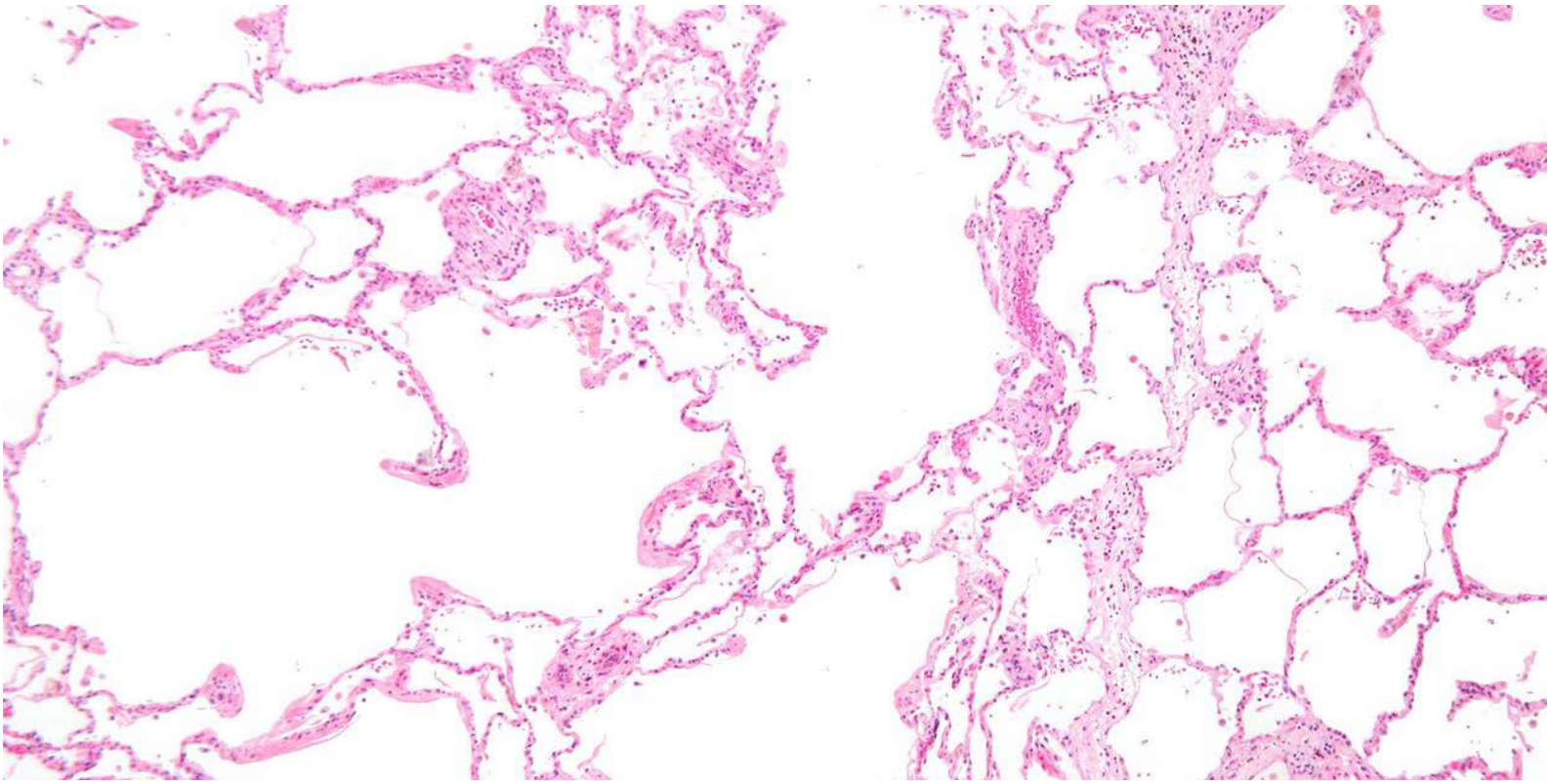
Psychosocial intervention in chronic obstructive pulmonary disease (COPD)

PhD dissertation



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Psychosocial intervention in chronic obstructive pulmonary disease (COPD)

PhD Dissertation

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In collaboration between

Unit for Psychooncology and Health Psychology,
Aarhus University and Aarhus University Hospital

and

Department of Respiratory Diseases and Allergy,
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Closer to now
In the crack between past and future
in the moment of nothingness
the universe is filled with joy
and infinity suddenly makes sense.

My friend Poul,
COPD-patient

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Ingeborg Farver-Vestergaard

Aarhus, July 2018

Contents

Overview

The present dissertation is the tangible result of a scientific and educational process initiated in 2013 with the purpose of investigating effects, mechanisms and delivery of psychosocial intervention in chronic obstructive pulmonary disease (COPD). The background for doing this is described in Section 1 and consists of, first, a description of relevant pieces of the pathological and clinical picture of COPD, followed by a general introduction to psychological issues that many patients with COPD are facing, and the theoretical reasons for why psychosocial intervention – and specifically mindfulness-based cognitive therapy (MBCT) – may be relevant in this regard. Lastly, the background for exploring tele-based delivery of MBCT is presented. Section 2 begins with a presentation of the aims of the present dissertation, followed by summaries of methods, results and conclusions of the included studies: A systematic review and meta-analysis of psychosocial intervention on psychological and physical outcomes in COPD (Study 1), a cluster-randomised controlled trial of MBCT in COPD (Study 2) and a mixed-methods feasibility study of tele-delivered MBCT (Tele-MBCT) in COPD (Study 3). Section 3 opens with a discussion of the main results of the three studies. This is followed by a general discussion of limitations, clinical implications and suggestions for future studies. Finally, concluding remarks are presented in Section 4. The results of the three studies are published in three separate scientific papers, which are included as appendices (Appendices A, B and C) together with the MBCT treatment manual adapted to COPD for the purpose of Study 2 (Appendix D).

List of papers

The present dissertation is based on the following original papers:

Paper 1

Farver-Vestergaard, I., Jacobsen, D. & Zachariae, R. (2015). Efficacy of psychosocial interventions on psychological and physical health outcomes in chronic obstructive pulmonary disease: a systematic review and meta-analysis. *Psychotherapy and Psychosomatics* 84: 37-50.

Paper 2

Farver-Vestergaard, I., O'Toole, M. S., O'Connor, M., Løkke, A., Bendstrup, E., Basdeo, S. A., Cox, D., Dunne, P., Ruggeri, K., Early, F. & Zachariae, R. (2018). Mindfulness-based cognitive therapy in COPD: a cluster-randomised controlled trial. *European Respiratory Journal* 51: 1702082.

Paper 3

Farver-Vestergaard, I., O'Connor, M., Smith, N. C., Løkke, A., Bendstrup, E. & Zachariae, R. (2018). Tele-delivered mindfulness-based cognitive therapy in chronic obstructive pulmonary disease: a mixed-methods feasibility study. *Journal of Telemedicine and Telecare* [e-pub ahead of print]. DOI: 10.1177/1357633X18780563.

Abbreviations and definitions

ANOVA=Analysis of variance. Statistical analysis method.

ATS=American Thoracic Society.

BCS=Breathlessness Catastrophizing Scale. Self-reported measure of breathlessness catastrophizing.

CAT=COPD Assessment Test. Self-reported measure of physical health status (i.e., COPD symptoms).

CBT=Cognitive behavioural therapy. Specific type of psychosocial intervention.

COPD=Chronic Obstructive Pulmonary Disease.

CSES=COPD Self-Efficacy Scale. Self-reported measure of COPD-specific self-efficacy.

ERS=European Respiratory Society

Exacerbation=an acute change in respiratory symptoms, which is beyond normal day-to-day variation.

FEV_1=Forced Expiratory Volume in 1 second. The volume of air exhaled during the first second of the exhalation. See also FVC and Spirometry.

FFMQ=Five Facet Mindfulness Questionnaire. Self-reported measure of mindfulness.

FVC=Forced vital capacity. The volume of air forcibly exhaled from the point of maximal inspiration. See also FEV_1 and Spirometry.

GOLD=Global Initiative for Chronic Obstructive Pulmonary Disease.

HADS=Hospital Anxiety and Depression Scale. Self-reported measure of psychological distress.

IL-6=Interleukin 6. A pro-inflammatory cytokine.

IL-8=Interleukin 8. A pro-inflammatory cytokine.

IL-17E=Interleukin 17E. Also known as Interleukin 25 (IL-25). A cytokine involved in inflammatory processes.

MBCT=Mindfulness-based cognitive therapy. Specific type of psychosocial intervention.

MBI=Mindfulness-based intervention. Overarching term for intervention programmes based on mindfulness training.

MBSR=Mindfulness-based stress reduction. Specific type of psychosocial intervention.

MBI:TAC=Mindfulness-Based Interventions–Teaching Assessment Criteria. A tool for the assessment and quantification of intervention integrity (adherence, differentiation, competence) in MBCT and MBSR.

MLM=Multilevel modelling. Statistical analysis method.

MRC=Medical Research Council dyspnea score. Self-reported or doctor administrated measure of breathlessness.

NRCT=Non-randomised controlled trial.

PR=Pulmonary rehabilitation. A standardised intervention programme consisting of supervised physical exercise and COPD-specific education.

QoL= Quality of life.

RCT=Randomised controlled trial.

SCS=Self Compassion Scale. Self-reported measure of self-compassion.

SGRQ=St. George's Respiratory Questionnaire. Self-reported measure of quality of life in respiratory illness.

Spirometry=a spirometer measures the volume of air that can be in- or exhaled and is the most objective measurement of airflow limitation (lung function). See also FEV_1 and FVC.

Tele-MBCT=Tele-delivered mindfulness-based cognitive therapy.

TNF-α=Tumour necrosis factor alpha. A pro-inflammatory cytokine.

1 Background

1.1 Chronic obstructive pulmonary disease (COPD)

Chronic obstructive pulmonary disease (COPD) is characterised by persistent obstruction of the airways, lung function impairment and chronic inflammation (GOLD Global Initiative for Chronic Obstructive Pulmonary Disease, 2018). The most common physical symptoms of the disease are breathlessness (dyspnea), cough and excessive sputum production, often accompanied by fatigue and low physical activity levels (GOLD Global Initiative for Chronic Obstructive Pulmonary Disease, 2018). Additionally, nutritional abnormalities, musculoskeletal dysfunction and cardiovascular disease are all recognised systemic effects of COPD (Agusti, 2007).

More than 10% of the global population suffers from COPD, and the burden of the disease is expected to increase over the coming decades due to continued risk factor exposure and ageing of the population (Adeloye et al., 2015; Mathers & Loncar, 2006). In Denmark, the total prevalence of COPD among adults across all grades of airflow obstruction severity is 17.4%, out of which a large proportion of patients (15.4%) currently in the group that is characterised by mild-to-moderate airflow obstruction, is expected to demand treatment over the coming decades as the illness progresses (Fabricius, Løkke, Marott, Vestbo, & Lange, 2011).

It has long been known that the main factors influencing the development and progression of COPD include tobacco smoking and exposure to toxic substances, for example indoor, outdoor and occupational pollution (Mannino & Buist, 2007). Individuals can be genetically predisposed, and more recent research indicates that childhood exposure interacts with later exposure in increasing the risk of developing COPD (Allinson et al., 2017). It is mainly the well-educated who succeed in smoking cessation before the onset of COPD later in life, which is one of the main reasons why COPD has been characterised as a major driver of social health inequality (Vestbo & Lange, 2017).

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) expert board has developed and regularly updates evidence-based guidelines for the diagnosis, management and prevention of COPD (GOLD Global Initiative for Chronic Obstructive Pulmonary Disease, 2018). According to the guidelines, a diagnosis of COPD should be considered in all individuals with 1) dyspnea, cough and/or sputum production, and/or 2) a history of exposure to risk factors. The diagnosis is spirometry-based, and a post-bronchodilator FEV_1/FVC ratio of less than 0.70 confirms the presence of airflow limitation and is thereby an indicator of COPD. Upon diagnosis, a more comprehensive clinical assessment

is performed with the purpose of understanding the impact of COPD on an individual patient's daily functioning and, consequently, guiding treatment. COPD assessment include 1) a classification of severity of airflow limitation, 2) assessment of the nature and magnitude of physical symptoms, 3) assessment of exacerbation risk and 4) assessment of possible comorbidities.

Classification of airflow limitation: The specific cut-points for airflow limitation severity are shown in Table 1. Here, FEV_1 is expressed as a percentage of the predicted value of a normative population of a given age and gender (FEV_1 % predicted). As there is only a weak correlation between GOLD grade and a patient's overall physical health status (Jones, Miravitlles, van der Molen, & Kulich, 2012), accompanying assessment of symptoms, exacerbation risk and comorbidity is needed.

Table 1. Grading of airflow limitation severity in COPD (based on post-bronchodilator FEV_1)

In patients with $FEV_1/FVC < 0.70$:		
GOLD 1	Mild	$FEV_1 \geq 80\%$ predicted
GOLD 2	Moderate	$50\% \leq FEV_1 < 80\%$ predicted
GOLD 3	Severe	$30\% \leq FEV_1 < 50\%$ predicted
GOLD 4	Very severe	$FEV_1 < 30\%$ predicted

Abbreviations: FEV_1=Forced expiratory volume in 1 s. FVC=Forced vital capacity.
Source: (GOLD Global Initiative for Chronic Obstructive Pulmonary Disease, 2018).

