cope with problems (e.g. 'get emotional support from friends and family') (Chesney et al., 2006). The three factors in the CSE scale are consistent with the three major aspects of coping – problem-focused coping, emotion-focused coping and social support. Although the scales are moderately correlated, the results of the concurrent validity analyses indicate that the scales assess self-efficacy with respect to different types of coping and lend support to using the factors separately (Chesney et al., 2006). Respondents answered on an 11-point scale. A higher score indicates a higher ability to cope with a particular situation (Chesney et al., 2006). In our sample, the Cronbach's alphas were 0.94 for self-efficacy for the use of problem-focused coping, 0.86 for coping self-efficacy for the ability to get support, and 0.93 for the ability to stop unpleasant emotions and thoughts, respectively.

Sleep-related problems

Sleep-related problems concerned night-time sleep quality and daytime sleepiness. *Night-time sleep quality* was measured using the Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989). The PSQI is a self-rated questionnaire to assess sleep disturbances and sleep quality over a one-month time interval. The PSQI consists of 19 self-report questions which cover seven domains: sleep duration, subjective sleep quality, sleep latency, habitual sleep efficiency, sleep disturbances, use of sleep medication and daytime dysfunction. The score ranges from 0 to 21, with higher scores reflecting poor night-time sleep quality. A cut-off score of 5 separates good from poor sleepers (Buysse et al., 1989). Cronbach's alpha in our sample was 0.85.

Daytime sleepiness was measured using the self-report Epworth Sleepiness Scale (ESS), an eight-item questionnaire describing the tendency to fall asleep in various daytime scenarios (Miletin and Hanly, 2003). The score ranges from 0 to 24, with higher scores indicating higher daytime sleepiness. An ESS total score greater than 10 indicates excessive daytime sleepiness (Miletin and Hanly, 2003). Cronbach's alpha in our sample was 0.86.

Sociodemographic and clinical data

Information on age, gender and marital status was obtained from patient records. Body Mass Index (BMI; height and weight) was assessed by a physician. BMI was categorized as: underweight (<18.5), normal (18.5–24.99), overweight (25.0–29.99) and obese (30+). Polysomnography (PSC) was used to determine whether the diagnosis of OSA was present and to identify the severity of the disorder. PSC consists of a simultaneous recording of multiple physiological parameters related to sleep and wakefulness which directly monitor and quantify the number of respiratory events, related hypoxemia and arousals. PSC included standard central and occipital electroencephalogram, bilateral electrooculogram, submental electromyogram (EMG), oral and nasal airflow using a thermistor, thoracic and abdominal excursions using respiratory inductive plethysmography and bilateral tibialis EMG. OSA severity was determined based on an AHI score (American Academy of Sleep Medicine, 2005), with three categories: mild OSA (AHI ≥ 5 and ≤ 15), moderate OSA (AHI > 15 and ≤ 30) and severe OSA (AHI > 30).

Statistical analyses

Firstly, we described the background characteristics of the sample and calculated means and standard deviations for hostility (CMHo), coping self-efficacy (CSE) and psychological distress (GHQ-28) and sleep-related problems. We calculated frequencies and percentage for sociodemographic and clinical variables. Secondly, we assessed the correlations between the variables under study. Thirdly, using regression analyses we assessed the crude associations of hostility and coping self-efficacy with psychological distress. Multicollinearity was assessed using the variance inflation factor (VIF <2.0). We applied the enter selection in multiple linear regression models to determine the factors associated with psychological distress. For each factor, beta coefficients represent the mean variation of the psychological distress score. As the choice of coping strategies may be influenced by clinical and sleep-related variables, the associations between hostility, coping self-efficacy and psychological distress were adjusted for OSA severity, night-time sleep quality and daytime sleepiness. The first model of the variables included sociodemographic data (age, gender). A second model included a clinical variable (OSA severity – measured by AHI), and a third model included night-time sleep quality and daytime sleepiness. In the fourth and fifth model, hostility and all dimensions of coping self-efficacy were included separately (following Bardwell et al., 2001; Mikula et al., 2016; Gassara et al., 2017) to assess the explained amount of the total variance of psychological distress.

Finally, we performed mediation analyses to investigate whether the associations between hostility and psychological distress were mediated by the coping self-efficacy. According to Baron and Kenny (1986), the following conditions must be met to establish mediation: the independent variable (hostility) must affect the dependent variable (psychological distress); secondly, the independent variable (hostility) must affect the mediator (separate coping self-efficacy dimensions); and lastly, the mediator (separate coping self-efficacy dimensions) must affect the dependent variable (psychological distress). The proportion of the effect which is mediated was calculated as the indirect effect divided by the total effect and multiplied by 100, while the as-advised standardized total effect was at least ± 0.2 (Kenny, 2016). Sobel z-tests were used to examine the mediating effects of the coping self-efficacy on the associations between hostility and psychological distress. Power analysis revealed that the statistical power for multivariate analysis exceed 95% at $\alpha=0.05$. The statistical power for univariate analysis was 0.99 at $\alpha=0.05$ (Faul et al., 2009). A p-value of <0.05 was considered to be statistically significant. All analyses were performed using the Statistical Package for the Social Sciences (IBM SPSS 23) and MedGraph.

Results

Sample characteristics

A total of N=150 OSA patients (68% male; mean age 48.9±9.5 years) were included in the study. The majority of patients had secondary education (57.3%). A total of 44.7% were obese and 49.3% had severe OSA (Table 5.1).

Table 5.1 Baseline characteristics of the OSA patients (AHI≥5)

Characteristics	N=150
Age in years; mean, sd	48.9±9.5
Gender; male, N (%)	102 (68.0%)
Marital status; single, N (%)	36 (24.0%)
Education; N (%)	
Elementary	8 (5.3%)
Secondary	86 (57.3%)
University	56 (37.3%)
Body Mass Index; mean, sd	30.2±7.7
Body Mass Index; N (%)	
Underweight (<18.50)	9 (6.0%)
Normal (18.50-24.99)	42 (28.0%)
Overweight (25.00-29.99)	32 (21.3%)
Obese (≥30.00)	67 (44.7%)
Apnoea-hypopnoea index (AHI) in events/h; mean, sd	36.1±22.3
OSA severity; N (%)	
Mild (AHI≥5≤15)	23 (15.3%)
Moderate (AHI>15≤30)	52 (34.7%)
Severe (AHI>30)	74 (49.3%)
Night-time sleep quality; mean, sd (PSQI; 0-21)	9.7±4.1
Excessive daytime sleepiness; mean, sd (ESS; 0-24)	11.0±5.3
Hostility (CMHo; 0-27)	15.1±5.6
Problem-focused coping self-efficacy (CSE; 0-120)	79.5±24.1
Get support from friends and family (CSE; 0-50)	32.9±10.0
Stopping unpleasant emotions and thoughts (CSE; 0-90)	56.1±19.6
Psychological distress (GHQ-28; 0-84)	32.6± 18.4
Psychological distress (GHQ-28 ≥24)	79 (56.0%)

AHI – Apnoea-Hypopnoea Index; OSA – Obstructive Sleep Apnoea; PSQI – Pittsburgh Sleep Quality Index; ESS – Epworth Sleepiness Scale; CMHo – Cook-Medley Hostility Scale; CSE – Coping Self-Efficacy Scale; GHQ-28 – General Health Questionnaire; Missing values: OSA severity (0.7%), age (1.0%), ESS (1.0%), PSQI (1.0%), CMHo (1.0%), GHQ-28 (6.0%), Problem-focused coping self-efficacy (6.0%), Get support from friends and family (2.0%), Stopping unpleasant emotions and thoughts (3.0%).

Correlations between hostility, coping self-efficacy and psychological distress

Table 5.2 shows the correlations between hostility, coping self-efficacy and psychological distress. Small but significant correlations were found between hostility, self-efficacy for the use of problem-focused coping and coping self-efficacy for getting support from family and friends. A moderate correlation was found between hostility and ability to stop unpleasant emotions and thoughts. The correlations between hostility, all dimensions of coping self-efficacy and psychological distress were high.

Table 5.2 Correlation coefficients between hostility, coping self-efficacy and psychological distress

	Hostility	Problem-focused coping self-efficacy	Get support from friends and family	Stopping unpleasant emotions and thoughts
Problem-focused coping self-efficacy	-0.24*	-	-	-
Get support from friends and family	-0.23*	0.89***	-	-
Stopping unpleasant emotions and thoughts	-0.26**	0.90***	0.82***	-
Psychological distress	0.58***	-0.50***	-0.35***	-0.53***

*p<0.05; **p<0.01; ***p<0.001. Higher score indicates higher psychological distress.

Associations between hostility, coping self-efficacy and psychological distress

A crude effect on psychological distress was found for OSA severity, sleep-related problems, hostility and coping self-efficacy (Table 5.3). The associations between hostility, coping self-efficacy and psychological distress were adjusted for sociodemographic variables (age, gender), the clinical variables (OSA severity, BMI) and sleep-related variables (night-time sleep quality, daytime sleepiness). Model 4, with hostility added, explained 59% of the total variance of psychological distress. All coping self-efficacy dimensions were strongly associated with a lower level of psychological distress. The regression models for coping self-efficacy for the ability to get support from family and friends, self-efficacy for the use of problem-focused coping and coping self-efficacy for the ability to stop unpleasant emotions and thoughts explained 63%, 67%, and 70% of the total variance of psychological distress (Model 5 A, B, C), respectively.

Table 5.3 Hostility and coping self-efficacy on psychological distress (N=150)

Psychological distress (GHQ-28)																
	Crude		Model 1		Model 2		Model 3		Model 4		Model 5 A		Model 5 B		Model 5 C	
	B	(95%CI)	B	(95%CI)	B	(95%CI)	B	(95%CI)	B	(95%CI)	B	(95%CI)	B	(95%CI)	B	(95%CI)
Age	-0.22	(-0.54; 0.12)	-0.26	(-0.59; 0.06)	-0.33	(-0.65; -0.02)*	-0.33	(-0.56; -0.11)**	-0.22	(-0.44; 0.03)	-0.19	(-0.39; 0.00)	-0.21	(-0.42; 0.00)	-0.18	(-0.37; 0.00)
Gender	6.06	(-0.43; 12.55)	6.63	(-0.09; 13.17)	5.40	(-0.91; 11.70)	1.85	(-2.92; 6.61)	0.97	(-3.61; 5.55)	0.18	(-3.91; 4.26)	0.63	(-3.63; 4.88)	0.46	(-3.46; 4.39)
Body mass index	0.62	(0.23; 1.02)**	-		0.91	(-0.30; 0.69)	0.13	(-0.22; 0.49)	0.06	(-0.29; 0.40)	-0.06	(-0.36; 0.25)	-0.01	(-0.36; 0.31)	0.01	(-0.28; 0.30)
OSA severity	0.24	(0.11; 0.36)**	-		0.20	(0.03; 0.37)*	0.06	(-0.07; 0.81)	0.08	(-0.04; 0.20)	0.12	(-0.01; 0.23)	0.13	(-0.01; 0.24)	0.13	(-0.03; 0.23)
Night-time sleep quality	2.89	(2.32; 3.45)***	-		-		2.60	(2.08; 3.13)***	2.15	(1.59; 2.71)***	1.85	(1.34; 2.36)***	2.00	(1.48; 2.53)***	1.79	(1.29; 2.27)***
Daytime sleepiness	1.44	(0.91; 1.97)***	-		-		0.89	(0.46; 1.32)***	0.71	(0.29; 1.14)**	0.68	(0.31; 1.06)***	0.69	(0.30; 1.09)**	0.68	(0.33; 1.04)***
Hostility	1.91	(1.47; 2.36)***	-		-		-		0.79	(0.36; 1.23)***	0.72	(0.33; 1.12)***	0.72	(0.31; 1.12)**	0.67	(0.30; 1.03)***
Problem-focused	-0.37	(-0.48; -0.26)***	-		-		-		-		-0.23	(-0.31; -0.15)***	-		-	
Get support	-0.62	(-0.91; -0.34)***	-		-		-		-		-		-0.39	(-0.59; -0.20)***	-	
Stopping emotions/thoughts	-0.49	(-0.62; -0.35)***	-		-		-		-		-		-		-0.32	(-0.41; -0.22)***
F Change	-		2.99		6.35**		59.88***		12.78***		32.83***		16.62***		44.59***	
Adjusted R ²	-		0.03		0.12		0.54		0.59		0.67		0.63		0.70	

Crude: effect of each variable separately on functional status; Model 1: effect of age and gender on GHQ-28 score; Model 2: effect of age, gender, BMI and OSA severity on GHQ-28 score; Model 3: effect of age, gender, BMI, OSA severity and sleep-related problems on GHQ-28 score; Model 4: effect of age, gender, BMI, OSA severity, sleep-related problems and hostility on GHQ-28 score; Model 5 A: effect of age, gender, BMI, OSA severity, sleep-related problems, hostility and coping self-efficacy for the ability to get support from friends and family on GHQ-28 score; Model 5 B: effect of age, gender, BMI, OSA severity, sleep-related problems, hostility and coping self-efficacy for the ability to stop unpleasant emotions and thoughts on GHQ-28 score; Model 5 C: effect of age, gender, BMI, OSA severity, sleep-related problems, hostility and coping self-efficacy for stopping unpleasant emotions and thoughts on GHQ-28 score; B: unstandardized regression coefficient; BMI: body mass index; CI – confidence interval; Gender – male gender was set as the reference; OSA – Obstructive Sleep Apnoea; GHQ-28 – General Health Questionnaire; F Change – significance of prediction improvement in model fit; Adjusted R² – explained variance adjusted for the number of predictors in the particular model; GHQ-28 – higher score indicates higher psychological distress; *p<0.05; **p<0.01; ***p<0.001.

Coping self-efficacy as a mediator between hostility and psychological distress
The mediation analyses showed that all three coping self-efficacy dimensions partially mediated the associations between hostility and psychological distress in OSA patients. The indirect effects of all three coping self-efficacy dimensions were significant. They accounted for 10.0% of coping self-efficacy for getting support from family and friends, 15.0% of self-efficacy for the use of problem-focused coping and 17.0% of coping self-efficacy for the ability to stop unpleasant emotions and thoughts (Table 5.4). Figure 5.1 shows the mediating effects of separate coping self-efficacy dimensions on the association between hostility and psychological distress.

Table 5.4 Mediating effect of coping self-efficacy on the association between hostility and psychological distress

Coping self-efficacy	Sobel z-value	Psychological distress	
		Direct effect	Indirect effect
Problem-focused coping self-efficacy	2.60***	0.49***	15.0%
Get support	2.16*	0.53***	10.0%
Stopping emotions and thoughts	2.85***	0.48***	17.0%

*p<0.05; *** p<0.001.

Figure 5.1 Mediating role of coping self-efficacy on the association between hostility and psychological distress

Mediations were conducted separately for each particular coping-self-efficacy dimension *p<0.05; **p<0.01; *** p<0.001.

Discussion

The aims of this study were 1) to assess whether hostility and coping self-efficacy are associated with psychological distress in Obstructive Sleep Apnoea (OSA) patients when controlled for sociodemographic, clinical and sleep-related variables, and 2) to examine whether coping self-efficacy mediates the association between hostility and psychological distress. We found that high levels of hostility and poor coping self-efficacy were strongly associated with psychological distress in OSA patients. Compared with self-efficacy for the use of problem-focused coping and coping self-efficacy for the ability to get support from friends and family, poor coping self-efficacy for stopping unpleasant emotions and thoughts was more strongly associated with psychological distress. All coping self-efficacy dimensions mediated the association between hostility and psychological distress. Coping self-efficacy for stopping unpleasant emotions and thoughts was identified as the strongest mediator in the association between hostility and psychological distress.

We found a strong association between high levels of hostility and psychological distress in OSA patients, even after controlling for sociodemographic variables, disease severity, body-mass index and sleep-related problems. Earlier, it was shown that individuals with OSA demonstrated along with the presence of irritability, also frustration and increased engagement in conflict (Bardwell et al., 1999; Yue et al., 2003, Unal et al. 2017). Hostility and anger were also found to be higher in OSA patients when compared to healthy controls in a Korean population (Lau and Lee, 2014). Vandervoort et al. (2006) showed that individuals with a high level of hostility reported poorer mental health and used avoidant coping strategies more often than individuals with a low level of hostility (Vandervoort, 2006).

As sleep-related symptoms in OSA may increase hostility, which may consequently potentiate the negative health consequences of the disease, coping self-efficacy may represent one of the key determinants in adaptation to sleep disorders. Our analyses showed that poor coping self-efficacy was strongly associated with psychological distress in OSA patients. This results confirm previous findings on the association between coping self-efficacy and a lower level of psychological distress (Chesney et al. 2006; Benka et al., 2014) and a better quality of life (Mikula et al., 2016) in the context of chronic diseases. Self-efficacy for the ability to stop unpleasant emotions and thoughts in our sample explained the most variance of all the coping self-efficacy dimensions in the psychological distress. One possible explanation why stopping unpleasant emotions and thoughts might be the most adaptive coping self-efficacy dimension in OSA is that the patients have very little control (e.g. Cheng, 2001) over the symptoms of their disease. When patients do not have the ability to control the disease and have to learn how to live with it, this kind of coping self-efficacy can help them to reduce the stress that breathing and sleep-related symptoms bring and thus may diminish their psychological distress. In line with the strategy-situation-fit hypothesis, well-being may thus represent a function of the “goodness of fit” between emotion-regulation efforts and the contextual characteristics (Conway and Terry, 1992) of OSA. This interpretation is consistent with previous research on chronic conditions, which suggests that coping self-efficacy

for stopping unpleasant emotions and thoughts is more adaptive when little control over disease is possible (De Ridder and Schreurs 2001; Mikula et al., 2014). In line with our findings, previous research also showed that individuals scoring higher on hostility were also more likely to employ escape-avoidance coping styles while handling psychological distress (Vandervoort, 2006) and were less likely to use problem-focused coping (Sasaki and Yamasaki, 2002).

Next, we found the ability to get support from friends and family to be the least adaptive coping self-efficacy domain in the association with psychological distress, including diminishing the negative effect of hostility on psychological well-being. This finding may be explained by the results of previous research, in which sleep-related problems represented an important predictor of daytime functioning, including engagement in social activities (Dew et al., 1994). Therefore, due to sleep-related OSA symptoms, such as daytime sleepiness, the sources of social support may be less utilized and thus may be of less importance. As hostility was found to be associated with poor levels of social support (Smith, 1992), social dysfunction (Sasaki and Yamasaki, 2002) and involves an oppositional orientation toward others and negative beliefs and feelings toward others (Houston and Vavak, 1991), it may be assumed that patients with OSA may be even less motivated to participate in social activities, when potentiated by the presence of hostility. Furthermore, hostility was found to lead to difficulty in extracting the needed social support (Vandervoort, 1999).

In contrast, Bardwell et al. (2001) concluded that the more active and less passive coping strategies reported by OSA patients, the lower level of depressive symptoms they experienced. Depressive symptoms were associated with more emotional coping and with less problem-focused coping in the study by Cassara et al. (2017). Although our results differ from those of previous studies (Bardwell et al., 2001; Cassara et al., 2017), these discrepancies may be associated with the difference in OSA diagnosis criteria; e.g. patients in the study by Bardwell et al. (2001) were diagnosed using a Respiratory Disturbance Index of ≥ 15 , while in our study OSA diagnosis was stated based on an Apnoea-Hypopnoea Index of ≥ 5 . Another possible explanation for the inconsistency in the above studies could be caused by the use of univariate statistical procedures in the study by Cassara et al. (2017). Moreover, the discrepancies in the role of passive coping strategies could be influenced by the different assessment of psychological distress, with a focus on depression. These discrepancies may also concern the difference in theoretical perspective of the tools used to measure coping (e.g. Vaske et al., 2017).

We also found that all coping self-efficacy dimensions mediated the association between hostility and psychological distress. Thus, active as well as passive coping may be adaptive when dealing with OSA. Moreover, coping self-efficacy may serve as a trigger or perpetuator for psychological distress in OSA patients. In line with our findings, efficient coping strategies were associated with a low levels of hostility in previous research (Comijs et al., 1999). One of the first investigations on coping and hostility in people with a chronic condition found that efficient coping was associated with reacting to stress with a minimum of hostility either expressed

or suppressed (Schill et al., 1985). The transactional model of the relationship between hostility and disease suggests that personality, cognitive and behavioural factors operate in reciprocal interaction with the environment and lead to a variety of frequent physiological reactions and related pathophysiological consequences (Williams and Williams, 2001).

Mediation analyses in our study revealed that coping self-efficacy for stopping unpleasant emotions and thoughts was the most effective in diminishing the strength of the association between hostility and psychological distress in OSA patients. In line with these findings, previous research also showed that escape-avoidance-oriented coping strategies had a significant mediating role in the relationship between hostility and self-rated health outcomes in a sample of healthy individuals (Vandervoort, 2006). This finding is not surprising, as the affective component of hostility consists of the tendency to experience several negative emotions (Barefoot et al., 1989).

Finally, we wanted to ensure that the choice of coping self-efficacy and its association with psychological distress was not simply a result of sociodemographic or clinical variables. Therefore, gender and age were employed as controlled variables, along with body mass index (BMI), AHI and sleep-related problems. We found no significant association between sociodemographic variables and psychological distress. Similarly, the association between clinical variables, measured as OSA severity and BMI, was no longer significant in complex models. Previous studies have shown that age (Ryff and Singer, 2013), overweight and obesity were found to be associated with poor levels of subjective health status, particularly in terms of physical well-being (Doll et al., 2000). Other studies, have not found any association between BMI and psychological disturbances or psychosocial functioning (Klesges et al., 1992). The missing associations between age, obesity and psychological distress may be a result of confounding by the presence of accompanying chronic illness (Doll et al., 2000).

Strengths and limitations

Patients in our sample were diagnosed by polysomnography, which is an asset of the study. Moreover, this is the first study which examines the mechanism between hostility, coping self-efficacy and psychological distress using comprehensive measurements in a rarely studied population of OSA patients. It is plausible that a number of limitations could have influenced our findings. First, we used cross-sectional data; thus, we can not make any causal inferences. Second, self-report hostility may be prone to providing socially acceptable answers (Davidson and Hall, 1997); thus, replication with more objective measures would provide an important comparison. Finally, although emotional suppression may reduce the outward expression of emotion and possibly the subjective experience of emotion in the short term, it was found to be less effective in reducing emotion and physiological arousal over a long-term period (Gross and Thompson, 2007). Previous studies have also suggested that long-term suppression of negative thoughts may prevent habituation to emotional stimuli and as such may result in hypersensitivity to psychological

distress and symptoms (Wenzlaff and Wegner, 2000). Thus, longitudinal studies are needed to assess the influence of coping self-efficacy for the ability to stop unpleasant emotions and thoughts on psychological distress.

Implications for future research and practice

Psychological distress in OSA patients is clearly associated with hostility and poor coping self-efficacy and requires attention in both clinical care and research. We recommend that our study should be replicated with a larger sample and a longitudinal design. Further, future research is needed to understand the causal mechanisms between hostility, coping self-efficacy and psychological distress in OSA patients. It would also be interesting to examine the actual sleep disturbances among patients scoring high and low on the Cook-Medley hostility scale in the laboratory. Hostility levels are well known to fluctuate considerably over time, and thus a longitudinal study including repeated measures is needed. Poor coping self-efficacy may represent a background factor partially underlying the adverse effect of hostility on psychological well-being.

Psychological distress was found to have the capacity for interventions (Farrand et al., 2016; and various protective efforts, including self-efficacy and effective coping strategies (Hopman et al., 2009; Trojan et al., 2012; Mikula et al., 2016). From a clinical perspective, knowing which coping strategies a patient uses and how much hostility they experience and express may be useful in OSA management. Therefore, the assessment of hostility and particular coping self-efficacy dimension may help to identify those patients who might benefit most from the direct treatment of psychological symptoms, in addition to treatment of sleep-disordered breathing itself. Our findings suggest that it is necessary to monitor hostility in OSA patients during clinical care. Understanding these associations may be beneficial for therapy, as well. A person who believes in his/her ability to produce a desired effect can conduct a more active and self-determined health-behaviour (Schwarzer and Renner, 2000). Therefore, education about the role of coping self-efficacy can be included in shorter pragmatic programs (Goudsmith et al., 2009; Wersebe et al., 2018). As disease occurs in people having premorbidly varying coping self-efficacy in general and illness-related stress in particular, personality and behavioural patterns may play a key role in determining which OSA patients will experience higher levels of psychological distress. Thus, rather than solely focusing on patients' medical parameters and standard OSA treatment, patients should be encouraged to use adaptive coping strategies. When our findings are confirmed in longitudinal studies, screening for hostility and treatment focused on decreasing high levels of hostility, in addition to standard therapy of the disordered breathing, might help to handle psychological distress experienced by OSA patients. Feelings of hostility may be decreased by cognitive behavioural therapy (Seligman et al., 2005), controlled interventions and behavioural modifications (Barefoot et al., 1989).

Conclusion

This study has led us to conclude that the presence of psychological distress in OSA patients may not be solely due to the effect of OSA itself. Rather, hostility and the choice of coping strategies may play a key role in examining which OSA patients will experience higher level of psychological distress. Thus, interventions focused on reducing hostility and enhancement of adaptive coping may help to optimize standard treatment in OSA patients and be paramount in diminishing psychological distress in OSA patients. Further longitudinal research is necessary to confirm the causality, however.

References

- American Academy of Sleep Medicine (2005) International Classification of Sleep Disorders: Diagnostic and Coding Manual (2nd ed). Sleep Disorders Association, Rochester, MN (ICSD-2).
- Antic NA, Catcheside P, Buchan C, et al. (2011) The effect of CPAP in normalizing daytime sleepiness, quality of life, and neurocognitive function in patients with moderate to severe OSA. *Sleep* 34(1): 111-119.
- Bandura A, Adams NE, Beyer J (1977) Cognitive processes mediating behavioral change. *Journal of Personality and Social Psychology* 35(3): 125-139.
- Bandura A (1999) Social cognitive theory: an agentic perspective. *Asian Journal of Social Psychology* 2(1): 21-41.
- Bardwell W, Berry C, Ancoli-Israel S, et al. (1999) Psychological correlates of sleep apnea. *Journal of Psychosomatic Research* 47(6): 583-596.
- Bardwell WA, Ancoli-Israel S, Dimsdale JE (2001) Types of coping strategies are associated with increased depressive symptoms in patients with obstructive sleep apnea. *Sleep* 24(8): 905-909.
- Barefoot JC, Dodge KA, Peterson BL, et al. (1989) The Cook-Medley hostility scale: item content and ability to predict survival. *Psychosomatic Medicine* 51(1): 46-57.
- Baron RM, Kenny DA (1986) The moderator-mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. *Journal of Personality and Social Psychology* 51(6): 1173-1182.
- Benka J, Nagyova I, Rosenberger, J et al. (2014) Is coping self-efficacy related to psychological distress in early and established rheumatoid arthritis patients?. *Journal of Developmental and Physical Disabilities* 26(3): 285-297.
- Bonanno GA and Burton CL (2013) Regulatory flexibility: An individual differences perspective on coping and emotion regulation. *Perspectives on Psychological Science* 8(6): 591-612.
- Booth BD, Paul Fedoroff J, Curry SD, et al. (2006) Sleep Apnea as a Possible Factor Contributing to Aggression in Sex Offenders. *Journal of Forensic Sciences* 51(5): 1178-1181.
- Brezo J, Paris J, and Turecki G. (2006) Personality traits as correlates of suicidal ideation, suicide attempts, and suicide completions: a systematic review. *Acta Psychiatrica Scandinavica* 113(3): 180-206.
- Brissette I and Cohen S (2002) The contribution of individual differences in hostility to the associations between daily interpersonal conflict, affect, and sleep. *Personality and Social Psychology Bulletin* 28(9): 1265-1274.
- Buysse DJ, Reynolds CF, Monk TH, et al. (1989) The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Research* 28(2): 193-213.
- Comijs HC, Jonker C, van Tilburg W, et al. (1999) Hostility and coping capacity as risk factors of elder mistreatment. *Social Psychiatry and Psychiatric Epidemiology* 34(1): 48-52.
- Conway VJ and Terry DJ (1992) Appraised controllability as a moderator of the effectiveness of different coping strategies: A test of the goodness of fit hypothesis. *Australian Journal of Psychology* 44: 1-7.
- Cook WW and Medley DM (1954) Proposed hostility and pharisaic-virtue scales for the MMPI. *Journal of Applied Psychology* 38(6): 414-418.
- Davidson K and Hall P (1997) Potential for hostility and faking-good in high-hostile men. *Journal of Behavioral Medicine* 20(1): 47-54.
- De Ridder D, Schreurs K (2001) Developing interventions for chronically ill patients: is coping a helpful concept? *Clinical Psychology Review* 21(2): 205-240.
- Dew MA, Reynolds III CF, Monk TH, et al. (1994) Psychosocial correlates and sequelae of electroencephalographic sleep in healthy elders. *Journal of Gerontology* 49(1): 8-18.
- Dimsdale JE, Lored JS, and Profant J (2000) Effect of continuous positive airway pressure on blood pressure. *Hypertension* 35(1): 144-147.

Doll HA, Petersen SE, Stewart-Brown SL (2000) Obesity and physical and emotional well-being: associations between body mass index, chronic illness, and the physical and mental components of the SF-36 questionnaire. *Obesity* 8(2): 160-170.

Farrand P, Matthews J, Dickens C, et al. (2016) Psychological interventions to improve psychological well-being in people with dementia or mild cognitive impairment: systematic review and meta-analysis protocol. *British Medical Journal Open* 6(1): e009713.

Faul F, Erdfelder E, Buchner A, et al. (2009) Statistical power analyses using G*Power 3.1: Tests for correlation and regression analyses. *Behavior Research Methods* 41: 1149-1160.

Folkman S, Lazarus RS, Dunkel-Schetter C, et al. (1986) Dynamics of a stressful encounter: Cognitive appraisal, coping, and encounter outcomes. *Journal of Personality and Social Psychology* 50(5): 992-1003.

Freitag L, Ireland J, and Niesten IJM (2017) Exploring the relationship between sleep quality, emotional well-being and aggression levels in a European sample. *Journal of Aggression, Conflict and Peace Research* 9(3): 167-177.

Gassara I, Thabet JB, Msaad S, et al. (2017) Impact of coping strategies on emotional status in patients with obstructive sleep apnea syndrome. *European Psychiatry*. DOI:<https://doi.org/10.1016/j.eurpsy.2017.01.602>.

Goldberg DP, Hillier VF (1979) A scaled version of the General Health Questionnaire. *Psychological Medicine* 9(1): 139-145.

Goudsmit EM, Ho-Yen DO, Dancey CP (2009) Learning to cope with chronic illness. Efficacy of a multi-component treatment for people with chronic fatigue syndrome. *Patient Education and Counseling* 77(2): 231-236.

Graven LJ and Grant JS (2013) Coping and health-related quality of life in individuals with heart failure: An integrative review. *Heart & Lung: The Journal of Acute and Critical Care* 42(3): 183-194.

Gross JJ and Thompson RA (2007) Emotion regulation: Conceptual foundations. In J. J. Gross (Ed.), *Handbook of emotion regulation* New York: Guilford Press pp 3-24.

Haines SJ, Gleeson J, Kuppens P et al. (2016) The wisdom to know the difference: Strategy-situation fit in emotion regulation in daily life is associated with well-being. *Psychological Science* 27(12): 1651-1659.

Hall M, Vasko R, Buysse DJ, et al. (2004) Acute stress affects heart rate variability during sleep. *Psychosomatic Medicine* 66: 56-62.

Harmell AL, Mausbach BT, Roepke SK, et al. (2011) The relationship between self-efficacy and resting blood pressure in spousal Alzheimer's caregivers. *British Journal of Health Psychology* 16(2): 317-328.

Heponiemi T, Elovainio M, Pekkarinen L, et al. (2006) The moderating effect of employee hostility on the association of long-term elderly care unit's negative resident characteristics to employee stress and well-being. *Journal of Occupational Health Psychology* 11(2): 157.

Hopman WM, Harrison MB, Coo H, et al. (2009) Associations between chronic disease, age and physical and mental well-being. *Chronic Diseases in Canada* 29(3): 108-116.

Houston BK, and Vavak CR (1991) Cynical hostility: Developmental factors, psychosocial correlates, and health behaviors. *Health Psychology* 10(1): 9-17.

Cheng C (2001) Assessing coping flexibility in real-life and laboratory settings: a multimethod approach. *Journal of personality and social psychology* 80(5): 814-833.

Chesney M, Neilands TB, Chambers DB (2006) A validity and reliability study of the coping self-efficacy scale. *British Journal of Health Psychology* 11(3): 421-437.

Ireland JL and Culpin V (2006) The relationship between sleeping problems and aggression, anger, and impulsivity in a population of juvenile and young offenders. *Journal of Adolescent Health* 38(6): 649-655.

Kang EW, Abdel-Kader K, Yabes J, et al. (2012) Association of sleep disorder breathing with cognitive dysfunction in CKD stages 4-5. *American Journal of Kidney Disease* 60(6): 949-958.

Kenny DA (2016) Mediation. Available at: <http://davidakenny.net/cm/mediate.htm> (accessed 10 May 2017).

Klesges RC, Isbell TR, Klesges, LM (1992) Relationship between dietary restraint, energy intake, physical activity, and body weight: a prospective analysis. *Journal of Abnormal Psychology* 101(4): 668-674.

Lau EYY, Ip MSM, Lee TMC (2014) Neurocognitive and psychosocial outcomes of obstructive sleep apnea in Hong Kong Chinese. *Hong Kong Medical Journal* 20(7): 19-23.

Lazarus R, Folkman S (1984) *Stress, Appraisal and coping*. Springer Publishing Company. ISBN 0-8261-4191-9.

Legier D, Bayon V, Laaban J, et al. (2012) Impact of sleep apnea on economics. *Sleep Medicine Reviews* 16(5): 455-462.

Lemogne C, Fossati P, Limosin F, et al. (2011) Cognitive hostility and suicide. *Acta Psychiatrica Scandinavica* 124(1): 62-69.

Luberto CM, Cotton S, McLeish AC et al. (2014) Mindfulness skills and emotion regulation: The mediating role of coping self-efficacy. *Mindfulness* 5(4): 373-380.

Mackay C and Pakenham KI (2012) A stress and coping model of adjustment to caring for an adult with mental illness. *Community Mental Health Journal* 48(4): 450-462.

Manarino MR, Fillipo FD, Piro M. (2012) Obstructive sleep apnea syndrome. *European Journal of Internal Medicine* 23(7): 586-593.

Mezick EJ, Matthews, KA, Hall M, (2010) Low life purpose and high hostility are related to an attenuated decline in nocturnal blood pressure. *Health Psychology* 29(2): 196-204.

Mikula P, Nagyova I, Krokavcova M, et al. (2014) Coping and its importance for quality of life in patients with multiple sclerosis. *Disability and Rehabilitation* 36(9): 732-736.

Mikula P, Nagyova I, Krokavcova M, et al. (2016) Do coping strategies mediate the association between Type D personality and quality of life among people with multiple sclerosis?. *Journal of Health Psychology*. 23(12): 1557-1565.

Miletin MS, Hanly PJ (2003) Measurement properties of the Epworth sleepiness scale. *Sleep Medicine* 4(3): 195-199.

Nabi H, Kivimäki M, Zins, M, et al. (2008) Does personality predict mortality? Results from the GAZEL French prospective cohort study. *International Journal of Epidemiology* 37(2): 386-396.

Park CL and Folkman S (1997) Meaning in the context of stress and coping. *Review of General Psychology* 1(2): 115-144.

Rezaeitalab F, Moharrari F, Saberi S, et al. (2014) The correlation of anxiety and depression with obstructive sleep apnea syndrome. *Journal of Research in Medical Sciences* 19(3): 205-210.

Ryff CD and Singer BH (2013) Know thyself and become what you are: A eudaimonic approach to psychological well-being. In *The exploration of happiness*. Springer, Dordrecht: 97-116.

Sasaki M and Yamasaki K (2002) Causal relationship between hostility and health status and the mediating role of stress coping. *Japanese Journal of Health Psychology* 15(2): 1-11.

Seligman ME, Steen TA, Park N, et al. (2005) Positive psychology progress: empirical validation of interventions. *American Psychologist* 60(5): 410-421.

Scharloo M, Kaptein AA, Weinman, JA, et al. (2000) Physical and psychological correlates of functioning in patients with chronic obstructive pulmonary disease. *Journal of Asthma* 37(1): 17-29.

Schill T, Ramanaiah N, O’Laughlin S (1985) Relation of expression of hostility to coping with stress. *Psychological Reports* 56(1): 193-194.

Schwarzer R and Renner B (2000) Social-cognitive predictors of health behavior: action self-efficacy and coping self-efficacy. *Health Psychology* 19(5): 487-495.

Silarova B, Nagyova I, Rosenberger J, et al. (2016) Sense of coherence as a mediator between hostility and health-related quality of life among coronary heart disease patients. *Heart & Lung: The Journal of Acute and Critical Care* 45(2): 126-131.

Smith TW (1992) Hostility and health: current status of a psychosomatic hypothesis. *Health Psychology* 11(3): 139-150.

Spiteri MC, Jomeen J, Martin CR (2013) Reimagining the General Health Questionnaire as a measure of emotional wellbeing: a study of postpartum women in Malta. *Women and Birth* 26(4): 105-111.

Su VYF, Chen YT, Lin WC, et al. (2015) Sleep apnea and risk of panic disorder. *The Annals of Family Medicine* 13(4): 325-330.

Tiemensma J, Gaab E, Voorhaar M, et al. (2016) Illness perceptions and coping determine quality of life in COPD patients. *International Journal of Chronic Obstructive Pulmonary Disease* 11:2001-2007.

Tippin J, Aksan N, Dawson J, et al. (2016) Sleep remains disturbed in patients with obstructive sleep apnea treated with positive airway pressure: a three-month cohort study using continuous actigraphy. *Sleep Medicine*. 24: 24-31.

Tkacova R, Dorkova Z (2010) Clinical presentations of OSA in adults. *European Respiratory Society Monograph* 50: 86-103.

Trojan DA, Kaminska M, Bar-Or A, et al. (2012) Polysomnographic measures of disturbed sleep are associated with reduced quality of life in multiple sclerosis. *Journal of the Neurological Sciences* 316(1): 158-163.

Tsara V, Kaimakamis E, Serasli E, et al. (2009) Health related quality of life in Greek patients with sleep apnea-hypopnea syndrome treated with continuous positive airway pressure. *Sleep Medicine* 10(2): 217-225.

Unal Y, Inanc L, Kutlu G, et al. (2017) Psychiatric morbidity of the patients with obstructive sleep apnea. *Sleep Medicine* 40: 330-331.

Vandervoort D (1999) Quality of social support in mental and physical health. *Current Psychology* 18(2): 205-221.

Vandervoort DJ (2006) Hostility and health: Mediating effects of belief systems and coping styles. *Current Psychology* 25(1): 50-66.

Vaske I, Kenn K, Keil DC, et al. (2017) Illness perceptions and coping with disease in chronic obstructive pulmonary disease: effects on health-related quality of life. *Journal of Health Psychology* 22(12): 1570-1581.

Weaver TE. (2013) “Don’t start celebrating—CPAP adherence remains a problem.” *Journal of Clinical Sleep Medicine* 9(6): 551-552.

Wenzlaff RM and Wegner DM (2000) Thought suppression. *Annual review of psychology* 51(1): 59-91.

Wersebe H, Lieb R, Meyer AH (2018) The link between stress, well-being, and psychological flexibility during an Acceptance and Commitment Therapy self-help intervention. *International Journal of Clinical and Health Psychology* 18(1): 60-68.

Williams B and Williams VP (2001) Managing Hostile Thoughts, Feelings, and Actions: The LifeSkills Approach In: Snyder CR (Ed.) (2001) *Coping with stress: Effective people and processes*. Oxford University Press.

Xiao Y, Han D, Zang H, et al. (2016) The effectiveness of nasal surgery on psychological symptoms in patients with obstructive sleep apnea and nasal obstruction. *Acta Oto-laryngologica* 136(6): 626-632.

Yue W, Hao W, Liu P, et al. (2003) A case-control study on psychological symptoms in sleep apnea-hypopnea syndrome. *Canadian Journal of Psychiatry* 48(5): 318-323.

Suicidal ideation in patients with obstructive sleep apnoea and its relationship with disease severity, sleep-related problems and social support

Vladimira Timkova, Iveta Nagyova, Sijmen A. Reijneveld, Ruzena Tkacova,
Roy E. Stewart, Jitse P. van Dijk, Ute Bültmann

Journal of Health Psychology. 2018;
Feb 1 DOI: 1359105318758859

"When it becomes really
impossible to get away
and sleep, then the will to
live evaporates of its own
accord."

Louis-Ferdinand CELINE

Abstract

Background and aim

Recently, an increased level of Suicidal Ideation (SI) has been observed in Obstructive Sleep Apnoea (OSA) patients. Social support has been shown to have relevance in many chronic diseases and is supposed to decrease SI. However, evidence is lacking on the association between sleep-related problems and social support with SI in OSA patients. Thus, we aimed to assess the prevalence of SI and to examine the relationships OSA severity, sleep-related problems, social support and SI in OSA patients.

Methods

We included 149 patients (68% male; mean age 48.99 ± 9.57 years) with diagnosed OSA (Apnoea-Hypopnoea Index–AHI ≥ 5) based on full-night polysomnography. All patients completed the General Health Questionnaire-28 subscale regarding SI, the Pittsburgh Sleep Quality Index, the Epworth Sleepiness Scale, the Multidimensional Fatigue Inventory and the Multidimensional Scale of Perceived Social Support. Structural equation modelling (SEM) was used to analyze the data.

Results

The prevalence of SI among OSA patients was 20.1%. Structural equation modelling showed that SI in OSA was strongly related to poor sleep quality and high fatigue levels. No relationship between social support and SI in OSA patients was found.

Conclusion

SI in OSA is strongly related to poor sleep quality and high fatigue levels. Understanding the pathways among these symptoms and SI in OSA patients is important, as it may contribute to better disease management.

Introduction

Obstructive Sleep Apnoea (OSA) is an incapacitating chronic disease caused by pharyngeal collapse during sleep (Manarino et al., 2012), which is characterized by repeated breathing pauses. OSA, along with insomnia, is one of the most common sleep disorders in adults (Subramanian et al., 2011), with an estimated prevalence of 2–10% (Leger et al., 2012).

Recently an increased level of suicidal ideation (SI) has been observed in patients treated in medical sleep centres (Krakow et al., 2011), including among OSA patients (Choi et al., 2015). Suicide is an important cause of death worldwide. Globally more than 800,000 people take their own life every year, and there are many more suicide attempts (World Health Organization, 2016). Recent approaches have defined suicide as a health behaviour, in the sense that a person makes a decision to take his/her own life, so an appreciation of the psychology of the suicidal mind is crucial to suicide prevention (O'Connor, 2017). The annual prevalence of SI in the general population according the World Mental Health Survey is around 2% (Borges et al., 2010). The cross-national lifetime prevalence of SI in the general population is 9.2% (Nock et al., 2008), while 13% of participants treated in medical sleep centres reported SI, 4.5% of whom had clinically significant SI (Krakow et al., 2011). In 2015, Choi et al. (2015) reported an SI prevalence of 20.5% in a South Korean population of OSA patients, but information about the prevalence of SI in OSA patients in other countries is lacking.

Sleep disturbances were not included in the recent suicide risk factor lists compiled by the World Health Organization (2012). Nonetheless, the potential association between sleep-related problems and suicide has been recognized. In a meta-analysis by Pigeon et al. (2012), sleep disturbances were identified as a risk factor for SI and suicidal behaviour beyond the effects of depression in various clinical and healthy population groups. Poor sleep quality was found to be associated with an increased risk of committing suicide in one decade, even when adjusted for depressive symptomatology (Bernert et al., 2014). Krakow et al. (2011) found an association between sleep-related problems and SI in patients treated in medical sleep centres, which remained significant after controlling for depression. A Korean study on OSA patients found that they suffered from insomnia and SI, and that the concepts of SI, insomnia and depression showed overlap (Choi et al., 2015).

Adequate social support may have a positive influence on SI and suicidal behaviour (Kleiman and Liu, 2013). In recent years, increasing attention has been paid to the protective effect of social support in many chronic diseases (Reblin and Uchino, 2008). Lower social support was associated with worse health status (Bucholz et al., 2014) and more depressive symptoms (Bucholz et al., 2014; Lee et al., 2016a) in men and women with acute myocardial infarction (Bucholz et al., 2014) and chronic arthritis pain (Lee et al., 2016a). However, OSA patients may experience lower levels of social support compared to other populations. Some previous studies have demonstrated for example that the partners of OSA patients were unable to engage in social activities due to poor energy levels (Luyster et al., 2016), and their overall

quality of life was adversely affected by OSA (McArdle et al., 2001; Luyster et al., 2016).

Another source of concern is that individuals with sleep problems suffering from psychological distress rarely seek formal mental health evaluation and treatment (Weissman et al., 1997; Wojnar et al., 2009). Therefore, the idea of depending solely on the available psychological and psychiatric care to detect individuals at risk of SI may be insufficient for early suicide prevention efforts, especially for people with chronic diseases such as OSA. However, in general little is known about the relationships between OSA severity, sleep-related problems, social support and SI in OSA patients. Understanding the pathways of and interrelationships between these constructs is of major importance, as better knowledge may contribute to better disease management and may be useful in enhancing our ability to predict and prevent death by suicide.

The aims of the present study were to: (a) assess the prevalence of SI, and (b) examine the relationships between OSA severity, sleep-related problems, social support and SI, in OSA patients. Based on previous findings in OSA populations, we hypothesized that OSA severity is related to poor night-time sleep quality, contributing to higher levels of fatigue and daytime sleepiness which may in turn contribute to a higher level of SI. Further, we hypothesized that OSA severity and sleep-related problems may be directly related to higher level of SI. Social support was expected to be associated with SI; i.e. poorer social support could contribute to a higher level of SI.

Methods

Sample and procedure

This cross-sectional study was conducted at the Department of Pneumology and Phthisiology, L. Pasteur University Hospital and the Medical Faculty of PJ Safarik University in Kosice, Slovak Republic. All patients who visited the Department for one-night polysomnography (PSG) from July 2013 to June 2016 and underwent PSG were eligible for the study. Indication for PSG was based on a general practitioner referral form. OSA was diagnosed based on an overnight sleep study. PSG was used to determine whether the diagnosis of OSA was present and to identify the severity of the disorder.

Only patients between 18 and 65 years old were included due to possible functional changes, increased vulnerability and a decline in abilities and performance related to age. The study sample consisted of patients with an Apnoea Hypopnoea Index (AHI; number of apnoeas + hypopnoeas per hour of sleep) score of 5 or more (American Academy of Sleep Medicine, 2005), who had no previous continuous positive airway pressure treatment or other OSA treatment, were Slovak-speaking and had no major comorbidities. Out of N=260 patients, N=39 refused to participate in the study (response rate 85.0%). Another N=72 patients were excluded because of major comorbidities (a coexisting major sleep disorder such as insomnia, narcolepsy, or circadian rhythm sleep disorder; major cardiovascular diseases,

primary pulmonary hypertension, chronic obstructive pulmonary disease, diabetes, Pickwick syndrome, a history of cancer in the past twelve months, neurological deficit, a major psychiatric diagnosis in the medical record such as schizophrenia, bipolar disorder or cognitive decline, and/or current usage of psychiatric medications such as sedative-hypnotics, or narcoleptics or drug abuse in the past six months) and regular shift work. Medical examinations were conducted by a pulmonologist specialized in sleep-disordered breathing. Clinical diagnoses were stated according to the International Classification of Diseases-10 codes. Screening on comorbidities was based on medical data and an initial clinical interview prior to data collection. The final sample consisted of N=149 OSA patients (68% male; mean age 48.99 ± 9.57 years). Patients received a self-reporting questionnaire.

The study was approved by the Ethics Committee of PJ Safarik University in Kosice (approval no. 115/2011). All patients signed a written informed consent prior to study participation. Participation in the study was fully voluntary, with no incentives for participation.

Measures

Sociodemographic and clinical data

Information on age, gender and marital status was obtained from patient records. The Body Mass Index (BMI; height and weight) was assessed by a physician. BMI was used to sort patients into categories: underweight (<18.50), normal ($18.50-24.99$), overweight ($25.00-29.99$) and obese (≥ 30.00). OSA severity was determined using PSG and was based on the Apnoea Hypopnea Index (AHI; number of apnoeas + hypopnoeas per hour of sleep), starting with a score of 5 or more according to the standard criteria (American Academy of Sleep Medicine, 2005). According to this, OSA severity is mild ($AHI \leq 15$), moderate ($AHI > 15 \leq 30$) or severe ($AHI > 30$).

Sleep-related problems

Sleep-related problems included night-time sleep quality, daytime sleepiness and fatigue. *Night-time sleep quality* was measured using the Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989). The PSQI consists of 19 self-reported responses to questions covering seven domains: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication and daytime dysfunction. The total score with a maximum of 21 was used, with higher scores reflecting poor night-time sleep quality. A cut-off score of 5 points separates good sleepers from poor ones (Buysse et al., 1989). Cronbach's alpha in our sample was 0.86.

Daytime sleepiness was measured using the self-reporting Epworth Sleepiness Scale (ESS), an eight-item questionnaire assessing the tendency to fall asleep in various daytime scenarios (Miletin and Hanly, 2003). The score ranges from 0 to 24, with higher scores indicating higher daytime sleepiness. An ESS total score greater than 10 indicates excessive daytime sleepiness (Miletin and Hanly, 2003). Cronbach's alpha in our sample was 0.87.

Fatigue was measured using the Multidimensional Fatigue Inventory (MFI-20) (Smets et al., 1995). It consists of 20 individual items measuring five dimensions of fatigue: general fatigue, physical fatigue, reduced activity, reduced motivation and mental fatigue. Each dimension contains four items with a five-point response format; the total score in each dimension ranges from 4 (no fatigue) to 20 (highest possible fatigue). The values for Cronbach's alphas were: general fatigue: 0.80; physical fatigue: 0.89; reduced activity: 0.75; reduced motivation: 0.81; and mental fatigue: 0.83.

Social support

Social support was measured using the Multidimensional Scale of Perceived Social Support (MSPSS), a 12-item measure of subjectively-assessed social support using a seven-point Likert-type scale with responses ranging from 'very strongly disagree' (score 1) to 'very strongly agree' (score 7). The total score ranges from 12 to 84, with higher scores indicating perceived higher social support (Zimet et al., 1988). The scale, with four items for each subscale, measures support provided by a significant other, family and friends. In our sample Cronbach's alpha was 0.90 for each of the three items, and Cronbach's alpha for the total scale was 0.94.

Suicidal ideation

Suicidal ideation (SI) was assessed using the General Health Questionnaire (GHQ-28) (Goldberg and Hillier, 1979). Four items directly dealing with SI were used: "Have you thought about the possibility of killing yourself?", "Do you wish to be dead and far away from everything?", "Do you have continual thoughts about ending your life?", and "Do you have the impression that life is not worth of living?" The validated four-item SI subscale of the GHQ-28 has been previously used to assess SI (Gili-Planas et al., 2001; Watson et al., 2001). In some previous studies the threshold of $SI \geq 1$ was used to assess the presence of SI (Gili-Planas et al., 2001; Biddle et al., 2004). However, the GHQ threshold is partly determined by the prevalence of multiple diagnoses, with higher thresholds being associated with higher rates of both single and multiple diagnoses (Goldberg, et al. 1998). Thus, based on the presence of severe physical illness raising the best threshold to be adopted (Goldberg, et al. 1998), we determined the prevalence of SI with a cut off of $SI \geq 2$, in a binary manner, with the negative responses given a score of zero and the positive responses a score of one. The sum-score of the four items of SI therefore ranged from 0 to 4. SI was also used as a continuous variable (1-4) in SEM, with a range from 4 to 16. Higher scores indicated a higher level of SI. In our sample Cronbach's alpha was 0.83.

Statistical analyses

The analyses were performed using the Statistical Package for the Social Sciences (IBM SPSS 23). Structural equation modelling (SEM) was performed with Mplus 7.1 (Muthén and Muthén, 2015). Firstly, we described the background characteristics of the sample, determined the SI prevalence and calculated the mean values of OSA

severity, night-time sleep quality (PSQI), fatigue (MFI), daytime sleepiness (ESS) and social support (MSPSS) for the total sample and stratified by SI yes/no ($SI \geq 2$). Chi-square analyses were conducted on dichotomous variables. T-tests were conducted to assess the differences between OSA patients with SI (yes/no). Secondly, we used correlation analysis to assess the association between social support and SI when controlled for age, gender and marital status. Thirdly we used SEM to examine the relationships between OSA severity, night-time sleep quality, fatigue, daytime sleepiness, social support and SI in OSA patients. The used model fit criteria were: chi-square test, RMSEA (90% confidence interval, CI), Comparative Fit Index (CFI) and Tucker-Lewis Index (TLI). Swain's corrections of the model fit criteria were used because the sample size was small (Herzog and Boomsma, 2009). A p-value of <0.05 was considered statistically significant.

Results

Sample characteristics

The majority of the patients were male (68.0%), had secondary education (57.4%), had a partner (77.6%), 44.9% were obese, and 50.0% had severe OSA. Patients reporting SI scored significantly higher on sleep-related problems compared to non-SI patients. We observed no significant differences in the main clinical and sociodemographic data, OSA severity and social support between OSA patients with and without SI. Based on the increased level of the threshold due to the presence of physical disorder, the prevalence of SI among OSA patients was stated at 20.1% (Table 6.1).

Table 6.1 Baseline characteristics of the OSA patients (AHI ≥ 5), total sample and stratified by SI yes/no (SI ≥ 2)

	OSA (N=149)	OSA SI (N=30)	OSA non-SI (N=119)	p-value
Age in years, mean, sd	48.99 $\pm$ 9.57	46.47 $\pm$ 10.76	49.50 $\pm$ 9.34	0.15
Gender, male, N (%)	101 (68.0%)	18 (60.0%)	83 (69.7%)	0.22
Education level, mean, sd	4.99 $\pm$ 1.74	5.13 $\pm$ 1.91	4.97 $\pm$ 1.70	0.66
Education level, N (%)				0.07
Elementary	8 (5.3%)	3 (10%)	5 (4.2%)	
Secondary school	86 (57.4%)	14 (46.6%)	72 (60.0%)	
University	55 (36.3%)	13 (43.3%)	42 (34.7%)	
Employed, N (%)	127 (84.7%)	26 (86.6%)	101 (84.8%)	0.53
Marital status, single, N (%)	35 (23.4%)	3 (10.0%)	32 (26.8%)	0.52
Body Mass Index, mean, sd	30.24 $\pm$ 7.66	32.15 $\pm$ 7.70	29.80 $\pm$ 7.61	0.13
Body Mass Index, N (%)				0.28
Underweight (<18.5)	9 (6.0%)	0 (0%)	9 (7.5%)	
Normal (18.5-24.99)	41 (27.5%)	8 (26.6%)	33 (27.7%)	
Overweight (25.0-29.99)	32 (21.4%)	5 (16.6%)	27 (22.6%)	
Obese (≥ 30)	67 (44.9%)	17 (56.6%)	50 (42.0%)	
Apnoea-hypopnoea index, mean, sd	35.64 $\pm$ 22.30	40.37 $\pm$ 18.16	34.66 $\pm$ 23.12	0.21
OSA severity, N (%)				0.41
Mild (AHI ≤ 15)	22 (15.0%)	0 (0%)	22 (18.5%)	
Moderate (AHI $>15 \leq 30$)	52 (35.0%)	10 (33.3%)	41 (33.11%)	
Severe (AHI >30)	74 (50.0%)	20 (66.7%)	55 (48.3%)	
Night-time sleep quality, mean, sd (PSQI; 0-21)	9.65 $\pm$ 4.14	12.90 $\pm$ 4.18	8.88 $\pm$ 3.70	<0.001***
Daytime sleepiness, mean, sd (ESS; 0-24)	10.97 $\pm$ 5.30	12.76 $\pm$ 5.75	10.51 $\pm$ 5.10	0.04*
Fatigue, mean, sd (MFI; 4-20)				
General fatigue	14.01 $\pm$ 4.71	17.76 $\pm$ 2.47	13.02 $\pm$ 4.56	0.001**
Physical fatigue	13.52 $\pm$ 4.77	17.6 $\pm$ 3.39	12.45 $\pm$ 4.62	<0.001***
Reduced activity	11.91 $\pm$ 4.94	16.43 $\pm$ 3.29	10.77 $\pm$ 4.63	<0.001***
Reduced motivation	9.13 $\pm$ 3.63	12.26 $\pm$ 3.52	8.34 $\pm$ 3.28	<0.001***
Mental fatigue	11.97 $\pm$ 4.82	16.93 $\pm$ 2.79	10.71 $\pm$ 4.39	<0.001***
Social support, mean, sd (MSPSS; 12-84)	63.11 $\pm$ 13.48	58.86 $\pm$ 14.68	64.18 $\pm$ 12.99	0.05
SI, mean, sd (GHQ; 4-16)	6.67 $\pm$ 3.30	12.03 $\pm$ 2.14	5.31 $\pm$ 1.75	<0.001***
Prevalence of SI, N (%) (GHQ-28 SI ≥ 1)		54 (36.2 %)	-	
Prevalence of SI, N (%) (GHQ-28 SI ≥ 2)		30 (20.1%)	-	
Prevalence of SI, N (%) (GHQ-28 SI ≥ 3)		19 (12.8%)	-	
Prevalence of SI, N (%) (GHQ-28 SI=4)		13 (8.8%)	-	

OSA – Obstructive Sleep Apnoea; SI – Suicidal Ideation; PSQI – Pittsburgh Sleep Quality Index; ESS – Epworth Sleepiness Scale; MFI – Multidimensional Fatigue Inventory; MSPSS – Multidimensional Scale of Perceived Social support; GHQ-28 – General Health Questionnaire; *p<0.05; **p<0.01; ***p<0.001. Missing values: OSA severity: (0.7%); age, PSQI, MFI, ESS (1.0%); MSPSS: (2.0%).

Relationships between OSA severity, night-time sleep quality, daytime sleepiness, fatigue, social support and SI

Daytime sleepiness and social support were not significantly related to night-time sleep quality and SI in the hypothesized model (Figure S6.1, Supplement 6.1). As our hypothesis was not confirmed, we tested an alternative, modified model without sleepiness and social support (Figure 6.1, Table 6.2). The model fit criteria of the modified model were chi-square test = 29.909 (p value 0.04) and RMSEA = 0.066 (90%CI = 0.016, 0.107). The CFI was 0.984; TLI was 0.975. Swain's correction factor was 0.972. Swain's corrected chi-square statistic was 29.063 (p-value: 0.05). Swain's corrected RMSEA was 0.064 (90%CI = 0.007, 0.106), Swain's corrected TLI was 0.971 and Swain's corrected CFI was 0.991.

Sleep quality ($\beta = 0.28$, $p < 0.001$) and fatigue ($\beta = 0.49$; $p < 0.001$) were strongly related to SI. Sleep quality mediated the effect of OSA severity on SI ($\beta = 0.06$, $p < 0.05$), OSA severity was associated with poor sleep quality ($\beta = 0.21$; $p < 0.01$) while fatigue was associated with poor sleep quality ($\beta = 0.60$; $p < 0.001$). Social support was not significantly associated with SI using complex modelling, and adjustment for sociodemographic variables as potential confounders (age, gender and marital status) did not change the association between social support and SI either.

Figure 6.1 Modified model of the relationships among OSA severity, night-time sleep quality, fatigue and SI: beta (standard error)

AHI – Apnoea-Hypopnoea Index; OSA – Obstructive Sleep Apnoea; **p<0.01; ***p<0.001.

Table 6.2 Relationships between OSA severity, night-time sleep quality, fatigue and SI

	Standardized coefficients (S.E.)
Direct paths	
OSA severity – Night-time sleep quality	0.21** (0.08)
Night-time sleep quality – Fatigue	0.60*** (0.06)
Night-time sleep quality – Suicidal ideation	0.28*** (0.08)
Fatigue – Suicidal ideation	0.49*** (0.07)
Indirect paths	
OSA severity – Night-time sleep quality – Suicidal ideation	0.06* (0.03)
OSA severity – Night-time sleep quality – Fatigue – Suicidal ideation	0.06* (0.03)

OSA – Obstructive Sleep Apnoea; S.E. – Standard Error; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

Discussion

This study shows a 20.1% prevalence of Suicidal ideation (SI) in people with Obstructive sleep apnoea (OSA). Patients reporting SI scored higher on sleep-related problems compared to non-SI patients. Poor night-time sleep quality and fatigue were directly related to SI. Night-time sleep quality mediated the effect of OSA severity on SI. We found no relationship between social support and SI in OSA patients.

Based on the presence of OSA, which represents severe physical illness consistently raising the best threshold to be adopted (Goldberg et al., 1998), we can assume that 20.1% of OSA patients in our study reported SI. This finding is in line with Choi et al. (2015), who found an SI prevalence of 20.5% in a Korean population of OSA patients. This SI prevalence of 20.1% among OSA patients is alarming, especially when compared to the cross-national lifetime prevalence of SI (9.2%) in the general population (Borges et al., 2010) and the annual prevalence (2.0% to 2.1%) of SI in the general population (Borges et al., 2010).

OSA severity was not directly related to SI in our study. Choi et al. (2015) also found no correlation between OSA severity and SI in OSA patients. However, night-time sleep quality mediated the effect of OSA severity on SI in our study. Although one-night polysomnography (PSG) is sufficient for diagnosis of OSA (Scholle et al., 2003; Gouveris et al., 2010), significant variability in the apnoea-hypopnoea indexes (AHI) taken from two nights was revealed in people with OSA (Gouveris et al., 2010). Thus, the missing direct relationship between OSA severity and SI may be related, according to Choi et al. (2015), to individuals' adaptation to the combination of the hospital environment and the recording equipment. However, some previous studies suggest that AHI based on numbers of all apnoeas and hypopnoeas, but not severity of apnoeic events, may not be the most appropriate measure of OSA severity when considering the clinical impact of OSA on subjective quality of life assessment (Weaver et al., 2005; Lee et al., 2016b).

Our findings demonstrate that disturbed night-time sleep quality was directly related to SI. This finding aligns with Bernert et al. (2014), who showed that poor

night-time sleep quality in an older population was associated with increased risk of committing suicide, even after adjustment for depressive symptomatology. Therefore, SI may not only represent a symptom of major depression but has also been found to be driven by neurobiological processes (Fried and Nesse, 2015; Du et al., 2017). Another recent meta-analysis revealed that psychiatric patients with sleep disturbances, including sleep-related breathing disorders, are about twice as likely to report suicidal behaviours compared to patients without sleep related-problems (Malik et al., 2014). Similarly, Choi et al. (2015) found that higher insomnia levels correlated with higher level of SI in OSA patients.

We found that fatigue was most strongly related to SI. Patients reporting SI scored significantly higher on daytime sleepiness, but the association was weak and no relationship between daytime sleepiness and sleep quality or SI was observed using complex modelling. Within a medical framework, excessive daytime sleepiness and fatigue are generally considered a result of sleep deprivation or poor sleep quality (Nicassio et al., 2002; Fava, 2004). However, according to Chervin (2000), some OSA patients report fatigue more often than daytime sleepiness, and therefore treatment of fatigue complaints in the absence of clear daytime sleepiness warrants more attention in OSA treatment. Nevertheless, the possibility that daytime sleepiness in OSA patients may simply be masked by the presence of psychological distress associated with a chronic state of hypervigilance (Krakow et al., 2015) should also be considered.

Unexpectedly, the relationship between social support and SI was not significant. Some previous analyses have revealed that social support had a greater impact on well-being (Antonucci and Akiyama, 1987; Walen and Lachman, 2000) and health (Walen and Lachman, 2000) in female compared with male populations. However, we found no significant impact of gender on the association between social support and SI when controlled for sociodemographic variables.

Given the evidence that sleep disturbances may represent an important predictor of daytime functioning, including engagement in social activities (Dew et al., 1994), it may also be hypothesized that in the case of extreme fatigue or daytime sleepiness, the sources of social support may not be adequately utilized and thus may be of less importance. On the other hand, it is also plausible that the reverse pathway is true; i.e. sleep disturbances may lead to a more negative perception of the social environment (Troxel et al., 2010). Furthermore, social interactions may represent stressful situations for patients with OSA; e.g. OSA patients subjectively felt a lack of trust from co-workers which caused them subsequent embarrassment (Reishtein et al., 2006). In line with these assumptions, OSA symptoms were also found to be associated with reduced social participation (Liu et al., 2016). Nevertheless, Choi et al. (2015) identified significant correlation between social support and SI in OSA patients with comorbid insomnia. In line with their findings, most subjects in our study had a partner, were employed and had relatively high education. However, the patients in our study were observed to have higher mean scores for social support (63.11 ± 13.48) compared to the mean score of 44.38 ± 7.81 found by Choi et al. (2015) using the Multidimensional Scale of Perceived Social

Support. Another possible explanation may be that discrepancies in the results were caused by the different statistical methods used.

Strengths and limitations

To our knowledge, this is one of the first studies examining OSA severity, sleep-related problems, social support and SI in a rarely studied population of OSA patients using structural equation modelling (SEM). Another strength is that the patients in our sample were diagnosed by means of polysomnography, which is considered the criterion standard for diagnosing OSA and determining the severity of the disease. However, in interpreting our data one has to consider certain limitations. Firstly, the diagnosis of OSA was stated based on a single sleepover. Secondly, no formal psychiatric diagnosis of SI was established, but on the other hand the GHQ-28 items are frequently used to assess the presence of SI in various populations (Hamilton and Schweitzer 2000; Gili-Planas et al., 2001; Watson et al., 2001; Romeo et al., 2013; Kawabe et al., 2016). Furthermore, it should be noted that the four-item GHQ-28 SI subscale has shown good concurrent validity with Beck's Suicide Intent Scale (Watson et al., 2001). Different cut-off values of the GHQ-28 SI subscale were used in some previous studies (Gili-Planas et al., 2001; Biddle et al., 2004). In our study we set the cut-off value of $SI \geq 2$, considering this threshold to be a good representation of the clinical picture (Goldberg, et al. 1998). Another limitation to be mentioned is gender bias. In our sample 68% of the OSA patients were men; thus, our results may be less generalizable to the female population. However, the number of participants in our study is consistent with the man-to-woman ratio in OSA (3:1). Finally, the cross-sectional nature of this study does not allow firm conclusions about causality in the relationships between the variables. Nevertheless, it has been argued that SEM methods may offer the potential for tentative causal effects to be drawn when used with specified and controlled designs (Bullock et al., 1994).

Implications for practice and future research

This study shows that disturbed night-time sleep quality and fatigue are directly related to SI. Our findings, if confirmed in longitudinal studies, may highlight the necessity of monitoring SI in OSA patients during clinical care. Intervention studies may be helpful in determining whether the continuous positive airway pressure (CPAP) treatment is effective in reducing the level of SI via reduction of fatigue, although the results of previous research are less encouraging, indicating that OSA patients suffering from psychological distress have poor compliance with CPAP treatment (Kjelsberg et al. 2005; Hussain et al., 2014), which means that the role of compliance bias should additionally be considered. Next, in research and clinical practice, symptoms common to OSA and depressive symptomatology such as daytime sleepiness and fatigue represent obstacles in determining the presence, causality and severity of one condition in the presence of the other (Harris et al., 2009). As such, severe fatigue can contribute to longer and more severe depression, or

vice versa, fatigue may be aggravated by depressive symptomatology (Carney et al., 2014), and therefore the presence of reverse causality should be examined in OSA patients. However, the latter pattern may be more applicable to the general population than to OSA patients, as previous longitudinal studies defined OSA and its symptoms as risk factors for psychological distress. In particular, sleep fragmentation was identified as a primary cause of daytime sleepiness and fatigue in OSA patients, which is assumed to result in depressive symptomatology (Schröder and O'Hara, 2005).

Due to a lack of general consensus regarding the CPAP treatment effects on self-reported health outcomes such as functional status or quality of life in people with OSA (e.g. Weaver, 2013), current research and clinical practice should focus not just on treating OSA, but also on ensuring that the symptoms such as poor night-time sleep quality, fatigue or daytime sleepiness as well as depression and anxiety are managed. Based on the strong relationship between poor sleep quality, fatigue and SI, clinicians should consider investigating SI in people with sleep-related disorders. Furthermore, SI may suddenly lead to suicidal behaviour (Simon, 2014; Du et al., 2017), while across all countries, 60% of transitions from ideation to plan and attempt occur within the first year after ideation onset (Nock et al., 2008). This may be dangerous, especially for people with undiagnosed and untreated OSA. SI may be largely preventable (Stanley and Brown, 2012; Simon, 2014) through early detection. However, sleep disorders including OSA are very rarely assessed on a regular basis in patients suffering from psychological distress. This is of particular importance, as adjunct treatment for symptoms of depression such as sedative-hypnotics may exacerbate OSA (Pagel and Parnes, 2001). Another source of concern is that OSA patients with depressive symptomatology and/or fatigue may suffer from reduced activity and consequently may have poor motivation to visit hospital, get a diagnosis and receive appropriate OSA treatment. Thus, it may be beneficial to detect undiagnosed OSA in psychological and psychiatric care with simple and economical screening tools. Disturbed night-time sleep quality is largely modifiable through medication or behavioural interventions. The education of people with OSA on basic sleep hygiene may improve the quality of sleep and decrease fatigue. With a larger sample and a longitudinal design, the relationships should be further unveiled.

Conclusion

The prevalence of SI in OSA patients was found to be 20.1%. Poor night-time sleep quality and fatigue were strongly related to SI. Social support was not significantly related to SI. Our findings emphasize the necessity of monitoring SI in OSA patients during clinical care. Longitudinal research is needed as a source of better understanding of the pathways between OSA severity, sleep-related problems social support and SI in OSA patients, as this may contribute to better disease management.

References

- American Academy of Sleep Medicine (2005) International Classification of Sleep Disorders: Diagnostic and Coding Manual (2nd ed). Sleep Disorders Association, Rochester, MN (ICSD-2).
- Antonucci TC and Akiyama H (1987) An examination of sex differences in social support among older men and women. *Sex Roles* 17(11-12): 737-749.
- Bernert RA, Turvey CL, Conwell Y, et al. (2014) Association of poor subjective sleep quality with risk for death by suicide during a 10-year period: a longitudinal, population-based study of late life. *JAMA Psychiatry* 71(10): 1129-1137.
- Biddle L, Gunnell D, Sharp D, et al. (2004) Factors influencing help seeking in mentally distressed young adults: a cross-sectional survey. *British Journal of General Practice* 54(501): 248-253.
- Borges G, Nock MK, Abad JMH, et al. (2010) Twelve-month prevalence of and risk factors for suicide attempts in the World Health Organization World Mental Health Surveys. *Journal of Clinical Psychiatry* 71(12): 1617-1628.
- Bucholz EM, Strait KM, Dreyer RP, et al. (2014) Effect of low perceived social support on health outcomes in young patients with acute myocardial infarction: results from the variation in recovery: role of gender on outcomes of young AMI patients (VIRGO) study. *Journal of the American Heart Association* 3(5): 1-11.
- Bullock HE, Harlow, LL and Mulaik SA (1994) Causation issues in structural equation modeling research. *Structural Equation Modeling: A Multidisciplinary Journal* 1(3): 253-267.
- Buyse DJ, Reynolds CF, Monk TH, et al. (1989) The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Research* 28(2): 193-213.
- Carney CE, Moss TG, Lachowski AM, et al. (2014) Understanding mental and physical fatigue complaints in those with depression and insomnia. *Behavioral Sleep Medicine* 12(4): 272-289.
- Dew MA, Reynolds CF, Monk TH, et al. (1994) Psychological correlates and sequelae of electroencephalographic sleep in healthy elders. *Journal of Gerontology* 49(1): 8-18.
- Du L, Zeng J, Liu H, et al. (2017) Fronto-limbic disconnection in depressed patients with suicidal ideation: a resting-state functional connectivity study. *Journal of Affective Disorders* 215: 213-217.
- Fava M (2004) Daytime sleepiness and insomnia as correlates of depression. *Journal of Clinical Psychiatry* 65(16): 27-32.
- Fried EI and Nesse RM (2015) Depression sum-scores don't add up: why analyzing specific depression symptoms is essential. 3(1): 72
- Gili-Planas M, Roca-Bennasar M, Ferrer-Perez V, et al. (2001) Suicidal ideation, psychiatric disorder, and medical illness in a community epidemiological study. *Suicide Life-Threatening Behavior* 31(2): 207-213.
- Goldberg DP and Hillier VF. (1979) A scaled version of the General Health Questionnaire. *Psychological Medicine* 9(1): 139-145.
- Goldberg DP, Oldehinkel T and Ormel J (1998) Why GHQ threshold varies from one place to another. *Psychological Medicine* 28(4): 915-921.
- Gouveris H, Selivanova O, Bausmer U, et al. (2010) First-night-effect on polysomnographic respiratory sleep parameters in patients with sleep-disordered breathing and upper airway pathology. *European Archives of Otorhinolaryngology* 267(9): 1449-1453.
- Hamilton TK and Schweitzer RD (2000) The cost of being perfect: Perfectionism and suicide ideation in university students. *Australian and New Zealand Journal of Psychiatry* 34(5): 829-835.
- Harris M, Glozier N, Ratnavadivel R, et al. (2009) Obstructive sleep apnea and depression. *Sleep Medicine Reviews* 13(6): 437-444.
- Herzog W and Boomsma A (2009) Small-sample robust estimators of noncentrality-based and incremental model fit. *Structural Equation Modeling* 16(1): 1-27.
- Hussain SF, Irfan M, Waheed Z, et al. (2014) Compliance with continuous positive airway pressure (CPAP) therapy for obstructive sleep apnea among privately paying patients-a cross sectional study *BMC pulmonary medicine* 14(1): 188.
- Chervin RD (2000) Sleepiness, fatigue, tiredness, and lack of energy in obstructive sleep apnea. *Chest* 118(2): 372-379.
- Choi SJ, Joo EY, Lee YJ, et al. (2015) Suicidal ideation and insomnia symptoms in subjects with obstructive sleep apnea syndrome. *Sleep Medicine* 16(9): 1146-1150.
- Kawabe K, Horiuchi F, Ochi M, et al. (2016) Suicidal ideation in adolescents and their caregivers: a cross sectional survey in Japan. *BioMed Central Psychiatry* 16(1): 231-239.