Symptom assessment: Historically, dyspnea has been considered the most functionally invalidating symptom of COPD, and single-item measures assessing the intensity of dyspnea, such as the British Medical Research Council (MRC) dyspnea scale, are therefore widely used (Bestall et al., 1999). Over the recent years, however, it has been increasingly recognised that COPD affects patients beyond dyspnea, and composite symptom measures are currently the standard approach to the measurement of physical health status (Jones, 2001). The COPD Assessment Test (CAT) is a measure of physical health status impairment in COPD that is commonly used for symptom assessment in routine clinical practice (Jones et al., 2009; Smid, Franssen, Houben-Wilke, et al., 2017). The eight items yield a total score ranging from 0-40, with higher scores representing more impairment. A total score of ≥10 is currently considered as representing a high symptom burden (GOLD Global Initiative for Chronic Obstructive Pulmonary Disease, 2018), but a more conservative cut-point of ≥18 has recently been suggested (Smid, Franssen, Gonik, et al., 2017).

Risk of exacerbation: A COPD exacerbation can be defined as "an event in the natural course of the disease characterized by a change in the patient's baseline dyspnoea, cough, and/or sputum that is

beyond normal day-to-day variations, is acute in onset, and may warrant a change in regular medication in a patient with underlying COPD" (Wedzicha & Seemungal, 2007, p. 786). Mortality and morbidity is significantly increased during an exacerbation (Halpin, Miravitlles, Metzdorf, & Celli, 2017), and screening for its risk is therefore important with the purpose of initiating timely adjustments in medication. COPD exacerbations are associated with increased airway and systemic inflammation, usually triggered by bacteria, viruses or pollutants (Wedzicha & Seemungal, 2007). Specifically heightened levels of the inflammatory cytokines of IL-6, IL-8 and TNF-α are seen during an exacerbation or between events in patients with frequent exacerbations (Bathoorn et al., 2009; Bhowmik, Seemungal, Sapsford, & Wedzicha, 2000; Perera et al., 2007), and also the cytokine of IL-17E (also known as IL-25) is thought to be involved in COPD-related inflammation (Barnes, 2008). However, the exact underlying mechanism by with an exacerbation develops is unclear and, most likely, manifold, and there is considerable variation in exacerbation rates between patients (Hurst et al., 2010). Relatively robust predictors of frequent exacerbations (defined as two or more exacerbations per year) are spirometric GOLD grade 3-4 and/or a history of earlier treated events (Hurst et al., 2010). As early signs of exacerbations rely on the monitoring of bodily sensations, patients themselves play a central role in the early detection of exacerbation (Worth, 1997). Therefore, individuals with COPD at risk of exacerbation are instructed to pay close attention to their daily symptom levels and take proper action, e.g., by following an action plan developed in collaboration with medical healthcare professionals or by asking for help from appropriate sources, when changes in symptom intensity deviates from normal day-to-day variations (de Silva, 2011; Worth & Dhein, 2004).

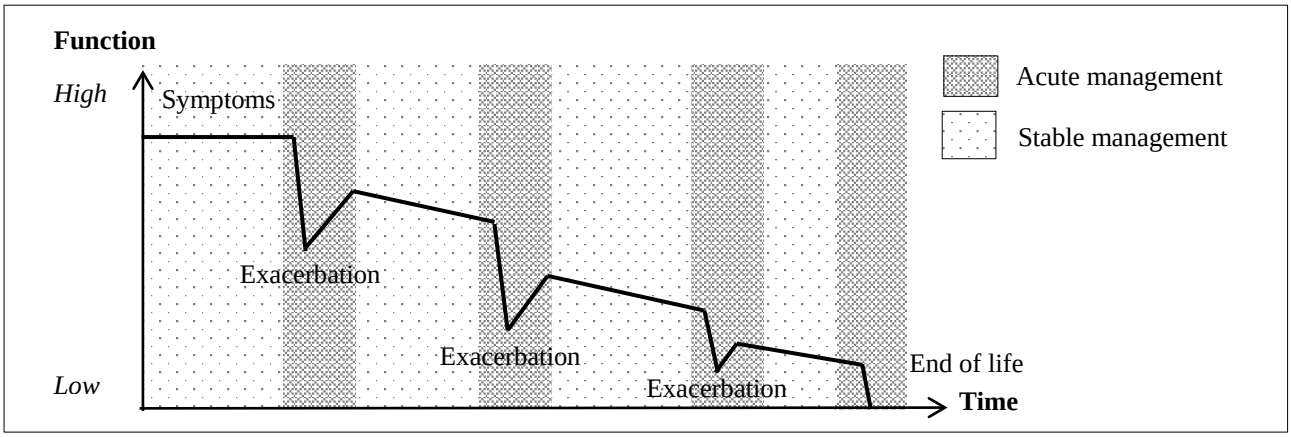
Assessment of comorbidity: Due to common risk factors, e.g., aging, smoking, inactivity and inflammation, comorbidity is high in COPD (Fabbri, Luppi, Beghé, & Rabe, 2008; Vanfleteren et al., 2013). Typical comorbidities include osteoporosis, cardiovascular disease, cancer, anxiety and major depression (Fabbri et al., 2008). High comorbidity leads to increased mortality and healthcare use and generally complicates the management of COPD (Barnes & Celli, 2009). Therefore, assessment of comorbidities and person-oriented treatment of complex comorbidity profiles is crucial in the context of COPD (Fabbri et al., 2008).

1.1.1 Illness and treatment trajectories in COPD

In contrast to the steady symptom progression and usually clear terminal phase of other chronic diseases, e.g., lung cancer, the illness trajectory of COPD is characterised by a gradual decline, punctuated by episodes of acute deterioration (Murray, Kendall, Boyd, & Sheikh, 2005). This particular

illness trajectory demands a corresponding treatment trajectory where the day-to-day management of relatively stable COPD is replaced by acute management of COPD exacerbations when needed (see Figure 1).

Figure 1: Typical illness and treatment trajectory for people with COPD (Murray et al., 2005).



According to the GOLD guidelines, the overall goal of the acute management phases is to minimise the impact of an actual exacerbation and to prevent the development of subsequent exacerbations. Depending on the severity of an exacerbation, treatment may consist of short-acting bronchodilators, antibiotics and/or corticosteroids. In the most severe cases, hospitalisation is required and the risk of death is significantly increased (GOLD Global Initiative for Chronic Obstructive Pulmonary Disease, 2018).

Conversely, the management of stable COPD is typically restricted to an outpatient setting. In addition to the management of co-existing pathologies (comorbidity), the main goals of stable COPD-treatment are to improve physical health status and quality of life (QoL) as well as to reduce symptoms and risk of exacerbations (GOLD Global Initiative for Chronic Obstructive Pulmonary Disease, 2018). In addition to pharmacological treatment, recommended non-pharmacological treatment initiatives include lifestyle intervention (e.g., smoking cessation, dietary and physical activity counselling typically delivered through a standardised pulmonary rehabilitation (PR) programme), oxygen therapy, and, in the most extreme cases, lung volume reduction and lung transplantation (Clini & Ambrosino, 2008).

Patients themselves play a central role after discharge from an exacerbation and in the stable management of COPD by monitoring changes in symptoms and adhering to life style changes, which takes a considerable amount of effort (Andersen, Thomsen, Bruun, Bødtger, & Hounsgaard, 2017;

Worth, 1997). As part of the treatment of stable COPD, it is recommended that all patients with moderate to very severe COPD are offered participation in a PR programme. PR primarily consists of physical exercise training supervised by healthcare professionals with additional components of health- and self-management related education. According to an official statement from the American Thoracic Society (ATS) and the European Respiratory Society (ERS) (Spruit et al., 2013), a standardised, group-based PR programme can be delivered both in hospital- and community-based settings. The duration should be of minimum eight weeks and the full course of the programme typically consists of 2-3 weekly sessions, each lasting from 1-4 hours. Furthermore, it is stated that the overall purpose of PR is to improve patients' overall QoL and to promote their long-term adherence to health-enhancing behaviours.

Usually, the effect of PR is assessed by applying outcomes of QoL, encompassing both physical and psychological domains (e.g., the St George's Respiratory Questionnaire (SGRQ) including subscales of dyspnea, fatigue, emotional function and mastery). A Cochrane review and meta-analysis of 65 RCTs, including a total of 3,822 COPD-patients, showed statistically and clinically significant positive effects of PR on exercise capacity and QoL (McCarthy et al., 2015). Meanwhile, a large proportion of COPD-patients entering PR report clinically significant levels of anxiety and depression (Janssen et al., 2010), which might not be captured in overall measures of QoL (Cafarella, Effing, Usmani, & Frith, 2012; Maurer et al., 2008), and there is a lack of evidence of the effect of PR on symptoms of mental illness (Maurer et al., 2008). Moreover, anxiety and depression have shown to be associated with increased dyspnea and reduced QoL not only before, but also *after* PR (von Leupoldt, Taube, Lehmann, Fritzsche, & Magnussen, 2011) as well as to predict non-adherence to PR (Garrod, Marshall, Barley, & Jones, 2006; Keating, Lee, & Holland, 2011). Therefore, while improvements in the multifaceted construct of QoL (i.e., including both physical and psychological domains) is evident, symptoms of anxiety and depression appear to form a distinct and unresolved issue in the management of COPD.

1.2 Psychological distress in COPD

Despite optimal medical treatment, COPD-patients across all illness grades continue to report clinically relevant levels of anxiety (40%) and depression (30%) symptoms (Bock, Bendstrup, Hilberg, & Løkke, 2017; Panagioti, Scott, Blakemore, & Coventry, 2014). Symptoms of anxiety and depression often appear together in patients with COPD (Maurer et al., 2008), and they form a distinct cluster of

comorbidity in COPD called the psychologic comorbidity cluster (Vanfleteren et al., 2013). Psychological distress will be used to label the larger non-specific distress factor of negative affectivity that can be said to encompass symptoms of anxiety and depression among patients with minor psychiatric conditions in a medical setting (Spinhoven et al., 1997).

Psychological distress has been shown to be associated with a larger physical symptom burden (von Leupoldt & Kenn, 2013; Yohannes & Alexopoulos, 2014a) and studies have shown that COPD-patients with high levels of psychological distress have an increased risk of exacerbation, hospitalisation and mortality post-discharge (Atlantis, Fahey, Cochrane, & Smith, 2013; Laurin, Moullec, Bacon, & Lavoie, 2011; Pooler & Beech, 2014). The underlying mechanisms explaining the co-existence of COPD and psychological distress are still unclear (Papava et al., 2016). It has been suggested, however, that factors related to smoking, nicotine dependence and systemic inflammation, e.g., increased activity in the systemic inflammation biomarkers of IL-6 and TNF-α, may play a significant role (Alshair et al., 2011; Barnes & Celli, 2009; Yohannes & Alexopoulos, 2014a).

Biological underpinnings can be supplemented by more holistic clinical models of the development and maintenance of psychological distress in COPD. Cognitive models of anxiety in COPD are typically based on Clark's fear-avoidance model of panic anxiety, suggesting that when a bodily symptom is cognitively appraised as threatening, an individual is likely to respond with anxiety, hypervigilance and avoidance of activity that could trigger the symptom (D. M. Clark, 1986). In COPD, cognitive processes of rumination and magnification of bodily symptoms, most often breathlessness, can amplify the psychophysiological processes, leading to a negative magnified interpretation of bodily symptoms, avoidance of physical activity, followed by gradual deconditioning and, thereby, further impairment of physical health status (Holas, Michałowski, Gaweda, & Domagała-Kulawik, 2017; Reardon, Lareau, & ZuWallack, 2006; von Leupoldt, Taube, Henkhus, Dahme, & Magnussen, 2010; ZuWallack, 2007). Moreover, avoidance is not limited to physical activity, but can encompass a refusal to enter any situation that could evoke breathlessness or in which COPD symptoms could be considered disturbing and/or self-inflicted (Holas et al., 2017; Malpass, Kessler, Sharp, & Shaw, 2015). In line with this, cognitive models of depression, in which automatic negative self-evaluations, expectancies and memories play a central role (Beck, 2008), can be applied in COPD. Here, a patient's negative thoughts about his or her own role in the development of the disease (e.g., smoking) as well as rumination about past and/or future exacerbations is linked with social isolation, and feelings of hopelessness (Hasson et al., 2008; Malpass et al., 2015).

Based on the bidirectional relationship between psychological distress and physical impairment in COPD, psychosocial intervention is thought to be an effective supplement to the already established management of stable COPD with the purpose of relieving both the psychological and physical symptom burden (von Leupoldt, 2017; von Leupoldt & Janssens, 2016).