- Kjelsberg FN, Ruud EA, and Stavem K (2005) Predictors of symptoms of anxiety and depression in obstructive sleep apnea. *Sleep Medicine* 6(4): 341-346.
- Kleiman EM and Liu RT (2013) Social support as a protective factor in suicide: Findings from two nationally representative samples. *Journal of Affective Disorders* 150(2): 540-545.
- Krakov B, Ribeiro JD, Ulibarri VA, et al. (2011) Sleep disturbances and suicidal ideation in sleep medical center patients. *Journal of Affective Disorders* 131(1): 422-427.
- Krakov BJ, Ulibarri VA, Moore BA, et al. (2015) Posttraumatic stress disorder and sleep-disordered breathing: a review of comorbidity research. *Sleep Medicine Reviews* 24:37-45.
- Lee JE, Kahana B and Kahana E (2016a) Social support and cognitive functioning as resources for elderly persons with chronic arthritis pain. *Aging & Mental Health* 20(4): 370-379.
- Lee W, Lee SA, Ryu HU, et al. (2016b) Quality of life in patients with obstructive sleep apnea: Relationship with daytime sleepiness, sleep quality, depression, and apnea severity. *Chronic Respiratory Disease* 13(1): 33-39.
- Leger D, Bayon V, Laaban JP, et al. (2012) Impact of sleep apnea on economics. *Sleep Medicine Reviews* 16(5): 455-462.
- Liu D, Myles H, Foley DL, et al. (2016) Risk factors for Obstructive Sleep Apnea are prevalent in people with psychosis and correlate with impaired social functioning and poor physical health. *Frontiers in Psychiatry* 7:139.
- Luyster FS, Dunbar-Jacob J, Aloia MS, et al. (2016) Patient and partner experiences with obstructive sleep apnea and CPAP treatment: a qualitative analysis. *Behavioral Sleep Medicine* 14(1): 67-84.
- Malik S, Kanwar A, Sim LA, et al. (2014) The association between sleep disturbances and suicidal behaviors in patients with psychiatric diagnoses: a systematic review and meta-analysis. *The Cochrane database of systematic reviews* 3(1): 18.
- Manarino MR, Fillipo FD and Piro M (2012) Obstructive sleep apnea syndrome. *European Journal of Internal Medicine* 23(7): 586-593.
- McArdle N, Kingshott R, Engleman H, et al. (2001) Partners of patients with sleep apnoea/hypopnoea syndrome: effect of CPAP treatment on sleep quality and quality of life. *Thorax* 56(7): 513-518.
- Miletin MS and Hanly PJ (2003) Measurement properties of the Epworth sleepiness scale. *Sleep Medicine* 4(3): 195-199.
- Muthén LK and Muthén BO (2015) Mplus User's Guide (7.4). Los Angeles, CA: Muthén & Muthén 16(1): 1-27.
- Nicassio PM, Moxham EG, Schuman CE, et al. (2002) The contribution of pain, reported sleep quality, and depressive symptoms to fatigue in fibromyalgia. *Pain* 100(3): 271-279.
- Nock MK, Borges G, Bromet EJ, et al. (2008) Suicide and suicidal behavior. *Epidemiologic Reviews* 30(1): 133-154.
- O'Connor R (2017) Suicide as (health) behaviour: towards a psychological understanding of suicidal behaviour. *European Health Psychologist* 19 (4): 333-334.
- Pagel JF and Parnes BL (2001) Medications for the treatment of sleep disorders: an overview. *Primary Care Companion to the Journal of Clinical Psychiatry* 3(3): 118-125.
- Pigeon WR, Pinquart M and Conner K (2012) Meta-analysis of sleep disturbance and suicidal thoughts and behaviors. *Journal of Clinical Psychiatry* 73(9): 1160-1167.
- Reblin M and Uchino BN (2008) Social and emotional support and its implication for health. *Current Opinion in Psychiatry* 21(2): 201-205.
- Reishtein JL, Pack AI, Maislin G, et al. (2006) Sleepiness and relationships in obstructive sleep apnea. *Issues in Mental Health Nursing* 27(3): 319-330.
- Romeo L, Balducci C, Quintarelli E, et al. (2013) MMPI-2 personality profiles and suicidal ideation and behavior in victims of bullying at work: A follow-up study. *Violence and Victims* 28(6): 1000-1014.
- Scholle S, Scholle HC, Kemper A, et al. (2003) First night effect in children and adolescents undergoing polysomnography for sleep-disordered breathing. *Clinical Neurophysiology* 114(11): 2138-2145.
- Schröder CM and O'Hara R (2005) Depression and obstructive sleep apnea (OSA). *Annals of General Psychiatry* 4(1): 13-21.
- Simon RI (2014) Passive suicidal ideation: Still a high-risk clinical scenario. *Current Psychiatry* 13(3): 13-15.

Smets EMA, Garssen B, Bonke BD, et al. (1995) The Multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. *Journal of Psychosomatic Research* 39(3): 315-325.

Stanley B and Brown GK (2012) Safety planning intervention: a brief intervention to mitigate suicide risk. *Cognitive and Behavioral Practice* 19(2): 256-264.

Subramanian S, Guntupalli B, Murugan T, et al. (2011) Gender and ethnic differences in prevalence of self-reported insomnia among patients with obstructive sleep apnea. *Sleep and Breathing* 15(4): 711-715.

Troxel WM, Buysse DJ, Monk TH, et al. (2010) Does social support differentially affect sleep in older adults with versus without insomnia? *Journal of Psychosomatic Research* 69(5): 459-466.

Walen HR and Lachman ME (2000) Social support and strain from partner, family, and friends: Costs and benefits for men and women in adulthood. *The Journal of Social and Personal Relationships* 17(1): 5-30.

Watson D, Goldney R, Fisher L, et al. (2001) The measurement of suicidal ideation. *Crisis* 22(1): 12-14.

Weaver EM, Woodson BT, Steward DL (2005) Polysomnography indexes are discordant with quality of life, symptoms, and reaction times in sleep apnea patients. *Otolaryngology-Head & Neck Surgery* 132(2): 255-262.

Weaver TE (2013) "Don't start celebrating-CPAP adherence remains a problem." *Journal of Clinical Sleep Medicine* 9(6): 551-552.

Weissman MM, Greenwald S, Niño-Murcia G, et al. (1997) The morbidity of insomnia uncomplicated by psychiatric disorders. *General Hospital Psychiatry* 19(4): 245-250.

Wojnar M, Ilgen MA, Wojnar J, et al. (2009) Sleep problems and suicidality in the National Comorbidity Survey Replication. *Journal of Psychiatric Research* 43(5): 526-531.

World Health Organization (2012) Public Health Action for the Prevention of Suicide: A Framework. Available at: <http://apps.who.int/iris/bitstream/10665/75166/1/9789241503570eng.pdf> (accessed 4 January 2017).

World Health Organization (2016) Suicide. Fact Sheet no. 398. Available at: <http://www.who.int/mediacentre/factsheets/fs398/en/> (accessed 2 August 2016).

Zimet GD, Dahlem NW, Zimet SG, et al. (1988) The multidimensional scale of perceived social support. *Journal of Personality Assessment* 52(1): 30-41.

Social support, mastery, sleep-related problems and their association with functional status in untreated obstructive sleep apnoea patients

Vladimira Timkova, Iveta Nagyova, Sijmen A. Reijneveld,
Ruzena Tkacova, Jitse P. van Dijk, Ute Bültmann

Heart & Lung: The Journal of Acute and Critical Care.
2018; 47(4): 371–379.

"No one in my family, not one of my friends ...realized that I was going through life asleep... My body had no more feeling than a drowned corpse. My very existence, my life in the world, seemed like a hallucination. A strong wind would make me think my body was about to be blown to the end of the earth, to some land I had never seen or heard of, where my mind and body would separate forever. 'Hold tight,' I would tell myself, but there was nothing for me to hold on to."

Haruki MURAKAMI

Abstract

Background and aim

Social support and mastery are important aspects in the treatment of chronic diseases, however their role in connection with Obstructive Sleep Apnoea (OSA) remains unclear. The purpose of this study was to examine the associations between social support, mastery, sleep-related problems and functional status in untreated patients with OSA and to assess the mediating role of social support and mastery in the association between sleep-related problems and functional status in patients with OSA.

Methods

All patients completed the Multidimensional Scale of Perceived Social Support, the Pearlin Mastery Scale, the Pittsburgh Sleep Quality Index, the Epworth Sleepiness Scale and the Functional Outcomes of Sleep Questionnaire. Multiple linear regression and mediation analyses were used to analyse the data.

Results

Participants were 150 newly diagnosed OSA patients (Apnoea-Hypopnoea Index–AHI ≥ 5 ; 68% male; mean age 48.9 ± 9.5 years). Compared with social support, mastery was more strongly associated with functional status. Moreover, mastery mediated the association between sleep-related problems and functional status. The direct effects of sleep-related problems on functional status varied between 76.7% and 82.3%, whereas the indirect effects via mastery varied between 17.7% and 23.3%.

Conclusions

Supporting OSA patients' sense of mastery over one's life and circumstances may significantly contribute to better disease management.

Introduction

Obstructive Sleep Apnoea (OSA) is an incapacitating chronic disease caused by pharyngeal collapse during sleep (Manarino et al., 2012). OSA, along with insomnia, is considered to be one of the most common sleep disorders in adults, with an estimated prevalence of 2–10% (Leger et al., 2012), and is related to higher all-cause mortality (Marshall et al., 2008). OSA has been shown to be associated with night-time sleep disturbance (Krakow et al., 2015; Tippin et al., 2016) and daytime sleepiness (Antic et al., 2011). These disabling symptoms pose multiple challenges for functional status in patients with OSA (Weaver et al., 2007), with a larger effect in females (Chervin, 2000; Quintana-Gallego et al., 2004; Silva et al., 2016; Boccabella and Malouf, 2017). Recent studies have also emphasized the importance of studying patients' functional status in sleep medicine research, because of its ability to provide insights which may go beyond the pathophysiology of commonly investigated OSA-related symptoms (Boccabella and Malouf, 2017).

Despite the acceptance of continuous positive airway pressure (CPAP) as a standard OSA treatment, there is a lack of consensus regarding the CPAP treatment effect on functional status in patients with OSA. Several studies have concluded that patients with OSA, even with a good CPAP treatment adherence, do not achieve normal functional status (Weaver et al., 2007; Reishtein et al., 2010; Weaver, 2013; Tippin et al., 2016) when compared to the general population. This suggests that other key factors may play a role (Reishtein et al., 2010). Moreover, personalization of the OSA treatment (Hesselbacher et al., 2014), which includes overall evaluation of functional status and the psychosocial aspects of disease, becomes more important in current clinical practice (Boccabella and Malouf, 2017).

Social support may be one of the essential, though under-investigated, protective factors associated with healthier sleep and better functional status in people with OSA (Günbey and Karabulut, 2014). There are several plausible pathways which may link social support with sleep, including protecting against social isolation, attenuating stress responses, encouraging healthy sleep behaviours, and entraining circadian rhythms (Troxel et al., 2010). Patients with OSA may experience lower levels of social support compared to other populations with chronic diseases. A study by Glenn et al. (2015) revealed an association between a low level of social support and the presence of sleep disordered breathing symptoms. Poor social support was also found to be independently associated with short sleep duration when controlled for sociodemographic variables (Glenn et al., 2015). Moreover, partners of patients with OSA also described their relationship as adversely affected by their partners' OSA symptomatology (Luyster et al., 2016). Lack of social support has a significant impact on health-related behaviour and risk of illness (Reblin and Uchino, 2008; Alemi et al., 2003). Moreover, lack of social support was associated with poorer self-rated health in patients with acute myocardial infarction (Buchholz et al., 2014) chronic arthritis pain (Lee et al., 2016), multiple sclerosis (Krokavcova et al., 2008a) and depression (Liu et al., 2016). Social support also had a positive influence on sleep in people with insomnia (Troxel et al., 2010). Although it has been posited that social support may be a key indicator of how patients with

OSA manage their disease (Günbey and Karabulut, 2014), to date only one study (Choi et al., 2015) has been performed regarding social support in the association with health outcomes in patients with OSA. Social support was also found to have a positive effect on CPAP treatment adherence (Luyster et al., 2016). Insufficient emotional (e.g., encouragement) and instrumental (e.g. help with putting on mask, verbal reminders) support from partners of OSA patients was identified as a barrier for adherence with CPAP treatment (Luyster et al., 2016).

As patients with OSA have very little control over the symptoms of their disease and have to learn how to live with it, mastery may help them to reduce the stress that breathing, and sleep-related symptoms bring about, and may thus improve their functional status (De Ridder and Schreurs, 2001). According to Pearlin and Schooler (1978), mastery is defined as a general sense of control over one's life and circumstances. In line with this, a diminished sense of mastery was associated with a decrease in overall functional ability (Kempen et al., 2006), physical, mental and social functioning (Kroavcova et al., 2008b; Sloan et al., 2009), and with increased mortality rates (Surtees et al., 2006) in patients with various chronic conditions or the general population (Tang, 2009). In older people a greater sense of mastery was found to be associated with seeking treatment at an early stage of disease and more efficient use of healthcare services (Menec and Chipperfield, 1997). In OSA patients with comorbid insomnia, the positive associations between mastery and both physical and mental quality of life remained significant even after adjustment for age, obesity, chronic diseases, erectile dysfunction, sleepiness, mood and financial strain (Lang et al., 2016). It has also been suggested that the relationship between social support and mastery may be reciprocal, and that higher levels of mastery may help to facilitate needed social support, while greater perceived social support may lead to greater feeling of mastery over one's life and circumstances (Green and Rodgers, 2001).

Sleep-related problems are associated with functional status in patients with chronic conditions (Kim et al., 2015), including OSA (Boccabella and Malouf, 2017). Previous studies have shown that sleep disruption (Mermigkis et al., 2009) poor sleep quality and daytime sleepiness (Lau et al., 2013) were associated with impaired functional status in patients with idiopathic pulmonary fibrosis (Mermigkis et al., 2009) and OSA (Lau et al., 2013). Research and clinical practice should therefore focus not only on treating OSA, but also on ensuring that all OSA-related symptoms, including sleep related problems, are managed adequately. To achieve this, we first need to understand how these symptoms and constructs relate to functioning in untreated patients with OSA.

Patients with OSA are known to have a high level of sleep-related problems; in contrast, the role of social support and mastery in the association between poor sleep quality, daytime sleepiness and functional status is less clear. Therefore, the purpose of this study was to examine the associations between social support, mastery, sleep-related problems and functional status in untreated patients with OSA, and to assess the mediating role of social support and mastery in the association between sleep-related problems and functional status in patients with OSA.

Methods

Sample and procedure

This cross-sectional study was conducted at the Department of the Department of Pneumology and Phthisiology, L. Pasteur University Hospital and the Medical Faculty of PJ Safarik University in Kosice, Slovak Republic. All patients who visited the Department for one-night polysomnography (PSG) between July 2013 and June 2016 and underwent PSG were eligible for the study. Indication for PSG was based on a general practitioner referral form. OSA was diagnosed based on an overnight sleep examination. Only patients with OSA between 18 and 65 years of age were included due to possible functional changes, increased vulnerability and decline in abilities and performance related to age. The study sample comprised patients with an Apnoea Hypopnoea Index (AHI; number of apnoeas+ hypopnoeas per hour of sleep) score of 5 or more (American Academy of Sleep Medicine, 2005) who had no previous continuous positive airway pressure (CPAP) therapy or other OSA treatment, were Slovak-speaking and had no major comorbidities. Out of 263 eligible patients, 41 patients who underwent PSG refused to participate in the study, yielding a total response of 84.0%. Another 72 were excluded because of major comorbidities. The reasons for exclusion were major comorbidities related to sleep (co-existing sleep disorder such as insomnia, narcolepsy, or circadian rhythm sleep disorder); major cardiovascular diseases (e.g. myocardial infarction, angina pectoris; primary pulmonary hypertension); pulmonary conditions (e.g. chronic obstructive pulmonary disease; Pickwick syndrome); and a history of cancer in the past twelve months. Neurological and psychological comorbidities included neurological condition (e.g. stroke, epilepsy); major psychiatric diagnosis (e.g. psychotic disorders, major depression) in the medical record, and/or current usage of psychiatric medications which may affect cognitive functions (e.g. benzodiazepine, antipsychotics or antidepressants); drug abuse in the past six months, and regular shift work in the past six months. Due to assessment of health outcomes related to sexual functioning, we excluded patients with diabetes and those using hypotensive medication, which may affect sexual functioning (following Hockema et al., 2007). Screening for comorbidities was based on medical data and an initial clinical interview prior to data collection. The clinical diagnoses were established according to the standard International Classification of Diseases-10 revision Codes. Medical examinations of patients were conducted by a pulmonologist specialized in sleep-disordered breathing. Patients with non-respiratory sleep-related complaints (e.g. narcolepsy, insomnia) were routinely referred to another group of clinical specialists. The invitation letter, the informed consent and the questionnaires were sent to participants by postal mail three weeks before the medical examination. One week before the medical examination, patients were reminded about the questionnaires by phone call. Patients filled in self-report questionnaires at home.

To maintain ethical principles with regard to the participants, we explained the purpose of the study and guaranteed confidentiality. We also explained that the collected data would only be used for the purposes of this research. Each patient

completed and signed an informed consent form prior to their participation in the study, which was fully voluntary and included no incentives for participation. The study was approved by the Ethics Committee of PJ Safarik University in Kosice (approval no. 115/2011).

Measures

Functional status

Functional status was assessed using the Functional Outcomes of Sleep Questionnaire (FOSQ). (Weaver et al., 1997). The FOSQ is a 30-item self-report, disease-specific measure designed to assess the impact of sleep disorders or excessive daytime sleepiness on multiple activities of daily living. The FOSQ has five subscales: activity level, vigilance, intimacy and sexual relationships, general productivity, and social outcomes. Responses are averaged (excluding missing responses) to create a subscale score of 1 to 4, and then subscale scores are summed for the total score (5–20), with higher scores indicating less effect of sleepiness on daily life (Billings et al., 2014). In our sample, Cronbach's alpha was 0.90 for the total scale, 0.90 for the activity level, 0.84 for vigilance, 0.95 for intimacy and sexual relationships, 0.90 for the general productivity subscale and 0.82 for the social outcomes subscale.

Social support

The Multidimensional Scale of Perceived Social Support (MSPSS) is a 12-item self-report measure of social support (Zimet et al., 1988). It uses a seven-point Likert-type scale, with scores ranging from 'very strongly disagree' (1) to 'very strongly agree' (7), so the total score ranges from 12 to 84, with higher scores indicating greater social support (Zimet et al., 1988). The MSPSS has three subscales: significant others, family and friends. In our sample, Cronbach's alpha was 0.90 for all three separate subscales. Cronbach's alpha of the total scale was 0.94.

Mastery

Mastery was measured using the Pearlin Mastery Scale (PMS) (Perlin and Schooler, 1978). The PMS measures an individual's level of mastery, a psychological resource that has been defined as "the extent to which one regards one's life-chances as being under one's own control in contrast to being fatalistically ruled" (Perlin and Schooler, 1978). The scale includes 7 items (five negatively-worded items and two positively-worded items), e.g. "You have little control over the things that happen to you", and "What happens to you in the future mostly depends upon you". The negatively-worded items require reverse coding prior to scoring, resulting in a score range of 7 to 35, with higher scores indicating higher levels of mastery (Perlin and Schooler, 1978). Cronbach's alpha of the total scale was 0.85.

Sleep-related problems

Sleep-related problems concerned night-time sleep quality and daytime sleepiness. *Night-time sleep quality* was measured using the Pittsburgh Sleep Quality Index

(PSQI) (Buysse et al., 1989). The PSQI is a self-rated questionnaire to assess sleep quality and disturbances over a one-month time interval. The PSQI consists of 19 self-report questions which cover seven domains: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication and daytime dysfunction. The score ranges from 0 to 21, with higher scores reflecting poor night-time sleep quality. A cut-off score of 5 separates good from poor sleepers (Buysse et al., 1989). Cronbach's alpha in our sample was 0.85.

Daytime sleepiness was measured using the self-report Epworth Sleepiness Scale (ESS), an eight-item questionnaire assessing the tendency to fall asleep in various daytime scenarios (Miletin and Hanly, 2003). The score ranges from 0 to 24, with higher scores indicating greater daytime sleepiness. An ESS total score greater than 10 indicates excessive daytime sleepiness (Miletin and Hanly, 2003). Cronbach's alpha in our sample was 0.86.

Sociodemographic and clinical data

Information on age, gender and marital status was obtained from patient records. The Body Mass Index (BMI; height and weight) was assessed by a physician. BMI was used to sort patients into categories: underweight (<18.50), normal (18.50–24.99), overweight (25.00–29.99) and obese (≥ 30.00). PSG was used to determine whether the diagnosis of OSA was present and to identify the severity of the disorder. PSG consists of a simultaneous recording of multiple physiological parameters related to sleep and wakefulness, which directly monitor and quantify the number of respiratory events, related hypoxemia and arousals. PSG consisted of the overnight recording of left and right electrooculograms, standard central and occipital electroencephalogram, submental electromyogram (EMG), bilateral tibialis EMG, nasal and oral airflow using a thermistor and thoracic, and abdominal excursions using respiratory inductive plethysmography. OSA severity was determined using PSG and was based on an AHI (number of apnoeas + hypopnoeas per hour of sleep) score of 5 or more, according to standard criteria (American Academy of Sleep Medicine, 2005). According to this, OSA severity is mild ($AHI \geq 5 \leq 15$), moderate ($AHI > 15 \leq 30$) or severe ($AHI > 30$).

Statistical analyses

All analyses were performed using the Statistical Package for the Social Sciences (IBM SPSS 23) and MedGraph. Firstly, we described the background characteristics of the sample and calculated means and standard deviations for functional status (FOSQ), social support (MSPSS), mastery (PMS), night-time sleep quality (PSQI), daytime sleepiness (ESS) and OSA severity (AHI) for the total sample and stratified by gender. T-tests were conducted to assess gender differences in the continuous variables. Differences in the categorical variables were analysed using Chi-square tests. Secondly, we investigated the bivariate correlations between all variables. Thirdly, multiple linear regressions were used to examine the associations between social support, mastery, sleep-related problems and functional status for the total scale and by subscales, controlled for sociodemographic and clinical variables.

Using regression analyses we firstly assessed the crude effects (i.e. associations unadjusted for the number of predictors) of each variable separately on functional status, and then we continued with multiple regression analyses. Multicollinearity was assessed using the variance inflation factor ($VIF < 2.0$). We applied the enter method in linear regression to identify the factors associated with summary score of functional status in the total scale and in the subscales. For each factor, beta coefficients represent the mean variation of functional status for the total scale and by subscales. The first model of the variables included sociodemographic data (age, gender, marital status). A second model included a clinical variable (OSA severity – measured by AHI), and a third model included night-time sleep quality and daytime sleepiness. Finally, in the fourth and fifth models, social support and mastery were included separately to assess the increase in the explained amount of total variance in functional status.

Mediation analyses were used to assess the role of social support and mastery in the association between sleep-related problems and functional status. According to Baron and Kenny (1986), the following conditions must be met to establish mediation: the independent variable must affect the dependent variable; secondly, the independent variable must affect the mediator; and lastly, the mediator must affect the dependent variable. The proportion of the effect which is mediated was calculated as the indirect effect divided by the total effect and multiplied by 100, while the as-advised standardized total effect was at least ± 0.2 . The Sobel z-test was used to examine the mediating effects of social support and mastery on the association between sleep-related problems and functional status in patients with OSA. We used partial correlation analyses to assess the association between variables under study when controlled for age, gender, marital status and OSA severity.

A p-value of < 0.05 was considered statistically significant. Missing data were expressed as percentage of total number of patients for each variable. Power analysis revealed that the statistical power for multivariate analyses exceeded 93%, with medium effect size at $\alpha = 0.05$. The statistical power for univariate analysis was 98%, with medium effect size at $\alpha = 0.05$ (Faul et al., 2009).

Results

Sample characteristics

The final sample consisted of 150 patients with OSA ($AHI \geq 5$). The mean age of participants was 48.9 ± 9.5 years. The majority of patients were male (68.0%), had secondary education (57.3%) and had a partner (76.0%). A total of 47.7% were obese and 49.3% had severe OSA. The mean score for functional status was 13.68 ± 4.04 . Female patients with OSA reported a significantly poorer level of perceived social support, greater sleep-related problems and poorer functional status compared with male patients with OSA (Table 7.1).

Table 7.1 Baseline characteristics of the patients with OSA with $AHI \geq 5$

Characteristics	OSA patients (N=150)	Male (N=102)	Female (N=48)	p-values
Age in years; mean, sd	48.9±9.5	47.9±9.5	51.4±9.3	0.04*
Gender; male, N (%)	102 (68.0%)	102 (68.0%)	48 (32.0%)	
Education; N (%)				0.27
Elementary	8 (5.3%)	4 (3.9%)	4 (8.3%)	
Secondary	86 (57.3%)	56 (54.9%)	30 (62.5%)	
University	56 (37.3%)	42 (41.2%)	14 (29.2%)	
Marital status; single, N (%)	36 (24.0%)	26 (25.5%)	10 (20.8%)	0.53
Body Mass Index; mean, sd	30.2±7.7	30.1±7.4	30.6±8.2	0.73
Body Mass Index; N (%)				0.28
Underweight (<18.50)	9 (6.0%)	4 (3.9%)	5 (10.4%)	
Normal (18.50-24.99)	42 (28.0%)	32 (31.4%)	10 (20.8%)	
Overweight (25.00-29.99)	32 (21.3%)	23 (22.5%)	9 (18.8%)	
Obese (>30.00)	67 (44.7%)	43 (42.2%)	24 (50.0%)	
Apnoea Hypopnoea index; mean, sd	36.1±22.3	33.9±21.0	39.4±24.6	0.16
OSA severity; N (%)				0.41
Mild ($AHI \leq 15$)	23 (15.3%)	16 (15.7%)	7 (14.6%)	
Moderate ($15 < AHI \leq 30$)	52 (34.7%)	38 (37.2%)	14 (29.2%)	
Severe ($AHI > 30$)	74 (49.3%)	47 (46.1%)	27 (56.2%)	
Night-time sleep quality; mean, sd (PSQI; 0-21)	9.7±4.1	9.2±4.0	10.7±4.1	0.03*
Excessive daytime sleepiness; mean, sd (ESS; 0-24)	11.0±5.3	10.2±4.9	12.5±5.8	0.01*
Perceived social support; mean, sd (MSPSS; 12-84)	62.9±13.5	63.6±12.6	62.0±15.3	0.50
Perceived social support; family; mean, sd	21.2±5.4	21.4±5.2	20.8±5.8	0.50
Perceived social support; friends; mean, sd	19.9±4.9	19.9±4.3	19.8±5.5	0.92
Perceived social support; signif. other; mean, sd	22.0±5.1	22.3±4.7	21.4±5.4	0.31
Mastery; mean, sd (PMS; 7-35)	20.4±4.3	20.9±4.5	19.4±3.6	0.05
Functional status; mean, sd (FOSQ; 5-20)	13.7±4.0	14.5±3.9	11.8±4.2	0.001**
Activity level	2.8±0.8	2.9±0.9	2.5±0.8	0.01*
Vigilance	2.11±0.8	2.3±0.8	1.7±0.7	p<0.001***
Intimacy and sexual relationships	2.6±1.3	2.8±1.1	2.1±1.4	p<0.001***
General productivity	3.0±0.8	3.2±0.8	2.7±0.9	p<0.001***
Social outcome	3.2±1.0	3.3±0.9	2.9±1.3	0.001**

OSA – Obstructive Sleep Apnoea; PSQI – Pittsburgh Sleep Quality Index; ESS – Epworth Sleepiness Scale; MSPSS – Multidimensional Scale of Perceived Social Support; SS – Social Support; PMS – Pearlman Mastery Scale; FOSQ – Functional Outcomes of Sleep Questionnaire; *p<0.05; **p<0.01; ***p<0.001. Missing values: OSA severity: (0.7%); age: (1%); ESS, PSQI (1%); MSPSS: (2.0%).

Correlations between the study variables

Table 7.2 shows the correlations between the study variables. Poor social support, low level of mastery, poor night-time sleep quality and daytime sleepiness were significantly correlated with functional status impairment in patients with OSA.

Table 7.2 Correlations between age, gender, marital status, OSA severity, social support, mastery, night-time sleep quality and daytime sleepiness

	Age	Gender	Marital status	OSA severity	Social support	Mastery	Night-time sleep quality	Daytime sleepiness
Gender	0.18*	-						
Marital status	-0.13		-					
OSA severity	0.13	0.11	0.13	-				
Social support	0.06	-0.07	-0.12	0.07	-			
Mastery	0.07	-0.17*	0.08	-0.12	0.20**	-		
Night-time sleep quality	0.05	0.17*	-0.09	0.19*	-0.16*	-0.28**	-	
Daytime sleepiness	-0.00	0.21**	0.10	0.24**	-0.14	-0.29***	0.15*	-
Functional status	-0.05	-0.34***	-0.05	-0.35***	0.26**	0.57***	-0.43***	-0.56***

Associations between social support, mastery, sleep-related problems and functional status (total scale)

Significant crude associations on functional status were found for gender (B: -2.68; 95%CI= -4.07; -1.30; $p<0.001$), OSA severity (B: -0.06; 95%CI= -0.09; -0.03; $p<0.001$), sleep quality (B: -0.43; 95%CI= -0.58; -0.28; $p<0.001$), daytime sleepiness (B: -0.43; 95%CI= -0.53; -0.33; $p<0.001$), social support (B: 0.08; 95%CI= 0.03; 0.13; $p<0.01$), and mastery (B: 0.54; 95%CI= 0.42; 0.67; $p<0.001$) (Table 7.3). In the subsequent multivariate models, the effects of gender, OSA severity and sleep-related problems on functional status were statistically significant (Model 1 - Model 3). The association between social support (B: 0.04; 95%CI= 0.01; 0.08; $p<0.05$) and functional status (Model 4) was no longer statistically significant (B: 0.03; 95%CI= -0.00; 0.06; $p=0.06$) when mastery was added to the model (Model 5). The association between mastery and functional status was strong (B: 0.33; 95%CI= 0.22; 0.43; $p<0.001$), and the final model (Model 5) explained 62% of the functional status total variance.

Table 7.3 Multiple linear regression analyses: associations of social support, mastery and sleep-related problems with total functional status scale

Functional status (FOSQ)	Crude	Model 1	Model 2	Model 3	Model 4	Model 5
	B (95%CI)	B (95%CI)	B (95%CI)	B (95%CI)	B (95%CI)	B (95%CI)
Age	-0.05 (-0.12; 0.02)	-0.01 (-0.08; 0.06)	0.01 (-0.06; 0.07)	-0.01 (-0.06; 0.04)	-0.01 (-0.06; 0.04)	-0.03 (-0.07; 0.02)
Gender	-2.68 (-4.07; -1.30)***	-2.94 (-4.30; -1.58)***	-2.67 (-3.97; -1.38)***	-1.50 (-2.54; -0.46)**	-1.44 (-2.46; -0.41)**	-1.18 (-2.09; -0.27)*
Marital status	-0.95 (-2.53; 0.63)	-0.68 (-2.15; 0.80)	-0.24 (-1.66; 1.18)	-0.26 (-1.38; 0.86)	-0.05 (-1.16; 1.05)	-0.46 (-1.45; 0.53)
OSA severity	-0.06 (-0.09; -0.03)***	-	-0.06 (-0.08; -0.03)***	-0.03 (-0.05; -0.00)*	-0.03 (-0.05; -0.01)**	-0.03 (-0.05; -0.01)**
Night-time sleep quality	-0.43 (-0.58; -0.28)***	-	-	-0.36 (-0.47; -0.24)***	-0.34 (-0.45; -0.21)***	-0.26 (-0.37; -0.16)***
Daytime sleepiness	-0.43 (-0.53; -0.33)***	-	-	-0.33 (-0.42; -0.23)***	-0.31 (-0.40; -0.22)***	-0.25 (-0.34; -0.17)***
Social support	0.08 (0.03; 0.14)**	-	-	-	0.04 (0.01; 0.08)*	0.03 (-0.00; 0.06)
Mastery	0.54 (0.42; 0.67)***	-	-	-	-	0.33 (0.22; 0.43)***
F Change		6.68***	16.61***	46.63***	6.68*	38.74***
Adjusted R ²		0.10	0.19	0.50	0.52	0.62

Crude: effect of each variable separately on functional status; Model 1: effect of age, gender and marital status on FOSQ score; Model 2: effect of age, gender, marital status and disease severity on FOSQ score; Model 3: effect of age, gender, marital status, disease severity and sleep-related problems on FOSQ score; Model 4: effect of age, gender, marital status, disease severity, sleep-related problems and social support on FOSQ score; Model 5: effect of age, gender, marital status, disease severity, sleep-related problems, social support and mastery on FOSQ score; B: unstandardized regression coefficient; CI - confidence interval; Gender - male gender was set as the reference; Marital status: single was set as the reference; OSA - Obstructive Sleep Apnoea; FOSQ - Functional Outcomes of Sleep Questionnaire; F Change - significance of prediction improvement in model fit; Adjusted R² - explained variance adjusted for the number of predictors in the model; FOSQ - higher scores indicating less impaired daily life; * $p<0.05$; ** $p<0.01$; *** $p<0.001$.

Associations between social support, mastery, sleep-related problems and functional status by subscale

Significant crude effects on all functional status subscales were found for social support, mastery, sleep quality and daytime sleepiness. Social support was significantly associated with intimacy-sexual relationships only, while mastery was associated with all functional status subscales in the final models (with an explained total variance of 38% for activity level, 48% for vigilance, 45% for intimacy-sexual relationships, 63% for general productivity and 38% for social outcome). Sleep-related problems were associated with all functional status subscales in the final models, except for the association between night-time sleep quality and vigilance (Table S7.4).

Mediating effect of social support on the association between sleep-related problems and functional status

No mediating role of social support was observed in the association between night-time sleep quality and functional status (Sobel z-value=-1.55, p=0.12).

Mediating effect of mastery on the association between sleep-related problems and functional status

A significant partial mediating effect of mastery on the association between night-time sleep quality (Sobel z-value= -3.202; p<0.001), daytime sleepiness (Sobel z-value=-3.302; p<0.001) and functional status was found. Standardized coefficients showed that 17.7% of the total effect of night-time sleep quality (PSQI) on functional status was mediated by mastery (-0.08), and 82.3% of the total effect was direct (-0.35) (Figure 7.1).

Figure 7.1 The mediating role of mastery in the association between night-time sleep quality and functional status

PSQI – Night-time sleep quality; PMS – Pearlman Mastery Scale; FOSQ – Functional Outcomes of Sleep Questionnaire; **p<0.01; ***p<0.001.

Further, standardized coefficients showed that 23.3% of the total effect of daytime sleepiness (ESS) on functional status was mediated by mastery (-0.13), and 76.7% of the total effect was direct (-0.43) (Figure 7.2).

Figure 7.2 The mediating role of mastery in the association between daytime sleepiness and functional status

ESS – Epworth Sleepiness Scale; PMS – Pearlman Mastery Scale; FOSQ – Functional Outcomes of Sleep Questionnaire; ***p<0.001.

Discussion

Our results provide evidence that suggests that poor social support, low levels of mastery, poor night-time sleep quality and daytime sleepiness were associated with impaired functional status in patients with OSA. The association between social support and functional status was weak, and no longer significant when mastery was added to the model. Mastery was strongly associated with functional status. Furthermore, mastery mediated the association between sleep-related problems and functional status.

We found a small but significant association between social support and functional status in patients with OSA. Given the evidence that sleep disturbances may represent an important predictor of daytime functioning, including engagement in social activities (Dew et al., 1994), it may be hypothesized that in cases of extreme daytime sleepiness, the sources of social support may not be adequately utilized and thus may be of less importance. Furthermore, it is also plausible recent studies have suggested that sleep disturbances may lead to more negative perceptions of the social environment (Troxel et al., 2010). Previous research has shown that disturbed sleep in people with OSA and their partners was associated with mood swings and aggression which affected relationships in a negative way. Patients with OSA also had difficulties initiating new intimate relationships or friendships (Broström et al.,

2007). In line with these assumptions, OSA symptoms were also associated with reduced social participation (Liu et al., 2016). Nevertheless, the subscale analyses in our study showed that social support was significantly associated only with one functional status subscale, i.e. intimacy-sexual relationships, while mastery was strongly associated with all functional status subscales. Thus, it may be assumed that mastery, together with social support, may improve intimate and sexual functioning in patients with OSA. This may be crucial as better relationship quality was identified as being the most important need expressed by untreated patients with OSA (Broström et al., 2007).

Mastery was strongly associated with overall functional status and explained an additional 10% of the variance in functional status beyond the variance explained by sociodemographic, clinical, sleep-related variables and social support. Moreover, the association between social support and functional status was attenuated and no longer significant when mastery was added to the model. These results are in line with findings from studies of other incapacitating diseases (Krokavcova et al., 2008b; Sloan et al., 2009; Raaijmakers et al., 2014), including one preliminary study involving OSA patients with comorbid insomnia (Lang et al., 2016), where higher levels of mastery were associated with better self-rated health and quality of life. As expected, our study identified a significant association between poor sleep quality, daytime sleepiness and consequent functional impairment in patients with OSA. Furthermore, mastery mediated the association between sleep-related problems and functional status. The associations between mastery, sleep-related problems, and functional status were statistically significant after controlling for sociodemographic variables and OSA severity.

Our results suggest that adequate mastery may have the potential to diminish the negative effects of sleep-related problems on functional status. As patients with OSA were found to have reduced energy and activity levels (measured with the Functional Outcomes of Sleep Questionnaire-FOSQ) even after treatment with continuous positive airway pressure treatment (CPAP) (Lau et al., 2013), mastery may help in diminishing the negative effects of sleep-related symptoms on functional status. The establishment of new strategies for functional status improvement may be crucial in patients with OSA, as reduced general productivity, poor energy and impaired vigilance lead to work-related and vehicle accidents (Karimi et al., 2013; Allen et al., 2016) and impaired work functioning in these patients (Mulgrew et al., 2007). Thus, greater levels of mastery may contribute to better functional status and better OSA management and treatment.

Since OSA is diagnosed according to a cut-off score in the Apnoea-Hypopnoea Index (AHI), a logical assumption is that higher AHI indicates higher sleep-related problems. Previous research has shown that AHI does not correlate well with the presence or degree of daytime sleepiness (Bixler et al., 2005; Roure et al., 2008; Macey et al., 2010; Dündar et al., 2015), poor sleep quality (Kezirian et al., 2009; Macey et al., 2010), psychological symptomatology (Macey et al., 2010; Lau et al., 2013; Rezaeitalab et al., 2014) or female sexuality (Hoekema et al., 2007). Moreover, contrary to the common belief, sleepy patients showed longer sleep duration and

increased slow-wave sleep compared to non-sleepy patients with OSA (Roure et al., 2008). In contrast, we found significant associations between AHI, sleep-related problems and functional status both in univariate as well as multivariate analyses. This profound role of OSA severity revealed in our study may occur due to lack of major comorbidities which are expected to influence sleep and affective symptoms (Macey et al., 2010). Also, unlike previous research, participants with regular shift works in the past six months were excluded from our study, which may strengthen the role of AHI.

Additionally, our results reveal possible gender differences in the impact of OSA on functional status. We found that despite the absence of a significant difference in age, marital status, body mass index and AHI, newly-diagnosed female patients with OSA reported significantly greater sleep-related problems and functional status impairment when compared with male OSA patients. In previous studies, functional status and sleep quality were also more impaired in female OSA patients compared with male patients (Chervin, 2000; Quintana-Gallego et al., 2004; Ye et al., 2009; Silva et al., 2016) despite similarity in sociodemographic and clinical variables (Ye et al., 2009). This larger impact of OSA severity on health outcomes cannot be explained only by female gender per se (Chervin, 2000; Quintana-Gallego et al., 2004); there are other attendant factors, for instance that women may be more often underdiagnosed regarding OSA when compared with men due to circumstances related to family lifestyle, sociocultural factors and different OSA clinical expressions (Chervin, 2000; Quintana-Gallego et al., 2004).

Strengths and limitations

The strength of our study lies in the objective assessment of OSA using PSG. To our knowledge, this is the first study examining the ways in which social support and mastery are associated with functional status in patients with OSA. Some limitations should be noted, however. Due to the cross-sectional design of our study, causal relationships cannot be established. In addition, in our sample 68% of the patients with OSA were men; thus, our results may be less generalizable to female patients with OSA. However, the number of participants in our study is consistent with the man-to-woman ratio in OSA (3:1). Another limitation is the length of the questionnaires used, which may influence the data quality, especially in patients with sleep-related problems. This limitation was mitigated by our sending the questionnaires to the patients three weeks in advance by postal mail, so they had enough time to fill them in.

Implications for practice and future research

This study shows that social support, mastery and sleep-related problems are associated with functional status in patients with OSA, and that mastery may contribute to functional status improvement. As elimination of OSA symptoms with CPAP does not lead to complete restoration of daytime energy, subjective and objective sleepiness (Pack et al., 2001; Lau et al., 2013), and overall functional status (Weaver et al., 2007; Weaver, 2013; Tippin et al., 2016) in many adherent patients, present

research and clinical practice should focus not just on standard treatment of OSA, but also on functional status in these patients. In line with this, health care professionals should be aware of the possibility that interventions focusing on mastery enhancement may help improve functional status in patients with OSA. Mastery as a part of patient empowerment (Aujoulat et al., 2008) was also found to be associated with individuals' capacity to make decisions about their health behaviour and to have or to take control over aspects of their lives that are related to health (McAllister et al., 2012). Moreover, as psychological resources associated with control over one's life, such as self-efficacy (Baron et al., 2011) or internality (Wild et al., 2004), were found to contribute to CPAP treatment adherence, the role of mastery may have a similar effect.

As mastery is not considered as a fixed personality trait but as an adaptive self-concept born of pivotal experience (Pearlin et al., 2007), education of patients with OSA, provided by psychologists or trained nurses focusing on personal empowerment for maintaining an adequate level of mastery in people affected by OSA, may be important. Mastery may also be improved by relaxation techniques (O'Brien et al., 2012), or by chronic disease management programmes which have been found to be effective in patients with pulmonary disease (Rea et al., 2004). Thus, health practitioners' education about the role of mastery and counselling supporting mastery for patients with OSA may be one of the important components of effective patient management. Additionally, we found that these interventions should be aimed especially at the group of female patients with a severe condition, who have higher probability of experiencing significant impairment in functional status.

Research advancing our knowledge of protective factors to enhance functional status in patients with OSA may help to develop comprehensive multidisciplinary strategies designed to improve self-management skills in patients with OSA. Further research should identify risk groups of patients with low mastery levels, so that counselling and interventions can be tailored to these patients. Future longitudinal intervention studies targeting patients with OSA should be designed to cast more light on the causality in the associations between social support, mastery and functional status. We recommend that our study should be replicated with a larger sample and in a longitudinal setting. As mastery may reflect components of negative affectivity or neuroticism (Surtees et al., 2006), future studies should examine the associations between mastery and psychological symptomatology. Finally, future studies may verify the association between mastery and CPAP treatment adherence. General CPAP treatment adherence has been found to be poor (Aloia et al., 2004; Haniffa et al., 2004; Weaver and Grunstein, 2008) due to various reasons including discomfort and feelings of claustrophobia due to the mask (Aloia et al., 2004), as well as other unspecified reasons (Haniffa et al., 2004). However, interventions to increase patients' autonomous motivation (e.g. self-efficacy) have demonstrated increased nightly use (Richards et al., 2007). Similarly, mastery is likely to increase patients' autonomous motivation to manage their condition (Raaijmakers et al., 2014), so it may be useful for improvement of CPAP treatment adherence.

Conclusion

While poor social support was weakly associated with impaired functional status in patients with OSA, we found a strong association between low mastery and impaired functional status. Mediation analysis showed that mastery may have the potential to diminish the negative effect of sleep-related problems on functional status. As supporting mastery of patients with OSA may play an important role in management of the condition, patients and health care professionals should learn more about the concept of mastery in connection with sleep-related problems and functional status.

References

- Alemi F, Stephens R, Llorens S, et al. (2003) The orientation of social support measure. *Addictive Behaviors* 28(7): 1285-1298.
- Allen AH, Park JE, Daniele PR, et al. (2016) Obstructive sleep apnoea and frequency of occupational injury. *Thorax* 71(7): 664-666.
- Aloia, MS, Arnedt JT, Riggs RL et al. (2004) Clinical management of poor adherence to CPAP: Motivational enhancement. *Behavioral Sleep Medicine* 2(4): 205-222.
- American Academy of Sleep Medicine (2005) *International Classification of Sleep Disorders: Diagnostic and Coding Manual* (2nd ed): Sleep Disorders Association, Rochester, MN (ICSD-2).
- Antic NA, Catcheside P, Buchan C, et al. (2011) The effect of CPAP in normalizing daytime sleepiness, quality of life, and neurocognitive function in patients with moderate to severe OSA. *Sleep* 34(1): 111-119.
- Asghari A, Mohammadi F, Kamrava SK, et al. (2012) Severity of depression and anxiety in obstructive sleep apnea syndrome. *European Archives of Oto-Rhino-Laryngology* 269(12): 2549-2553.
- Aujoulat I, Marcolongo R, Bonadiman L, et al. (2008) Reconsidering patient empowerment in chronic illness: A critique of models of self-efficacy and bodily control. *Social Science & Medicine* 66(5): 1228-39.
- Baron KG, Berg CA, Czajkowski LA, et al. (2011) Self-efficacy contributes to individual differences in subjective improvements using CPAP. *Sleep and Breathing* 15(3): 599-606.
- Baron RM and Kenny DA (1986) The moderator-mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. *Journal of Personality and Social Psychology* 51(6): 1173-1182.

Billings ME, Rosen CL, Auckley D, et al. (2014) Psychometric performance and responsiveness of the Functional Outcomes of Sleep Questionnaire and Sleep Apnea Quality of Life Index in a randomized trial: the HomePAP study. *Sleep* 37(12): 2017-2024.

Bixler EO, Vgontzas AN, Lin HM, et al. (2005) Excessive daytime sleepiness in a general population sample: the role of sleep apnea, age, obesity, diabetes, and depression. *The Journal of Clinical Endocrinology & Metabolism* 90(8): 4510-4515.

Boccabella A, and Malouf J. (2017) How do sleep-related health problems affect functional status according to sex?. *Journal of Clinical Sleep Medicine* 13(5): 685-692.

Broström A, Johansson P, Strömberg A, et al. (2007) Obstructive sleep apnoea syndrome—patient's perceptions of their sleep and its effects on their life situation. *Journal of Advanced Nursing* 57(3): 318-327.

Bucholz EM, Strait KM, Dreyer RP, et al. (2014) Effect of low perceived social support on health outcomes in young patients with acute myocardial infarction: results from the variation in recovery: role of gender on outcomes of young AMI patients (VIRGO) study. *Journal of the American Heart Association* 3(5): 1-11.

Buyse DJ, Reynolds CF, Monk TH et al. (1989) The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Research* 28(2): 193-213.

Chervin RD (2000) Sleepiness, fatigue, tiredness, and lack of energy in obstructive sleep apnea. *Chest* 118(2): 372-379.

Choi SJ, Joo EY, Lee YJ, et al. (2015) Suicidal ideation and insomnia symptoms in subjects with obstructive sleep apnea syndrome. *Sleep Medicine* 16(9): 1146-1150.

De Ridder D and Schreurs K. (2001) Developing interventions for chronically ill patients: is coping a helpful concept? *Clinical Psychology Review* 21(2): 205-240.

Dew MA, Reynolds CF, Monk TH, et al. (1994) Psychological correlates and sequelae of electroencephalographic sleep in healthy elders. *Journal of Gerontology* 49(1): 8-18.

Dündar Y, Saylam G, Tatar EÇ, et al. (2015) Does AHI Value Enough for Evaluating the Obstructive Sleep Apnea Severity?. *Indian Journal of Otolaryngology and Head & Neck Surgery* 67(1): 16-20.

Faul F, Erdfelder E, Buchner A, et al. (2009) Statistical power analyses using G*Power 3.1: Tests for correlation and regression analyses. *Behavior Research Methods* 41(4): 1149-1160.

Glenn C, Enwerem N, Odeyemi, Y, et al. (2015) Social support and sleep symptoms in US adults. *Journal of Clinical Sleep Medicine* 11(08): 957-957.

Green BL and Rodgers A (2001) Determinants of social support among low-income mothers: a longitudinal analysis. *American Journal of Community Psychology* 29(3): 419-441.

Günbey E and Karabulut H (2014) Multidimensional scale of perceived social support in patients with obstructive sleep apnea syndrome. *European Archives of Oto-Rhino-Laryngology* 271(11): 3067-3071.

Haniffa M, Lasserson TJ and Smith I (2004) Interventions to improve compliance with continuous positive airway pressure for obstructive sleep apnoea. *The Cochrane Database of Systematic Reviews* DOI: 10.1002/14651858.CD003531.pub2.

Hesselbacher S, Subramanian S, Rao S, et al. (2014) Self-reported sleep bruxism and nocturnal gastroesophageal reflux disease in patients with obstructive sleep apnea: relationship to gender and ethnicity. *Open Respiratory Medicine Journal* 8: 34-40.

Hoekema A, Stel AL, Stegenga B et al. (2007) Sexual function and obstructive sleep apnea-hypopnea: A randomized clinical trial evaluating the effects of oral appliance and continuous positive airway pressure therapy. *The Journal of Sexual Medicine* 4(4): 1153-1162.

Karimi M, Eder DN, Eskandari D, et al. (2013) Impaired vigilance and increased accident rate in public transport operators is associated with sleep disorders. *Accident Analysis & Prevention* 51: 208-214.

Kempen GI, Ranchor AV, van Sonderen E, et al. (2006) Risk and protective factors of different functional trajectories in older persons: are these the same? *The Journals of Gerontology. Series B, Psychological Sciences and Social Sciences* 61(2): 95-101.

Kenny DA (2016) Mediation. Available at: <http://davidakenny.net/cm/mediate.htm> (accessed 7 April 2017).

Kezirian EJ, Harrison SL, Ancoli-Israel S, et al. (2009) Behavioral correlates of sleep-disordered breathing in older men. *Sleep* 32(2): 253-261.

Kim J, Kim Y, Yang KI, et al. (2015) The relationship between sleep disturbance and functional status in mild stroke patients. *Annals of Rehabilitation Medicine* 39(4): 545-552.

Krakow BJ, Ulibarri VA, Moore BA, et al. (2015) Posttraumatic stress disorder and sleep-disordered breathing: a review of comorbidity research. *Sleep Medicine Reviews* 24: 37-45.

Krokavcova M, Nagyova I, van Dijk JP, et al. (2008b) Mastery, functional disability and perceived health status in patients with multiple sclerosis. *European Journal of Neurology* 15(11): 1237-1244.

Krokavcova M, van Dijk JP, Nagyova I, et al. (2008a) Social support as a predictor of perceived health status in patients with multiple sclerosis. *Patient Education and Counselling* 73(1): 159-165.

Lang CJ, Appleton S, Vakulin A, et al. (2016) Psychological and quality of life factors in men with comorbid Obstructive Sleep Apnea (OSA) and insomnia (Ins): a population study. In: *Sleep DownUnder 2016: 28th ASM of Australasian Sleep Association and Australasian Sleep Technologists Association* (20 October - 22 October 2016: Adelaide, Australia). *Journal of Sleep Research* 25(2): 14.

Lau, EYY, Eskes, GA, Morrison DL, et al. (2013) The role of daytime sleepiness in psychosocial outcomes after treatment for obstructive sleep apnea. *Sleep Disorders*. DOI: <http://dx.doi.org/10.1155/2013/140725>.

Lee JE, Kahana B and Kahana E (2016) Social support and cognitive functioning as resources for elderly persons with chronic arthritis pain. *Aging & Mental Health* 20(4): 370-379.

Leger D, Bayon V, Laaban JP, et al. (2012) Impact of sleep apnea on economics. *Sleep Medicine Reviews* 16(5): 455-462.

Liu D, Myles H, Foley DL, et al. (2016) Risk Factors for Obstructive sleep apnea are Prevalent in People with Psychosis and correlate with impaired social Functioning and Poor Physical health. *Frontiers in Psychiatry* 7: 139.

Luyster FS, Dunbar-Jacob J, Aloia MS, et al. (2016) Patient and partner experiences with obstructive sleep apnea and CPAP treatment: a qualitative analysis. *Behavioral Sleep Medicine* 14(1): 67-84.

Macey PM, Woo MA, Kumar R, et al. (2010) Relationship between obstructive sleep apnea severity and sleep, depression and anxiety symptoms in newly-diagnosed patients. *PloS One* <https://doi.org/10.1371/journal.pone.0010211>.

Manarino MR, Fillipo FD, Piro M (2012) Obstructive sleep apnea syndrome. *European Journal of Internal Medicine* 23(7): 586-593.

Marshall NS, Wong KK, Liu PY, et al. (2008) Sleep apnea as an independent risk factor for all-cause mortality: the Busselton Health Study. *Sleep* 31(8): 1079-1085.

McAllister M, Dunn G, Payne K, et al (2012) Patient empowerment: the need to consider it as a measurable patient-reported outcome for chronic conditions. *BMC Health Services Research* 12(1): 157-165.

Mence VH and Chipperfield JG (1997) The interactive effect of perceived control and functional status on health and mortality among young-old and old-old adults. *Journals of Gerontology. Series B: Psychological Sciences and Social Sciences* 52(3): 118-126.

Mermigkis C, Stagaki E, Amfilochiou A, et al. (2009) Sleep quality and associated daytime consequences in patients with idiopathic pulmonary fibrosis. *Medical Principles and Practice* 18(1): 10-15.

Miletin MS and Hanly PJ (2003) Measurement properties of the Epworth sleepiness scale. *Sleep Medicine* 4(3): 195-199.

Mulgrew AT, Ryan CF, Fleetham JA, et al. (2007) The impact of obstructive sleep apnea and daytime sleepiness on work limitation. *Sleep Medicine* 9(1): 42-53.

O'Brien C, O'Brien PG, Kennedy WZ, et al. (2012) *Psychiatric Mental Health Nursing: an introduction to theory and practice*, 2nd edition Jones & Bartlett Publishers, 700 pgs. ISBN: 978-1-4496-5174-9.

Pack AI, Black JE, Schwartz JR, et al. (2001) Modafinil as adjunct therapy for daytime sleepiness in obstructive sleep apnea. *American Journal of Respiratory and Critical Care Medicine* 164(9): 1675-1681.

Pearlin LI and Schooler C (1978) The structure of coping. *Journal of Health and Social Behavior* 19(1): 2-21.

Pearlin LI, Nguyen KB, Schieman S, et al. (2007) The Life-Course Origins of Mastery among Older People. *Journal of Health and Social Behavior* 48(2): 164-179.

Quintana-Gallego E, Carmona-Bernal C, Capote F, et al. (2004) Gender differences in obstructive sleep apnea syndrome: a clinical study of 1166 patients. *Respiratory Medicine* 98(10): 984-989.

Raaijmakers LG, Martens MK, Hesselink, et al. (2014) Mastery and perceived autonomy support are correlates of Dutch diabetes patients' self-management and quality of life. *Patient Education and Counseling* 97(1): 75-81.

Rea H, McAuley S, Stewart A, et al. (2004) A chronic disease management programme can reduce days in hospital for patients with chronic obstructive pulmonary disease. *Internal Medicine Journal* 34(11): 608-614.

Reblin M and Uchino BN (2008) Social and emotional support and its implication for health. *Current Opinion in Psychiatry* 21(2): 201-205.

Reishtein JL, Maislin G and Weaver TE. (2010) Outcome of CPAP treatment on intimate and sexual relationships in men with obstructive sleep apnea. Multisite Study group. *Journal of Clinical Sleep Medicine* 6(3): 221-6.

Rezacitalab F, Moharrari F, Saberi S, et al. (2014) The correlation of anxiety and depression with obstructive sleep apnea syndrome. *Journal of Research in Medical Sciences: The Official Journal of Isfahan University of Medical Sciences* 19(3): 205-210.

Richards D, Bartlett DJ, Wong K, et al. (2007) Increased adherence to CPAP with a group cognitive behavioral treatment intervention: a randomized trial. *Sleep* 30(5): 635-640.

Roure N, Gomez S, Mediano O, et al. (2008) Daytime sleepiness and polysomnography in obstructive sleep apnea patients. *Sleep Medicine* 9(7): 727-731.

Silva GE, Goodwin JL, Vana KD, et al. (2016) Obstructive sleep apnea and quality of life: comparison of the SAQLI, FOSQ, and SF-36 questionnaires. *Southwest Journal of Pulmonary & Critical Care* 13(3): 137-149.

Sloan FA, Padrón NA and Platt AC (2009) Preferences, Beliefs, and Self-Management of Diabetes. *Health Services Research* 44(3): 1068-1087.

Surtees PG, Wainwright NW, Luben R, et al. (2006) Mastery, sense of coherence, and mortality: evidence of independent associations from the EPIC-Norfolk Prospective Cohort Study. *Health Psychology* 25(1):102-110.

Tang CSK (2009) The Influence of Family–Work Role Experience and Mastery on Psychological Health of Chinese Employed Mothers. *Journal of Health Psychology* 14(8): 1207-1217.

Tippin J, Aksan N, Dawson J, et al. (2016) Sleep remains disturbed in patients with obstructive sleep apnea treated with positive airway pressure: a three-month cohort study using continuous actigraphy. *Sleep Medicine* 24:24-31.

Troxel WM, Buysse DJ, Monk TH, et al. (2010) Does social support differentially affect sleep in older adults with versus without insomnia? *Journal of Psychosomatic Research* 69(5): 459-466.

Weaver TE (2013) “Don’t start celebrating—CPAP adherence remains a problem.” *Journal of Clinical Sleep Medicine* 9(6): 551-552.

Weaver TE and Grunstein RR (2008) Adherence to continuous positive airway pressure therapy: the challenge to effective treatment. *Proceedings of the American Thoracic Society* 5(2): 173-178.

Weaver TE, Laizner AM, Evans LK, et al. (1997) An instrument to measure functional status outcomes for disorders of excessive sleepiness. *Sleep* 20(10): 835-843.

Weaver TE, Maislin G, Dinges DF, et al. (2007) Relationship between hours of CPAP use and achieving normal levels of sleepiness and daily functioning. *Sleep* 30(6): 711-719.

Wild MR, Engleman HM, Douglas NJ, et al. (2004) Can psychological factors help us to determine adherence to CPAP? A prospective study. *European Respiratory Journal* 24(3): 461-465.

Ye L, Pien GW, Ratcliffe SJ, et al. (2009) Gender differences in obstructive sleep apnea and treatment response to continuous positive airway pressure. *Journal of Clinical Sleep Medicine* 5(6): 512-518.

Zimet, GD, Dahlem, NW, Zimet SG et al. (1988) The multidimensional scale of perceived social support. *Journal of Personality Assessment* 52(1): 30-41.

General discussion,
implications,
and conclusions

"I've always loathed the
necessity of sleep.
Like death, it puts even
the most powerful men on
their backs."

Frank UNDERWOOD

Obstructive sleep apnoea (OSA) has been linked with the exacerbation of physiological and psychological disturbances that not only contribute to decreased quality of life (QoL) (Bishop et al., 2018), and poor daytime functioning (Sharkey et al., 2013; Aaronson et al., 2016), but also may be associated with increased suicide risk (Bishop, et al., 2018; Gupta and Jarosz, 2018). Therefore, OSA is recommended to be approached as a chronic disease requiring multidisciplinary managerial and treatment implications, including behavioural treatments (Epstein et al., 2009). The burden of this long-term chronic condition poses a challenge for health-care professionals, and for a successful management of OSA, bio-psycho-social factors need to be taken into consideration (Weaver, 2013; Vaske et al., 2017; Hilbert and Yaggi, 2018). This thesis seeks to address the psycho-social factors that have been identified as key determinants in the adaptation to various chronic diseases but are less known in OSA yet. The thesis further aims to contribute to the understanding of the associations between biomedical factors and self-reported health outcomes in OSA patients that have been identified as ambivalent in previous research. Section 8.1 summarizes the main findings of Chapters 3-7. The next section 8.2 provides a general overview and discussion of the main findings. The methodological considerations of the study are addressed in section 8.3. Finally, implications of the study for practice along with opportunities for future research are discussed in section 8.4.

8.1 Main findings

Research question 1 (Chapter 3)

Has continuous positive airway pressure (CPAP) treatment a positive effect on quality of life (QoL) in OSA patients when compared to sham CPAP, placebo pills, and conservative treatment?

Meta-analysis of 13 randomised controlled trials showed no significant differences in overall (0.18; 95%CI = 0.10, 0.26) and psychological QoL (0.25; 95%CI = -0.23, 0.72) comparing values of CPAP treated patients with controls; however, physical QoL improved (0.20; 95%CI = 0.04, 0.35). Subgroup analyses and sensitivity analyses showed that CPAP significantly affected the overall QoL in studies with controls receiving sham CPAP, parallel design, low risk of bias, and mild OSA patients.

Research question 2a (Chapter 4)

Are OSA severity, sleep-related problems, and anxiety associated with work functioning in OSA patients when controlled for age, gender, and type of occupation?

Impaired work functioning was reported by 82% of the OSA patients. A weak association between OSA severity and impaired work functioning was found in the crude model that was no longer significant in the adjusted models. Multivariate analyses revealed that poor perceived sleep quality was more strongly associated with impaired work functioning than sleep efficiency and daily disturbances. We found no significant association between daytime sleepiness and work functioning. Anxiety was strongly associated with impaired work functioning (-0.61; 95%CI = -1.10, -0.15). After adding anxiety to age, gender, OSA severity, and night-time sleep quality, the explained variance of work functioning increased from 20% to 25%.

Research question 2b (Chapter 4)

Does anxiety moderate the associations between sleep-related problems and work functioning?

The moderating effect of anxiety on the association between overall night-time sleep quality and work functioning was especially strong in patients with better sleep quality, while the effect of anxiety on the association between overall night-time sleep quality and work functioning was negligible in case of high sleep quality problems. Separate analyses of the three night-time sleep quality factors showed that anxiety moderated the associations between low and medium levels of perceived sleep quality problems, daily disturbances and work functioning. No moderating effect of anxiety on the association of sleep efficiency with work functioning was found.

Research question 3a (Chapter 5)

Are hostility and coping self-efficacy associated with psychological distress in OSA patients when controlled for sociodemographic, clinical, and sleep-related variables?

A high level of hostility and poor coping self-efficacy were strongly associated with psychological distress in OSA patients. In the regression models, hostility and the three coping self-efficacy dimensions, a) the ability to get support from family and friends, b) problem-focused coping self-efficacy, and c) coping self-efficacy for stopping unpleasant emotions and thoughts explained 5%, 4%, 8%, and 11% of the variance of psychological distress, respectively.

Research question 3b (Chapter 5)

Does coping self-efficacy mediate the association between hostility and psychological distress?

All coping self-efficacy dimensions mediated the associations between hostility and psychological distress. The indirect effects of all three coping self-efficacy dimensions were significant. They accounted for 10% of coping self-efficacy for getting support from family and friends, 15% of problem-focused coping self-efficacy, and 17% of coping self-efficacy for stopping unpleasant emotions and thoughts.

Research question 4 (Chapter 6)

What is the prevalence of suicidal ideation in OSA patients? Are OSA severity, sleep-related problems, and social support related to suicidal ideation in OSA patients?

The prevalence of suicidal ideation in OSA patients was 20.1%. Patients reporting suicidal ideation scored higher on sleep-related problems compared to non-suicidal ideation patients. OSA severity was not directly related to suicidal ideation but the association was mediated by night-time sleep quality. Poor night-time sleep quality and fatigue were directly related to suicidal ideation; with fatigue most strongly related to suicidal ideation. Unexpectedly, the relationships between daytime sleepiness, social support and suicidal ideation were not significant. Adjustment for age, gender, and marital status did not change the associations between social support, daytime sleepiness and suicidal ideation.

Research question 5a (Chapter 7)

Is there an association between social support, mastery, sleep-related problems and functional status in OSA patients when controlled for sociodemographic and clinical variables?

Social support was weakly associated with functional status in OSA patients and this association was no longer significant when mastery was added to the model. Mastery was strongly associated with functional status in OSA patients. We also identified significant associations between poor night-time sleep quality, daytime sleepiness and functional impairment.

Research question 5b (Chapter 7)

Do social support and mastery mediate the association between sleep-related problems and functional status?

No mediating role of social support was observed in the association between sleep-related problems and functional status. Mastery, however, mediated the association between sleep-related problems and functional status. The direct effects of sleep-related problems on functional status varied between 76.7% and 82.3%, whereas the indirect effects via mastery varied between 17.7% and 23.3%.

8.2 Discussion of the main findings

This thesis focuses on the associations between bio-psycho-social factors and selected aspects of self-reported health outcomes in OSA patients, i.e. quality of life, functional status, work functioning, and overall psychological distress – with particular interest in suicidal ideation. Our health model, the choice of examined constructs, and related measures were partially inspired by Wilson and Cleary (1995) and the bio-psycho-social approach as proposed by Engel (1978). The chosen health model stresses the presence of interactive, causal, and complex relationships between symptoms of the disease, functional status, general health perceptions, and overall QoL, as experienced by individuals (Wilson and Cleary 1995; Krabbe, 2017). More detailed information about the used health model can be found in Chapter 1.

Figure 8.1. Conceptual model of the associations between constructs examined in the thesis

8.2.1 Biomedical and psychological factors and their association with self-reported health outcomes in obstructive sleep apnoea patients

The examined OSA-related biomedical factors in this thesis concerned CPAP treatment, OSA severity, and sleep-related problems – measured as night-time sleep quality, daytime sleepiness, and fatigue. Psychological factors in this thesis were operationalized as anxiety and hostility. Other important intra-individual psychological resources, considered as major features within the process of coping with chronic disease (Kempen et al., 1997), were defined as coping self-efficacy and sense of mastery over one's life and circumstances.

Continuous positive airway pressure treatment and quality of life

We identified no CPAP treatment effect on overall QoL in studies with a crossover design compared to a small but significant effect found in studies with a parallel design. This finding supports the results of prior research, as parallel-group trials were found to be more efficient at capturing the persistence of benefits from CPAP treatment (Richens, 2001; Jing et al., 2008). Subgroup analyses further showed that CPAP led to a small but significant improvement in overall QoL in studies with controls undergoing sham CPAP treatment, compared to negligible overall QoL improvement revealed in controls receiving placebo pills. This result is unexpected, as sham CPAP treatment is supposed to worsen both sleep quality and gas exchange (Engleman et al., 1999; Sanner et al., 2000). A possible explanation may be that most studies that used placebo pills as control condition also had very small study samples. Moreover, all studies with placebo pills as control condition had a crossover design – identified as less sensitive in capturing the effect of CPAP treatment due to short wash-out periods which are not able to eliminate the effects of the first treatment (Richens, 2001). We also found significant QoL improvement in studies with mild OSA patients and low risk of bias. Thus, disease severity and level of low risk of bias may also be relevant when measuring the effect of CPAP treatment on QoL in OSA patients.

In line with previous meta-analyses by Jing et al. (2008), we have further confirmed that CPAP treatment may help to improve physical symptoms of OSA, whereas impaired psychological QoL still cannot be alleviated. The suboptimal effect of CPAP treatment on psychological QoL may be explained by irreversible OSA-related brain injuries, confirmed by recent histopathological investigations of brain tissue autopsy in OSA patients (Owen et al., 2018). These neural alterations in OSA patients may contribute to the development of psychological symptomatology (Huang et al., 2019), including mood (Peiffer et al., 2001), anxiety disorders (Milad 2007), and disturbed social functioning (Jack and Pelphrey, 2015). Owen and colleagues (2018) further suggest that myelin in OSA patients is impacted and not protected by CPAP treatment. Moreover, poor neuropsychological function and psychological symptoms may diminish adherence with CPAP treatment (Kushida, 2007; Hussain et al., 2014; Jackson et al., 2018). Thus, if the hypothesis

on irreversible brain injuries and their contribution to psychological impairment in OSA patients can be confirmed, the next step is to better understand OSA-related psychological symptoms and to adopt appropriate psycho-social interventions in disease management. Another possible explanation for the lack of a CPAP treatment effect on QoL is that there is no “perfect placebo” for CPAP and each approach has limitations and difficulties in blinding. For example, even a patient on sham CPAP treatment may be made aware of persisting snoring or observed apnoeas by a bed partner (Kushida et al., 2007).

Finally, the results of our meta-analyses may also be explained by the relatively low CPAP compliance level (with the highest value of 5.0 hours per night) in the included studies. It is well known that CPAP adherence is often suboptimal and remains persistently low over twenty years of reported data (Rotenberg et al., 2016b). Due to problematic adherence, the real effectiveness of CPAP may be poor, with a large proportion of users abandoning the machine within one year of prescription (Rotenberg et al., 2016a). These low rates of adherence consequently call into question the status of CPAP as first line treatment for OSA (Rotenberg et al., 2016b). Moreover, the question of what level of CPAP yields optimal health outcomes and defines adherence has not yet been clearly established and varies between 4 and 7.5 hours per night (Zimmerman et al., 2006; Weaver et al., 2007; Masa and Corral-Peñafiel, 2014), while some patients are not able to achieve normal daily functioning or remain excessively sleepy despite optimal CPAP treatment (Weaver et al., 2007; Antic et al., 2011; Jackson et al., 2018). The aforementioned findings may serve as a reminder that a “one size fits all” approach may not be appropriate in OSA and that decisions concerning the effectiveness of evaluation of CPAP treatment and its management need to be more individualized (Hilbert and Yaggi, 2018).