1.3 Psychosocial intervention in COPD

There appears to be broad consensus that psychological distress is largely undiscovered and undertreated in COPD (Cafarella et al., 2012; Deb & Sambamoorthi, 2016; Maurer et al., 2008; von Leupoldt & Kenn, 2013). The efficacy of a psychopharmacological treatment approach is limited and patients are reluctant to take more medication (Fritzsche, Clamor, & von Leupoldt, 2011; Yohannes & Alexopoulos, 2014b). Psychosocial intervention can be defined as intervention programmes with a psychosocial aim that does not include the prescription of medications or include only a physical focus (e.g., PR programmes without an explicit psychological component; acupuncture; massage therapy). In comparison with other chronic diseases, such as cancer, diabetes and asthma, non-pharmacological approaches to the management of psychological distress in COPD have not received the same level of research activity (Kaptein et al., 2009; von Leupoldt, Fritzsche, Trueba, Meuret, & Ritz, 2012). However, some efforts do exist, and a number of systematic reviews of the effect of psychosocial intervention in COPD have been conducted (see overview in Table 2).

In 2002, Rose et al. concluded that there was a lack of evidence that psychosocial intervention reduce anxiety in COPD (Rose et al., 2002). More than half a decade later, in 2008, Coventry and Gellatly published a systematic review of non-randomised controlled trials (NRCT) and randomised controlled trials (RCT) of cognitive behavioural therapy (CBT) in which they emphasised that there was inconclusive evidence for its effect on anxiety and depression (Coventry & Gellatly, 2008). In 2011, Baraniak and Sheffield conducted a meta-analysis of the efficacy of psychosocial intervention for anxiety, depression and QoL, which revealed a medium combined effect size on anxiety only, corresponding to a standardised mean difference (Cohen's *d*) of 0.57 (Baraniak & Sheffield, 2011). With three-year intervals, Smith et al. (2014) and Usmani et al. (2017) published the results of their meta-analyses. Smith et al. found no statistically significant pooled effect of psychosocial intervention on anxiety (d=0.49) and depression (d=0.37). Conversely, in their Cochrane-review, Usmani et al. found a statistically significant pooled effect of CBT-based psychosocial interventions on anxiety (d=0.43, calculated by dividing the MD in Table 2 with the average SD for BAI in the three included studies).

Table 2. Summary of existing systematic reviews of controlled trials on psychosocial intervention in COPD.

	Interventions[a]	Designs[b]	Outcomes	Included studies	Effect
Rose et al. (2002)	CBT-inspired=1; Mind-body=3; Analytic= 1; Comprehensive PR=1	RCTs (K=6; n=324)	Anxiety	Lustig (1970) Rosser et al. (1983) Weiner (1988) Gift et al. (1992) Sassi-Dambron et al. (1995) Emery et al. (1998)	Anxiety: Direction in favour of psychosocial intervention, but no stat. sig. between-group effects reported.
Coventry & Gellatly (2008)	CBT	NRCTs, RCTs (K=4; n=173)	Anxiety, depression	Eiser et al. (1997) Emery et al. (1998) Kunik et al. (2001) de Godoy et al. (2003)	Anxiety: Direction in favour of CBT, but only one study reported stat. sig. btw-group effect. Depression: Direction in favour of CBT, but only one study reported stat. sig. btw-group effect
Baraniak & Sheffield (2011)	CBT=6; CBT-inspired=1; Analytic=1; Mind-body=1	NRCTs, RCTs, Pre-post (K=9; n=523)	Anxiety, depression, QoL	Rosser et al. (1983) Gift et al. (1992) Lisansky et al. (1996) Eiser et al. (1997) Emery et al. (1998) Kunik et al. (2001) de Godoy et al. (2005) Kunik et al. (2008) Heslop et al. (n.d.)	Anxiety: Combined ES (*r*)= -0.273; CI= -0.42 – -0.14; *p*=0.00004 Depression and QoL: Results not reported due to file-drawer and heterogeneity problems.
Smith et al. (2014)	CBT=5; CBT-inspired=2	RCTs (K=7; n=691)	Anxiety Depression	De Godoy et al. (2003) Hynninen et al. (2010) Jiang et al. (2012) Kunik et al. (2001) Kunik et al. (2008) Lamers et al. (2010) Livermore et al. (2010)	Anxiety: SMD= -0.49; CI= -1.04 – 0.06; p=0.08; I^2=80% Depression: SMD= -0.37: CI)=-0.86 – 0.11; *p*=0.13; I^2=74%
Usmani et al.(2017)	CBT=2; CBT-inspired=1	RCTs (K=3; n=319)	Anxiety	De Godoy et al. (2003) Hynninen et al. (2010) Kunik et al. (2008)	Anxiety: MD BAI= -4.41; CI=-8.28 – -0.53; *p*=0.03; I^2=62%

Abbreviations: BAI=Beck Anxiety Inventory. CBT=Cognitive behavioural therapy. CI=95% confidence interval. ES=Effect size. MD=Mean difference. NRCT=Non-randomised controlled trial. QoL=Quality of life. RCT=Randomized controlled trial. SMD=Standardised mean difference.

[a]= Number of studies and the specific intervention types applied.

[b]= Number of included studies (K) and total number of participants (n) are reported in parentheses.

Taken together, the five systematic reviews, altogether representing a development over 15 years, indicate that there is only limited – and methodologically low-quality – evidence for psychosocial intervention on psychological distress. However, the reviews took a relatively narrow approach concerning 1) outcomes as well as 2) intervention types, and it has been argued that a broader approach

– with exploration of reasons for potentially non-homogeneous results – strengthens the clinical relevance and credibility of a meta-analysis (Gøtzsche, 2000). Firstly, none of the described reviews quantitatively summarised the effect on physical impairment. This is in spite of existing work suggesting that psychosocial intervention, in addition to improving psychological outcomes, also have the potential of influencing physical outcomes such as pulmonary function and exercise capacity – and even biomarkers of systemic inflammation (N. M. Clark, Dodge, Partridge, & Martinez, 2009; O'Toole et al., 2018). Secondly, the reviews predominantly included studies of CBT-based psychosocial intervention types in which a central goal is to *change* the content of cognitive patterns triggering what is considered to be maladaptive affective-behavioural responses. For example by substituting thoughts such as "It is dangerous; I have no control of the situation" with thoughts such as "It is not dangerous; I am in control" (Bove, Overgaard, Lomborg, Lindhardt, & Midtgaard, 2015). The issue remains, however, that while CBT techniques relies on an assumption that the thoughts are distorted, the automatic thoughts experienced by COPD-patients may not simply be distortions; increases in symptoms *could* potentially be dangerous, and patients *should* to a certain extent react to their physical sensations with the purpose of detecting a potentially impending exacerbation. Addressing these issues in psychosocial intervention may be beneficial for patients with the purpose of managing their psychological and physical condition. This may in part explain the lack of effect of psychosocial intervention types that are based on 'classical' cognitive strategies. Mind-body approaches to psychosocial intervention include components of relaxation, yoga and/or meditation and have received increased attention in the field of respiratory medicine over the recent decades (Coventry et al., 2013; Harrison, Lee, Janaudis-Ferreira, Goldstein, & Brooks, 2016; Volpato, Banfi, Rogers, & Pagnini, 2015; Yohannes, Junkes-Cunha, Smith, & Vestbo, 2017). Therefore, including such intervention types in a systematic review of psychosocial intervention in COPD, may yield different results.

1.4 Mindfulness-based cognitive therapy (MBCT)

Mindfulness has been defined as "the awareness that emerges through paying attention on purpose, in the present moment, and non-judgementally to the unfolding of experience moment by moment" (Kabat-Zinn, 2006, p. 145). Stimulating this form of awareness through regular meditation practice is supposed to have positive effects in both somatic and mental illness (Alsubaie et al., 2017) and has therefore been incorporated in specific mind-body types of psychosocial interventions alongside other therapeutic elements.

1.4.1 Mindfulness-based intervention

The first standardised mindfulness-based intervention (MBI) was developed by Jon Kabat-Zinn under the name of mindfulness-based stress reduction (MBSR) and predominantly consists of mindfulness meditation, yoga exercises and psycho-education with the purpose of coping with stress, pain and illness in a general – and not necessarily clinical – population (Kabat-Zinn, 1990). More recently, Segal, Williams, and Teasdale (2002) combined MBSR elements with CBT components under the name of mindfulness-based cognitive therapy (MBCT), which is a clinical programme designed with the purpose of preventing relapse in major depression. MBCT for depression consists of 8 weekly 2-hour group-sessions together with 45 minutes of daily home-practice during the intervention period (Segal, Williams, & Teasdale, 2013).

MBIs have been shown to improve physical (e.g., pain) and psychological (e.g., anxiety and depression) outcomes in chronic illnesses such as cancer and cardiovascular disease (Gotink et al., 2015; Johannsen et al., 2016; Piet, Würtzen, & Zachariae, 2012; Schellekens et al., 2017), but the efficacy of MBI in COPD is relatively understudied. A recent systemic review of MBI in people with a respiratory diagnosis (Harrison et al., 2016) reported only two RCTs in COPD (Chan, Giardino, & Larson, 2015; Mularski et al., 2009). The effects found for respiratory rate, dyspnea and QoL did not reach statistical significance or were in the opposite of the expected direction, i.e., associated with increased respiratory rate. However, one of the studies included a sample of male veterans unlikely to be representative of the COPD population (Mularski et al., 2009), while the other was a pilot study, including a relatively small sample (n=41) (Chan et al., 2015). Neither of the two studies included long-term follow-up. Moreover, the MBIs tested in the two trials followed the overall format of MBSR adapted to COPD and did not include elements of cognitive therapy.

In contrast, reports of qualitative and case studies describe MBI as a meaningful type of psychosocial intervention in COPD (Addy, 2007; Chan & Lehto, 2016; Harrison, Lee, Goldstein, & Brooks, 2017; Malpass et al., 2015). In a case study, it is suggested that MBI should be preferred over CBT for COPD-patients who experience increased breathlessness as an objective consequence of physical activity. It is argued that these patients will not be directly capable of disconfirming the feared consequences (breathlessness) when omitting safety behaviours (avoidance of physical activity), which is a central behavioural strategy in COPD (Addy, 2007). MBI introduces a more acceptance-based approach where the immediate goal is not to make unpleasant physical symptoms go away, but instead coming to see physical sensations, thoughts and emotions as natural, passing events and responding

to such situations on the basis of more awareness and clarity instead of acting automatically. This is line with a qualitative study by Malpass et al. (2015), exploring COPD- and asthma-patients' experiences of attending MBCT. Here, an acceptance-based approach to their own physical vulnerability, paired with a more decentred attitude towards anxiety-related catastrophizing and depression-specific rumination, seemingly enabled participants to choose an appropriate and helpful response in difficult situations, instead of reacting automatically with panic and/or lowered mood. Results from another study, based on qualitative interviews with patients and healthcare professionals with or without previous experience with mindfulness-training, suggested that MBI should be delivered as an 'opt in' add-on to PR programmes with shorter-than-two-hours sessions and very clear and concise contents to facilitate the understanding of the concept of mindfulness (Harrison et al., 2017). Participant narratives from one of the previously described RCTs of 8-wk MBI in COPD (Chan et al., 2015) emphasised the following benefits of the intervention: 1) transformative benefits, e.g., increased acceptance of self and COPD, improved mood, decreased reactivity, decreased COPD-related anxiety, 2) improved physical symptoms, e.g., improved breathing, less severe dyspnea exacerbations, improved non-COPD symptoms and 3) improved self-care, e.g., improved disease management, closer connection with physical self (Chan & Lehto, 2016). However, the study also revealed important barriers related to scepticism towards mindfulness, no need of help ("I suppose if I was sicker, I might need it"), problems getting to class and difficulties understanding the complexities of mindfulness.

In summary, while there is a lack of quantitative evidence in favour of MBI in COPD, qualitative studies indicate that MBIs could be acceptable in COPD if delivered in a more easily accessible and comprehensible, COPD-specific version. Based on the assumption that rumination and magnification in the cognitive appraisal of breathlessness lead to increases in physical impairment and psychological distress (see Section 1.2), the application of MBCT, which is designed to target cognitive patterns associated with affective disorder, may yield more positive results that previously evaluated MBSR-based programmes in COPD.