OSA severity and self-reported health outcomes

Mostly weak and inconsistent associations between OSA severity and self-reported health outcomes were found. The missing association between OSA severity and subjective health outcomes may be related to the lack of adaptation to the hospital environment and the recording equipment during the first night of polysomnography (PSG) assessment (Choi et al., 2015). We may further assume that this lack of adaptation may be especially significant in patients experiencing psychological distress. Therefore, issues such as abbreviated PSG monitoring, night-to-night variability, or the “first-night effect” of the PSG may partly explain the variability of OSA severity across different studies and outcomes (Punjabi, 2008). Furthermore, the Apnoea-Hypopnoea Index (AHI) does not capture the range of physiological variability related to adverse health outcomes of OSA, such as sleep fragmentation, degree of hypoxemia, or arousal threshold (Butler et al., 2019). All in all, considering the aforementioned problems, we believe that many controversies in the field of OSA may be caused due to the inability of AHI to measure the exact severity of the disease in a reliable and valid way (e.g. Asghari et al., 2012; Asghari and Mohammadi, 2013; Ryu et al., 2016).

Daytime sleepiness and work functioning

No significant association between daytime sleepiness and work functioning was found. We assume that the perception of subjective daytime sleepiness may be confounded by the patients' habituation to the increased sleep fragmentation that may occur with the long duration of the untreated disease. Perhaps, daytime napping could also be a confounding factor in the expression of the symptoms of sleepiness, e.g. people with more flexible working hours may have more nap opportunities, when compared to people with fixed working hours. Sleepiness, further, represents an interaction of physiological systems that increase sleep tendency and other systems opposing sleep drive. These complementary factors provide a dynamic equilibrium that oscillates over the course of a day depending on homeostasis between sleep debt and circadian phase. Thus, it may be difficult to objectively assess the level of daytime sleepiness as it may inevitably vary during the day (Kushida, 2007; Hurdie et al., 2018). Moreover, the levels of daytime sleepiness were found to be significantly influenced by a deterioration of the circadian rhythm, especially in OSA patients with poor sleep quality (Burioka et al., 2008; More et al., 2019).

Other observations indicate that the Epworth Sleepiness Scale may be an unreliable screening tool for OSA (Al Houqani and Arora, 2019). Sleepiness is a subjective, physiological, and behavioural construct and this may lead to a certain amount of confusion in the discussion of its prevalence, mechanisms, and societal implications (Cappuccio et al., 2010). The subjective evaluation of daytime sleepiness is often complicated by the fact that patients may complain about a lack of energy, exhaustion, and tiredness, rather than sleepiness itself (Chervin, 2000; Sharkey et al., 2013). Therefore, if OSA patients underestimate these symptoms, we recommend health care professionals to accompany self-reported measures of daytime sleepiness by clinical judgement and objective assessment – using technological devices to monitor sleepiness and alertness with documented validity (e.g. Cappuccio et al., 2010; Kaplan et al., 2018).

Finally, the lack of an association between daytime sleepiness and work functioning may be attributed to the hyperarousal theory, which links the symptoms of poor sleep quality and anxiety (Perlis et al., 2005). More specifically, both sleep-disordered breathing and anxiety may be associated with waking or sleeping hyperarousal activity (Krakow, 2015). Thus, anxiety in OSA patients may develop into a chronic state of hypervigilance, which refers to being on high alert much more than normal. This arousal may ultimately lead to a state of chronic anxiety and may eventually obliterate the natural daytime sleepiness or cause sleeplessness (Perlis et al., 2005; Krakow, 2015).

Night-time sleep quality and work functioning: the moderating role of anxiety

One of the most interesting findings of the moderation analysis was that the role of anxiety in the association between sleep quality and work functioning was weakest in OSA patients with the highest levels of sleep quality problems. Moderation analyses revealed that high sleep quality problems may become more significant in the association with poor work functioning than anxiety, while the moderating

effect of anxiety on work functioning may be especially profound in patients with better sleep quality. Thus, it can be assumed that in case of very poor night-time sleep quality, anxiety symptoms in OSA patients may become less dominant. An explanation may be that very poor sleep quality may cause fatigue, which may decrease the levels of (work-related) anxiety. Due to fatigue, OSA patients may have a lack of energy and may thus avoid work-related social interactions (e.g. Haack and Mullington, 2005), which are perceived by OSA-patients as stressful (Reishtein et al., 2006). Prior research showed that OSA patients may have difficulties to complete work tasks and that they perceived a lack of trust from coworkers which led to embarrassment (Reishtein et al., 2006). Thus, it should be considered that an increased prevalence of anxiety as identified in our study may also be social or work-related (e.g. adverse work environment, poor relationships at work) and not solely OSA-related.

Although the Beck Anxiety Inventory (BAI) represents a reliable indicator of anxiety in primary care (Wetherell and Gatz, 2005; Muntingh et al., 2011), its focus on psychophysiological symptoms linked to panic disorder such as a racing heart or dizziness (Julian, 2011), should be considered when interpreting our results (Beck and Steer, 1991; Cox et al., 1996), including the relatively high prevalence of anxiety identified in our study. It seems that the mechanism of the association between sleep and anxiety in OSA is complicated, e.g. a previous study reported a higher anxiety dream incidence in OSA patients (Carrasco et al., 2006) and OSA-related snoring when compared to controls (de Groen et al., 1993). OSA also appears to confer a higher risk for future development of nocturnal panic attacks due to breathing-related OSA symptoms (Edlund et al., 1991; Su et al., 2015), as well as somatic symptoms of anxiety such as excessive sweating, or nightmares (Wiersema et al., 2018). In light of these findings, it can be assumed that anxiety as measured in our study may be associated with psychophysiological symptomatology related to panic attacks, rather than with anxiety in general. As the BAI does not assess other aspects of anxiety, such as cognitive symptomatology, further research should include additional anxiety measures to distinguish between symptoms linked to panic disorder and other anxiety disorders (e.g. generalized anxiety disorder) in OSA patients.

Sleep-related problems and suicidal ideation

We found that disturbed night-time sleep quality and fatigue were directly related to suicidal ideation. There is a large body of evidence showing that disrupted night-time sleep quality may directly affect mental functioning in several ways including increased impulsivity, decreased executive functioning, and emotional exhaustion (Krakow et al., 2000; Weaver and George, 2011; Bernert et al., 2014) all of which may consequently diminish the capacity to inhibit suicidal ideation or behaviour (e.g. Malik et al., 2014). Notable is also the recent study by Bishop et al. (2018) which described that self-reported OSA was significantly associated with suicidal ideation and suicide planning, after controlling for key covariates such as depression, substance use disorders, and comorbid physical diseases. Nonetheless, sleep disturbances were not included in the recent suicide risk factor lists compiled by

the World Health Organization (2012). Therefore, the associations between disturbed night-time sleep quality, fatigue, and suicidal ideation revealed in our study may provide an additional support for the importance of sleep-related problems in the course and development of suicidal ideation in OSA patients beyond major depression (Krakow et al., 2011; Bishop et al., 2018), when confirmed in longitudinal studies.

Several mechanisms may explain our findings. First, it seems that repeated OSA-related arousal during sleep may exacerbate suicidality through the effects on night-time sleep quality (e.g. Krakow et al., 2000; Tseng et al., 2018). Second, the theory of entrapment may apply. Entrapment represents a core component of the psychological mechanisms underlying suicidal ideation. The term entrapment is derived from the concept of “arrested flight,” whereby a powerful motivation to escape from a situation, driven by threat-related psychobiological systems, is blocked (Gilbert and Allan, 1998). As poor sleep quality was found to alter the association between pre-sleep entrapment and awakening suicidal ideation (Littlewood et al., 2019), OSA patients may represent a group endangered by suicide. Moreover, OSA may lead to a low perception of control over the disease and its symptoms, which may potentiate the feeling of entrapment. Sleep may further be seen as an alternative way to escape these perceptions of entrapment. The potential downside to this occurs when people start ‘escaping’ via daytime napping, because this can disrupt night-time sleep. Subsequently, this behaviour may reinforce the disturbed sleep patterns, which in turn contribute to increased suicidal ideation and behaviours (Littlewood et al., 2016). Furthermore, if the hypothesis on the ‘escaping’ via sleep in the daytime is valid, it may be used as a possible explanation for the lack of the significant association between daytime sleepiness and suicidal ideation. Finally, the lack of an association between daytime sleepiness and suicidal ideation can be explained by the conceptual difference between fatigue and sleepiness. More specifically, daytime sleepiness can be defined as drive for sleep while fatigue can be described as drive for rest. Fatigue was also found to be strongly associated with psychological symptoms (Harvey et al., 2009) and involves neurastenic qualities (Kushida, 2007) and thus may better reflect the presence of psychological distress, including SI, when compared to daytime sleepiness.

Hostility and psychological distress: the mediating effect of coping self-efficacy

All assessed coping self-efficacy dimensions mediated the association between hostility and psychological distress. The coping self-efficacy for stopping unpleasant emotions and thoughts was the most adaptive strategy in attenuating the association between hostility and psychological distress. An explanation why coping self-efficacy for stopping unpleasant emotions and thoughts may be most adaptive in OSA patients is that they have very little control over the symptoms of their disease. When patients lack the ability to control disease-related symptoms and need to learn how to manage them, the avoidance-oriented coping strategies may help them to diminish the level of psychological distress (e.g. De Ridder and Schreurs 2001; Mikula et al., 2014). Furthermore, our results corroborate with previous studies showing that

hostile individuals were more likely to employ escape-avoidance coping styles to handle psychological distress (Vandervoort, 2006). All in all, our findings support the hypothesis that healthy emotion-regulation may not merely be about using the “right” problem focused strategies (Haines et al. 2016) and that coping can diminish psychological distress only when used in appropriate contexts (Bonanno and Burton, 2013; Haines et al. 2016).

However, our findings coincide with previous research among OSA patients. Two former studies (Bardwell et al., 2001; Cassara et al., 2017) concluded that the more active coping strategies reported by OSA patients, the lower the level of depressive symptoms they experienced. A possible explanation for the inconsistency with our findings may be the difference in OSA diagnosis criteria (Bardwell et al., 2001) and different measurements of coping and psychological symptomatology (Bardwell et al., 2001; Cassara et al., 2017). Recent studies also identified active coping processes as potential behavioural intervention targets to promote CPAP use (Dieljens et al., 2013; Saconi et al., 2018), while passive coping was significantly associated with poor adherence with treatment. Thus, it may be assumed that during the solution-oriented CPAP treatment process, active coping strategies may become more useful when compared with passive-oriented coping. Therefore, an important issue to resolve in future research is the role of the different coping self-efficacy dimensions in the management of CPAP treatment.

Sleep-related problems and functional status: the mediating role of mastery

Mastery over one’s life and circumstances was significantly associated with all functional status subscales in terms of activity level, vigilance, general productivity, social outcomes, and intimate and sexual relationships. Our findings are in line with previous studies showing that mastery was found to facilitate QoL, psychological well-being, and adaptation under stressful situations, including medical events (Kempen et al., 1997; Lang et al., 2016). Furthermore, when looking at the mediating effect of mastery on the association between sleep-related problems and functional status, we found that mastery mediated the association between night-time sleep quality, daytime sleepiness and functional status. As OSA patients were found to experience reduced energy and activity levels even after treatment with CPAP (Lau et al. 2013; Weaver, 2013) with optimal compliance (Antic et al., 2011; Jackson et al., 2018), adequate mastery may help in diminishing the negative effects of sleep-related symptoms on functional status. As mastery is not considered a stable element of personality but is understood as a personal resource that may evolve and change over the lifespan in response to circumstances and interventions (Pearlin et al., 2007; Zautra et al., 2012), the development of new strategies for the improvement of mastery may be beneficial.

8.2.2 Social factors and self-reported health outcomes

It is now generally accepted that health and illness are not only the result of an interaction between biological and psychological factors, but also social factors (Haslam et al., 2018). The impact of OSA is significant and the disease does not only affect

physical and psychological health but the whole person in the context of his or her social life. OSA itself may cause changes in the social environment which may inevitably affect health outcomes of the individual. In this thesis, we were particularly interested in the associations between social support (measured as perceived social support) and health-related outcomes (assessed as functional status and suicidal ideation).

Social support and functional status

We identified only a weak association between social support and overall functional status in OSA patients. Still, we found that social support was strongly associated with one functional status subscale, i.e. intimacy-sexual relationships. Beyond the increasing interest in the associations between sleep disorders and a couple's intimate relationships, some specific consequences of OSA such as the high incidence of erectile dysfunction (Schulz et al., 2019), or experienced sexual dysfunction in female OSA patients (Yilmaz et al., 2017) make the investigation of intimate relationships worthwhile. The role of social support in couples may be significant, since relationship satisfaction represents a relevant variable in enhancing the QoL and helps to diminish psychological distress in OSA patients (Baron et al., 2009). Moreover, improving intimate relationships may be crucial as better relationship quality was identified as being the most important need expressed by untreated OSA patients (Broström et al., 2007).

Social support and suicidal ideation

The importance of social support was consistently described across multiple theories of suicidal behaviour. The sociological theory of suicide (Durkheim and Simpson, 1951), the psychache theory of suicide (Shneidman, 1993), the arrested flight model (Williams, 2001), and the interpersonal-psychological theory of suicide (Joiner, 2007; Mars et al., 2019) suggest that inadequate social support, lack of strong interpersonal relationships, and perception of low belongingness may increase the risk for suicidal ideation and suicidal attempts. Perception of social support was found to represent a protective factor for suicidal ideation and behaviours (Rowe et al., 2006). Surprisingly, we found only a weak, non-significant association between perceived social support and suicidal ideation in OSA patients. The lack of the association between social support and suicidal ideation in our study may be explained by the presence of severe sleep-related problems in OSA patients. In line with this hypothesis, individuals with severe sleep deprivation report being less sociable (Haack and Mullington, 2005). Previous research also showed that the association between perceived and received social support may be reciprocal and people who reported giving less social support also reported getting less support (Piferi et al., 2006). Families of OSA patients also described their relationships and their overall QoL as negatively affected by OSA of their relatives or partners (Parish and Lyng 2003; Brown, 2005; Luyster et al., 2016; Bergeron et al., 2017). Moreover, people may be less willing to interact with an extremely sleep-deprived person (Sundelin et al., 2017). Thus, it should be considered that in case of extreme sleep-related OSA

symptoms, the sources of social support may be of less importance as well as of less adequacy, which may reduce resilience and increase the risk of suicidal behaviour when difficulties are encountered.

8.2.3 Towards a bio-psycho-social approach for OSA

*“Macbeth does murder sleep, the innocent sleep,
Sleep that knits up the ravell'd sleeve of care,
The death of each day's life, sore labour's bath,
Balm of hurt minds, great nature's second course,
Chief nourisher in life's feast”*

William Shakespeare, Macbeth

The aforementioned findings of the lack of the CPAP treatment effect on overall and psychological QoL call into question the identification of factors that may help to improve impaired health outcomes in OSA patients. All in all, the studies presented in this thesis revealed that sleep-related problems, including night-time sleep quality, daytime sleepiness, and fatigue explained more variance in health outcomes, when compared to psychological or social factors. Thus, the treatment of sleep-related problems should be recommended as a main practical tool for promoting mental health and daily functioning in OSA patients.

This thesis also revealed that factors related to external resources such as self-perceived social support and coping self-efficacy for the ability to get support from family and friends explained less variance in health outcomes when compared to intra-individual psychological resources such as mastery and coping-self-efficacy for the ability to stop unpleasant emotions and thoughts and problem-focused coping.

A possible explanation may be that sleep-related problems hamper social interactions (Haack and Mullington, 2005; Cappuccio et al., 2010). Moreover, because of the tendency to disengage from stressful situations (e.g. Reishtein et al., 2006; Kang et al., 2018), interpersonal sensitivity (Kang et al., 2018), or negative feedback provided from patients' relatives, partners (Parish and Lyng 2003; Brown, 2005; Schwarzer, 2014; Luyster et al., 2016; Bergeron et al., 2017; Sundelin et al., 2017), or co-workers (Reishtein et al., 2006), OSA patients may do little to improve their social interactions. Another reason why the social support may be insufficient is that the person is not able to cope in an adaptive manner. Paradoxically, those individuals who have valuable personal resources such as competence, high self-esteem, internal locus of control, and optimism were found to elicit a stronger tendency in others to provide social support. The expression of too much distress strains the social network, evokes negative reactions, and turns away those who would have been supportive (Schwarzer, 2014).

Negative feedback from others may further booster social inhibition and serve as precursor to social isolation and loneliness. Neuroimaging techniques also showed that loneliness may consequently lead to an increased level of hypervigilance to hostile

cues and a negative attitude towards others (Cacioppo et al., 2016). Moreover, higher levels of anxiety or hostility identified in OSA patients (Lau et al., 2014; Unal et al., 2017; Wiersema et al., 2018) may be associated with a lack of ability to communicate with others (Perfect et al., 2013), social inhibition, social dysfunction (Sasaki and Yamasaki, 2002), and oppositional orientation towards others (Houston and Vavak, 1991). Thus, it may be assumed that patients with OSA, identified as hostility-prone, may have even poorer motivation to participate in social activities.

Nevertheless, we should also consider the ways in which the bio-psycho-social factors have the capacity to influence and restructure each other over time (Jull, 2017; Haslam et al., 2018). Moreover, if the hypothesis based on the hyperarousal theory and the theory of entrapment can be confirmed, then the next step is to reveal whether a decrease in psychological distress with adequate treatment induces daytime sleepiness in OSA patients (Krakow et al., 2015).

We may also ask: “Are sleep problems only symptoms or also causes and consequences of other OSA-related problems?” Shakespeare says it rather well: it may be all three. First, lack of sleep is a cause of distress and ill health. If we miss sleep, we miss the balm of hurt minds. Second, Macbeth’s distress murders sleep. Sleep disturbance is a consequence of the circumstances of people’s life. Third, Lady Macbeth’s heart is sorely charged and her sleep is disturbed. Sleep disturbance is a symptom of psychological distress or perhaps other disease. Moreover, these three domains – causes, consequences, and symptoms, can all interact. Sleep-related problems can not only be a result of disorder, but can in turn, cause other problems (Marmot, 2010).

The abovementioned examples illustrate that the possibility of interaction between causes, consequences, and symptoms in the bio-psycho-social model must always be considered, as it is important to sort out which of the three is dominant, as interventions might differ (Marmot, 2010). All in all, failure to recognise the ‘fluidity’ in the bio-psycho-social model lessens the appreciation of the variety within, as well as the associations between its domains, and the relative importance of each factor in the individual patient at initial and progressive time points could have negative impact on disease management. Thus, the graphical presentation of the bio-psycho-social factors as three mainly symmetrical areas can cause misleading information or errors in the clinical reasoning (Haslam et al., 2018). Therefore, when interpreting our results, we need to consider the relative and variable contributions of each domain of the bio-psycho-social model to individual patients’ presentations over time (Jull, 2017; Haslam et al., 2018).

Although the bio-psycho-social model has been successfully applied to obtain a better theoretical understanding of the causes of the disease and its processes, or for public health purposes (Alonso, 2004), unfortunately, it has not yet been included in a model of medical practice (Wade and Halligan, 2017; Hadi et al., 2017). Nevertheless, as Engel (1978) pointed out, even though both patient and doctor may culturally adhere to the biomedical model, the patient’s needs and ultimate criteria for defining disease are always psycho-social, even when the health complaints are physical. Thus, despite many drawbacks related to greater knowledge, personnel,

and time investment, which will probably continue to relegate the bio-psycho-social model to a secondary position in clinical practice (Wade and Halligan, 2017), the broadening of the health-care professionals’ knowledge of the importance of psychological and social aspects may be beneficial for the patient (Alonso, 2004). Moreover, if the findings of OSA-related biological mechanisms involved in the spread of brain injuries resistant to CPAP treatment (Owen et al., 2018) and their consequent contribution to psychological symptomatology in OSA patients (Huang et al., 2019) can be confirmed, the next step should definitely include the adoption of appropriate psycho-social interventions in disease management.

8.3 Methodological considerations

The strengths and limitations of the studies are described in more detail in the separate chapters of this thesis. A short synopsis of the main methodological considerations is presented below. First, the quality of the study sample will be discussed. Second, the quality of the measuring instruments will be described. Finally, causality and confounding will be considered.

8.3.1 Quality of the sample

A strength of the study is that it was based on a sample with a wide age range (25–65 years) and a man-to-woman ratio of 3:1. Next, patients were diagnosed using PSG, which is considered the criterion standard for diagnosing OSA and determining disease severity. The indication for PSG was based on a general practitioner referral form while OSA was diagnosed based on an overnight sleep study carried out at a clinical laboratory. Medical examinations were carried out by a pulmonologist specialized in sleep-disordered breathing. To ensure that health outcomes were not influenced by major comorbidities such as stroke, comorbid sleep-disorders or diseases associated with the use of sedatives or hypnotics, we studied recently-diagnosed, mild to severe OSA patients with minimal comorbidities, who had not started treatment. Only OSA patients between 18 and 65 years of age were included due to possible increased vulnerability, functional changes and a decline in abilities and/or performance related to age. We also excluded participants in shift work, due to the negative impact of shift work on QoL (Kaliterna et al., 2004), well-being (Nezamodini et al., 2014), mood, alertness (Cori et al., 2018), and quality of sleep (Nezamodini et al., 2014). Thus, the findings are not generalizable to the general working population including shift workers, only to workers with regular working time arrangements. It may be assumed that the results may be even worse when shift workers are included. It should further be noted, that our sample with minimal co-morbidities and recent diagnosis may be not fully representative of the general OSA population. Another major limitation concerns the small sample size. Finally, in our sample, the majority of OSA patients was male. Thus, the results may be less generalizable to female OSA patients.

8.3.2 Quality of the measuring instruments

Patients' reported outcome measures (PROMS) increasingly accompany the traditional clinical way of measuring health and the effect of treatment in various chronic diseases (Weldring and Smith, 2013; Appleby et al., 2016), including OSA (Tam et al., 2014). A clear strength of this thesis is that it aimed to get more insight into less known factors underlying adaptive functioning of OSA patients. To our best knowledge, this is the first time that the Work Role Functioning Questionnaire has been used in a sample of OSA patients. It is also the first study using the Pittsburgh Sleep Quality Inventory factor structure in an OSA population. Although we used valid and reliable measures of the relevant constructs, some limitations should be noted. A major limitation concerns that we used self-reported measures and no formal psychiatric diagnosis of suicidal ideation or anxiety was established. Another limitation is that the OSA diagnosis was based on a single sleepover. Although a one-night PSG is sufficient for the diagnosis of OSA (Scholle et al., 2003; Gouveris et al., 2010), significant variability in the AHIs taken from two nights was revealed in OSA patients (Gouveris et al., 2010). Many studies have further shown that AHI may not be able to quantify the disease severity (e.g. Ryu et al., 2016) and complications such as clinical impact of OSA on self-reported health outcomes, including QoL (Moyer et al., 2001), or psychological distress (Asghari et al., 2012). Another source of concern may be the length of the used questionnaires, which may have influenced the data quality, especially in patients with sleep-related problems. To overcome this methodological limitation, the questionnaires were sent to the patients three weeks before the PSG examination by postal mail, so they had enough time to fill them in at home.

8.3.3 Causality and confounding

Due to the cross-sectional design of the study, causal inferences cannot be made. Although we adjusted for key covariates that have consistently been associated with health outcomes in OSA patients, including sociodemographic and clinical variables; we did not adjust for all possible confounders. Thus, we cannot rule out the possibility of residual confounding that may account for the associations between the examined variables.

8.4 Implications

In clinical sleep medicine, the focus has shifted from OSA diagnosis to OSA management, with the emergence of new, integrated models of care (Heatley et al., 2013). Multidisciplinary OSA treatment can help to minimize fragmentation of care (Shelgikar et al., 2014), to improve the risk assessment for the consequences of untreated OSA, and can lead to better treatment strategies (Kapur, 2018). Results of this study may be helpful in identifying bio-psycho-social factors associated with poor health outcomes that can be modified by health care professionals and by the patients themselves.

8.4.1 Implications for clinical practice

We found that medical treatment of OSA may help to improve physical symptoms of the disease, whereas existing psychological impairment still cannot be successfully alleviated. Therefore, the current research and clinical practice should focus not only on the standard treatment of OSA, but also on ensuring that psychological symptoms are efficiently managed.

As impaired work functioning was reported by 82% of the OSA patients, employee assessment of their work functioning may be an important proxy for the health burden of OSA. There is also a need for workplace strategies that encourage behaviours and practices that may be helpful in reducing OSA-related symptoms and improve work functioning in OSA patients. Occupational health professionals may together with OSA patients find ways to address the specific work demands that are difficult to conduct. Management of unsatisfactory sleep through a variety of proven strategies, including naps, better management of work demands, regular exercise, duty hour considerations, and instruction on the basics of sleep hygiene including stimulating activities prior to bedtime, ingestions, and bedtime rituals (Jansson and Linton, 2006; Kushida, 2007) may be helpful.

Further, our findings may enhance health care professionals' understanding of the mental health problems in OSA patients. Health care professionals should keep in mind that OSA may not be immediately apparent but might present in an atypical fashion. The presence of some atypical psychological OSA-related symptoms revealed in this study, was also identified in previous research (Krakow et al., 2015; Choi et al., 2015; Unal et al., 2017) and may include anxiety, hostility, or suicidal ideation. A lack of knowledge regarding the heterogeneity of OSA's clinical presentation may pose critical challenges to its clinical recognition, resulting in missed or delayed diagnosis. Moreover, the lag time between initial OSA symptoms and OSA diagnosis can vary widely, with the average duration from seven to ten years (Guilleminault et al., 1995; Rahaghi and Basner, 1999). People with atypical or less known OSA symptomatology may have had a longer lag time, leading to a longer duration of exposure to untreated OSA and, thus, a higher probability of developing comorbidities. All in all, primary care providers represent the key to successful case finding. Therefore, it is essential to promote an understanding of the signs and symptoms of OSA. Simple questions about key OSA symptoms such as snoring, witnessed nocturnal apnoeas, and sleep-related problems, together with questions about atypical psychological symptoms should become a routine component of the medical interview.

Health care professionals also have to be informed about the alarming prevalence's of overall psychological distress (56.0%) and suicidal ideation (20.1%) in OSA patients. As suicidal ideation and behaviour may be largely preventable (Stanley and Brown, 2012; Simon, 2014) by early detection, preventive education of caregivers and relatives about the high prevalence of suicidal ideation in OSA patients may be important. Based on the strong relationship between poor sleep quality, fatigue and suicidal ideation, we recommend health care professionals to

consider investigating and monitoring suicidal ideation in people with sleep-related disorders. Sleep problems are a modifiable risk factor for suicidal thoughts and behaviours (Littlewood et al., 2019). Thus, the education of OSA patients on basic sleep hygiene may improve the quality of sleep and decrease fatigue. OSA patients with psychological symptoms and/or sleep-related problems may suffer from decreased activity and reduced social participation (e.g. Haack and Mullington, 2005), and consequently may have poor motivation to seek health care. Therefore, an OSA diagnosis may represent an early opportunity for health care providers to discuss mental health with their patients. Health care professionals' communication skills, particularly related to a frank and clear discussion of suicidality, should be developed through training courses. Because assessing suicidality in medical settings may be challenging, the use of self-administered screening questionnaires that identify patients at risk of suicidality could be a promising strategy (Kye and Park, 2017). Our results further indicated that anxiety was strongly associated with poor-nighttime sleep quality and impaired work functioning. Anxiety, especially at severe and panic levels, has a major impact on night-time sleep and breathing, which may in turn exacerbate OSA symptoms and contribute to difficulties with CPAP adaptation (Shapiro, 2014). Therefore, screening for anxiety at the time of OSA diagnosis with a simple, cost-effective self-rating tool may improve reporting of anxiety symptoms among OSA patients, and in turn, may help to improve assessment of OSA in primary care settings.

Another source of concern is that sleep disorders along with OSA are rarely assessed on a regular basis by mental health professionals in patients suffering from psychological distress. The presence of the sleep-wake complaints in a patient's profile, and the onset of those complaints prior to the development of the psychological symptomatology, should draw the mental health professional's attention to a potential concurrent or underlying OSA. Screening for symptoms associated with OSA can easily be integrated in symptom screening in a psychiatric interview (Braitman, 2018). Additionally, it is important for mental health professionals to understand that the routinely prescribed psychiatric medications may affect OSA. Thus, identifying patients with overlapping diagnoses of mental disorders and OSA may help to improve their treatment outcomes through more careful dosing of pharmacotherapy and CPAP treatment. Especially, sedation medications should be used with caution, as they were found to exacerbate OSA (Weatherspoon et al., 2016). Notably benzodiazepines are considered to be inappropriate due to potential adverse effects, such as increased risk for adverse respiratory events, decrease in wakefulness and airway muscle tone, as well as weak response to hypoxemia (Hanly and Powles, 1993; Kushida, 2007; Zhang, et al., 2014; Kao et al., 2018). Benzodiazepines have the potential to cause next-day hangover and may contribute to fatigue and cognitive impairment already experienced by individuals with OSA (Kushida, 2007). Furthermore, patients with coexisting OSA and mental disorders may respond less well to antipsychotic medications than psychiatric patients without OSA (Gupta and Simpson, 2015).

Targeted psychological interventions, such as psychotherapy which starts early in the OSA disease trajectory, may help to prevent serious problems later on. Our study revealed that both high hostility and poor coping self-efficacy may result in a higher level of psychological distress in OSA patients. Considering our findings, we may conclude that the use of adaptive coping self-efficacy may be used as a gateway to improve overall psychological well-being and to diminish the negative effect of hostility on psychological well-being in OSA patients. Although hostility is a relatively stable personality trait, coping self-efficacy can be actively modified, e.g. by cognitive behavioural therapy. Given that sense of mastery was found to represent a skill of importance to daily functioning, interventions focused on mastery enhancement may be a part of an integrated OSA care model. Specifically, brief interventions may be applied for the improvement of the functional status, as mastery seems to be responsive to short-term psychological treatment (Zautra et al., 2012).

8.4.2 Implications for future research

Clearly, more high-quality studies with larger study populations and with longer treatment duration are needed to better understand the effect of CPAP treatment on QoL in OSA patients. Yet, further longitudinal research is required to reveal how and to what extent social and psychological resources are relevant and effective in ameliorating the impact of OSA-related symptomatology and whether they can be of use in targeting interventions. The lack of widely acknowledged, tested and proven explanatory models of the pathophysiological mechanisms to understand the relationships between anxiety, suicidal ideation, sleep-related problems and OSA may be a barrier for understanding the clinical relevance of these conditions. Therefore, examining these factors over time may help to properly address the revealed associations in a more comprehensive way. Next, since major comorbidities may influence sleep and affective symptoms, a detailed assessment of OSA patients with various categories of major comorbidities will further extend our knowledge.

Another key challenge of future research is our limited knowledge of the factors that determine suicidal behaviour, i.e., which individual with suicidal ideation will act on this ideation (O'Connor, 2017). Thus, it is important to examine the inter-relationships between sleep disturbances, suicidal ideation, and other symptoms of OSA, which will provide novel insights into the specific pathways by which sleep-related symptoms contribute to the occurrence of suicidal ideation. Future research should include both objective and subjective assessments of key sleep parameters to ascertain suicide risk among OSA patients. Because suicidality can reflect a wide range of factors that can have various effects in different sociocultural contexts, more research is needed to explore the long-term effects of OSA on suicidality, while considering comprehensive psycho-social factors.

Our findings indicate that coping self-efficacy for the ability to stop unpleasant emotions and thoughts may be the most closely associated with diminishing of psychological distress in OSA out of the three studied coping strategies. Previous

research demonstrated that emotional suppression may be less adaptive in reducing psychological distress and symptoms over a longer time span (Wenzlaff and Wegner, 2000; Gross and Thompson, 2007). Thus, longitudinal studies are needed to verify the role of coping self-efficacy for the ability to stop unpleasant emotions and thoughts in diminishing the negative effect of OSA-related symptoms on psychological well-being in OSA patients. Finally, as social support was strongly associated with one functional status subscale, i.e. intimacy-sexual relationships, another area that merits further attention is the patient-partner dyad. With respect to the clinical importance of our study, the revealed significance of sources of social support in intimate relationships should be addressed as previous research identified poor health-related outcomes not only in OSA patients, but also in their bed-partners (Parish and Lyng 2003; Luyster et al., 2016).

Conclusion

The results of this thesis confirmed the previous findings of a very small improvement in self-reported health outcomes with CPAP treatment in OSA patients. Based on the results of our meta-analysis, we may assume that medical treatment of OSA may help to improve physical symptoms of OSA, whereas existing psychological impairment still cannot be successfully alleviated. We further found that psychological factors, together with some biological and social factors, are associated with health-related outcomes in OSA patients. As we found strong associations between sleep-related problems and self-reported health outcomes, we recommend health care professionals to intervene on sleep to reduce psychological distress and impaired daytime functioning in OSA patients. Our findings indicate that factors related to external resources such as social support and coping self-efficacy for the ability to get support from family and friends, may be of less importance in influencing health outcomes when compared with patients' intra-individual psychological factors such as coping self-efficacy for stopping unpleasant emotions and thoughts, problem focused coping, and mastery. Based on these results we may further assume that helping OSA patients to strengthen their intra-individual psychological resources may be an important strategy to attenuate the negative impact of OSA-related symptoms. However, longitudinal research is needed to confirm our results.

References

Aaronson JA, Hofman WF, van Bennekom CA, et al. (2016) Effects of continuous positive airway pressure on cognitive and functional outcome of stroke patients with obstructive sleep apnea: a randomized controlled trial. *Journal of Clinical Sleep Medicine: Official Publication of the American Academy of Sleep Medicine* 12(4): 533-541.

Al Houqani M and Arora T (2019) Comparison of Commonly Used Questionnaires to Identify Obstructive Sleep Apnea in Pilots. *Sleep* 42 (1) DOI: <https://doi.org/10.1093/sleep/zsz067.443>.

Alonso Y (2004) The biopsychosocial model in medical research: the evolution of the health concept over the last two decades. *Patient Education and Counseling* 53(2): 239-244.

Antic NA, Catcheside P, Buchan C, et al. (2011). The effect of CPAP in normalizing daytime sleepiness, quality of life, and neurocognitive function in patients with moderate to severe OSA. *Sleep* 34(1): 111-119.

Appleby J, Devlin N, Parkin D (2016) Using Patient Reported Outcomes to Improve Health Care. John Wiley & Son, Chichester. 978-111-894859-0. 109 pgs.

Asghari A and Mohammadi F (2013) Is Apnea-Hypopnea Index a proper measure for Obstructive Sleep Apnea severity?. *Medical Journal of The Islamic Republic of Iran (MJIRI)* 27(3): 161-162.

Asghari A, Mohammadi F, Kamrava SK, et al. (2012) Severity of depression and anxiety in obstructive sleep apnea syndrome. *European Archives of Oto-Rhino-Laryngology* 269(12): 2549-2553.

Bardwell WA, Ancoli-Israel S, Dimsdale JE (2001) Types of coping strategies are associated with increased depressive symptoms in patients with obstructive sleep apnea. *Sleep* 24(8): 905-909.

Barnes M, McEvoy RD, Banks S, et al. (2004) Efficacy of positive airway pressure and oral appliance in mild to moderate obstructive sleep apnea. *American Journal of Respiratory and Critical Care Medicine* 170(6): 656-664.

Baron KG, Smith TW, Czajkowski LA, et al. (2009) Relationship quality and CPAP adherence in patients with obstructive sleep apnea. *Behavioral Sleep Medicine* 7(1): 22-36.

Beck AT and Steer RA (1991) Relationship between the Beck Anxiety Inventory and the Hamilton Anxiety Rating Scale with anxious outpatients. *Journal of Anxiety Disorders* 5(3): 213-223.

Benka J, Nagyova I, Rosenberger J, et al. (2014) Is coping self-efficacy related to psychological distress in early and established rheumatoid arthritis patients? *Journal of Developmental and Physical Disabilities* 26(3): 285-297.

Bergeron M, Duggins AL, Ishman SL (2017) The impact of pediatric obstructive sleep apnea on patient and family quality of life. *Sleep Medicine* 40: 31-e32.

Bernert RA, Turvey CL, Conwell Y, et al. (2014) Association of poor subjective sleep quality with risk for death by suicide during a 10-year period: a longitudinal, population-based study of late life. *JAMA Psychiatry* 71(10): 1129-1137.