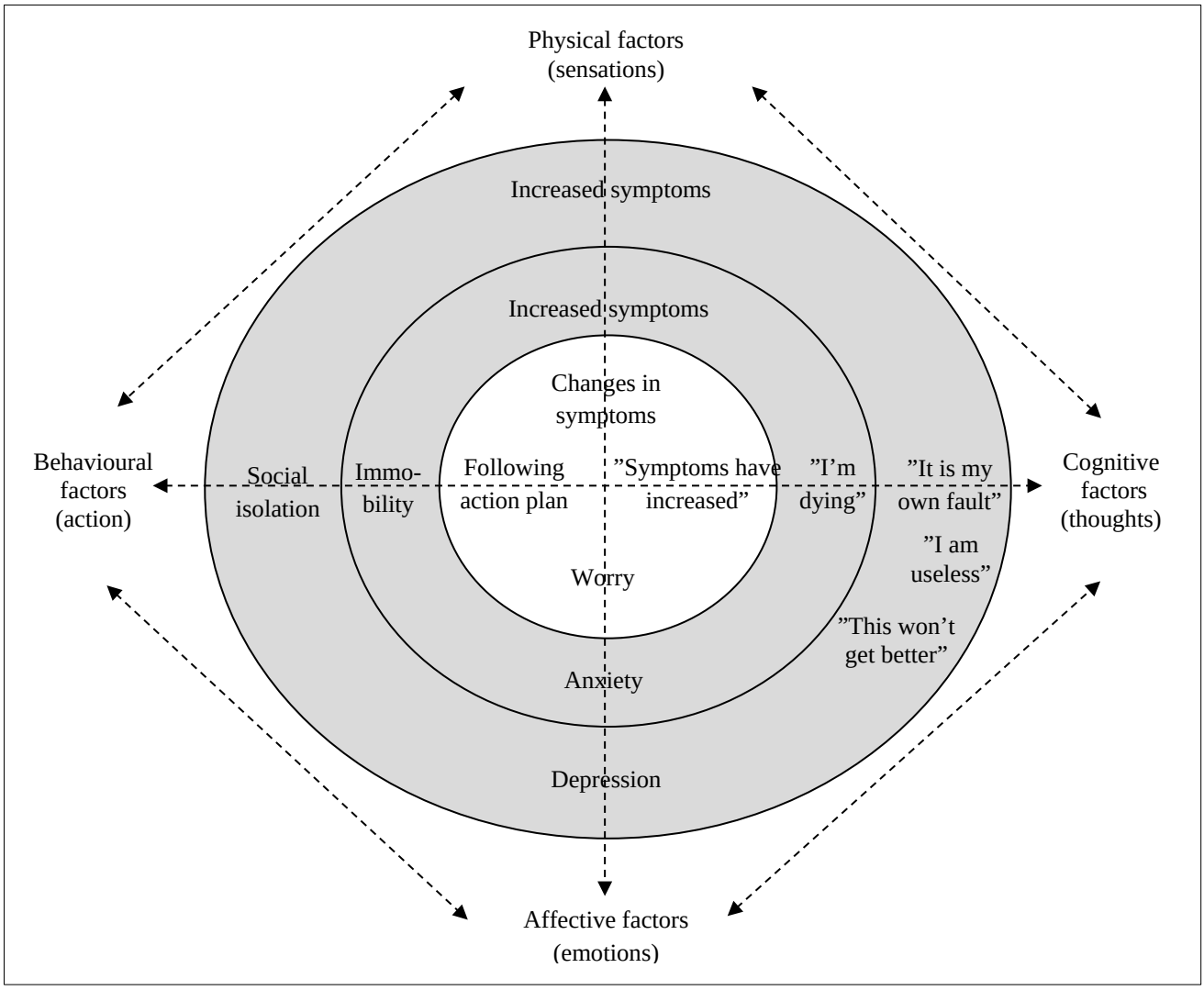
1.4.2 Mindfulness and the relief of suffering in COPD

> *"In healthy people, breathing is the most natural thing in the world. No need to think about it. No need to be concerned about it. It is not even the object of conscious perception. But when breathing becomes difficult, when it produces* suffering *[emphasis added], nothing else matters. Life discolours and shrinks around an act of breathing that has become elusive and uncertain, but pervasive. […] not being able to breathe freely is probably the worst thing that can happen to a human being."* (Similowski, 2018, p. 1).

Drawing on Buddhist philosophy, the relief of suffering through insight and compassion is a central matter in MBI (Bodhi, 2011). Applying Buddhist thought in the context of COPD, breathlessness can be described as an unavoidable aspect of living with COPD, whereas the *suffering* that emerges as a consequence of automatic attempts to interpret and avoid physical sensations such as breathlessness can be reduced through the ongoing practice of mindfulness.

Based on these fundamental assumptions, one can propose an illustrative model of psychological distress in COPD as depicted in Figure 2. At the core of the model (the white area), physical sensations of COPD-symptoms are inherent aspects of living with COPD, and thoughts, emotions and actions/behavior emerging as immediate and interrelated reactions to these physical sensations could be adaptive as long as they enable the participant to act according to what is helpful in a particular situation. For example, the physical sensations of changes in symptom levels beyond normal day-to-day variation could activate thoughts such as "symptoms have increased", which could lead to feelings of worry and subsequent behavioural responses such as using short-acting bronchodilators, applying breathing techniques or contacting primary or secondary health care according to a predefined action plan (see Section 1.1). If these reactions are in accordance with the immediate magnitude of change in experienced levels of COPD-symptoms, they are in fact adaptive in the sense that they allow the patient to monitor and respond wisely to underlying pathological changes that warrant patient self-management or medical attention.

Figure 2: Proposed psychological model of the development of suffering in COPD

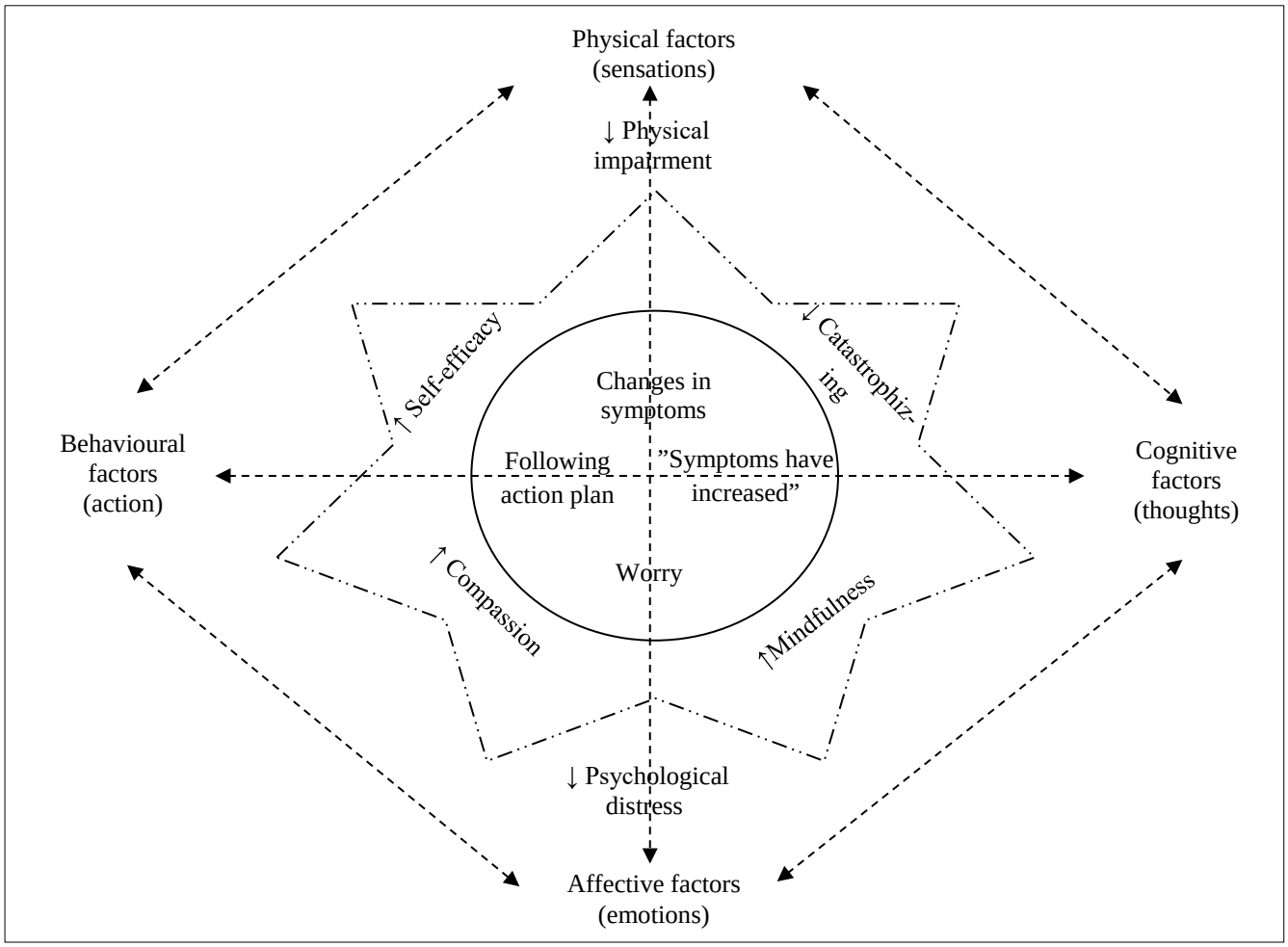


What is not adaptive, however, is when additional layers of suffering are added as ripples in the water (the grey area, Figure 2). The two outer levels of the model provide examples of interrelated cognitive, affective and behavioural responses to physical sensations that have spiraled out of control and thereby have become maladaptive. Here, a chain of cognitive reactions goes from an immediate, neutral ‘comment’ on the symptom (e.g. “symptoms have increased”) to catastrophizing appraisal (e.g. “I’m dying”) which bi-directionally influences affective-behavioural factors such as anxiety and immobilisation and an increase in symptom levels. At the same time, the cognitive chain reaction can also give way for negative depression-specific automatic thinking (e.g. “It is my own fault for being like this”, “This will never get better”, “I am useless”) with the interrelated affective-behavioral factors of depression and social isolation (Malpass et al., 2015).

1.4.3 Proposed drivers of change in MBCT for COPD

Following up on the proposed psychological model of suffering in COPD (Figure 2), moment-to-moment awareness of bodily sensations, thoughts and emotional states is thought to give an individual patient the opportunity of noticing when and how symptoms such as breathlessness arise, and to respond wisely and self-compassionately as an alternative to the automatic activation of additional layers of suffering in COPD. As illustrated in Figure 3, instead of leading to increases in physical impairment and psychological distress through cognitive mechanisms of catastrophizing, the immediate perception of COPD symptoms at the core of the model is surrounded and "contained" by direct, mindful awareness of immediate physical, cognitive, affective and behavioural factors and a compassionate attitude towards oneself and, thereby, an experience of self-efficacy (the proposed mediating effects of mindfulness, self-compassion, catastrophizing and self-efficacy are described in more detail below).

Figure 3: Proposed psychological model of the relief of suffering in COPD



The mindfulness-based approach to cognitive therapy differs from classical CBT in that it does not seek to change or control the content of thoughts but only how people relate and respond to them (Crane et al., 2017; Segal et al., 2013). Thus, the primary aims and intentions of MBCT in COPD are to (inspired by MBCT for depression (Segal et al., 2013; van der Velden et al., 2015)):

1) enable participants to notice the automatic activation of interrelated physical, cognitive, affective and behavioural responses, and how these can develop into maladaptive patterns of psychological distress and physical impairment
2) decenter from these processes by redirecting attention to stable physical sensations, such as the sensations of the heart beating, the blood flowing and the contact to the floor, and observing the unfolding of thoughts, emotions and physical sensations on that basis,
3) develop a meta-awareness and thereby come to see thoughts and feelings as temporary and automatic events in the mind that does or does not demand action, and
4) relate to the change and flux of thoughts, emotions and physical sensations with a curious and compassionate attitude (e.g. "how can I best take care of myself right now").

As can be seen in the star-shaped area of Figure 3, four specific constructs are proposed to act as mediators of the effect of MBCT in COPD: 1) increased mindfulness, 2) increased self-compassion, 3) decreased breathlessness catastrophizing and 4) increased COPD-specific self-efficacy.

Mindfulness: For meditation novices, the construct of mindfulness can be operationalised to include the facets of describing experiences, acting with awareness, non-judging of experiences and non-reactivity to experiences (Baer, Smith, Hopkins, Krietemeyer, & Toney, 2006; Williams, Dalgleish, Karl, & Kuyken, 2014). Mindfulness has been shown to mediate effects of MBCT on depressive symptoms in relation to recurrent depressive disorder (Batink, Peeters, Geschwind, van Os, & Wichers, 2013; Kuyken et al., 2010). Increasing non-judgemental present-moment awareness through mindfulness practice may enable COPD-patients to familiarise themselves with the nuances of the physical experience of breathlessness without subsequent intensification of psychosomatic responses and instead act with awareness on what is the most helpful action in a particular moment (Addy, 2007; Malpass et al., 2015; O'Donnell et al., 2007). Therefore, mindfulness may act as a mediator of MBCT's effect on psychological distress and physical impairment in COPD.

Self-compassion: The construct of self-compassion can be defined as being aware of, touched by, open to and non-judgemental of one's own suffering in a way that it is seen as part of the larger human

experience (Neff, 2003). Increased levels of self-compassion act as a mediating factor of MBCT in depression relapse prevention (Kuyken et al., 2010). Findings from qualitative studies indicate that COPD-patients consider their illness to be self-inflicted and feel guilty and shameful due to prior smoking (Giacomini, Dejean, Simeonov, & Smith, 2012; Lindqvist & Hallberg, 2010). Such self-blame and the experience of social stigma have been shown to be associated with social isolation and psychological distress in COPD (Johnson, Campbell, Bowers, & Nichol, 2007; Plaufcan, Wamboldt, & Holm, 2012). Increased levels of self-compassion through MBCT may prevent the cognitive chain reaction of depression-specific automatic thoughts, and the interrelated affective-behavioural factors of depression and social isolation, which may altogether reduce psychological distress and physical impairment in COPD (Malpass et al., 2015).

Breathlessness catastrophizing: Breathlessness catastrophizing is an example of a negative cognitive orientation in COPD where rumination about experiences with breathlessness, magnification of the threat value and perceived inability to control breathlessness can trigger and the reinforcement of psychological distress and physical impairment in COPD (Solomon et al., 2015). Previous studies indicate that MBCT may decrease rumination and cognitive reactivity and, thereby, depressive symptoms and relapse risk (Kuyken et al., 2010; Shahar, Britton, Sbarra, Figueredo, & Bootzin, 2010; van Aalderen et al., 2012). Moreover, a qualitative study indicates that MBCT helped COPD and asthma patients to realise that "thoughts are not facts", which appeared to change how they related to and focused on their breathlessness and left less attentional resources for catastrophizing and rumination (Malpass et al., 2015). Therefore, targeting breathlessness catastrophizing in MBCT for COPD is hypothesised to act as a mediator of effects on bi-directional psychological and physical outcomes.

COPD-specific self-efficacy: Self-efficacy refers to an individual's conviction that he or she can successfully execute a behaviour required to produce a desired outcome, and consequently enables initiation and persistence of coping behaviour (Bandura, 1977). In COPD-patients, negative expectations regarding their ability to manage breathing difficulties have been shown to be related to avoidance of situations that may cause breathlessness (e.g. physical activity; emotional and cognitive arousal; weather and environmental conditions) regardless of actual physical capability (Wigal, Creer, & Kotses, 1991). It has been suggested that mindfulness training achieves its beneficial outcomes through an increase in perceived self-efficacy (Baer, 2003; Grossman, Niemann, Schmidt, & Walach, 2004; Perez-Blasco, Viguer, & Rodrigo, 2013) which may also be the case in COPD. Indeed, the qualitative study of COPD- and asthma-patients' experiences of MBCT revealed that a richer and

more decentred understanding of subtle bodily sensations as early warning signs of breathlessness and affective-behavioural responses facilitated a sense of control of difficult situations (Malpass et al., 2015).

Following up on the proposed mediators, it is relevant to consider and explore potential moderators of the effect of MBCT in COPD (Holmes et al., 2018). In addition to the sociodemographic factors of age and gender, factors related to MBCT adherence and the therapeutic working alliance may moderate treatment outcomes. On the basis of the assumption that MBIs retrieve their effects primarily through a fundamental change in the way people relate to events and experiences in everyday life, research suggests that adherence to treatment curriculum is essential for the benefit of MBIs, e.g., by showing up to treatment sessions and by establishing a regular home practice between sessions that can be maintained also after the formal intervention programme has ended (Parsons, Crane, Parsons, Fjorback, & Kuyken, 2017). Therefore, it is relevant to explore the potentially moderating influence of attendance to MBCT sessions (i.e., number of sessions attended) and adherence to home practice (i.e., home practice diaries) on the outcomes of MBCT in COPD. Moreover, the therapeutic alliance can be defined as the affective bond and mutually agreed goals and tasks between client and therapist in psychosocial intervention (Horvath & Greenberg, 1989), and is thought to matter a great deal in MBIs as it potentially allows for modelling of mindfulness and compassion (Aalderen, Breukers, Reuzel, & Speckens, 2012; Goldberg, Davis, & Hoyt, 2013). Therefore, it is relevant to explore the possible moderating influence of the therapeutic alliance on outcomes of MBCT in COPD.

In summary, while RCTs to this date have not clearly been in favour of MBI in COPD, there is theoretical and qualitative empirical reasons to believe that MBCT specifically tailored to the needs of the COPD-population can increase mindfulness, self-compassion and self-efficacy as well as decrease breathlessness catastrophizing and thereby reduce psychological distress and physical impairment in COPD. With the additional purpose of examining the characteristics of those who benefit most of the intervention, it is relevant to explore the moderating influence of age, gender, adherence to MBCT curriculum (i.e., attendance to MBCT sessions and home practice adherence) and the therapeutic working alliance.

1.4.4 COPD-specific adjustments of the original MBCT manual

With the purpose of securing the integrity of the adapted MBCT intervention, essential ingredients of the mother programme (MBCT for depression (Segal et al., 2013)) should be maintained while certain elements are seen as more flexible and should be adjusted to suit the needs of the specific target

population, in this case patients with COPD (Crane et al., 2017). The essential elements of the COPD-specific programme are based on the foundational basis of MBCT for depression, and are reflected in the aims and intentions described in the previous section. The adaptions of the flexible elements of programme structure, length and delivery are described in the following and includes: 1) focus on the breath, 2) length and intensity of meditation exercises and home practice and 3) complexity of cognitive exercises. The complete adjusted treatment manual can be found in Appendix D.

Focus on the breath: In the original MBCT-programme, experiential awareness of the breath is used as an ever-present and stabilising connection to the present moment from the basis of which participants can investigate the impermanent character of unpleasant bodily sensations, thoughts and emotions in a decentred manner (Segal et al., 2013). For individuals with COPD, the breath is often experienced as an ever-present source of distress (Bailey, 2004; Hasson et al., 2008; Heinzer, Bish, & Detwiler, 2003), suggesting that the role of the breath should be modified for COPD in order to maintain the original purpose of the programme. The heartbeat, the blood flow and grounding (e.g., the sensation of the feet touching the floor) are ever-present physical mechanisms that can be used as alternative points of present-moment awareness. The sensation of grounding can be used to mobilise the gathering of attention, whereas the heartbeat and the blood flow can be used to mobilise an attitude of letting be – bringing a certain quality of softness and warmth to the awareness of uncomfortable physical sensations. To give an example, the body scan exercise (Appendix D, p. 146), which facilitates mindful awareness of each part of the body, originally instructs participants to use the sensations of the breath to move from one part of the body to another. In the COPD-specific version of this exercise, body awareness was facilitated by the sensation of the heart beat and the blood flow moving through the body. This does not mean that the sensation of the breath (or breathlessness) should be ignored in the programme, but rather that the focus of the breath should be changed from being a means of stabilisation to being a potential source of discomfort in line with awareness of other uncomfortable physical sensations. These specific adaptations are in line with other COPD-specific adaptations of MBSR (Chan et al., 2015) and MBCT (Malpass et al., 2015).

Length and intensity of treatment sessions and meditation practices: The original MBCT programme consists of two-hour sessions including guided meditation practices of 30-45 minutes duration during which participants are sitting in an upright position or lying down on a mat. In addition to relatively high age and debilitating comorbidities, COPD is associated with substantially poorer lower extremity function, poor balance and self-reported functional limitations such as standing, sitting and getting

up from a lying position (Eisner et al., 2008). Shorter treatment sessions (1 hours and 45 minutes) and meditation practices (20-30 minutes) is a way of taking care of the vulnerable physical condition of patients with COPD, which is an adaptation that is also suggested by patients and healthcare professionals in a qualitative study of attitudes towards MBI (Harrison et al., 2017). In a meta-analysis including 30 studies of MBSR in clinical and non-clinical populations (Carmody & Baer, 2009), the correlation between effect size on psychological distress and number of in-class hours was small and non-significant (r=-.25, p=0.18) with longer versions of MBSR showing smaller effects. This suggests that a reduction of in-class hours may be worthwhile in populations for whom longer time-commitment may be a barrier to their ability or willingness to participate. With regards to meditative yoga exercises included in MBCT, these were adjusted based on cancer-specific adaptations (Bartley, 2012) with the purpose of taking care of the restricted physical capacity of the COPD population. Examples of instructions include gentle stretching of upper and lower extremities from a sitting position.

The complexity of cognitive exercises: It has been suggested that comprehensive CBT programmes may be inappropriate in COPD due to the relatively high age, and hence low cognitive capabilities, of the population (Coventry & Gellatly, 2008). Furthermore, qualitative research of COPD-patients' attitudes towards MBI points to the need for simplification (Harrison et al., 2017). The complexity in the structure of certain cognitive exercises in the adapted MBCT programme should therefore be reduced. This is exemplified by an exercise in which participants explore links between activities of daily life and changes in their psychological state. In the original version of this exercise, participants are told to, first, make a list of typical everyday activities. Thereafter, they are instructed to mark each activity with an "N" (nourishing activities) and/or a "D" (depleting activities) and to consider ways of skilfully balancing the two categories in everyday life. As a third step, participants in the original programme are asked to mark activities with a "P" (activities that give pleasure) and/or an "M" (activities that give a sense of mastery) and to consider ways of expanding the list by including more of such activities in daily life (Segal et al., 2013). In the less complex COPD-specific version (Appendix D, pp. 130-131 and 139-140), participants are similarly instructed to make a list of everyday activities, but instead of using the words "nourishing" and "depleting", they are asked to mark activities with either a plus (+) and/or a minus (-) corresponding to whether the activity boosts or lowers their energy levels. To illustrate the point of skilfully balancing plus and minus activities, the metaphor of savings in the bank is introduced – one can only buy if there is money left to spend. Instead of additionally

marking pleasant and mastery activities, this is discussed more implicitly if there appears to be an imbalance in the plus and minus activities.

In addition to the three points mentioned above, more general adaptations in terms of working with unpleasant bodily sensations, thoughts and emotions through physical activity are applied in MBCT for COPD. In a non-systematic review of mindfulness in the promotion of physical activity amongst older adults, Rejeski (2008) posits that the body is where mindfulness is experienced. Bringing mindful awareness to physical activity can thereby serve as a laboratory, providing valuable lessons about the nature of suffering, the impermanence of sensations and experience, and how the mind functions as a reactive 'narrator' often leading to worry, self-critique and a cognitive clinging to past memories or future plans disconnected from the activity of the body in the present moment (Rejeski, 2008). In COPD, the body in motion can be said to form the scene on which the maladaptive patterns of affective-behavioural reactions to bodily sensations of breathlessness or other COPD symptoms are played out. Adding MBCT to PR, in which there is a strong focus on exercise and physical activity, is thought to enable the patients to realise how mindfulness can be applied in day-to-day moments with physical activity (Malpass et al., 2015). In MBCT adapted for COPD, the walking meditation is moved from MBCT Session 4 to Session 5 in the COPD-adaptation, based on the structural notion that Session 5 is where the programme starts focusing on applying the mindfulness-skills that has been learned in Sessions 1-4 on 'real-life' difficulties (Segal et al., 2013).

In summary, the essential elements of the mother programme (MBCT for depression) are maintained while the more flexible elements of the programme, including structure, length and delivery are changed in accordance with the needs of the target population (MBCT for COPD).

1.5 Home-based psychosocial intervention

There is an inherent paradox in, on the one hand, COPD-patients' undeniable need for help and, on the other hand, their poor uptake of and adherence to psychosocial and behavioural interventions (Blackstock, ZuWallack, Nici, & Lareau, 2016; Fischer et al., 2007; Keating et al., 2011). And ironically, the pattern of fear and avoidance in COPD described in Section 1.2, could be an underlying reason for COPD-patients' non-attendance to the psychosocial interventions that could potentially break the very same cycles of psychological distress and physical impairment. Generally, poor adherence to treatment regimens is a well-known problem in chronic illness (von Korff, Gruman, Schaefer, Curry, & Wagner, 1997). Barriers of participation in hospital-based treatment programmes typically include activity limitations, travels issues, poor confidence in treatment effect (Fischer et

al., 2007; Keating et al., 2011; Rochester et al., 2015; Sohanpal, Steed, Mars, & Taylor, 2015). Therefore, when delivering psychosocial intervention in COPD, it is crucial to explore alternative methods of delivery. As a home-based alternative to hospital-based outpatient treatment programmes, tele-delivered psychosocial intervention are showing promising results in both mental and somatic conditions (Eccleston et al., 2014; Perle, Langsam, & Nierenberg, 2011; Rogers, Lemmen, Kramer, Mann, & Chopra, 2017; Spijkerman, Pots, & Bohlmeijer, 2016; Zachariae, Lyby, Ritterband, & O'Toole, 2016).

1.5.1 Tele-delivered MBCT

A recent systematic review by Toivonen et al. (2017) examined studies of web-based MBIs for people with physical health conditions, e.g., cancer, epilepsy and chronic pain, without restrictions related to outcomes or study designs (randomised, non-randomised, controlled and uncontrolled trials were included). They concluded that web-based MBI may be helpful in alleviating psychological and physical symptom burden, particularly when interventions are tailored for specific physical health conditions. A number of individual studies have explored the effect of tele-delivered MBCT (Tele-MBCT), specifically. Three studies of Tele-MBCT delivered asynchronously, meaning that there is a time-lag in receiver-provider communication, reported post-treatment improvements in pain interference in chronic pain patients (Dowd et al., 2015) and fatigue severity and psychological distress in cancer (Bruggeman Everts, van der Lee, & de Jager Meezenbroek, 2015). Participant-reported advantages of asynchronously delivered Tele-MBCT are related to time management (i.e., programme at own time improves receptivity) and the individual setting (e.g., sense of autonomy; not having to cope with other patients' stories) (Compen et al., 2017). Asynchronous, self-directed intervention types, however, may be challenging for the present generation of COPD-patients – an elderly population with relatively limited computer skills (Horton, 2008).