- Bishop TM, Ashrafioun L, Pigeon WR (2018) The association between sleep apnea and suicidal thought and behavior: an analysis of national survey data. *Journal of Clinical Psychiatry* 79(1): DOI: 10.4088/JCP.17m1480.
- Bonanno GA and Burton CL (2013) Regulatory flexibility: An individual differences perspective on coping and emotion regulation. *Perspectives on Psychological Science* 8(6): 591-612.
- Braitman DV (2018) Screening for Sleep Apnea in Psychiatry. *American Journal of Psychiatry Residents' Journal*, 13(5): 5-7.
- Broström A, Johansson P, Strömberg A, et al. (2007) Obstructive sleep apnoea syndrome—patients' perceptions of their sleep and its effects on their life situation. *Journal of Advanced Nursing* 57(3): 318-327.
- Brown WD (2005) The psychosocial aspects of obstructive sleep apnea. *Seminars in Respiratory and Critical Care Medicine* 26(1): 33-43.
- Burioka N, Koyanagi S, Endo M, et al. (2008) Clock gene dysfunction in patients with obstructive sleep apnoea syndrome. *European Respiratory Journal* 32(1): 105-112.
- Butler MP, Emch JT, Rueschman M, et al. (2019) Apnea-hypopnea event duration predicts mortality in men and women in the Sleep Heart Health Study. *American Journal of Respiratory and Critical Care Medicine* 199(7): 903-912.
- Cacioppo S, Bangee M, Balogh S, et al. (2016) Loneliness and implicit attention to social threat: A high-performance electrical neuroimaging study. *Cognitive Neuroscience* 7(1-4): 138-159.
- Cappuccio F, Miller MA and Lockley SW (Eds.) (2010) *Sleep, health, and society: From aetiology to public health*. Oxford University Press, USA. ISBN 978-0-19-956659-4.
- Carrasco E, Santamaria J, Iranzo A, et al. (2006) Changes in dreaming induced by CPAP in severe obstructive sleep apnea syndrome patients. *Journal of Sleep Research* 15(4): 430-436.
- Chervin RD (2000) Sleepiness, fatigue, tiredness, and lack of energy in obstructive sleep apnea. *Chest* 118(2): 372-379.
- Chesney M, Neilands TB, Chambers DB (2006) A validity and reliability study of the coping self-efficacy scale. *British Journal of Health Psychology* 11(3): 421-437.
- Choi SJ, Joo EY, Lee YJ, et al. (2015) Suicidal ideation and insomnia symptoms in subjects with obstructive sleep apnea syndrome. *Sleep Medicine* 16(9): 1146-1150.
- Conway VJ and Terry DJ (1992) Appraised controllability as a moderator of the effectiveness of different coping strategies: A test of the goodness of fit hypothesis. *Australian Journal of Psychology* 44: 1-7.
- Cox BJ, Cohen E, Drenfeld DM, et al. (1996) Does the Beck Anxiety Inventory measure anything beyond panic attack symptoms? *Behaviour Research and Therapy* 34(11): 949-954.
- De Groen JH, Op den Velde W, Hovens JE et al. (1993) Snoring and anxiety dreams. *Sleep* 16(1): 35-36.
- De Ridder D and Schreurs K (2001) Developing interventions for chronically ill patients: is coping a helpful concept? *Clinical Psychology Review* 21(2): 205-240.
- Dieltsjens M, Vanderveken OM, Van den Bosch D, et al. (2013) Impact of type D personality on adherence to oral appliance therapy for sleep-disordered breathing. *Sleep and Breathing* 17(3): 985-991.
- Du L, Zeng J, Liu H, et al. (2017) Fronto-limbic disconnection in depressed patients with suicidal ideation: a resting-state functional connectivity study. *Journal of Affective Disorders* 215: 213-217.
- Durkheim E and Simpson G (1951) *Suicide, a study in sociology*. Free Press, 405 pgs.
- Edlund MJ, McNamara ME, Millman RP (1991) Sleep apnea and panic attacks. *Comprehensive Psychiatry* 32(2): 130-132.
- Engel GL (1978) The biopsychosocial model and the education of health professionals. *Annals of the New York Academy of Sciences* 310: 169-81.
- Engleman HM, Kingshott RN, Wraith PK, et al. (1999) Randomized placebo-controlled crossover trial of continuous positive airway pressure for mild sleep apnea/hypopnea syndrome. *American Journal of Respiratory and Critical Care Medicine* 159(2): 461-467.
- Engleman HM, Martin SE, Deary IJ, et al. (1997) Effect of CPAP therapy on daytime function in patients with mild sleep apnoea/hypopnoea syndrome. *Thorax* 52(2): 114-119.
- Engleman HM, Martin SE, Kingshott RN, et al. (1998) Randomised placebo-controlled trial of daytime function after continuous positive airway pressure (CPAP) therapy for the sleep apnoea/hypopnoea syndrome. *Thorax* 53: 341-345.
- Epstein LJ, Kristo D, Strollo PJ Jr, et al. (2009) Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. *Journal of Clinical Sleep Medicine* 5(3): 263-276.

Faccenda JF, Mackay TW, Boon NA, et al. (2001) Randomized placebo-controlled trial of continuous positive airway pressure on blood pressure in the sleep apnea-hypopnea syndrome. *American Journal of Respiratory and Critical Care Medicine* 163(2): 344-348.

Freitag L, Ireland JL, Niesten IJ (2017) Exploring the relationship between sleep quality, emotional well-being and aggression levels in a European sample. *Journal of Aggression, Conflict and Peace Research* 9(3): 167-177.

Cassara I, Thabet JB, Msaad S, et al. (2017) Impact of coping strategies on emotional status in patients with obstructive sleep apnea syndrome. *European Psychiatry* 41: S492.

Gilbert P and Allan S (1998) The role of defeat and entrapment (arrested flight) in depression: An exploration of an evolutionary view. *Psychological Medicine* 28: 585-598.

Giles TL, Lasserson TJ, Smith B, et al. (2006) Continuous positive airways pressure for obstructive sleep apnoea in adults. *Cochrane Database of Systematic Reviews* 19(3): 1-113.

Gouveris H, Selivanova O, Bausmer U, et al. (2010) First night-effect on polysomnographic respiratory sleep parameters in patients with sleep-disordered breathing and upper airway pathology. *European Archives of Oto-Rhino-Laryngology* 267(9): 1449-1453.

Graven LJ and Grant JS (2013) Coping and health-related quality of life in individuals with heart failure: An integrative review. *Heart & Lung: The Journal of Acute and Critical Care* 42(3): 183-194.

Green BL and Rodgers A (2001) Determinants of social support among low-income mothers: a longitudinal analysis. *American Journal of Community Psychology* 29(3): 419-441.

Gross JJ and Thompson RA (2007) Emotion regulation: Conceptual foundations. In J. J. Gross (Ed.), *Handbook of emotion regulation* New York: Guilford Press.

Gross M and Lavie P (1994) Dreams in sleep apnea patients. *Dreaming* 4(3): 195-204.

Grunstein RR, Stenlöf K, Hedner JA, et al. (1995) Impact of self-reported sleep-breathing disturbances on psychosocial performance in the Swedish Obese Subjects (SOS) Study. *Sleep* 18(8): 635-643.

Guilleminault C (1990) Benzodiazepines, breathing, and sleep. *The American Journal of Medicine* 88(3): 25-28.

Guilleminault C, Stoohs R, Kim YD, et al. (1995) Upper airway sleep-disordered breathing in women. *Annals of Internal Medicine* 122: 493-501.

Gupta MA and Jarosz P (2018) Obstructive sleep apnea severity is directly related to suicidal ideation in posttraumatic stress disorder. *Journal of Clinical Sleep Medicine* 14(03): 427-435.

Gupta MA and Simpson FC (2015) Obstructive sleep apnea and psychiatric disorders: a systematic review. *Journal of Clinical Sleep Medicine* 11(2): 165-175.

Haack M and Mullington JM (2005) Sustained sleep restriction reduces emotional and physical well-being. *Pain* 119(1-3): 56-64.

Hadi MA, Alldred DP, Briggs M, et al. (2017) 'Treated as a number, not treated as a person': a qualitative exploration of the perceived barriers to effective pain management of patients with chronic pain. *Biomedical Journal Open* 7(6): <http://dx.doi.org/10.1136/bmjopen-2017-016454>.

Haines SJ, Gleeson J, Kuppens P, et al. (2016) The wisdom to know the difference: Strategy-situation fit in emotion regulation in daily life is associated with well-being. *Psychological Science* 27(12): 1651-1659.

Hanly P and Powles P (1993) Hypnotics should never be used in patients with sleep apnea. *Journal of Psychosomatic Research* 37: 59-65.

Harvey SB, Wessely S, Kuh D, et al. (2009). The relationship between fatigue and psychiatric disorders: evidence for the concept of neurasthenia. *Journal of Psychosomatic Research* 66(5): 445-454.

Haslam C, Jetten J, Cruwys T, et al. (2018) *The New Psychology of Health: Unlocking the Social Cure*, 1st Edition London Routledge: 510 pages, ISBN-13: 978-1138123885.

Heatley EM, Harris M, Battersby M et al. (2013) Obstructive sleep apnoea in adults: a common chronic condition in need of a comprehensive chronic condition management approach. *Sleep Medicine Reviews* 17(5): 349-355.

Hilbert J and Yaggi HK (2018) Patient-centered care in obstructive sleep apnea: a vision for the future. *Sleep Medicine Reviews* 37: 138-147.

Holt-Lunstad J, Smith, TW, Uchino BN (2008) Can hostility interfere with the health benefits of giving and receiving social support? The impact of cynical hostility on cardiovascular reactivity during social support interactions among friends. *Annals of Behavioral Medicine* 35(3): 319-330.

- Houston BK, and Vavak CR (1991) Cynical hostility: Developmental factors, psychosocial correlates, and health behaviors. *Health Psychology* 10(1): 9-17.
- Huang X, Tang S, Lyu X, et al. (2019) Structural and functional brain alterations in obstructive sleep apnea: a multimodal meta-analysis. *Sleep Medicine* 54: 195-204.
- Hurdie R, Riedy SM, Millet GP, et al. (2018) Cognitive performance and self-reported sleepiness are modulated by time-of-day during a mountain ultramarathon. *Research in Sports Medicine* 26(4): 482-489.
- Hussain SF, Irfan M, Waheed Z, et al. (2014) Compliance with continuous positive airway pressure (CPAP) therapy for obstructive sleep apnea among privately paying patients-a cross sectional study. *BioMed Central Pulmonary Medicine* 14(1): 188.
- Jack A and Pelphrey KA (2015) Neural correlates of animacy attribution include neocerebellum in healthy adults *Cerebral Cortex* 25(11): 4240-4247.
- Jackson ML, McEvoy RD, Banks S (2018) Neurobehavioral impairment and CPAP treatment response in mild-moderate obstructive sleep apnea. *Journal of Clinical Sleep Medicine* 14(1): 47-56.
- Jansson M and Linton SJ (2006) Psychosocial work stressors in the development and maintenance of insomnia: a prospective study. *Journal of Occupational Health Psychology* 11(3): 241-248.
- Jing J, Huang T, Cui W, et al. (2008) Effect on quality of life of continuous positive airway pressure in patients with obstructive sleep apnea syndrome: a meta-analysis. *Lung* 186(3): 131-144.
- Joiner TE (2007) Why people die by suicide. Harvard University Press, 288 pgs.
- Julian LJ (2011) Measures of anxiety: State-Trait Anxiety Inventory (STAI), Beck Anxiety Inventory (BAI), and Hospital Anxiety and Depression Scale-Anxiety (HADS-A). *Arthritis Care Research* 63(11): 467-472.
- Jull G (2017) Biopsychosocial model of disease: 40 years on. Which way is the pendulum swinging?. *BioMedical Journal*, <http://dx.doi.org/10.1136/bjsports-2016-097362>.
- Kaliterna LL, Prizmic LZ, Zganec N (2004) Quality of life, life satisfaction and happiness in shift-and non-shiftworkers. *Revista de Saúde Pública* 38: 3-10.
- Kaplan, RA, Hemink DA, Kenyon M (2018) *U.S. Patent No. 9,905,108*. Washington, DC: U.S. Patent and Trademark Office.
- Kang JM, Cho SJ, Lee YJ, et al. (2018) Comparison of Psychiatric Symptoms in Patients With Obstructive Sleep Apnea, Simple Snoring, and Normal Controls. *Psychosomatic Medicine* 80(2): 193-199.
- Kao CH Wang SH, Chen WS, et al. (2018) Benzodiazepines associated with acute respiratory failure in patients with obstructive sleep apnea. *Frontiers in Pharmacology* 9: 1513.
- Kapur VK (2018) Personalizing sleep apnea care. <https://doi.org/10.1093/sleep/zsy042>.
- Kempen GI, Jelicic M, Ormel J (1997) Personality, chronic medical morbidity, and health-related quality of life among older persons. *Health Psychology* 16(6): 539-546.
- Krabbe (2017) The Measurement of Health and Health Status: Concepts, Methods and Applications from a Multidisciplinary Perspective. Academic Press. Elsevier Inc. 380 pgs.
- Krakov B, Artar A, Warner TD, et al. (2000) Sleep disorder, depression and suicidality in female sexual assault survivors. *Crisis: The Journal of Crisis Intervention and Suicide Prevention* 21(4): 163-170.
- Krakov B, Ribeiro JD, Ulibarri VA, et al. (2011) Sleep disturbances and suicidal ideation in sleep medical center patients. *Journal of Affective Disorders* 131(1): 422-427.
- Krakov BJ, Ulibarri VA, Moore BA, et al. (2015) Posttraumatic stress disorder and sleep-disordered breathing: a review of comorbidity research. *Sleep Medicine Reviews*. 24: 37-45.
- Krokavcova M, Nagyova I, van Dijk JP, et al. (2008) Mastery, functional disability and perceived health status in patients with multiple sclerosis. *European Journal of Neurology* 15(11): 1237-1244.
- Kuhn E, Schwarz EI, Bratton DJ, et al. (2017) Effects of CPAP and MADs on health-related quality of life in OSA: a systematic review and meta-analysis. *Chest* 151(4): 786-794.
- Kushida CA (2007) *Obstructive sleep apnea: Diagnosis and treatment*. CRC Press. ISBN-1: 978-0-8493-9182-2.
- Kye SY and Park K (2017) Suicidal ideation and suicidal attempts among adults with chronic diseases: A cross-sectional study. *Comprehensive Psychiatry* 73: 160-167.

Lang CJ, Appleton S, Vakulin A, et al. (2016) Psychological and quality of life factors in men with comorbid Obstructive Sleep Apnea (OSA) and insomnia (Ins): a population study. In: *Sleep DownUnder 2016: 28th ASM of Australasian Sleep Association and Australasian Sleep Technologists Association* (20 October - 22 October 2016: Adelaide, Australia). *Journal of Sleep Research* 25(2): 14.

Lau EYY, Ip MSM, Lee TMC (2014) Neurcognitive and psychosocial outcomes of obstructive sleep apnea in Hong Kong Chinese. *Hong Kong Medical Journal* 20(7): 19-23.

Lau, EYY, Eskes, GA, Morrison DL, et al. (2013) The role of daytime sleepiness in psychosocial outcomes after treatment for obstructive sleep apnea. *Sleep Disorders*. <http://dx.doi.org/10.1155/2013/140725>.

Littlewood DL, Gooding P, Kyle SD, et al. (2016) Understanding the role of sleep in suicide risk: qualitative interview study. *Biomedical Journal Open* 6(8): e012113.

Littlewood DL, Kyle SD, Carter LA, et al. (2019) Short sleep duration and poor sleep quality predict next-day suicidal ideation: an ecological momentary assessment study. *Psychological Medicine* 49(3): 403-411.

Luyster FS, Dunbar-Jacob J, Aloia MS, et al. (2016) Patient and partner experiences with obstructive sleep apnea and CPAP treatment: a qualitative analysis. *Behavioral Sleep Medicine* 14(1): 67-84.

Malik S, Kanwar A, Sim LA, et al. (2014) The association between sleep disturbances and suicidal behaviors in patients with psychiatric diagnoses: a systematic review and meta-analysis. *The Cochrane Database of Systematic Reviews* 3(1): 18.

Marmot (2010) Foreword. In Cappuccio F, Miller MA and Lockley SW (Eds.) (2010) *Sleep, health, and society: From aetiology to public health*. Oxford University Press, USA. ISBN 978-0-19-956659-4.

Mars B, Heron J, Klonsky ED, et al. (2019) What distinguishes adolescents with suicidal thoughts from those who have attempted suicide? A population-based birth cohort study. *Journal of Child Psychology and Psychiatry* 60(1): 91-99.

Marshall NS, Neill AM, Campbell AJ, et al. (2005) Randomised controlled crossover trial of humidified continuous positive airway pressure in mild obstructive sleep apnoea. *Thorax* 60(5): 427-432.

Masa JF and Corral-Peñafiel J (2014) *Should use of 4 hours continuous positive airway pressure per night be considered acceptable compliance?* 44: 1119-1120.

McMahon JP, Foresman BH, Chisholm, RC (2003) The influence of CPAP on the neurobehavioral performance of patients with obstructive sleep apnea hypopnea syndrome: a systematic review. *Wisconsin Medical Journal* 102(1): 36-43.

Merino JS, de Torres LAP, Gómez RM, et al. (2017) Impact of CPAP therapy on health-related quality of life in elderly patients with apnoea-hypopnea syndrome: a systematic review of randomised clinical trials. *European Respiratory Journal* 49(1): 1601644.

Mermigkis C, Stagaki E, Amfilochiou A, et al. (2009) Sleep quality and associated daytime consequences in patients with idiopathic pulmonary fibrosis. *Medical Principles and Practice* 18(1): 10-15.

Mikula P, Nagyova I, Krokavcova M, et al. (2014) Coping and its importance for quality of life in patients with multiple sclerosis. *Disability and Rehabilitation* 36(9): 732-736.

Mikula P, Nagyova I, Krokavcova M, et al. (2018) Do coping strategies mediate the association between Type D personality and quality of life among people with multiple sclerosis? *Journal of Health Psychology* 23(12): 1557-1565.

Milad MR, Quirk, GJ, Pitman RK et al. (2007) A role for the human dorsal anterior cingulate cortex in fear expression. *Biological Psychiatry* 62: 1191-1194.

Moyer CA, Sonnad SS, Garetz SL, et al. (2001) Quality of life in obstructive sleep apnea: a systematic review of the literature. *Sleep Medicine* 2(6): 477-491.

Mulgrew AT, Ryan CF, Fleetham JA, et al. (2007) The impact of obstructive sleep apnea and daytime sleepiness on work limitation. *Sleep Medicine* 9(1): 42-53.

Muntingh AD, van der Feltz-Cornelis CM, van Marwijk HW, et al. (2011) Is the beck anxiety inventory a good tool to assess the severity of anxiety? A primary care study in The Netherlands study of depression and anxiety (NESDA). *BioMed Central Family Practice* 12(1): 66.

Nezamodini Z, Parisa H, Elham B, et al. (2014) Relationship between Shift works with sleep disorders and public health in a Pipe Co. *Safety Promotion and Injury Prevention* 2(3): 189-195.

Nock MK, Borges G, Bromet EJ, et al. (2008) Suicide and suicidal behavior. *Epidemiologic Reviews* 30(1): 133-154.

O'Connor R (2017) Suicide as (health) behaviour: towards a psychological understanding of suicidal behaviour. *European Health Psychologist* 19(4): 333-334.

Omachi TA, Claman DM, Blanc PD. (2009) Obstructive sleep apnea: a risk factor for work disability. *Sleep* 32(6): 791-798.

Owen JE, Benediktsdóttir B, Gislason T, et al. (2018) Neuropathological investigation of cell layer thickness and myelination in the hippocampus of people with obstructive sleep apnea. *Sleep* 42(1): 199.

Pagel JF and Parnes BL (2001) Medications for the treatment of sleep disorders: an overview. *Primary Care Companion to the Journal of Clinical Psychiatry* 3(3): 118-125.

Pagel JF and Kwiatkowski C (2010) The nightmares of sleep apnea: nightmare frequency declines with increasing apnea hypopnea index. *Journal of Clinical Sleep Medicine* 6(01): 69-73.

Parish JM and Lyng PJ (2003) Quality of life in bed partners of patients with obstructive sleep apnea or hypopnea after treatment with continuous positive airway pressure. *Chest* 124(3): 942-947.

Pearlin LI, Nguyen KB, Schieman S, et al. (2007) The life-course origins of mastery among older people. *Journal of Health and Social Behavior* 48(2): 164-179.

Peiffer C, Poline JB, Thivard L, et al. (2001) Neural substrates for the perception of acutely induced dyspnea. *American Journal of Respiratory and Critical Care Medicine* 163(4): 951-957.

Perfect MM, Archbold K, Goodwin JL, et al. (2013) Risk of behavioral and adaptive functioning difficulties in youth with previous and current sleep disordered breathing. *Sleep* 36(4): 517-525.

Perlis ML, Smith MT, Pigeon WR (2005) Principles and practice of sleep medicine. 4th ed. Philadelphia: Elsevier Saunders; Chapter 60, Etiology and pathophysiology of insomnia. p. 714-725.

Piferi RL and Lawler KA (2006) Social support and ambulatory blood pressure: An examination of both receiving and giving. *International Journal of Psychophysiology* 62(2): 328-336.

Pigeon WR, Britton PC, Ilgen MA, et al. (2012) Sleep disturbance preceding suicide among veterans. *American Journal of Public Health* 102(S1): 93-97.

Punjabi NM (2008) The epidemiology of adult obstructive sleep apnea. *Proceedings of the American Thoracic Society* 5(2): 136-143.

Raaijmakers LG, Martens MK, Hesselink, et al. (2014) Mastery and perceived autonomy support are correlates of Dutch diabetes patients' self-management and quality of life. *Patient Education and Counseling* 97(1): 75-81.

Rahaghi F and Basner RC (1999) Delayed diagnosis of obstructive sleep apnea: don't ask, don't tell. *Sleep and Breathing* 3(4): 119-124.

Reishtein JL, Pack AI, Maislin G, et al. (2006) Sleepiness and relationships in obstructive sleep apnea. *Issues in Mental Health Nursing* 27(3): 319-330.

Richens A (2001) Proof of efficacy trials: cross-over versus parallel-group. *Epilepsy Research* 45(1-3): 43-47.

Rotenberg BW, Murariu D, Pang KP (2016) (b) Trends in CPAP adherence over twenty years of data collection: a flattened curve. *Journal of Otolaryngology-Head & Neck Surgery* 45(1): 43 DOI 10.1186/s40463-016-0156-0.

Rotenberg BW, Vicini C, Pang EB, Pang KP (2016) (a) Reconsidering first-line treatment for obstructive sleep apnea: a systematic review of the literature. *Journal of Otolaryngology-Head & Neck Surgery* 45(1): 23, DOI 10.1186/s40463-016-0136-4.

Rowe JL, Conwell Y, Schulberg HC, et al. (2006) Social support and suicidal ideation in older adults using home healthcare services. *The American Journal of Geriatric Psychiatry* 14(9): 758-766.

Ryu HS, Lee SA, Lee GH, et al. (2016) Subjective apnoea symptoms are associated with daytime sleepiness in patients with moderate and severe obstructive sleep apnoea: a retrospective study. *Clinical Otolaryngology* 41(4): 395-401.

Saconi B, Watach AJ, Yang H, et al. (2018) Coping Processes and CPAP Use Among Adults with Obstructive Sleep Apnea. *Sleep* 41(1): 196-197.

Sanner BM, Klewer J, Trumm A et al. (2000) Long-term treatment with continuous positive airway pressure improves quality of life in obstructive sleep apnoea syndrome. *European Respiratory Journal* 16(1): 118-122.

Sasaki M and Yamasaki K (2002) Causal relationship between hostility and health status and the mediating role of stress coping. *Japanese Journal of Health Psychology* 15: 1-11.

Sawyer AM, Gooneratne NS, Marcus, CL, et al. (2011) A systematic review of CPAP adherence across age groups: clinical and empiric insights for developing CPAP adherence interventions. *Sleep Medicine Reviews* 15(6): 343-356.

Scholle S, Scholle HC, Kemper A, et al. (2003) First night effect in children and adolescents undergoing polysomnography for sleep-disordered breathing. *Clinical Neurophysiology* 114(11): 2138–2145.

Schulz R, Bischof F, Galetke W, et al. (2019) CPAP therapy improves erectile function in patients with severe obstructive sleep apnea. *Sleep Medicine* 53: 189–194.

Schwarzer R (2014) *Self-efficacy: Thought control of action*. Taylor & Francis. ISBN 1-56032-269-1. 405 pgs.

Shapiro AL (2014) Anxiety in middle-aged men with obstructive sleep apnea: State of the science. *Journal of the American Association of Nurse Practitioners* 26(12): 689–695.

Sharkey KM, Orff HJ, Tosi C, et al. (2013) Subjective sleepiness and daytime functioning in bariatric patients with obstructive sleep apnea. *Sleep and Breathing* 17(1): 267–274.

Shelgikar AV, Durmer JS, Joynt KE, et al. (2014) Multidisciplinary sleep centers: strategies to improve care of sleep disorders patients.” *Journal of Clinical Sleep Medicine* 10(6): 693–697.

Shneidman ES (1993) Suicide as psychache: A clinical approach to self-destructive behavior. Jason Aronson, 258 pgs.

Siegmán AW and Smith TW (Eds.) (2013) *Anger, hostility, and the heart*. Psychology Press, 285 pgs.

Silarova B, Nagyova I, Rosenberger J, et al. (2016) Sense of coherence as a mediator between hostility and health-related quality of life among coronary heart disease patients. *Heart & Lung: The Journal of Acute and Critical Care* 45(2): 126–131.

Simon RI (2014) Passive suicidal ideation: Still a high-risk clinical scenario. *Current Psychiatry* 13(3): 13–15.

Sloan FA, Padrón NA, Platt AC (2009) Preferences, Beliefs, and Self-Management of Diabetes. *Health Services Research* 44(3): 1068–1087.

Somers TJ, Shelby RA, Keefe FJ, et al. (2010) Disease severity and domain-specific arthritis self-efficacy: Relationships to pain and functioning in patients with rheumatoid arthritis. *Arthritis Care & Research* 62(6): 848–856.

Stanley B and Brown GK (2012) Safety planning intervention: a brief intervention to mitigate suicide risk. *Cognitive and Behavioral Practice* 19(2): 256–264.

Su VYF, Chen YT, Lin WC, et al. (2015) Sleep apnea and risk of panic disorder. *The Annals of Family Medicine* 13(4): 325–330.

Su VYF, Chen YT, Lin WC, et al. (2015) Sleep apnea and risk of panic disorder. *The Annals of Family Medicine* 13(4): 325–330.

Sundelin T, Lekander M, Sorjonen K. et al. (2017) Negative effects of restricted sleep on facial appearance and social appeal. *Royal Society Open Science* 4(5): 160918.

Tam S, Woodson BT, Rotenberg B (2014) Outcome measurements in obstructive sleep apnea: Beyond the apnea-hypopnea index. *The Laryngoscope* 124(1): 337–343.

Tiemensma J, Gaab E, Voorhaar M, et al. (2016) Illness perceptions and coping determine quality of life in COPD patients. *International Journal of Chronic Obstructive Pulmonary Disease* 11: 2001–2007.

Tramonti F, Maestri M, Carnicelli L, et al. (2017) Relationship quality of persons with obstructive sleep apnoea syndrome. *Psychology, Health & Medicine* 22(8): 896–901.

Tseng WC, Liang YC, Su MH, et al. (2018) Sleep apnea may be associated with suicidal ideation in adolescents. *European Child & Adolescent Psychiatry* 28(5): 635–643.

Ulfberg J, Carter N, Talbäck M, et al. (1996) Excessive daytime sleepiness at work and subjective work performance in the general population and among heavy snorers and patients with obstructive sleep apnea. *Chest* 110(3): 659–663.

Unal Y, Inanc L, Kutlu G, et al. (2017) Psychiatric morbidity of the patients with obstructive sleep apnea. *Sleep Medicine* 40: 330–331.

Vandervoort DJ (2006) Hostility and health: Mediating effects of belief systems and coping styles. *Current Psychology* 25(1): 50–66.

Vaske I, Kenn K, Keil DC, et al. (2017) Illness perceptions and coping with disease in chronic obstructive pulmonary disease: effects on health-related quality of life. *Journal of Health Psychology* 22(12): 1570–1581.

Wade DT and Halligan PW (2017) “The biopsychosocial model of illness: a model whose time has come.” 31: (8) 995–1004.

Weaver TE (2013) Don’t Start Celebrating—CPAP Adherence Remains a Problem. *Journal of Clinical Sleep Medicine* 9(6): 551–552.

Weaver TE and George CFP (2011) Cognition and performance in patients with obstructive sleep apnea. In: Kryger MH, Roth T, Dement WC, eds. *Principles and Practice of Sleep Medicine*. 5th ed. St. Louis, MO: Elsevier Saunders; 1194–1205.

Weaver TE, Maislin G, Dinges DF, et al. (2007) Relationship between hours of CPAP use and achieving normal levels of sleepiness and daily functioning. *Sleep* 30(6): 711–719.

Weldring T, Smith SMS (2013) Article Commentary: Patient-Reported Outcomes (PROs) and Patient-Reported Outcome Measures (PROMs). *Health Services Insights* 6: 61–68

Wenzlaff RM and Wegner DM (2000) Thought suppression. *Annual Review of Psychology* 51(1): 59–91.

Wetherell JL and Gatz M (2005) The Beck Anxiety Inventory in Older Adults With Generalized Anxiety Disorder. *Journal of Psychopathology and Behavioral Assessment* 27(1): 17–24.

Wiersema C, Van Zelst W, Voshaar RO (2018) When a patient with depression is feeling sleepy, be aware of sleep apnoea. *Biomedical Journal Case Reports*, bcr-2018.

Wild MR, Engleman HM, Douglas NJ, et al. (2004) Can psychological factors help us to determine adherence to CPAP? A prospective study. *European Respiratory Journal* 24(3): 461–465.

Williams JMG (2001) *The cry of pain: Understanding Suicide and Self-harm*. Penguin, London, 272 pgs.

Wilson IB and Cleary PD (1995) Linking clinical variables with health-related quality of life: a conceptual model of patient outcomes. *The Journal of the American Medical Association* 273(1): 59–65.

World Health Organization (2012) Public Health Action for the Prevention of Suicide: A Framework. Available at: <http://apps.who.int/iris/bitstream/10665/75166/1/9789241503570eng.pdf> (accessed 4 January 2018).

Ye L, Pien GW, Ratcliffe SJ, et al. (2014) The different clinical faces of obstructive sleep apnoea: a cluster analysis. *European Respiratory Journal* 44(6): 1600–1607.

Yilmaz Z, Sirinocak P, Voyvoda B, et al. (2017) Sexual Dysfunction in Premenopausal Women With Obstructive Sleep Apnea. *Urology Journal* 14(6): 5051–5056.

Zautra AJ, Davis MC, Reich JW, et al. (2012) Phone-based interventions with automated mindfulness and mastery messages improve the daily functioning for depressed middle-aged community residents. *Journal of Psychotherapy Integration* 22(3): 206–228.

Zhang XJ, Li QY, Wang Y, et al. (2014) The effect of non-benzodiazepine hypnotics on sleep quality and severity in patients with OSA: a meta-analysis. *Sleep and Breathing* 18(4): 781–789.

Zimmerman ME, Arnedt JT, Stanchina M, et al (2006) Normalization of memory performance and positive airway pressure adherence in memory-impaired patients with obstructive sleep apnea. *Chest* 130(6): 1772–1778.

"Unlike stories, real life, when
it has passed, inclines toward
obscurity, not clarity."

Elena FERRANTE

Summary

This thesis studied patients with obstructive sleep apnoea (OSA) who face the burden of this chronic disease in their everyday lives. OSA represents one of the most widespread sleep disorders that requires lifetime care. It has serious consequences, not only for patients and their families, but also for society as a whole. Thus, regarding clinical care, one of the main goals is to improve patients' daily functioning and well-being. While medical treatment of OSA may help to improve physical symptoms of the disease, existing psychological impairment still cannot be successfully cured. Therefore, in clinical sleep medicine, the main focus has shifted from OSA diagnosis to OSA management, with the emergence of new, integrated models of care. Thus, this thesis seeks to address the psycho-social factors that have been identified as one of the key factors in the adaptation to various chronic diseases, but less are known in OSA yet. This thesis further aims to contribute to the understanding of the associations between biomedical factors and self-reported health outcomes in OSA patients that have been identified as ambivalent in previous research.

Chapter 1 provides a general introduction of OSA. It further describes the key theoretical constructs of the thesis: continuous positive airway pressure (CPAP) treatment, sleep-related problems, anxiety, hostility, coping self-efficacy, mastery over one's life and circumstances, and social support. Health-related outcomes were identified as quality of life (QoL), functional status, work functioning, and psychological distress, including suicidal ideation. This chapter also introduces the conceptual model of the associations between constructs examined in the thesis.

Chapter 2 presents information about the study design. It describes the sample and procedure of the data collection, and settings used in the thesis. It also provides a description of the measures and used statistical analyses.

Chapter 3 examines the effect of CPAP treatment on QoL, when compared to placebo pills, sham CPAP, and conservative treatment. We found no significant differences in overall and psychological QoL between CPAP treated patients and controls. However, physical QoL improved in CPAP treated patients compared with control treatments. Furthermore, subgroup analyses and sensitivity analyses showed that the type of control group, the study design, OSA severity, and risk of bias may be relevant in capturing the effect of CPAP on QoL. However, high-quality trials with low risk of bias and more participants are needed for further investigation of the effect of CPAP treatment on QoL improvement.

Chapter 4 examines whether OSA-severity, sleep-related problems, and anxiety are associated with work functioning in OSA patients when controlled for age, gender, and type of occupation. It also investigates whether anxiety moderates the associations between sleep-related problems and work functioning. We found that the majority of working OSA patients was anxious and had impaired work functioning. The results of our study further showed that poor night-time sleep quality and anxiety

were associated with impaired work functioning. The moderating effect of anxiety on the association between night-time sleep quality and work functioning was especially strong in patients with better sleep quality, while the effect of anxiety on the association between night-time sleep quality and work functioning was negligible in case of worse sleep quality.

Chapter 5 examines the associations between hostility, coping self-efficacy and psychological distress in OSA patients when controlled for sociodemographic, clinical, and sleep-related variables. It further explores whether coping self-efficacy dimensions mediate the association between hostility and psychological distress. Our study revealed that hostility and poor coping self-efficacy were strongly associated with psychological distress in OSA patients. We also found that all coping self-efficacy dimensions mediated the association between hostility and psychological distress. Our study further provided the evidence that coping self-efficacy for stopping unpleasant emotions and thoughts was found to be the most adaptive strategy in OSA patients.

Chapter 6 describes the prevalence of suicidal ideation in patients with OSA. It also examines the associations between OSA severity, sleep-related problems, social support and suicidal ideation in OSA patients. Our findings suggest that suicidal ideation is highly prevalent among OSA patients (20.1%). Poor night-time sleep quality and fatigue were directly related to suicidal ideation, however OSA severity and social support were not. The adjustment for sociodemographic variables did not change the association between social support and suicidal ideation either. Sleep quality mediated the effect of OSA severity on suicidal ideation.

Chapter 7 examines the associations between social support, mastery, sleep-related problems and functional status in patients with OSA when controlled for sociodemographic and clinical variables. It also investigates the mediating role of social support and mastery in the association between sleep-related problems and functional status. Our results provided suggestive evidence that low level of social support, poor mastery, disturbed night-time sleep quality, and daytime sleepiness were associated with an impairment in functional status in OSA patients. While social support was weakly associated with functional status, we found a strong association between mastery and overall functional status in OSA patients. The subscale analyses showed that social support was strongly associated with one functional status subscale, i.e. intimacy-sexual relationships, while mastery was associated with all functional status subscales in the final models. We found that mastery mediated the association between sleep-related problems and functional status. However, no mediating role of social support in the association between sleep-related problems and functional status was observed.

Finally, in *Chapter 8* we summarise the key findings as presented in the Chapters 3-7, discussed them in the context of contemporary scientific research and provided implications. In line with previous studies, the results of our meta-analysis confirmed that CPAP treatment may help to improve physical symptoms of OSA, whereas existing psychological impairment still cannot be successfully cured. Therefore, the current research and clinical practice should focus not only on the standard treatment of OSA, but also on ensuring that psychological symptoms are efficiently managed.