Synchronous versions of Tele-MBCT, in which providers and patients communicate through a videoconference device in real time, have shown to reduce depressive symptoms in epilepsy (Thompson et al., 2010, 2015). In COPD, synchronously tele-delivered medical consultation and PR programmes have shown feasible and acceptable in COPD (Goldstein, 2014; McLean et al., 2012). To date, however, little is known about the clinical feasibility of tele-delivered *psychosocial* interventions in COPD, and Tele-MBCT has so far not been applied and explored in this population.

Using videoconferencing to deliver psychosocial intervention has received increasing empirical support, and studies indicate high levels of patient satisfaction (García-Lizana & Muñoz-Mayorga, 2010).

Yet, the field is still in its infancy, and concerns have been raised that tele-delivered psychosocial interventions could negatively impact the development of a productive therapeutic working alliance and complicate procedures for taking clinical responsibility of patients at a distance (Emmelkamp, 2011; Perle et al., 2011). Additional issues have been related to technology-mediated presence, e.g., whether technology-mediated experiences evoke that same bodily, emotional and cognitive dynamics as real experiences and how this may influence clinical outcomes. Moreover, relatively little is known about individual variation in the experience of and responses to technology-mediated environments (Bouchard, Dumoulin, Michaud, & Gougeon, 2011; Riva, 2011). Therefore, in addition to quantitative assessments of changes in pre-specified clinical parameters, it is relevant to qualitatively explore individual patients' experiences with receiving and engaging in tele-based psychosocial interventions when evaluating its clinical feasibility and identifying relevant design issues for future efficacy trials.

2 The PhD project

2.1 Summary of background

COPD is a persistent and debilitating lung condition causing physical symptoms of breathlessness, cough and excessive sputum production. A considerable proportion of patients with COPD also experience high levels of psychological distress in the form of anxiety and depression symptoms, which persists despite optimal medical treatment. The effects of psychopharmacological approaches are limited and patients are often unwilling to take more medication. Due to the bi-directional nature of psychological and physical symptoms in COPD, psychosocial interventions may both reduce psychological distress and improve physical health status in COPD.

To date, systematic reviews of psychosocial intervention in COPD have predominantly included studies of CBT-informed intervention types, and not 'mind-body' types of psychosocial intervention, which otherwise have gained a massive increase in attention and popularity over the recent decades. Moreover, meta-analyses have focused on the effect of psychosocial intervention on psychological outcomes and have not quantitatively summarised effects of psychosocial intervention on physical outcomes. Therefore, there is a need for meta-analyses that takes a broader approach to psychosocial intervention types and the outcomes they may improve.

Mindfulness-based cognitive therapy (MBCT) is a psychosocial intervention programme that combines elements from CBT and mind-body approaches. It is thought to have the potential to relieve psychological distress and physical impairment in COPD, but no studies have so far tested the efficacy of this particular psychosocial intervention.

Despite the apparent need for help, barriers related to poor accessibility have shown to prevent COPD-patients from taking part in potentially effective interventions. Consequently, there is a need for studies exploring alternative modes of delivery, e.g., tele-delivered psychosocial intervention.

2*.1.1 Aims of the PhD project*

On this background, the overall aim of the PhD project was to investigate effects, mechanisms and delivery of psychosocial intervention in COPD, with the more specific aims being:

- To systematically review and quantitatively summarise the existing evidence for the efficacy of psychosocial interventions in improving psychological and physical outcomes in COPD

- To adapt MBCT for COPD and investigate its efficacy as an add-on to a standardised PR programme in improving psychological distress and physical health status in COPD
- To explore possible mediators of the effect of MBCT in COPD (what works?)
- To explore possible moderators of the effect of MBCT in COPD (for whom?)
- To evaluate the clinical feasibility of tele-delivered MBCT in COPD.

The PhD dissertation includes three papers based on three separate studies: 1) A systematic review and meta-analysis of psychosocial intervention in COPD (Study 1; results presented in Paper 1, see Appendix A), 2) a cluster randomised controlled trial of MBCT in COPD (Study 2; results presented in Paper 2, see Appendix B) and 3) a feasibility study of tele-delivered MBCT in COPD (Study 2; results presented in Paper 3, see Appendix C). Moreover, the dissertation includes the adapted MBCT treatment manual for COPD (Appendix D).

Study 2 was approved by the Central Denmark Region Committee on Health Research Ethics (number: 1-10-72-253-13) and pre-registered at ClinicalTrials.gov (registration number: NCT02042976). Participants in Study 3 were recruited from the control group of Study 2.

2.2 Summaries of included papers

2.2.1 Paper 1

Title: "Efficacy of psychosocial interventions on psychological and physical health outcomes in chronic obstructive pulmonary disease: a systematic review and meta-analysis." (Appendix A)

Aim: The primary study objective was to summarise the existing evidence of the efficacy of psychosocial intervention on relevant psychological and physical outcomes in COPD. Additionally, it was explored whether some types of psychosocial interventions are more effective than others and to what degree the effects are related to the methodological quality of the studies.

Methods: A systematic review of the databases of PubMed, PsychINFO, Embase, Web of Science, Cochrane Library and CINAHL was performed by combining key words related to 1) the population, 2) the intervention and 3) the outcomes of interest. English-language reports describing controlled trials and published in peer-reviewed journals were considered eligible. Two independent researchers extracted relevant data from included studies and rated their methodological quality based on the Jadad criteria (Jadad et al., 1996) and five additional criteria developed for the purpose of the present study. Heterogeneity was explored using Q and I^2 statistics. Standardised effect sizes (Hedges' g) in

the included studies were computed based on pre- and postintervention means or medians and their standard deviations or ranges. Pooled overall effect sizes were calculated for the effect of psychosocial intervention on psychological and physical outcomes, respectively. Subsequently, possible between-study differences in effect sizes were explored by comparing the effect sizes of studies according to the study characteristics of active v. passive control, intervention type and methodological quality, treatment duration, number of sessions, age, gender and lung function at baseline, using meta-ANOVA and meta-regression. Publication bias was evaluated by inspecting funnel plots and using Egger's test (Egger, Smith, Schneider, & Minder, 1997). Possible publication bias was followed up with Duval and Tweedie's method (Duval & Tweedie, 2000) and calculation of fail-safe numbers (Copas & Shi, 2000).

Results: Twenty independent studies investigating a total of 1,361 patients were included and subjected to meta-analytic evaluation. After adjusting for potential publication bias, a statistically significant overall effect was found for the combination of psychological outcomes (i.e., anxiety and depression) (g=0.38, p<0.001), but not for the combination of physical outcomes (i.e., dyspnea, exercise capacity, fatigue, lung function) (g=0.20, 95% CI=-0.05–0.44). Moreover, we found a statistically significant, but small, effect on QoL (g=0.24, p=0.018), an outcome where psychological and physical domains are combined. Regarding individual intervention types, CBT appeared to be effective for improving the combination of psychological outcomes (g=0.39, p=0.001), whereas for the combination of physical outcomes, only mind-body intervention (e.g. mindfulness-, yoga- and relaxation-based psychosocial interventions) revealed a statistically significant effect (g=0.40, p=0.042). Near-significant results of meta-regression analyses indicated that longer treatment duration was associated with smaller effect sizes for psychological (B=-0.06, p=0.054) and physical (B=-0.05, p=0.066) outcomes. Neither of the remaining variables (i.e., study quality, number of sessions, age, gender, lung function at baseline) showed to moderate the effect.

Conclusion: Overall, the results suggest that psychosocial intervention is efficacious in improving psychological outcomes in COPD. Specifically, CBT intervention types appeared to improve psychological outcomes, whereas mind-body type interventions appeared to improve physical outcomes. However, due to indications of possible publication bias towards positive findings, the results should be interpreted with caution, and more high quality research is needed.

Preliminary results of an updated version of the systematic review and meta-analysis: At the time of the systematic literature search for Study 1, an alert system was set up in PubMed using the key words

presented in Paper 1. In May 2018, a screening of all the received notifications of recently published studies yielded 8 eligible clinical trials published after March 2014 (see Table 3). Updated meta-analyses of main effects showed psychosocial intervention to be efficacious for both psychological (g=0.325, p=0.000, K=21, I^2=36.06) and physical outcomes (g=0.279, p=0.000, K=24, I^2=49.76), and there were no indications of publication bias. These results suggest that there is currently a low risk of publication bias in studies of psychosocial intervention in COPD. While psychosocial intervention improved both psychological and physical outcomes, there appeared to be larger effects of psychological compared to physical outcomes based on a descriptive characterisation of the magnitude of the effects.

Table 3. Eligible clinical trials published after publication of Paper 1.

	Study design (sample size[a]; mean age; % women)	Groups	Intervention type[b] (number of sessions/treatment duration in weeks	Physical outcome measure(s)	Psychological outcome measure(s)
Howard & Dupont (2014)	RCT (222/139; mean age for the total sample not reported; 51.8%)	(1) AC (COPD information booklets) (119/68) (2) COPD breathlessness manual + facilitator contact (112/71)	CBT (5/5)	(1) Dyspnea: CRQ dyspnea subscale (2) Fatigue: CRQ fatigue subscale	(1) Anxiety: HADS anxiety subscale (2) Depression: HADS depression subscale
Chan et al. (2015)	RCT (41/38; 69.5 yrs; 65.9%)	(1) PC (22/22) (2) Mindful meditation intervention, MBSR-format (19/16)	Mind-body (8/8)	(1) Dyspnea: CRQ dyspnea subscale (2) Fatigue: CRQ fatigue subscale	(1) Anxiety: ASI-3
Ranjita et al. (2016)	RCT (81/72; 54 yrs; 0.0%)	(1) PC (40/36)) (2) Comprehensive meditative yoga programme (41/36	Mind-body (72/12)	(1) Exercise capacity: 6MWT (2) Dyspnea: Borg scale (3) Fatigue: Borg scale	-
Bove et al. (2016)	RCT (88/58; 70.20 yrs; 66.7%)	(1) PC (33/28) (2) Minimal home-based psychoeducative intervention (33/30)	CBT (1/1)	(1) Dyspnea: CRQ dyspnea subscale (2) Fatigue: CRQ fatigue subscale	(1) Anxiety: HADS anxiety subscale
Luk et al. (2017)	NRCT (34/28; 72.4 yrs; 53.6%)	(1) AC (PR only) (18/14) (2) CBT + PR (16/14)	CBT (6/8)	(1) Exercise capacity: 6MWT (2) Dyspnea: CRQ dyspnea subscale (3) Fatigue: CRQ fatigue subscale	(1) Anxiety: DASS anxiety subscale (2) Depression: DASS depression subscale
Doyle et al. (2017)	RCT (110/95; 68.0 yrs; 65.5%)	(1) AC (Telephone-delivered 'befriending' intervention) (56/52) (2) Telephone-delivered CBT (54/43)	CBT (8/8)	-	(1) Anxiety: BAI (2) Depression: PHQ-9

Perkins-Porras et al. (2018)	RCT (80/50; mean age for the total sample not reported; 48.8%)	(1) AC (10-min natural history audio recording) (40/24) (2) 10-min mindfulness intervention (40/26)	Mind-body (1/1)	(1) Dyspnea: Borg scale	(1) Anxiety: HADS anxiety subscale (2) Depression: HADS depression subscale
Volpato et al. (2018)	RCT (39/38; 72.66 yrs; 39.5%)	(1) AC (Documentary movie with neutral contents) (20/19) (2) One-session mindful breathing relaxation exercise (19/19)	Mind-body (1/1)	(1) Lung function: spirometry	(1) Anxiety: STAI state subscale

Abbreviations: AC=Active control. ASI-3=Anxiety Sensitivity Index-3. BAI= Beck Anxiety Inventory. CAT=COPD Assessment Test. CBT=Cognitive behavioural therapy. CRQ=Chronic Respiratory Questionnaire. DASS=Depression Anxiety Stress Scales. HADS=Hospital Anxiety and Depression Scale. NRCT=Non-randomised controlled trial. PC=Passive control. PHQ-9=Patient Health Questionnaire 9-item depression scale. PR=Pulmonary rehabilitation. STAI=State-Trait Anxiety Inventory. RCT=Randomised controlled trial.

[a]= Reported total sample size, with analysed sample-size reported in parentheses.

[b]=Specific psychosocial intervention programmes are categorized as either CBT or mind-body (e.g., relaxation-, mindfulness-, yoga-, taichi- or quigoing-based psychosocial intervention).

2.2.2 Paper 2

Title: "Mindfulness-based cognitive therapy in COPD: a cluster randomised controlled trial" (Appendix B)

Aim: The primary aim of the study was to test the efficacy of MBCT as an add-on to a standard PR programme in improving the outcomes of psychological distress and physical health status impairment in COPD. Secondarily, the efficacy on activity levels and the expression of certain inflammatory cytokines was evaluated. In addition, we explored the possible moderating effects of age, gender, MBCT attendance rate and patients' perception of the therapeutic working alliance, together with the potential mediating effects of mindfulness, self-compassion, breathlessness catastrophizing and COPD-specific self-efficacy.

Methods: COPD-patients eligible for PR were cluster randomised to receive either an 8-week, group-based MBCT-programme as an add-on to an 8-week PR programme (MBCT+PR; n=39), or PR alone (PR-only; n=45). The primary outcomes of psychological distress and physical health status impairment were measured with the Hospital Anxiety and Depression Scale (HADS) total score (combining the measurement of anxiety and depression subscales) and the COPD Assessment Test (CAT) before randomisation (T1), mid- (T2) and post-intervention (T3), and at three (T4) and six (T5) months follow-up. The secondary outcome of physical activity level was measured by triaxial accelerometers carried around the waist for two periods of 7 days (T1 and T3), while blood samples were collected at T1 and T3 for the analysis of the secondary outcome of inflammatory cytokine expression (i.e., the biomarkers of TNF-α, IL-6, IL-8 and IL-17E). Regarding moderators, age and gender were registered at T1, the number of MBCT sessions attended was registered for patients in the MBCT+PR arm at T3, and patient perceptions of the therapeutic working alliance was assessed with the Working Alliance Inventory (WAI) at T2. For the assessment of home practice attendance, patients were asked to keep a diary of the frequency and duration of meditation practice between sessions. Potential mediators were assessed with the Five-Facet Mindfulness Questionnaire (FFMQ) (total score of four facets only, which has been suggested in samples of previously non-meditators (Williams et al., 2014)), the Self-Compassion Scale (SCS), the Breathlessness Catastrophizing Scale (BCS) and the COPD-specific Self-Efficacy Scale (CSES). *A priori* sample size calculations indicated that 2 × 56 patients would be sufficient to detect an average three-point reduction in CAT scores after PR with 80% statistical power (two-sided α, 5%) (Dodd et al., 2011). In addition, the chosen sample size also allowed for detection of a between-group minimal clinically important difference in HADS total scores over

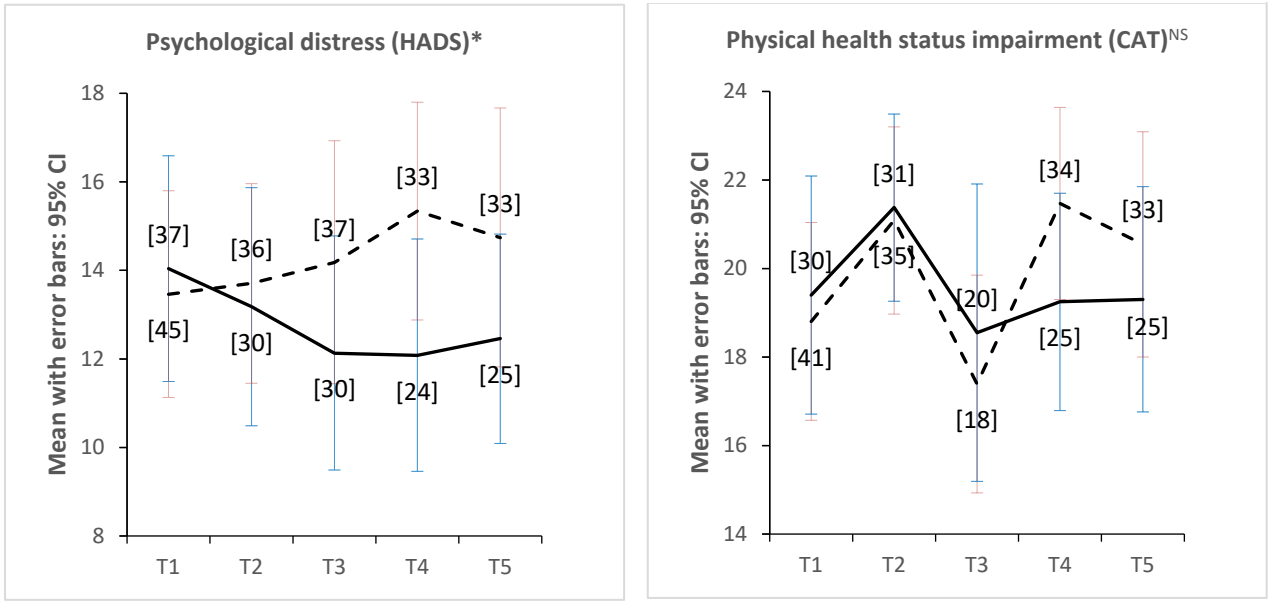
time of 1.5 points (Puhan, Frey, Büchi, & Schünemann, 2008) with a statistical power of 78%. Multilevel models (MLM) were used to evaluate treatment effects of primary outcomes and the secondary outcome of activity level over time, i.e., time × arm (Tasca, Illing, Joyce, & Ogrodniczuk, 2009; Verbeke & Molenberghs, 2000). Two-way ANOVAs were used to compare cytokine expression levels in the treatment arms from T1 to T3. Treatment moderators were explored as two-way interaction terms (time × moderator) when measures were only available in the MBCT-PR arm (i.e., MBCT attendance rate and working alliance) and as three-way interaction terms (time × arm × moderator) when measures were available in both arms (i.e., gender and age). If treatment effect was detected, potential mediators were explored in time-lagged analyses (Verbeke & Molenberghs, 2000) in the MBCT+PR group only.

Results: In the period between February 2014 and January 2016, 84 COPD-patients (inclusion rate=52%), divided over 12 PR clusters, took part in the present study (MBCT+PR: n= 39, number of clusters=6; PR-only: n=45, number of clusters=6). Participants had a mean age of 67.2 years (SD=7.74), and 57.1% were women. Fourteen patients from the intent-to-treat population withdrew from the study, and 12 patients failed to return questionnaires. Average PR attendance did not differ significantly between study arms (MBCT+PR=10.7 out of 16 sessions; PR-only=10.0 out of 16 sessions; p=0.434). Participants in the MBCT+PR arm attended an average of 4 out of 8 MBCT sessions (SD=2.74).

A graphical overview of means and confidence intervals for primary outcomes over time can be found in Figure 4. A statistically significant time × arm effect was found for the HADS total score (Cohen's d=0.62, p=0.010). The result remained significant when adjusting for multiple comparison (Benjamini-Hochberg correction) and when testing its robustness (MLM with last observation carried forward for study dropouts). Supplementary analyses of the HADS depression and anxiety subscales showed a statistically significant time × arm effect on depression (d=0.51, p=0.009), but not anxiety (d=0.26, p=0.136). The treatment effect on the CAT failed to reach statistical significance (d=0.42, p=0.061). Concerning secondary outcomes, the effect on activity level did not reach statistical significance. A statistically significant increase in the expression of the inflammatory cytokine of TNF-α from T1 to T3 was found in the PR-only arm (mean diff. (mRNA fold change value): 0.42, p=0.04), whereas TNF-α remained unchanged in the MBCT+PR arm (mean diff.: 0.05, p=0.31). The between-arm difference did not reach statistical significance. No statistically significant changes were found in IL-6 and IL-8 mRNA from T1 to T3, and IL-17E mRNA was not detectable in the blood samples

and could therefore not be subjected to statistical analysis. A moderating effect of age was found for the effect on the HADS (d=0.38, p=0.040), indicating a better outcome for younger patients. The moderating effects of gender, the WAI and attendance rate did not reach statistical significance, and data on home practice attendance were not subjected to analysis as only three patients completed their diaries. Concerning mediators, changes in self-compassion (SCS) statistically significantly preceded changes in HADS scores (B=0.24, p=0.035), while the reverse pattern was not significant (B=0.20, p=0.227). Changes in the FFMQ total, the BCS and the CSES were not statistically significant predictors of subsequent change in the HADS.

Figure 4. Means and 95% confidence intervals for primary outcomes



Notes: [N]: No. of respondents. T1: Baseline. T2: Mid-intervention. T3: Post-intervention. T4: 3 months follow-up. T5: 6 months follow-up.
Abbreviations: CAT=COPD Assessment Test. HADS=Hospital Anxiety and Depression Scale.
* Marks a statistically significant time x arm effect (p<0.05)
NS Marks a statistically near-significant time x arm effect (p<0.10)

Conclusion: Our main findings indicated that MBCT as an add-on to PR led to a clinically relevant reduction (1.5 points (Puhan et al., 2008)) of psychological distress in COPD, which was maintained six months after termination of the 8-week intervention period. Additional analyses suggested that MBCT relieved psychological distress primarily by reducing symptoms of depression rather than anxiety. The only near-significant effect on the primary outcome of physical health status impairment

did not reach clinical significance (2.0 point reduction (Kon et al., 2014)). Concerning moderator analyses, MBCT appeared to be more efficacious for younger patients, and mediation analyses suggested that the effect of MBCT on psychological distress may be facilitated through increased levels of self-compassion. The final sample was smaller than expected which could explain the statistically non-significant effect on physical health status impairment. Moreover, the results should be interpreted with caution, as a psychological component (e.g., competing or attention control) was not added to the PR programme in the control arm. To increase the validity of the results, future trials including larger samples and attention control arms are recommended.

2.2.3 Paper 3

Title: "Tele-delivered mindfulness-based cognitive therapy in chronic obstructive pulmonary disease: a mixed-methods feasibility study" (Appendix C)

Aim: The aim of the study was to evaluate the clinical feasibility of tele-delivered MBCT (Tele-MBCT) in COPD in relation to the three overall areas of 1) clinical change, 2) attendance and 3) working alliance. The combination of quantitative and qualitative methods enabled both a deductive (i.e., assessment of pre-specified clinical parameters) and inductive (i.e., spontaneous individual experiences) approach to the evaluation.

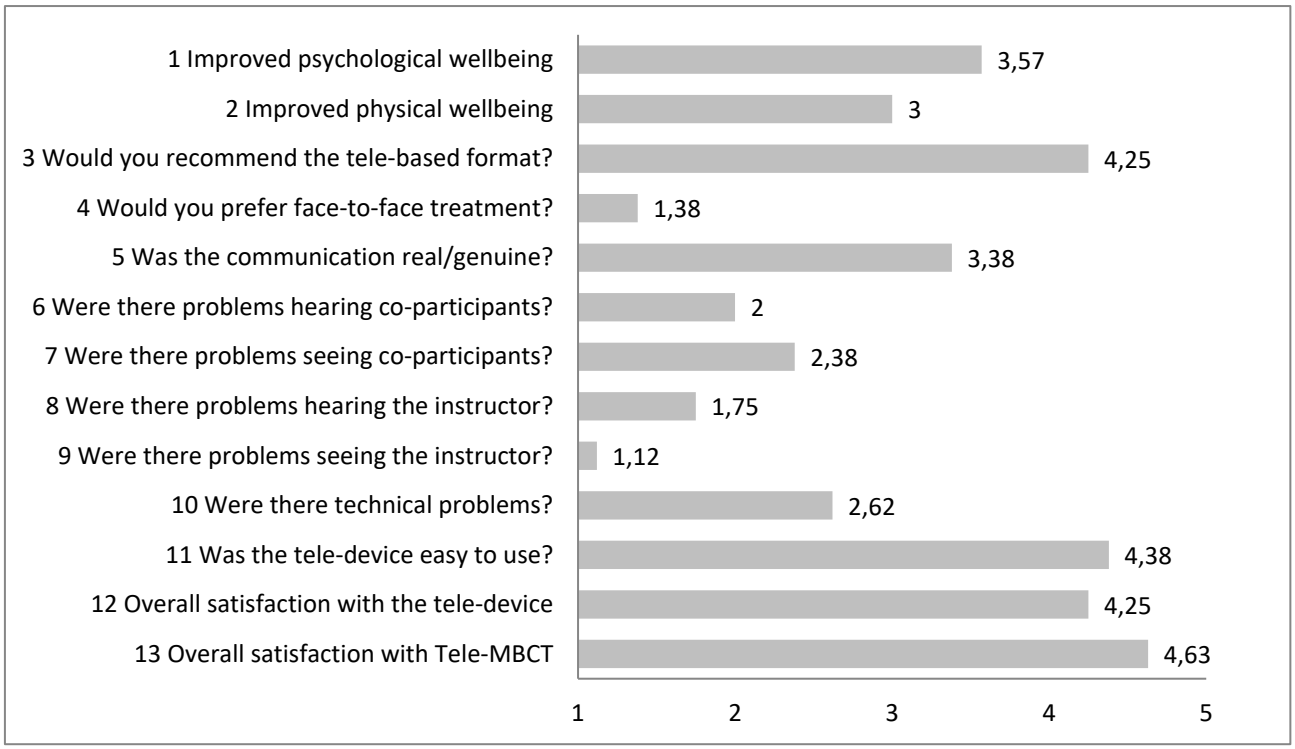
Methods: Participants were recruited from the control arm of Study 2 after termination of the follow-up data collection (mean time since enrolment=519 days (SD=201)). All included participants received the 8-week MBCT programme adjusted for COPD and delivered via home-based video-conferences in groups of four. Clinical change in the predefined quantitative measures of psychological distress (Hospital Anxiety and Depression Scale (HADS)) and physical health status (COPD Assessment Test (CAT)) was measured before and after the intervention. Attendance rate was recorded for all patients at the end of the intervention. Between Tele-MBCT session four and five, the quality of the therapeutic working alliance was measured using the Working Alliance Inventory (WAI). After the intervention, semi-structured interviews were conducted with all participants with the purpose of exploring areas of the evaluation in a more inductive fashion.