Our findings may also enhance health care professionals' understanding of the mental health problems in OSA patients. Next, our study provided evidence for high prevalence of overall psychological distress in OSA patients including suicidal ideation and anxiety. Thus, the necessity of monitoring psychological symptoms in OSA patients during clinical care should be highlighted. The education of people with OSA on basic sleep hygiene and application of behavioural interventions may improve the quality of sleep and decrease fatigue strongly associated with self-reported health outcomes. Health care professionals may also directly recommend targeted psychological care, which starts early in the OSA trajectory and may help to prevent serious problems later on. Moreover, identifying patients with overlapping symptoms of mental disorders and OSA may help to improve the diagnostic process and treatment outcomes through careful dosing of pharmacotherapy and use of CPAP treatment.

Another interesting observation to emerge from our study was that the external resources related to social support explained less variance in health outcomes when compared to intra-individual psychological resources such as mastery and coping-self-efficacy focused on stopping unpleasant emotions and thoughts or problem focused coping self-efficacy. Based on these results we may conclude that helping OSA patients to strengthen their intra-individual resources may be one of the important protective strategies, attenuating the negative impact of OSA-related symptoms. Therefore, encouraging mastery over one's life and circumstances, and dispelling coping self-efficacy may be paramount in improving functional status and handling the psychological distress in OSA patients. Still, we found that social support was strongly associated with one functional status subscale, i.e. intimacy-sexual relationships. Thus, the revealed significance of sources of social support in intimate relationships should be addressed as previous studies identified poor health-related outcomes not only in OSA patients, but also in their bed-partners.

Chapter 8 also addresses the methodological considerations and future research implications of the study. Strengths of this study include OSA diagnosis stated using polysomnography. Results of our study may be helpful in identifying bio-psycho-social risk factors of poor health outcomes that can be modified by health care professionals or by the patients themselves. Multidisciplinary OSA care can help to reduce effort duplication, minimize fragmentation of care, control costs, improve risk assessment for the consequences of untreated OSA, and lead to better treatment strategies. All in all, our study has led us to conclude that impairment of health outcomes in OSA patients may not be solely due to biomedical factors or the effect of OSA itself. Rather, psychological factors such as anxiety, hostility, the choice of coping strategies, or mastery, may play a key role in determining the experience of poor health. However, further longitudinal confirmation of our results is needed.

Sammenvattig

Dit proefschrift bestudeert patiënten met obstructieve slaapapneu (OSA) die in hun dagelijks leven geconfronteerd worden met de last van deze chronische ziekte. OSA is een van de meest voorkomende slaapstoornissen waarvoor levenslang zorg nodig is. Het heeft ernstige gevolgen, niet alleen voor patiënten en hun families, maar ook voor de samenleving als geheel. Wat klinische zorg betreft, is één van de hoofddoelen het verbeteren van het dagelijks functioneren en welzijn van patiënten. Hoewel medische behandeling van OSA kan helpen de fysieke symptomen van de ziekte te verbeteren, kunnen bestaande psychische klachten nog steeds niet met succes worden genezen. In de klinische slaapgeneeskunde is met de opkomst van nieuwe, geïntegreerde zorgmodellen de nadruk verschoven van de OSA-diagnose naar het omgaan met OSA. Dit proefschrift zal ingaan op de psychosociale factoren die zijn geïdentificeerd als sleutelfactoren bij de aanpassing aan verschillende chronische ziekten, maar bij OSA zijn er minder zulke factoren bekend. Dit proefschrift beoogt verder bij te dragen aan het begrip van de associaties tussen biomedische factoren en zelfgerapporteerde gezondheid bij OSA-patiënten die in eerder onderzoek als niet-doorslaggevend zijn geïdentificeerd.

In *Hoofdstuk 1* wordt een algemene introductie van OSA gegeven. De belangrijkste theoretische constructen van het proefschrift worden beschreven: continue positieve luchtweg-druk (CPAP), slaapgerelateerde problemen, angst, vijandigheid, zelfredzaamheid, eigen effectiviteit, beheersing van iemands leven en omstandigheden, en sociale steun. De gezondheidsgelateerde uitkomstmaten die zijn gebruikt zijn kwaliteit van leven (KvL), functionele status, functioneren in het werk en psychische klachten, inclusief zelfmoordgedachten. Dit hoofdstuk introduceert ook het conceptuele model van de verbanden tussen de constructen die in het proefschrift zijn onderzocht.

Hoofdstuk 2 geeft informatie over de onderzoeksopzet. Het beschrijft de steekproef en de procedure van de gegevensverzameling die in het proefschrift zijn gebruikt. Het geeft ook een beschrijving van de meetinstrumenten en gebruikte statistische analyses.

In *Hoofdstuk 3* wordt het effect van CPAP-behandeling op KvL onderzocht, in vergelijking met placebo-pillen, schijn-CPAP en conservatieve behandeling. We vonden geen significante verschillen in de totale en psychologische KvL tussen met CPAP behandelde patiënten en controles. De fysieke KvL verbeterde echter bij met CPAP behandelde patiënten in vergelijking met de controlebehandelingen. Verder toonden subgroepanalyses en sensitiviteitsanalyses aan dat het type controlegroep, de onderzoeksopzet, de ernst van OSA en het risico op bias relevant kunnen zijn bij het bepalen van het effect van CPAP op de KvL. Kwalitatief hoogwaardige onderzoeken met een laag risico op bias en meer deelnemers zijn nodig voor verder onderzoek naar het effect van CPAP-behandeling op KvL verbetering.

In *Hoofdstuk 4* wordt onderzocht of de ernst van OSA, slaapgerelateerde problemen en angst geassocieerd zijn met het functioneren in het werk bij OSA-patiënten als gecontroleerd wordt voor leeftijd, geslacht en type beroep. Ook wordt onderzocht of angst de verbanden tussen slaapgerelateerde problemen en functioneren in het werk beïnvloedt. We vonden dat de meerderheid van de werkende OSA-patiënten angstig was en dat het functioneren in het werk belemmerd was. De resultaten van onze studie toonden verder aan dat slechte nachtelijke slaapkwaliteit en angst geassocieerd waren met een verminderd functioneren in het werk. Het modererende effect van angst op het verband tussen nachtelijke slaapkwaliteit en functioneren in het werk was vooral sterk bij patiënten met een betere slaapkwaliteit, terwijl het effect van angst op het verband tussen nachtelijke slaapkwaliteit en functioneren in het werk te verwaarlozen was in het geval van slechte slaapkwaliteit.

In *Hoofdstuk 5* worden de verbanden onderzocht tussen vijandigheid, eigen effectiviteit en psychische klachten bij OSA-patiënten als deze gecontroleerd worden voor sociodemografische, klinische en slaapgerelateerde variabelen. Verder wordt onderzocht of dimensies van eigen effectiviteit het verband tussen vijandigheid en psychische klachten mediëren. Onze studie toonde aan dat vijandigheid en lage eigen effectiviteit sterk geassocieerd waren met psychische klachten bij OSA-patiënten. We ontdekten ook dat alle dimensies van eigen effectiviteit het verband mediëerden tussen vijandigheid en psychische klachten. Ons onderzoek leverde verder op dat eigen effectiviteit in de zin van het stoppen van onaangename emoties en gedachten de meest adaptieve strategie bleek te zijn bij OSA-patiënten.

In *Hoofdstuk 6* wordt de prevalentie beschreven van suïcidale gedachten bij patiënten met OSA. Ook worden de verbanden onderzocht tussen de ernst van OSA, de slaapgerelateerde problemen, de sociale steun en de suïcidale ideeën bij OSA-patiënten. Onze bevindingen suggereren dat suïcidale ideeën zeer gangbaar zijn bij OSA-patiënten (20,1%). Slechte nachtelijke slaapkwaliteit en vermoeidheid waren direct gerelateerd aan suïcidale ideeën, maar de ernst van OSA en sociale steun waren dat niet. De controle voor sociodemografische variabelen veranderde ook het verband tussen sociale steun en suïcidale ideeën niet. Slaapkwaliteit mediëerde het effect van OSA-ernst op suïcidale gedachten.

In *Hoofdstuk 7* worden de verbanden onderzocht tussen sociale steun, beheersing, slaapgerelateerde problemen en functionele status bij patiënten met OSA die gecontroleerd werden voor sociodemografische en klinische variabelen. Ook wordt de mediërende rol van sociale steun en beheersing in het verband tussen slaapgerelateerde problemen en functionele status onderzocht. Onze resultaten leverden suggestief bewijs op dat een laag niveau van sociale steun, een slechte beheersing, verstoorde nachtelijke slaapkwaliteit en slaperigheid overdag een verband hebben met een verslechtering van de functionele status bij OSA-patiënten. Hoewel er tussen sociale steun en functionele status een zwak verband was, vonden we een sterk verband tussen beheersing en functionele status bij OSA-patiënten. De subschaalanalyses toonden aan dat sociale steun sterk geassocieerd was met één subschaal van functionele status, te weten die van intimiteit-seksuele relaties, terwijl beheersing geassocieerd was met alle subschalen van functionele status in de uiteindelijke modellen. We ontdekten

dat beheersing het verband tussen slaapgerelateerde problemen en functionele status mediëerde. Zo een mediërende rol werd niet van sociale steun waargenomen met betrekking tot het verband tussen slaapgerelateerde problemen en functionele status.

Tenslotte vatten we in *hoofdstuk 8* de belangrijkste bevindingen samen zoals gepresenteerd in de hoofdstukken 3-7, we bespreken de bevindingen in de context van het hedendaags wetenschappelijk onderzoek en geven implicaties aan. In overeenstemming met eerdere studies, bevestigden de resultaten van onze meta-analyse dat CPAP-behandeling kan helpen om fysieke symptomen van OSA te verbeteren, terwijl bestaande psychische klachten nog steeds niet met succes kunnen worden behandeld. Daarom moet het huidige onderzoek en de klinische praktijk niet alleen gericht zijn op de standaardbehandeling van OSA, maar ook op het waarborgen van een efficiënte behandeling van psychische problemen. Onze bevindingen kunnen ook de kennis van zorgverleners over psychische problemen bij OSA-patiënten verbeteren. Vervolgens liet ons onderzoek een hoge prevalentie van algemene psychische klachten bij OSA-patiënten zien, inclusief zelfmoordgedachten en angst. Daarom is het uitermate belangrijk deze psychische klachten bij OSA-patiënten tijdens de klinische zorg te monitoren. Het kennisniveau van OSA-patiënten over elementaire slaaphygiëne en de toepassing van gedragsinterventies kan de slaapkwaliteit verbeteren en vermoeidheid verminderen, en is sterk verbonden met de zelfgerapporteerde gezondheid. Gezondheidszorgprofessionals kunnen ook direct psychologische zorg op maat aanbevelen, die vroeg in het OSA-traject begint en later kan helpen ernstige problemen te voorkomen. Bovendien kan het identificeren van patiënten met symptomen van zowel psychische problemen en OSA helpen het diagnostische proces en de behandelresultaten door zorgvuldige dosering van farmacotherapie en het gebruik van de CPAP-behandeling te verbeteren.

Een andere interessante observatie die uit onze studie naar voren kwam, was dat de externe bronnen met betrekking tot sociale steun minder variantie in gezondheidsuitkomsten verklaarden in vergelijking met intra-individuele psychologische bronnen zoals beheersing en eigen effectiviteit die gericht is op het stoppen van onaangename emoties en gedachten of probleemgericht omgaan met zelfredzaamheid. Op basis van deze resultaten kunnen we concluderen dat het helpen versterken van intra-individuele bronnen bij OSA-patiënten één van de belangrijke beschermende strategieën kan zijn, waardoor de negatieve impact van OSA-gerelateerde symptomen wordt verzacht. Het aanmoedigen van beheersing van iemands leven en omstandigheden en eigen effectiviteit kunnen van groot belang zijn bij het verbeteren van de functionele status en het omgaan met de psychische klachten bij OSA-patiënten. Ook vonden we een sterk verband tussen sociale steun en één subschaal van functionele status, te weten de subschaal intimiteit-seksuele relaties. Daarom zou sociale steun in intieme relaties moeten worden aangepakt, ook omdat eerdere studies slechte gezondheidsgerelateerde uitkomsten rapporteerden, niet alleen bij OSA-patiënten zelf, maar ook bij hun bedpartners.

Hoofdstuk 8 behandelt ook de methodologische overwegingen en toekomstige implicaties van het onderzoek voor verder onderzoek en de praktijk. Sterke punten van deze studie zijn dat de diagnose OSA gesteld is met behulp van polysomnografie.

Resultaten van ons onderzoek kunnen helpen bij het identificeren van bio-psycho-sociale risicofactoren voor slechte gezondheidssuitkomsten, die kunnen worden aangepast door gezondheidszorgprofessionals of door de patiënten zelf. Multidisciplinaire OSA-zorg kan helpen een verdubbeling van inspanningen te verminderen, versnippering van zorg te minimaliseren, kosten te beheersen, risicobeoordeling voor de gevolgen van onbehandelde OSA te verbeteren en kan tot betere behandelstrategieën leiden. Al met al heeft ons onderzoek ons ertoe gebracht te concluderen dat een verslechtering van de gezondheidssuitkomsten bij OSA-patiënten mogelijk niet alleen te wijten is aan biomedische factoren of aan het effect van OSA zelf. Integendeel, psychologische factoren zoals angst, vijandigheid, de keuze van strategieën met betrekking tot eigen effectiviteit of beheersing kunnen een belangrijke rol spelen bij het bepalen van de ervaring van slechte gezondheid. Een bevestiging van onze resultaten in longitudinaal onderzoek is echter nodig.

Obštrukčné spánkové apnoe (OSA) predstavuje jednu z najrozšírenejších porúch spánku, ktorá si vyžaduje celoživotnú liečbu. Toto ochorenie má vážne dôsledky nielen pre pacientov a ich rodiny, ale aj pre spoločnosť ako celok. Jedným z hlavných cieľov klinickej starostlivosti je zlepšiť každodenné fungovanie pacientov a ich well-being. Medicínska starostlivosť môže pomôcť zlepšiť fyzické príznaky ochorenia ale existujúce psychologické symptómy však stále nie je možné u pacientov s OSA úspešne vyliečiť. Vzhľadom na to presúva súčasná spánková medicína primárny dôraz z diagnostiky OSA na manažment ochorenia s využitím nových, integrovaných modelov starostlivosti. Cieľom tejto štúdie je popísať úlohu psycho-sociálnych faktorov, ktoré boli identifikované ako jeden z kľúčových aspektov pri adaptácii na rôzne chronické ochorenia, ale sú menej známe v oblasti OSA. Táto práca sa ďalej snaží prispieť k pochopeniu asociácií medzi biomedicínskymi faktormi a seba-posudzovaným zdravím u pacientov s OSA, ktoré boli v predchádzajúcom výskume identifikované ako ambivalentné.

Prvá kapitola poskytuje všeobecný úvod do problematiky OSA. Ďalej opisuje kľúčové teoretické konštrukty tejto práce: liečbu kontinuálnym pozitívnym tlakom v dýchacích cestách (CPAP), problémy súvisiace so spánkom, anxiétu, hostilitu, copingovú seba-účinnosť, schopnosť zvládania životných okolností a sociálnu oporu. Výstupy súvisiace so seba-posudzovaným zdravím boli identifikované ako kvalita života, funkčný stav, úroveň pracovnej funkčnosti a psychologické symptómy vrátane samovražedných myšlienok. Táto kapitola ďalej definuje konceptuálny model asociácií medzi konštruktnými skúmanými v tejto štúdii a jednotlivé výskumné otázky.

V druhej kapitole poskytujeme informácie o dizajne štúdie. V tejto kapitole popisujeme výskumnú vzorku, postup zberu údajov, použité nástroje merania a štatistické analýzy.

Tretia kapitola skúma efekt CPAP liečby na kvalitu života v porovnaní s placebo tabletami, simulovanou CPAP a konzervatívnou liečbou. U pacientov liečených CPAP sme nezistili významné rozdiely v celkovej a psychologickej kvalite života v porovnaní so skupinou pacientov podstupujúcou kontrolnú liečbu. Na druhej strane sme zistili, že fyzická kvalita života sa u pacientov liečených CPAP sa v porovnaní s kontrolnou skupinou významne zlepšila. Analýzy ďalej ukázali, že typ kontrolnej skupiny, dizajn štúdie, závažnosť ochorenia a risk of bias môžu zohrávať relevantnú úlohu pri meraní účinku CPAP na kvalitu života. Na presnejšie stanovenie úrovne účinku CPAP liečby na kvalitu života pacientov s OSA je však potrebné väčšie množstvo kvalitných štúdií s nízkou úrovňou risk of bias a väčšou výskumnou vzorkou.

Štvrtá kapitola skúma či závažnosť OSA, problémy súvisiace so spánkom a anxieta súvisia s úrovňou pracovnej funkčnosti u pacientov s OSA. Pri overovaní našej výskumnej otázky sme uplatnili kontrolu asociácií vzhľadom na vek, pohlavie a typ zamestnania. Ďalším predmetom skúmania bolo posúdenie moderačného efektu

anxiety na asociácie medzi problémami súvisiacimi so spánkom a úrovňou pracovnej funkčnosti. Zistili sme, že väčšina pracujúcich pacientov s OSA vykazovala zvýšenú úroveň anxiety a zníženú úroveň pracovnej funkčnosti. Výsledky našej štúdie ďalej ukázali, že nízka kvalita nočného spánku a zvýšená úroveň anxiety súviseli so zníženou úrovňou pracovnej funkčnosti. Moderačný efekt anxiety na asociáciu medzi kvalitou nočného spánku a úrovňou pracovnej funkčnosti bol obzvlášť signifikantný u pacientov s lepšou kvalitou spánku, zatiaľ čo moderačný vplyv anxiety na asociáciu medzi kvalitou nočného spánku a úrovňou pracovnej funkčnosti bol zanedbateľný v prípade nízkej kvality spánku.

Piatá kapitola skúma asociácie medzi hostilitou, copingovou seba-účinnosťou a psychologickým distresom u pacientov s OSA. Skúmané asociácie boli kontrolované berúc do úvahy sociodemografické, klinické a spánkové premenné. Táto kapitola ďalej skúma, či jednotlivé dimenzie copingovej seba-účinnosti mediujú asociáciu medzi hostilitou a psychologickým distresom. Naša štúdia ukázala, že hostilita a nízka úroveň copingovej seba-účinnosti boli u pacientov s OSA silne spojené s psychologickým distresom. Taktiež sme zistili, že všetky posudzované dimenzie copingovej seba-účinnosti mali mediačný efekt na asociáciu medzi hostilitou a psychologickým distresom. Táto štúdia ďalej poskytla dôkazy o tom, že najúčinnnejšiu copingovú stratégiu u pacientov s OSA predstavuje seba-účinnosť zameraná na zastavenie nepríjemných emócií a myšlienok.

Šiesta kapitola opisuje výskyt samovražedných myšlienok u pacientov s OSA. Skúma tiež súvislosť medzi závažnosťou OSA, problémami súvisiacimi so spánkom, sociálnou oporou a samovražednými myšlienkami u pacientov s OSA. Naše zistenia naznačujú, že suicidálne myšlienky sú u pacientov s OSA alarmujúco prevalentné (20.1%). Nízka kvalita nočného spánku a únava vykazovali priamu súvislosť so samovražednými myšlienkami, avšak naša štúdia nenašla signifikantný vzťah medzi závažnosťou OSA, ospalosťou počas dňa, sociálnou oporou a suicidálnymi myšlienkami. Kontrola pre sociodemografické premenné neovplyvnila absentujúcu signifikanciu vzťahu medzi ospalosťou počas dňa, sociálnou oporou a samovražednými myšlienkami. Kvalita spánku mala mediačný efekt na vzťah medzi závažnosťou OSA a samovražednými myšlienkami.

Siedma kapitola skúma asociácie medzi sociálnou oporou, úrovňou zvládania životných okolností, problémami súvisiacimi so spánkom a funkčným stavom u pacientov s OSA. Skúmané asociácie boli kontrolované berúc do úvahy sociodemografické a klinické premenné. Táto kapitola zároveň skúma mediačný efekt sociálnej opory a úrovne zvládania životných okolností na asociáciu medzi problémami súvisiacimi so spánkom a funkčným stavom. Naše výsledky poskytli sugestívne dôkazy o tom, že nízka úroveň sociálnej opory, nízka schopnosť zvládania, narušená kvalita nočného spánku a denná ospalosť boli u pacientov s OSA spojené s nízkou úrovňou funkčného stavu. Zatiaľ čo sociálna opora bola len nevýrazne asociovaná s celkovým funkčným stavom, zistili sme signifikantnú asociáciu medzi schopnosťou zvládania a celkovým funkčným stavom. Analýzy subškál ukázali, že sociálna opora bola signifikantne asociovaná s jednou subškálou funkčného statusu, t. j. intimita-sexuálne vzťahy, zatiaľ čo schopnosť zvládania bola asociovaná so všetkými subškálami funkčného stavu. Zistili

sme, že schopnosť zvládania mala mediačný efekt na asociáciu medzi problémami súvisiacimi so spánkom a funkčným stavom. Nepozorovali sme však mediačný efekt sociálnej opory na asociáciu medzi problémami súvisiacimi so spánkom a funkčným stavom.

Ôsma kapitola sumarizuje kľúčové zistenia prezentované v kapitolách 3-7, obsahuje diskusiu našich zistení v kontexte súčasných vedeckých poznatkov a poskytuje implikácie pre prax a ďalší výskum. V súlade s predchádzajúcimi štúdiami, výsledky našej metaanalýzy potvrdili, že liečba CPAP môže pomôcť zlepšiť fyzické príznaky OSA, zatiaľ čo existujúce psychologické poškodenia často nie je možné úspešne minimalizovať. Súčasný výskum a klinická prax by sa preto mali zamerať nielen na štandardnú liečbu OSA, ale aj na zabezpečenie efektívneho manažmentu psychologických symptómov. Naše zistenia môžu tiež zlepšiť pochopenie problematiky duševného zdravia u pacientov s OSA. Naša štúdia poskytla dôkazy o zvýšenej prevalencii celkového psychologického distresu u pacientov s OSA, vrátane samovražedných myšlienok a anxiety. Preto je následne potrebné zdôrazniť adekvátnosť monitorovania psychologických symptómov u pacientov s OSA počas klinickej starostlivosti. Vzdelávanie ľudí s OSA v oblasti základnej spánkovej hygieny a aplikácie behaviorálnych intervencií môže zlepšiť kvalitu spánku a znížiť únavu, ktorá je u týchto pacientov významne spojená so seba-posudzovaným zdravím. Zdravotnícki pracovníci môžu pacientom priamo odporučiť ciele a včasnú psychologickú starostlivosť, ktorá môže zamedziť neskoršiemu vzniku vážnych problémov. Identifikácia pacientov s prekrývajúcimi sa príznakmi duševných porúch a OSA môže navyše pomôcť k zlepšeniu diagnostických procesov a výsledkov liečby prostredníctvom starostlivého dávkovania farmakoterapie a aplikácie CPAP liečby.

Ďalším zaujímavým pozorovaním, ktoré vyplynulo z našej štúdie, bolo, že externé zdroje súvisiace so sociálnou oporou boli menej signifikantne asociované so seba-posudzovaným zdravím v porovnaní s inter-individuálnymi psychologickými zdrojmi, ako je celková úroveň zvládania životných okolností a coping zameraný na zastavenie nepríjemných emócií a myšlienok. Na základe týchto výsledkov predpokladáme, že facilitácia inter-individuálnych zdrojov môže predstavovať jednu z dôležitých ochranných stratégií, pri zmiernení negatívneho vplyvu symptómov OSA na seba-posudzované zdravie. Podpora schopnosti zvládania a copingovej seba-účinnosti môže preto predstavovať jeden z rozhodujúcich faktorov v rámci zlepšovania funkčného stavu a zvládania psychologického distresu u pacientov s OSA. Nesmieme však zabudnúť na naše zistenie, že sociálna opora bola významne spojená s jednou funkčnou subškálou, t. j. intímne-sexuálne vzťahy. Vzhľadom na skutočnosť, že predchádzajúce štúdie identifikovali negatívne zdravotné dôsledky OSA nielen u pacientov s týmto ochorením, ale u ich partnerov, význam sociálnej opory v partnerských vzťahoch by mal byť ďalším predmetom skúmania.

Ôsma kapitola následne popisuje limity tejto štúdie a sumarizuje odporúčania pre klinickú prax a ďalší výskum. Silné stránky tejto štúdie zahŕňajú diagnostiku OSA s využitím polysomnografie. Výsledky našej štúdie môžu byť užitočné pri identifikácii bio-psycho-sociálnych faktorov, ktoré môžu ovplyvniť zdravie pacientov s OSA, a ktoré môžu byť následne manažované zdravotníckymi pracovníkmi a v neposlednom

rade aj samotnými pacientmi. Multidisciplinárna starostlivosť o pacientov s OSA môže zamedziť duplikovaniu úkonov, minimalizovať fragmentáciu starostlivosti, znížiť náklady na kontrolu, zlepšiť posúdenie rizika následkov neliečeného OSA a viesť k efektívnejším stratégiám liečby. Naša štúdia viedla k záveru, že zhoršenie seba-posudzovaného zdravia u pacientov s OSA nemusí byť spôsobené len biomedicínskymi faktormi alebo samotným ochorením. Psychologické faktory ako sú anxieta, hostilita, typ copingovej seba-účinnosti alebo celková schopnosť zvládať životné okolnosti môžu zohrávať kľúčovú úlohu pri určovaní úrovne seba-posudzovaného zdravia u pacientov s OSA. Výsledky našej štúdie je však potrebné potvrdiť longitudinálnymi štúdiami.

Acknowledgements

*"We are such stuff as dreams are made on,
and our little life is rounded with a sleep."*

William Shakespeare, The Tempest

Getting a PhD can be challenging and isolating. As my favourite novelist Haruki Murakami says; sometimes I just felt like like being in a "sandstorm that keeps changing directions. You change direction but the sandstorm chases you. You turn again, but the storm adjusts. And you really will have to make it through that metaphysical, symbolic storm. And once the storm is over you won't remember how you made it through.... You won't even be sure, in fact, whether the storm is really over. But one thing is certain. When you come out of the storm you won't be the same person who walked in. That's what this storm's all about." Thankfully, I was not alone and there were many people who were willing to give me helping hand, supported me, cheered me and helped me to not give up, and for that, I am grateful. The range of people I intrinsically would like to thank is broad.

First of all, I want to thank to my family. *Mamka, ocko, ďakujem vám za zázemie, ktoré ste mi vytvorili, za vašu lásku a za všetku oporu a dôveru. Veľmi Vás ľúbim. Moja vďaka patrí aj Vám, drahá babka a Teta Babika. Ďakujem za múdre rady a podporu. My dearest uncle, you had to stand in the most difficult storm I could ever imagine. So all you could do was "give in to it, inside the storm, closing your eyes and plugging up your ears so the sand doesn't get in, and walk through it, step by step. There was no sun there, no moon, no direction, no sense of time." I am so sorry we were not able to beat this storm, there was no "safe flight" as you used to say, and we could just brace for impact. You gave me one of the most important lessons by showing me how brave you were in your fight. I will always love you. I couldn't have had better uncle.*

The next thank you goes to my soulmate. *Rištek, ďakujem, že si mi ukázal, čo je v živote dôležité, že si ma veľa naučil, že to so mnou nikdy nevzdal. Ďakujem z celého srdca za tvoju oporu, silu, rozvahu, lásku, pokoru a trpezlivosť v zdraví aj chorobe, krásnych aj ťažkých časoch. Lúbim ťa, liebling.*

Next, I would like to say big thank you to my colleagues and former colleagues – my office soulmate Pavol Mikula, my dear Alexandra Husivargova, Katarina Petrikova, Martina Behanova, Peter Kolarcik, Janka Holubcikova, Janka Buckova, Laura Kundratova, and Julius Evelley. *You made my journey fullfilled with nice memories. You are very smart, nice, and hardworking people with sense of humour and great personalities.* I would like thank Zuzana Katreniakova, Marcela Linkova, Marta Nemcikova, and Anna Beresova for all the support.

A big thank you belongs also to my friends. *Monzi, thank you for all the help with TIFFs forming and sarcastic jokes. Tina a Kamil, Lydka, Jana, Stef, Ludka, Kings family, Pili family, Pokatcho family, Milan, Miso, Matej, Jozo, Ondrik, and Dusan thank you for your friendship and all good memories.*

Specifically, I would like to offer huge thanks to my supervisors – my promoters Prof. Ute Bultman and Prof. Ruzena Tkacova, co-promoters Dr. Iveta Nagyova and Dr. Jitse van Dijk. Thank you for keeping an eye on me during my long PhD track. You shared with me your knowledge, writing style, and statistical skills. Thank you for all the support and patience during a very long period of my struggle with the manuscripts. In the words of Italo Calvino *“what matters is not the enclosure of the work within a harmonious figure, but the centrifugal force produced by it -- a plurality of language as a guarantee of a truth that is not merely partial.”* Thank you for all your remarks, questions, comments, and all the inspiring meetings. Thank you belongs also to Prof. Menno Reijneveld, head of the Department of Health Sciences, Community and Occupational Medicine at RuG who made this collaboration be possible, and Dr. Roy Stewart for his help with statistical analyses. I am very thankful to David McLean and Andy Billingham for their skills in proof reading of the manuscripts.

Special thanks goes to the best research assistants: Martina Sukenikova, Henrieta Salokyova and Nicol Hendrichovska. Furthermore, I wish to express my gratitude to Dr. Tomeckova and Dr. Paranicova for the recruitment of patients, their clinical management and the scoring of the sleep studies, and to Mrs. Anna Schejbalova and Zuzana Lazarova for all the technical work in the sleep laboratory. I would also like to thank to Dr. Femke Abma for providing the Work Role Functioning Questionnaire 2.0., the syntax and guidance in the analyses. I would like to thank Ms Truus van Ittersum-Gritter, clinical librarian, who was of great help in the data collection. I would also wish to express gratitude to Dr. Tialda Hoekstra for the help with the methodology. My gratitude belongs to all patients who participated in this study. This project would not have been realized without their willingness to participate in the data collection and to share their problems, feelings, and thoughts.

Grants

This work was supported by the Slovak Research and Development Agency under contracts APVV-15- 0719 (80%); and by the Agency of the Ministry for Education of the Slovak Republic for the Structural Funds of the European Union, Operational Programme Research and Development (Contract No. 034/2009/2.1/OPRandD) (20%).

Vladimira Timkova was born on 15 November, 1987 in Kosice, Slovakia. She completed her bachelor's degree in psychology in June 2010 and her master's degree in psychology in June 2012, both at the Pavol Jozef Safarik University in Kosice, Faculty of Arts. Her qualifying area is clinical psychology and her master thesis was focused on problematic internet use. After her masters study her interest in the clinical area of psychology encouraged her to seek experience in working with patients suffering from mental illness. Therefore, she started her clinical internship at the Department of Psychiatry. Due to her interest in the field of research she started to work as researcher at the Pavol Jozef Safarik University in Kosice, Medical Faculty and also began her PhD program at the University of Groningen, The Netherlands. In her PhD project she explored the associations between bio-psycho-social factors and self-reported health outcomes in patients with obstructive sleep apnoea. While doing her research, she acquired skills in methodology, data analyses, dissemination of scientific results, including publishing. She currently participates in projects on integrated care, social care, and health-related behaviour change. In addition to scientific and research activities, she is also involved in teaching. She delivered lectures and practicals on Social Medicine, Behavioral Medicine and Qualitative and Quantitative Methods in Research.

Supplements

Supplement 3.1: TableS3.2 Search strings

Web of Knowledge: (“Sleep apnea” OR “sleep apnoea” OR OSA) AND (“quality of life” OR “health status” OR “functional status” OR “self-perceived health” OR “self-perceived health” OR “self-rated health” OR “self-rated health”) AND (CPAP OR “continuous positive airway pressure”).

Pubmed: (“Sleep Apnea Syndromes”(Mesh) OR sleep apnea(tiab) OR sleep apnoea(tiab) OR OSA(tiab)) AND (“Continuous Positive Airway Pressure”(Mesh) OR CPAP(tiab) OR continuous positive airway pressure(tiab)) AND (“Quality of Life”(Mesh) OR “Health Status”(Mesh) OR quality of life(tiab) OR health status(tiab) OR functional status(tiab) OR self-rated health(tiab) OR self-perceived health(tiab)).

PsycINFO: (DE “Sleep Apnea” OR TI („sleep apnea” OR “sleep apnoea” OR OSA) OR AB („sleep apnea” OR “sleep apnoea” OR OSA)) AND (TI (“continuous positive airway pressure” OR CPAP) OR AB (“continuous positive airway pressure” OR CPAP)) AND (DE “Quality of Life” OR TI (“quality of life” OR “health status” OR “functional status” OR “self-rated health” OR “self-perceived health”) OR AB (“quality of life” OR “health status” OR “functional status” OR “self-rated health” OR “self-perceived health”)).

The Cochrane Library: (“sleep apnea” or “sleep apnoea” or OSA:ti,ab,kw) and (“continuous positive airway pressure” or CPAP:ti,ab,kw) and (“quality of life” or “health status” or “functional status” or “self-rated health” or “self-perceived health”:ti,ab,kw)

EMBASE: (((‘sleep apnea’:ti,ab,kw OR ‘sleep apnoea’:ti,ab,kw OR ‘osa’:ti,ab,kw) AND ‘continuous positive airway pressure’:ti,ab,kw OR ‘cpap’:ti,ab,kw) AND ‘quality of life’:ti,ab,kw OR ‘health status’:ti,ab,kw OR ‘self-rated health’:ti,ab,kw OR ‘self-perceived health’:ti,ab,kw OR ‘functional status’:ti,ab,kw)).

CINAHL: “sleep apnea OR sleep apnoea OR OSA AND continuous positive airway pressure OR CPAP AND quality of life OR health status OR functional status OR self-rated health OR self-perceived health on 2019-03-03 09:15 AM”

Supplement 3.2: Overview of the included studies: exclusion criteria, sociodemographic and clinical data, level of compliance with CPAP

Table S3.4 Overview of the included studies

Study	Exclusion criteria	Sociodemographic and clinical data Mean (SD/SE, range)	CPAP compliance, Mean (SD/ SE, range)
Engleman 1997, Scotland	neurological disorder; co-existing sleep disorder	Age: 52±2.0 years Gender: 12 men, 4 women AHI: 12.5±0.5 events/h BMI: 29.8±1.8 kg/m ² ESS: 14±1.0	8 patients: 5.00.6± h/ per night
Engleman 1998, Scotland	lung disease; neurological disorder; co-existing sleep disorder	Age: 47±12.0 years Gender: 21 men, 2 women AHI: 43.0±12.0 events/h BMI: 30.0±7.0 kg/m ² ESS: 12.04.0±	2.8±2.0 h/per night
Engleman 1999, Scotland	shift workers; co-existing sleep disorder; neurologi- cal disease; lung disease	Age: 44.0±8.0 years Gender: 21 men, 13 women AHI: 10.0±3.0 events/h BMI: 30.0±5 kg/m ² ESS: 13.0±3.0	2.8±2.1 h/per night
Jenkinson 1999, UK	mental impairment; major psychoses; alcohol depen- dence; learning difficulties	Age: real CPAP: 50.0 (33-71) years Age: sham CPAP: 48.0 (36-68) years Gender: 101 men, 0 women AHI: NA Oximeter: >4% SaO ₂ (dips/h) Sham CPAP: 28.5 (10.7-68.7) Real CPAP: 32.9 (15.5-63.4) BMI: real CPAP: 35.1 (25.8-44.3) kg/m ² BMI: sham CPAP: 35.0 (26.9- 51.4) kg/m ² ESS: real CPAP: 16.0 ESS: Sham CPAP: 17.0	controls: 4.6 h/per night real CPAP: 5.4 h/per night
Barbé 2001, Spain	cognitive deterioration; chronic underlying dis- ease; cardiac disease; less than 8 years of formal education Illicit drugs; alcohol abuse	Age: real CPAP: 54±2.0 years Age: sham CPAP: 52±2.0 years Gender: 5 female, 49 male AHI: real CPAP: 54±2.0 events/h AHI: sham CPAP: 52±2.0 events/h BMI: 29.0±1.0 (26.9-51.4) kg/m ² BMI: sham CPAP: (29±0.4) kg/m ² ESS: real CPAP: 7.0±0.4 ESS: sham CPAP: 7.0±0.4 multicentre; 6 hospitals	controls: 4.0±0.5 h/ per night real CPAP: 5.0±0.4 h/ per night

Table S3.4 Overview of the included studies - continued

Study	Exclusion criteria	Sociodemographic data and clinical data Mean (SD/SE, range)	CPAP compliance, mean (SD, SE, range)
Faccenda 2001, UK	shift workers; diabetes; taking medication which may alter blood pressure	Age: 50.0 (29-72) years Gender: 55 males, 13 females AHI: 35.0 (15-129) events/h BMI: 30.0 (21-53) kg/m ² ESS: 15.0 (16-24)	3.3±0.8 h/per night
Montserrat 2001, Spain	severe cardiovascular disease; hazardous job coincidentally with OSA	Age: 54.0±10.0 years Gender: 41 male, 4 female AHI: 54.0±19.0 events/h BMI: 32.0±6.0 kg/m ² ESS: 16.0±5.0	not specified
Chakravorty 2002, UK	neuromuscular disorders; hypothyroidism; associat- ed respiratory diseases; acute abdomen; chest infection; visual impair- ment	Age: 50.0±11.0 years Gender: not specified AHI: 49.0±28.0 events/h BMI: 37.0±12.0 kg/m ² ESS: 14.0±5.0	not specified
Barnes 2004, Australia	not specified	Age: 46.6±1.1 years Gender: 64 male, 16 female AHI: 5-30 events/h BMI: 31.0±0.6 kg/m ² ESS: 10.0±0.5	3.6± 0.3 h/per night
Marshall 2005, New Zealand	history of somnolence requiring immediate treat- ment; shift work; chronic sleep restriction; currently taking sedatives, antide- pressants, psychotropics or stimulants; an alcohol intake of 0.3 standard units/24 hours or caffeine dependency (unable to forego caffeine on testing days); had undergone upper airway surgery; or had any clinically signifi- cant co-existing disease or additional sleep disorders	Age: 50.5 (25-67) years Gender: 23 male, 6 female AHI: 21.67.5± events/h BMI: 3.5 (6.0) kg/m ² ESS: 12.5 (0.8)	4.9 (0-8.4) h/per night
Siccoli 2008, UK	respiratory failure	Age: real CPAP: 48.1±9.5 years Age: sham CPAP: 48.7±10.6 years Gender: 102 male; 0 female BMI: real CPAP: 35.8±7.3 kg/m ² BMI: sham CPAP: 34.5±5.0 kg/m ² ESS: real CPAP: 15.8±4.0 ESS: sham CPAP: 15.2±4.0	controls: 3.9±2.5 h/ per night real CPAP: 4.7±2.1 h/ per night

Table S3.4 Overview of the included studies - continued

Study	Exclusion criteria	Sociodemographic data and clinical data Mean (SD/SE, range)	CPAP compliance, mean (SD, SE, range)
Weaver, 2012 USA	unstable medical condition in the past 3 months; greater than fifth grade reading level; and no history of other sleep disorder, current pregnancy, substance abuse, sleepiness-related driving accident, or sleepiness-sensitive occupation	Age: real CPAP: 49.5±10.9 years Age: sham CPAP: 51.7±11.9 years Gender: 223 patients; 140 male; 122 female Black: 79.3%; whites: 76.3% AHI: real CPAP: 12.8±6.4 events/h AHI: sham CPAP: 12.5±6.5 events/h BMI: real CPAP: 33.2±6.3 kg/m ² BMI: sham CPAP: 34.2±7.8 kg/m ² ESS: real CPAP: 15.0±3.4 ESS: sham CPAP: 14.7±3.0	controls: 3.1±2.1 h/per night real CPAP: 4.0±2.0 h/per night
Batool-Anwar, 2016 USA	previous treatment for OSA with CPAP or surgery, oxygen saturation on baseline PSG < 75% for > 10% of the recording time, history of motor vehicle accident related to sleepiness within the past 12 months, chronic medical conditions, use of various medications known to affect sleep or neurocognitive function, health and social factors that may impact testing procedures (e.g. shift work)	Age: real CPAP: 52.0±12.0 years Age: sham CPAP: 51.0±12.0 years Gender: male; female AHI: real CPAP: 40.0±24.0 events/h AHI: sham CPAP: 41.0±25.0 events/h BMI: real CPAP: NA BMI: sham CPAP: NA ESS: real CPAP: 10.3±4.5 ESS: sham CPAP: 14.7±3.0 multi-centre study	controls: 2.922.92± h/per night real CPAP: 3.69±3.10 h/per night

CPAP: continuous positive airway pressure

Supplement 4.1
Supplementary Table S4.1 Multiple linear regression analysis: associations of OSA severity, perceived sleep quality, daytime sleepiness and anxiety with work functioning

Work functioning (WRFQ)						
	Crude B (95%CI)	Model 1 B (95%CI)	Model 2 B (95%CI)	Model 3 B (95%CI)	Model 4 B (95%CI)	Model 5 B (95%CI)
Age	-0.22 (-0.79; 0.36)	-0.10 (-0.67; 0.47)	-0.10 (-0.48; 0.68)	-0.12 (-0.64; 0.40)	-0.19 (-0.71; 0.32)	-0.19 (-0.69; 0.31)
Gender	14.70 (2.56; 26.84)*	14.36 (1.97; 26.74)*	12.56 (-0.74; 25.10)	7.86 (-3.61; 19.33)	6.15 (-5.08; 17.38)	4.88 (-6.22; 15.78)
Occupation	-4.03 (-15.40; 7.34)	-	-	-	-	-
OSA severity	-0.27 (-0.53; -0.01)*	-	-0.21 (-0.48; 0.06)	-0.13 (-0.37; 0.11)	-0.10 (-0.34; 0.13)	-0.10 (-0.33; 0.13)
Perceived sleep quality	-5.76 (-7.90; -3.61)***	-	-	-5.28 (-7.48; -3.08)***	-3.41 (-5.99; -0.83)*	-9.76 (-16.25; -3.27)**
Daytime sleepiness	-0.61 (-1.70; 0.48)	-	-	-	-	-
Anxiety	-1.02 (-1.40; -0.63)***	-	-	-	-0.60 (-1.06; -0.14)*	-1.49 (-2.44; -0.54)**
Perceived sleep quality × Anxiety	-0.05 (-0.07; -0.03)***	-	-	-	-	0.18 (0.10; 0.35)*
F Change	-	2.93	2.47	22.76***	6.58*	4.45*
Adjusted R ²	-	0.04	0.05	0.23	0.27	0.29

Crude effects: effect of each variable separately on work functioning; Model 1: effect of age and gender on work functioning; Model 2: effect of age, gender and OSA severity on work functioning; Model 3: effect of age, gender, OSA severity and perceived sleep quality on work functioning; Model 4: effect of age, gender, OSA severity, perceived sleep quality and anxiety on work functioning; Model 5: interaction between perceived sleep quality and anxiety; B: unstandardized regression coefficient; CI – confidence interval; Gender – male gender was set as the reference; Blue-white collar – white collar was set as the reference; OSA – Obstructive Sleep Apnoea; F Change – significance of prediction improvement in the model fit; Adjusted R² – explained variance adjusted for the number of predictors in the model; *p<0.05; **p<0.01; ***p<0.001.

Supplementary Table S4.2 Multiple linear regression analysis: associations of OSA severity, sleep efficiency, daytime sleepiness and anxiety with work functioning

Work functioning (WRFQ)						
	Crude	Model 1	Model 2	Model 3	Model 4	Model 5
	B (95%CI)	B (95%CI)	B (95%CI)	B (95%CI)	B (95%CI)	B (95%CI)
Age	-0.22 (-0.79; 0.36)	-0.06 (-0.62; 0.51)	0.01 (-0.56; 0.58)	-0.09 (-0.65; 0.46)	-0.21 (-0.74; 0.32)	-0.28 (-0.79; 0.23)
Gender	14.70 (2.56; 26.84)*	16.15 (3.71; 28.59)*	14.41 (1.76; 27.05)*	8.58 (-4.26; 21.42)	5.58 (-6.64; 17.80)	2.20 (-9.62; 14.01)
Occupation	-4.03 (-15.40; 7.34)	-	-	-	-	-
OSA severity	-0.27 (-0.53; -0.01)*	-	-0.18 (-0.45; 0.08)	-0.09 (-0.35; 0.18)	-0.08 (-0.33; 0.17)	-0.07 (-0.31; 0.17)
Daily disturbances	-7.88 (-11.93; -3.84)***	-	-	-6.45 (-10.92; -1.99)**	-3.49 (-8.00; 1.03)	-21.78 (-33.67; -9.89)**
Daytime sleepiness	-0.61 (-1.70; 0.48)	-	-	-	-	-
Anxiety	-1.02 (-1.40; -0.63)***	-	-	-	-0.80 (-1.24; -0.36)**	-3.18 (-4.68; -1.68)**
Daily disturbances x Anxiety	-0.05 (-0.07; -0.03)***	-	-	-	-	0.56 (0.22; 0.90)**
F Change	-	3.55*	1.88	8.24**	12.90**	10.75**
Adjusted R ²	-	0.05	0.06	0.16	0.22	0.29

Crude effects: effect of each variable separately on work functioning; Model 1: effect of age and gender on work functioning; Model 2: effect of age, gender and OSA severity on work functioning; Model 3: effect of age, gender, OSA severity and sleep efficiency on work functioning; Model 4: effect of age, gender, OSA severity, sleep efficiency and anxiety on work functioning; Model 5: interaction between sleep efficiency and anxiety; B: unstandardized regression coefficient; CI – confidence interval; Gender – male gender was set as the reference; Blue-white collar – white collar was set as the reference; OSA – Obstructive Sleep Apnoea; F Change – significance of prediction improvement in the model fit; Adjusted R² – explained variance adjusted for the number of predictors in the model; *p<0.05; **p<0.01; ***p<0.001.

Supplementary Table S4.3 Multiple linear regression analysis: associations of OSA severity, daily disturbances, daytime sleepiness and anxiety with work functioning

Work functioning (WRFQ)						
	Crude B (95%CI)	Model 1 B (95%CI)	Model 2 B (95%CI)	Model 3 B (95%CI)	Model 4 B (95%CI)	Model 5 B (95%CI)
Age	-0.22 (-0.79; 0.36)	-0.10 (-0.67; 0.47)	-0.02 (-0.59; 0.56)	0.07 (-0.50; 0.64)	-0.15 (-0.69; 0.39)	-0.16 (-0.70; 0.38)
Gender	14.70 (2.56; 26.84)*	14.36 (1.96; 26.74)*	12.58 (0.07; 25.08)*	13.27 (0.98; 25.56)*	7.81 (-3.84; 19.46)	7.34 (-4.40; 19.09)
Occupation	-4.03 (-15.40; 7.34)	-	-	-	-	-
OSA severity	-0.27 (-0.53; -0.01)*	-	-0.21 (-0.48; 0.06)	-0.17 (-0.44; 0.09)	-0.12 (-0.36; 0.13)	-0.13 (-0.37; 0.12)
Sleep efficiency	-3.55 (-6.60; -0.51)*	-	-	-3.31 (-6.35; -0.27)*	-1.14 (-4.14; 1.85)	-4.33 (-13.26; 4.60)
Daytime sleepiness	-0.61 (-1.70; 0.48)	-	-	-	-	-
Anxiety	-1.02 (-1.40; -0.63)***	-	-	-	-0.89 (-1.31; -0.47)***	-1.03 (-1.60; -0.46)***
Sleep efficiency x Anxiety	-0.05 (-0.07; -0.03)***	-	-	-	-	0.09 (-0.14; 0.32)
F Change	-	2.93	2.47	4.66*	17.40***	0.57
Adjusted R ²	-	0.04	0.05	0.09	0.22	0.22

Crude effects: effect of each variable separately on work functioning; Model 1: effect of age and gender on work functioning; Model 2: effect of age, gender and OSA severity on work functioning; Model 3: effect of age, gender, OSA severity and daily disturbances on work functioning; Model 4: effect of age, gender, OSA severity, daily disturbances and anxiety on work functioning; Model 5: interaction between daily disturbances and anxiety; B: unstandardized regression coefficient; CI – confidence interval; Gender – male gender was set as the reference; Blue-white collar – white collar was set as the reference; OSA – Obstructive Sleep Apnoea; F Change – significance of prediction improvement in the model fit; Adjusted R² – explained variance adjusted for the number of predictors in the model; *p<0.05; **p<0.01; ***p<0.001.

Crude effects

	Work Scheduling and Output demands B (95%CI)	Physical demands B (95%CI)	Flexibility demands B (95%CI)	Mental and Social demands B (95%CI)
Age	-0.15 (-0.78; 0.48)	-0.17 (-0.85; 0.51)	-0.72 (-0.82; 0.39)	-0.29 (-0.92; 0.33)
Gender	10.75 (-2.84; 24.34)	20.60 (6.95; 34.25)**	20.35 (7.40; 33.31)*	17.70 (4.35; 31.05)*
Occupation	-0.74 (-13.34; 11.86)	-2.03 (-15.38; 11.33)	-3.99 (-1.45; 1.04)	-5.04 (-17.34; 7.27)
OSA severity	-0.19 (-0.48; 0.11)	-0.36 (-0.66; -0.05)*	-0.22 (-0.50; 0.08)	-0.26 (-0.54; 0.03)
Night-time sleep quality	-3.43 (-4.69; -2.16)***	-2.02 (-3.47; -0.56)**	-2.82 (-4.08; -1.57)***	-2.73 (-3.70; -1.05)**
Daytime sleepiness	-0.12 (-1.34; 1.11)	-0.99 (-2.22; 0.24)	-0.20 (-1.46; 1.05)	-0.29 (-1.51; 0.94)
Anxiety	-1.17 (-1.81; -0.93)***	-0.93 (-1.44; -0.42)***	-0.93 (-1.35; -0.51)**	-0.82 (-1.26; -0.38)***
Night-time sleep quality x Anxiety	-0.06 (-0.08; -0.04)***	-0.04 (-0.06; -0.01)**	-0.04 (-0.06; -0.02)***	-0.04 (-0.06; -0.01)**

Adjusted models

	Work Scheduling and Output demands B (95%CI)	Physical demands B (95%CI)	Flexibility demands B (95%CI)	Mental and Social demands B (95%CI)
Age	-0.16 (-0.67; 0.46)	0.04 (-0.62; 0.71)	-0.11 (-0.66; 0.44)	-0.20 (-0.79; 0.39)
Gender	2.72 (-9.83; 15.27)	15.43 (1.60; 29.26)*	14.40 (1.58; 27.22)*	13.18 (0.30; 26.65)*
OSA severity	-	-0.17 (-0.48; 0.14)	-	-
Night-time sleep quality	-2.13 (-3.66; -0.61)**	-0.51 (-2.23; 1.20)	-1.64 (-3.16; -0.12)	-1.31 (-2.92; 0.31)
Anxiety	-1.79 (-3.06; -0.52)**	-0.65 (-1.27; -0.03)*	-0.48 (-1.00; 0.05)	-0.45 (-1.01; 0.11)
F Change	734**	4.32*	3.26	2.58
Adjusted R ²	0.26	0.16	0.23	0.15

Crude effects: effect of each variable separately on work functioning subscales; Model Work Scheduling and Output demands: effect of age, gender, night-time sleep quality and anxiety on work scheduling and output demands level score; Model Physical demands: effect of age, gender, disease severity, night-time sleep quality and anxiety on physical demands; Model Flexibility demands: effect of age, gender, night-time sleep quality and anxiety on flexibility demands; Model Mental and Social demands: effect of age, gender, night-time sleep quality and anxiety on mental and social demands score; B: unstandardized regression coefficient; CI – confidence interval; Gender – male gender was set as reference; Blue-white collar – white collar was set as a reference; OSA – Obstructive Sleep Apnoea; F Change – significance of prediction improvement in the model fit; Adjusted R² – explained variance adjusted for the number of predictors in the model. *p<0.05; **p<0.01; ***p<0.001.

Supplement 6.1

Figure S6.1: Hypothesized model of the relationships among OSA severity, night-time sleep quality, daytime sleepiness, fatigue, social support and SI: beta (standard error)

AHI – Apnoea-Hypopnoea Index; OSA – Obstructive Sleep Apnoea; **p<0.01; ***p<0.001.

Table S7.4 Multiple linear regression analyses: associations of social support, mastery and sleep-related problems with functional status subscales (N=150)

Crude effects					
	Activity level B (95%CI)	Vigilance B (95%CI)	Intimacy-sexuality B (95%CI)	General productivity B (95%CI)	Social outcome B (95%CI)
Age	0.01 (-0.02; 0.01)	-0.01 (-0.02; 0.00)	-0.02 (-0.04; 0.00)	-0.01 (-0.02; 0.01)	-0.02 (-0.03; -0.00)*
Gender	-0.41 (-0.70; -0.11)***	-0.60 (-0.87; -0.33)***	-0.78 (-1.20; -0.36)***	-0.49 (-0.78; -0.20)**	-0.41 (-0.71; -0.10)*
Marital status	-0.23 (-0.52; 0.13)	-0.10 (-0.41; 0.21)	-0.44 (-0.91; 0.04)	-0.13 (-0.45; 0.20)	-0.09 (-0.44; 0.25)
OSA severity	-0.01 (-0.02; -0.00)**	-0.01 (-0.01; -0.00)**	-0.02 (-0.03; -0.01)***	-0.01 (-0.02; -0.01)***	-0.01 (-0.02; -0.01)***
Nighttime sleep quality	-0.09 (-0.12; -0.05)***	-0.05 (-0.08; -0.02)**	-0.12 (-0.16; -0.07)***	-0.09 (-0.12; -0.06)***	-0.09 (-0.12; -0.05)***
Daytime sleepiness	-0.08 (-0.10; -0.06)***	-0.09 (-0.11; -0.07)***	-0.11 (-0.14; -0.07)***	-0.09 (-0.11; -0.07)***	-0.06 (-0.09; -0.04)***
Social support	0.02 (0.01; 0.03)**	0.01 (0.00; 0.03)*	0.03 (0.01; 0.04)***	0.01 (0.00; 0.02)**	0.01 (0.00; 0.02)**
Mastery	0.11 (0.01; 0.14)***	0.10 (0.07; 0.12)***	0.14 (0.09; 0.18)***	0.12 (0.09; 0.14)***	0.08 (0.05; 0.11)***
Adjusted models					
	Activity level B (95%CI)	Vigilance B (95%CI)	Intimacy-sexuality B (95%CI)	General productivity B (95%CI)	Social outcome B (95%CI)
Age	0.00 (-0.01; 0.01)	-0.00 (-0.01; 0.00)	-0.01 (-0.03; 0.00)	-0.00 (-0.01; 0.01)	-0.01 (-0.02; 0.00)
Gender	-0.13 (-0.34; 0.07)	-0.37 (-0.58; -0.15)***	-0.38 (-0.72; -0.03)*	-0.17 (-0.36; 0.02)	-0.14 (-0.39; 0.12)
Marital status	-0.10 (-0.33; 0.12)	-0.01 (-0.24; 0.22)	-0.34 (-0.71; 0.03)	-0.03 (-0.23; 0.17)	0.02 (-0.26; 0.30)
OSA severity	-0.00 (-0.01; 0.00)	-0.00 (-0.01; 0.00)	-0.01 (-0.01; 0.00)	-0.01 (-0.01; -0.00)*	-0.01 (-0.01; -0.00)**
Nighttime sleep quality	-0.06 (-0.08; -0.03)***	-0.02 (-0.04; 0.01)	-0.07 (-0.11; -0.03)**	-0.06 (-0.08; -0.04)***	-0.06 (-0.09; -0.03)***
Daytime sleepiness	-0.05 (-0.07; -0.03)***	-0.06 (-0.08; -0.04)***	-0.06 (-0.09; -0.03)***	-0.05 (-0.07; -0.04)***	-0.03 (-0.06; -0.01)**
Social support	0.01 (-0.00; 0.01)	0.00 (-0.01; 0.01)	0.01 (0.00; 0.03)*	0.00 (-0.00; 0.01)	0.01 (-0.00; 0.02)
Mastery	0.07 (0.05; 0.10)***	0.06 (0.04; 0.09)***	0.08 (0.04; 0.12)***	0.07 (0.05; 0.09)***	0.04 (0.01; 0.07)**
F	24.49***	18.41***	16.25***	32.42***	12.53***
Adjusted R ²	0.38	0.48	0.45	0.63	0.38

Crude effects: effect of each variable separately on functional status subscales; Model Activity level: effect of age, gender, marital status, disease severity, sleep-related problems, social support and mastery on activity level score; Model Vigilance: effect of age, gender, marital status, disease severity, sleep-related problems, social support and mastery on vigilance score; Model Intimacy-sexuality: effect of age, gender, marital status, disease severity, sleep-related problems, social support and mastery on intimacy and sexual relationships score; Model General productivity: effect of age, gender, marital status, disease severity, sleep-related problems, social support and mastery on general productivity score; Model Social outcome: effect of age, gender, marital status, disease severity, sleep-related problems, social support and mastery on social outcome score; B: unstandardized regression coefficient; CI – confidence interval; Gender – male gender was set as the reference; Marital status: single was set as the reference; OSA – Obstructive Sleep Apnoea; F – significance of prediction in model fit; Adjusted R² – explained variance adjusted for the number of predictors in the model; FOSQ – higher scores indicating less impaired daily life; *p<0.05; **p<0.01; ***p<0.001

Graduate School Kosice Institute for Society and Health (KISH) and previous dissertations

The Graduate School Kosice Institute for Society and Health (KISH) was established in 2004 and is hosted by the Medical Faculty of the Pavol Jozef Safarik University in Kosice, Slovakia. Its interdisciplinary research programs focus on Youth and Health and on Chronic Disease. The Graduate School KISH is collaborating closely with the Department of Community and Occupational Medicine, University Medical Center Groningen, University of Groningen, The Netherlands.

Previous dissertations from the Graduate School Institute for Society and Health (KISH)

Belak A (2019)

The health of segregated Roma: first-line views and practices

Supervisors: Prof. S.A. Reijneveld Prof. A. Geckova

Co-supervisors: Assoc. Prof. Dr. JP van Dijk

Kopcakova Rondosova J (2018)

Physical activity, screen-based activities and their potential determinants: Active living during adolescence

Supervisors: Prof. Dr. SA Reijneveld, Prof. Dr. A Madarasova Geckova

Co-supervisors: Assoc. Prof. Dr. JP van Dijk, Assoc. Prof. Dr. Z Dankulincova

Husarova D (2017)

Barriers to active participation of school-aged children

Supervisors: Prof. Dr. SA Reijneveld, Prof. Dr. A Madarasova Geckova

Co-supervisor: Assoc. Prof. Dr. JP van Dijk

Holubcikova J (2016)

Eating habits, body image and health and behavioural problems of adolescents.

The role of school and family context

Supervisors: Prof. Dr. SA Reijneveld, Prof. Dr. A Madarasova Geckova

Co-supervisors: Assoc. Prof. Dr. JP van Dijk, Dr. P Kolarcik

Vitkova M (2015)

Poor sleep quality and other symptoms affecting quality of life in patients with multiple sclerosis

Supervisors: Prof. Dr. SA Reijneveld, Prof. Dr. Z Gdovinova
Co-supervisors: Assoc. Prof. Dr. JP van Dijk, Dr. J Rosenberger

Sudzinova A (2015)

Roma ethnicity and outcomes of Coronary Artery Disease: Mortality, clinical status and self-rated health

Supervisor: Prof. Dr. SA Reijneveld
Co-supervisors: Assoc. Prof. Dr. JP van Dijk, Dr. J Rosenberger

Skorvanek M (2014)

Apathy, fatigue and quality of life in patients with Parkinson's disease

Supervisors: Prof. Dr. JW Groothoff, Prof. Dr. Z Gdovinova
Co-supervisors: Assoc. Prof. Dr. JP van Dijk, Dr. J Rosenberger

Kolvek G (2014)

Etiology and prognosis of chronic kidney disease in children: Roma ethnicity and other risk factors

Supervisors: Prof. Dr. SA Reijneveld, Prof. Dr. L Podracka
Co-supervisors: Assoc. Prof. Dr. JP van Dijk, Dr. J Rosenberger

Mikula P (2014)

Health related quality of life in people with multiple sclerosis : the role of coping, social participation and self-esteem

Supervisors: Prof. Dr. JW Groothoff, Prof. Dr. Z Gdovinova
Co-supervisors: Assoc. Prof. Dr. JP van Dijk, Dr. I Nagyova

Prihodova L (2014)

Psychosocial and medical determinants of long-term patient outcomes. A specific focus on patients after kidney transplantation and with haemophilia

Supervisor: Prof. Dr. JW Groothoff
Co-supervisors: Assoc. Prof. Dr. JP van Dijk, Dr. I Nagyova, Dr. J Rosenberger

Behanova M (2014)

Area- and individual-level socioeconomic differences in health and health-risk behaviours

Supervisor: Prof. Dr. SA Reijneveld
Co-supervisors: Assoc. Prof. Dr. JP van Dijk, Dr. I Nagyova, Dr. Z Katreniakova

Silarova B (2014)

Unraveling the role of sense of coherence in coronary heart disease patients

Supervisor: Prof. Dr. SA Reijneveld
Co-supervisors: Assoc. Prof. Dr. JP van Dijk, Dr. I Nagyova

Pitel L (2013)

Sociocultural determinants, gender and health-related behaviour in adolescence

Supervisor: Prof. Dr. SA Reijneveld
Co-supervisors: Assoc. Prof. Dr. JP van Dijk, Assoc. Prof. Dr. A. Geckova

Majernikova M (2013)

Self-rated health and mortality after kidney transplantation

Supervisor: Prof. Dr. JW Groothoff
Co-supervisors: Assoc. Prof. Dr. JP van Dijk, Dr. J Rosenberger, Dr. R Roland

Rosicova K (2013)

Regional mortality in Slovakia: socioeconomic indicators and ethnicity

Supervisor: Prof. Dr. JW Groothoff
Co-supervisors: Assoc. Prof. Dr. JP van Dijk, Assoc. Prof. Dr. A. Geckova

Bobakova D (2013)

Youth subcultures and problem behaviours in Slovakia: Hip-Hop, Techno-scene, Metal, Punk, Skinheads and Roma

Supervisor: Prof. Dr. SA Reijneveld
Co-supervisors: Assoc. Prof. Dr. JP van Dijk, Assoc. Prof. Dr. A. Geckova

Benka J (2012)

Living with Rheumatoid Arthritis: do personal and social resources make a difference?

Supervisors: Prof. Dr. JW Groothoff, Prof. Dr. JJL van der Klink
Co-supervisors: Assoc. Prof. Dr. JP van Dijk, Dr. I Nagyova

Kalina O (2012)

Sexual risky behaviour among Slovak adolescents and young adults: social and psychological factors

Supervisor: Prof. Dr. SA Reijneveld
Co-supervisors: Assoc. Prof. Dr. JP van Dijk, Assoc. Prof. Dr. A. Geckova

Salonna F (2012)

Health inequalities among Slovak adolescents over time.

Supervisors: Prof. Dr. SA Reijneveld, Prof. Dr. JW Groothoff
Co-supervisors: Assoc. Prof. Dr. JP van Dijk, Assoc. Prof. Dr. A. Geckova

Kolarcik P (2012)

Self-reported health and health risky behaviour of Roma adolescents in Slovakia. A comparison with the non-Roma

Supervisor: Prof. Dr. SA Reijneveld
Co-supervisors: Assoc. Prof. Dr. JP van Dijk, Assoc. Prof. Dr. A. Geckova

Tomcikova Z (2011)*Parental divorce and adolescent excessive drinking: Role of parent - adolescent relationship and other social and psychosocial factors*

Supervisor: Prof. Dr. SA Reijneveld

Co-supervisors: Assoc. Prof. Dr. JP van Dijk, Assoc. Prof. Dr. A. Geckova

Veselska Z (2010)*Intrapersonal factors, social context and health-related behavior in adolescence*

Supervisor: Prof. Dr. SA Reijneveld

Co-supervisors: Assoc. Prof. Dr. JP van Dijk, Assoc. Prof. Dr. A. Geckova

Dubayova T (2010)*Parkinson's Disease – Psychological Determinants of Quality of Life*

Supervisor: Prof. Dr. JW Groothoff

Co-supervisors: Assoc. Prof. Dr. JP van Dijk, Dr. I Nagyova, Assoc. Prof. Dr. Z Gdovinova, Dr. LJ Middel

Sarkova M (2010)*Psychological well-being and self-esteem in Slovak adolescents*

Supervisor: Prof. Dr. W.J.A. van den Heuvel

Co-supervisors: Assoc. Prof. Dr. JP van Dijk, Dr. Z. Katreniakova, Assoc. Prof. Dr. A. Geckova

Krokavcova M (2009)*Perceived Health Status in Multiple Sclerosis Patients*

Supervisor: prof dr JW Groothoff

Co-Supervisors: dr JP van Dijk, dr I Nagyova, dr Z Gdovinova, dr LJ Middel

Havlikova E (2008)*Fatigue, mood disorders and sleep problems in patients with Parkinson's disease*

Supervisor: prof dr JW Groothoff

Co-supervisors: dr JP van Dijk, dr J Rosenberger, dr Z Gdovinova, dr LJ Middel

Skodova Z (2008)*Coronary heart disease from a psychosocial perspective: socioeconomic and ethnic inequalities among Slovak patients*

Supervisor: prof dr SA Reijneveld

Co-supervisors: dr JP van Dijk, dr I Nagyova, dr LJ Middel, dr M Studencan

Sleskova M (2006)*Unemployment and the health of the Slovak adolescents*

Supervisors: prof dr SA Reijneveld, prof dr JW Groothoff

Co-supervisors: dr JP van Dijk, dr A Geckova

Rosenberger J (2006)*Perceived Health Status after Kidney Transplantation*

Supervisors: prof dr JW Groothoff, prof dr WJA van den Heuvel

Co-supervisors: dr JP van Dijk, dr R Roland

Nagyova I (2005)*Self-Rated Health and Quality of Life in Slovak Rheumatoid Arthritis Patients*

Supervisor: prof dr WJA van den Heuvel

Co-supervisor: dr JP van Dijk

Geckova A (2002)*Inequality in health among Slovak adolescents*

Supervisors: prof dr D.Post, prof dr JW Groothoff

Co-supervisor: dr JP van Dijk

Groningen

Graduate School of Medical Sciences – Research Institute SHARE and previous dissertations

This thesis is published within the Research Institute SHARE (Science in Healthy Ageing and healthcaRE) of the University Medical Center Groningen /University of Groningen. Further information regarding the institute and its research can be obtained from our internetsite: <http://www.share.umcg.nl/>

More recent theses can be found in the list below.
((co-) supervisors are between brackets)

2020

Havinga P

Breaking the cycle?

(Prof dr RA Schoevers, Dr CA Hartman, Dr L Boschloo)

Stoter I

Staying on track: The road to elite performance in 1500m speed skating.

(Dr MT Elferink-Gemser, Prof C Visscher, Prof FJ Hettinga)

Bos J

Physical activity and physical fitness in children with chronic conditions

(Prof dr PU Dijkstra, Prof dr JHB Geertzen)

Akkerman M

Functioning beyond pediatric burns

(Prof dr LHV van der Woude, Dr LJ Mouton, Dr MK Nieuwenhuis)

Bekhuis E

A body-mind map: Epidemiological and clinical aspects of the relation between somatic, depressive and anxiety symptomatology

(Prof dr JGM Rosmalen, Prof dr RA Schoevers, Dr L Boschloo)

Renting N

Clinical workplace-learning today

(Prof dr ROB Gans, Prof dr ADC Jaarsma, Prof dr JCC Borleffs)

van der Fels I

Movement, cognition and underlying brain functioning in children
(Dr E Hartman, Prof dr C Visscher, Prof dr RJ Bosker, Dr J Smith)

Braaksma P

Moving matters for children with developmental coordination disorder
(Prof dr R Dekker, Prof dr CK van der Sluis, Dr MM Schoemaker, Dr I Stuive) **2019**

Dierselhuis EF

Advances of treatment in atypical cartilaginous tumours
(Prof SK Bulstra, Prof AJH Suurmeijer, Dr PC Jutte, Dr M Stevens)

Gils A van

Developing e-health applications to promote a patient-centered approach to medically unexplained symptoms
(Prof JCM Rosmalen, Prof RA Schoevers)

Notenbomer A

Frequent sickness absence; a signal to take action
(Prof U Bultmann, Prof W van Rhenen, Dr CAM Roelen)

Bishanga DR

Improving access to quality maternal and newborn care in low-resource settings: the case of Tanzania
(Prof J Stekelenburg, Dr YM Kim)

Tura AK

Safe motherhood: severe maternal morbidity and mortality in Eastern Ethiopia
(Prof SA Scherjon, Prof J Stekelenburg, Dr TH van den Akker)

Vermeiden CJ

Safe motherhood : maternity waiting homes in Ethiopia to improve women's access to maternity care
(Prof J Stekelenburg, Dr TH van den Akker)

Schrier E

Psychological aspects in rehabilitation
(Prof PU Dijkstra, Prof JHB Geertzen)

Malinakova K

Spirituality and health: their associations and measurement problems
(Prof SA Reijneveld, Prof P Tavel, Dr JP van Dijk)

Dijkhuizen A

Physical fitness and performance of daily activities in persons with intellectual disabilities and visual impairment; towards improving conditions for participation
(Prof CP van der Schans, Dr A Waning, Dr WP Krijnen)

Graaf MW de

The measurement and prediction of physical functioning after trauma
(Prof E Heineman, Dr IHF Reininga, Dr KW Wendt)

Vrijen C

Happy faces and other rewards; different perspectives on a bias away from positive and toward negative information as an underlying mechanism of depression
(Prof AJ Oldehinkel, Prof CA Hartman, Prof P de Jonge)

Moye Holz DD

Access to innovative medicines in a middle-income country; the case of Mexico and cancer medicines
(Prof HV Hogerzeil, Prof SA Reijneveld, Dr JP van Dijk)

Woldendorp KH

Musculoskeletal pain & dysfunction in musicians
(Prof MF Reneman, Prof JH Arendzen, Dr AM Boonstra)

Mooyaart JE

Linkages between family background, family formation and disadvantage in young adulthood
(Prof AC Liefbroer, Prof F Billari)

Maciel Rabello L

The influence of load on tendons and tendinopathy; studying Achilles and patellar tendons using UTC
(Prof J Zwerver, Prof RL Diercks, Dr I van den Akker-Scheek, Dr MS Brink)

Holvast F

Depression in older age
(Prof PFM Verhaak, Prof FG Schellevis, Prof RC Oude Voshaar, Dr H Burger)

Schaap F

Towards a person-centred approach for older people with intellectual disabilities
(Prof dr SA Reijneveld, Dr GJ Dijkstra, Dr EJ Finnema)

Maters G

Lungs under a cloud
(Prof Dr R Sanderman, Dr JB Wempe Dr G Pool)

Beemster T

Quality improvement of vocational rehabilitation in patients with chronic musculo-skeletal pain and reduced work participation

(Prof dr MF Reneman, Prof dr MHW Frings-Dresen, Prof dr CAM, van Bennekom, Dr JM van Velzen)

Leving MT

Understanding the motor learning process in handrim wheelchair propulsio

(Prof LHV van der Woude, Dr S de Groot, Dr RJK Vegter)

Sas AA

(Genetic) Epidemiology of Inflammation, Age-related Pathology and Longevity

(Prof Dr H Snieder, Dr H Riese)

Hagedoorn EI

Collaborative partnership between family caregivers and nurses in the care of older hospitalized persons

(Prof dr CP van der Schans, Prof dr T Jaarsma, Dr W Paans, Dr JC Keers)

Willems M

Lifestyle change in adults with intellectual disabilities

(Prof dr CP van der Schans, Dr A Waninge Dr J de Jong, Dr TIM Hilgenkamp)

Notenbomer A

Frequent sickness absence, a signal to take action

(Prof dr U Bültmann, Prof dr W van Rhenen, Dr CAM Roelen)