Results: In the period from February to May 2016, a total of 8 out of 47 invited COPD-patients (17%) were enrolled in the study and allocated to two treatment groups of four participants each (reasons for non-participation: 8 preferred face-to-face MBCT; 25 were not interested in receiving any form of MBCT at the time of recruitment; 6 did not respond to telephone calls).

Concerning the area of clinical change, quantitative data showed statistically non-significant reductions in psychological distress (Cohen's d=0.504; p=0.399) and physical health status impairment (d=0.743; p=0.156) from pre- to post-intervention. Participant narratives focused on changes in the way of relating to unpleasant sensations, i.e., through attentional flexibility, taking a pause and acceptance of difficult thoughts and feelings. Concerning the area of attendance, the average attendance rate was 7.5 (SD=0.8) out of 8 sessions and no participants dropped out. Qualitatively, most participants expressed that the tele-based format made the planning of the day easier, which promoted their ability and wish to participate in an intervention with a relatively large number of treatment sessions. Concerning the area of working alliance, the average WAI score was 68.88 (SD=10.72), which is comparable to the WAI scores of Study 2 using the same MBCT-instructor (Mean=63.67 (SD=13.63)). In contrast, the qualitative data indicated that participants experienced reduced and disturbed personal contact, e.g., due to technical problems, which for some participants led to difficulties in creating an atmosphere of trust and safety. Meanwhile, most participants reported that, over time, the personal contact with the instructor and co-participants developed more positively, and certain participants described advantages of the tele-based format being 1) better management of group dynamics and 2) smaller group size that they were used to in face-to-face interventions.

Results not included in the paper: After the Tele-MBCT intervention, participants completed a number of single items measuring aspects of satisfaction and developed for the purpose of the present study. As illustrated in Figure 5, satisfaction levels were generally high across single items, despite some degree of technical problems (Item 10). Participants reported some degree of issues with with seeing and hearing co-participants (Item 6 and 7). Moreover, the mean rating of real/genuine communication were only just above average (Item 5). Yet, the mean overall satisfaction with Tele-MBCT was high (Item 13), and participants appeared to be willing to recommend the tele-based format to others (Item 3).

Figure 5. Self-reported participant satisfaction (mean scores)



Abbreviations: Tele-MBCT (Tele-delivered mindfulness-based cognitive therapy)
Notes: 1 (not at all) – 5 (very much)

Conclusion: Tele-MBCT appeared to be feasible in COPD. In the future, large-scale RCTs are needed with the purpose of testing the efficacy of Tele-MBCT on the outcomes of psychological distress and physical health status. Such studies could preferably include a) inclusion criteria related to baseline levels of psychological distress and physical health status, b) mediational analyses of MBCT-related factors, e.g., attentional flexibility and acceptance, and moderating influences of tele-related factors, e.g., distance communication and tele-presence, c) monitoring of session attendance and between-sessions adherence as well as underlying reasons for (non-)attendance and d) careful consideration and description of ethical and safety procedures. Moreover, the evaluation of cost-efficacy was out of the scope of the present feasibility study but should be a central matter in future studies within the area.

3 Discussion

The overall aim of the present PhD project was to investigate effects, mechanisms and delivery of psychosocial intervention in COPD. More specifically, the objectives were to, first, summarise the existing evidence for the efficacy of psychosocial intervention in improving psychological and physical health outcomes (Study 1). Secondly, our aim was to evaluate the efficacy of a specific psychosocial intervention programme, namely COPD-adapted mindfulness-based cognitive therapy (MBCT), on psychological distress and physical health status in COPD, as well as to explore potential mediators (what works?) and moderators (for whom?) of the effect (Study 2). Finally, poor uptake and attendance rates of face-to-face MBCT in the RCT led us to explore the clinical feasibility of a tele-delivered version of MBCT (Study 3). In the following, the main results of the three studies will be discussed in the light other existing evidence. Then a discussion of limitations and methodological considerations will be presented, followed by clinical implications and suggestions for future research.

3.1 Main findings

3.1.1 Effects on psychological outcomes

Results from Study 1 indicated that psychosocial intervention in general was efficacious for improving the combination of psychological outcomes (i.e., anxiety and depression). Additional analyses suggested, that psychosocial intervention also reduced anxiety and depression, separately. This finding is in discordance with the reviews by Rose et al. (2002), Coventry & Gellatly (2008) and Smith et al. (2014) who did not find support for the efficacy of psychosocial intervention on the outcomes of anxiety and depression, analysed separately. Moreover, the meta-analysis of Baraniak and Sheffield (2011) reported statistically significant effects on anxiety, but not depression. Possible explanations of these inconsistent findings could be related to the fact that previous systematic reviews and meta-analyses focused predominantly on CBT – whereas studies of mind-body interventions were also included in the meta-analysis of the present dissertation. Consequently, the results of Study 1 is based on data from a larger combined sample of COPD-patients and reflect a more inclusive picture of the types of psychosocial interventions that are being applied in the context of COPD.

MBCT is a type of psychosocial intervention that combines elements from CBT and mind-body approaches, and findings from Study 2 found MBCT to be efficacious in reducing psychological distress in COPD-patients. This finding is generally in accordance with the results found for psychosocial intervention in Study 1. However, the result is in conflict with other studies exploring the efficacy of

MBI in COPD which showed statistically non-significant results on the psychological outcomes of anxiety and perceived stress (Chan et al., 2015; Mularski et al., 2009). Additional analyses of Study 2 suggested that MBCT relieved psychological distress primarily by reducing symptoms of depression rather than anxiety, which may explain the null-findings in earlier studies that did not assess the outcome of depression. Furthermore, earlier studies applied MBSR, which does not include cognitive elements, and combining elements from mind-body interventions and CBT in the MBCT programme for COPD may thus be more efficacious than focusing predominantly on mindfulness meditation in MBSR-based approaches.

Quality of life (QoL) is a construct that encompasses psychological as well as physical domains, and the results of Study 1 showed that there was a statistically significant, but small combined effect of psychosocial intervention on QoL, which is in conflict with the findings of the previously mentioned meta-analysis by Baraniak and Sheffield (2011) where there was no effect on QoL. Possible explanations for these conflicting findings may again be related to the fact that Study 1 included studies of mind-body interventions in which there is a strong focus on psychophysiological mechanisms and targets (e.g., meditative yoga in which balance of mind and body are sought (Ranjita et al., 2016)), and thereby the improvement of physical domains, which could drive the effect on overall QoL. A measure of QoL including both psychological and physical domains was not applied in Study 2, but the COPD Assessment Test (CAT), which was used to assess physical health status impairment in Study 2, has been shown to correlate strongly with the SGRQ (r=0.73) (Ringbaek, Martinez, & Lange, 2012), which was a commonly used measure of QoL in Study 1. Study 2's results of MBCT on the CAT will be presented in the following section.

3.1.2 Effects on physical outcomes

The results of Study 1 showed a statistically significant positive effect of psychosocial intervention on the combination of physical outcomes (i.e., dyspnea, exercise capacity, fatigue and lung function) in COPD. At the time when Study 1 was conducted, there were indications of possible publication bias, and after adjusting the results accordingly, the effect on physical outcomes became only statistically near-significant. However, preliminary results of a recently updated version of the systematic review and meta-analysis (see Table 3, p. 27) indicated that the risk of publication bias is currently low, and psychosocial intervention now appeared efficacious for the improvement of physical outcomes.

In partial agreement with these findings, the results of Study 2 showed a statistically near-significant effect of MBCT on physical health status, which is a concept that involves the combination of the most functionally impairing physical consequences of COPD (e.g., dyspnea, cough, sputum, sleep, exercise capacity). In addition, exploratory analyses of inflammatory cytokine expression in the blood suggested that MBCT may prevent increases in TNF-α-related inflammation, which is considered a target in the treatment of COPD (Matera, Calzetta, & Cazzola, 2010). This in is line with another study showing mindfulness practice to be associated with reductions in TNF-α after stress induction in healthy individuals (Rosenkranz et al., 2013) and, more broadly, studies indicating that MBIs may improve immune function (Davidson et al., 2003). Further exploratory analyses of physical outcomes in Study 2 showed no effect of MBCT on physical activity measured by accelerometers, which conflicts with the results of Study 1 where improvements in exercise capacity were seen post-treatment. Yet, physical activity and exercise capacity are separate constructs, and improvements in the *capacity* of exercise does not necessarily lead to incorporation of exercise and increased physical activity levels in everyday life (Zwerink, van Der Palen, van Der Valk, Brusse-Keizer, & Effing, 2013). Moreover, the extrapolation of physical activity levels from standard tests of exercise capacity (e.g., the six-minute walk test or the incremental shuttle walk test) are poor indicators of physical activity measured by a pedometer (Zwerink et al., 2013). Based on a relatively recent review of physical activity measurement in COPD (Thyregod & Bødtger, 2016), relying solely on accelerometers might compromise the validity and test-retest reliability of results (i.e., patient adherence problems; different devices have different ways of calculating and summarising outcomes of physical activity). The triangulation of accelerometers and self-reported physical activity levels is therefore recommended (Thyregod & Bødtger, 2016).

Taken together, psychosocial intervention can potentially improve physical as well as psychological outcomes in COPD-patients. Study 1 is among the first to report a quantitative summary of the efficacy of psychosocial intervention on physical outcomes, while Study 2, exploring the efficacy of a specific psychosocial intervention programme (MBCT), is among the first to include analyses of physical outcomes across multiple levels of units of analysis, ranging from biomarkers (i.e., inflammatory cytokines) through behavioural monitoring (e.g., accelerometers) to self-reported physical health status (e.g., the CAT) (an approach that is requested by the Lancet Psychiatry Commision (Holmes et al., 2018)). The findings are promising, but more high-quality studies with larger samples are needed for more robust results.

3.1.3 What works for whom?

Demonstrating efficacy is merely the first step in the scientific exploration of psychosocial intervention in COPD. In addition to investigating *if* psychosocial intervention works in terms of improving certain clinical outcomes, there is a need to explore questions related to what type of therapy works best compared to others, what particular elements or mechanisms make the intervention work, and who appear to benefit most from this or that specific intervention (Holmes et al., 2018; Kazdin, 2007).

Results of Study 1 indicated that different types of psychosocial intervention yielded different effects, such that that only CBT, but not mind-body interventions, significantly improved psychological outcomes, while the opposite result was found for physical outcomes where only the results of mind-body interventions reached statistical significance. This may to a certain extent explain the results of Study 2, indicating that the combination of CBT and mind-body techniques, i.e., MBCT, has the potential of improving both psychological and physical outcomes. However, it should be noted that the differences in effects between CBT and mind-body types of intervention in Study 1 did not reach statistical significance, limiting the trustworthiness of the conclusion. Moreover, as no competing psychosocial intervention was applied to the control arm condition in Study 2, we cannot be sure whether similar or even better results could have been obtained with other types of psychosocial intervention. Exploratory mediational analyses indicated that increases in self-compassion preceded subsequent reductions in psychological distress, which may suggest that the participants' cultivation of a non-judgemental attitude towards themselves through MBCT may have been an essential active mechanism in MBCT for COPD. On the other hand, it could be argued that similar results could have been obtained through other psychosocial intervention programmes stimulating self-compassion, such as compassion-based therapy (Gilbert, 2010). Especially as mindfulness, which is logically thought to be a main active ingredient in MBCT, did not appear to statistically mediate the effect of MBCT on psychological distress in Study 2.

As breathlessness catastrophizing has been proposed to play a central role in the escalation of psychological distress and physical impairment in COPD (see Section 1.4.3) – and as MBCT is designed to target such ruminative cognitive patterns – it is surprising that the mediating effect of breathlessness catastrophizing on psychological distress did not appear as a statistically significant mediator. Perhaps catastrophizing in relation to bodily sensation of breathlessness may be more directly connected to the development of anxiety, which was – as reflected in the supplementary analyses of primary outcomes in Study 2 – not reduced by MBCT. Therefore, as indicated in Study 1, CBT may

be the most efficacious intervention for the more specific treatment of anxiety in COPD. However, perhaps other results could have been obtained in Study 2 by applying a more specific measure of panic anxiety, since it is an outcome which may be more directly reduced through reductions in breathlessness catastrophizing (von Leupoldt & Janssens, 2016). Meanwhile, despite statistically non-significant mediating effects of mindfulness, breathlessness catastrophizing and COPD-specific self-efficacy, it cannot be ruled out that these or other mechanisms could act as drivers of the effect of MBCT in COPD as the limited number of measurement points and the lack of competing mediators did not allow for a more fine-grained and precise analysis of the mechanisms of change in treatment outcomes (Holmes et al., 2018; Kazdin, 2007).

Concerning who benefits most, the sociodemographic variables of age and gender did not appear to moderate the effect of psychosocial intervention on neither psychological nor physical outcomes in Study 1. In contrast, relatively younger participants appeared to experience larger reductions in psychological distress after MBCT in Study 2. The finding of Study 2 corresponds to results of another study stating that younger COPD-patients may be more adept at learning the skills and tools taught in psychosocial intervention (Coventry & Gellatly, 2008). It is somewhat surprising that there appeared to be no differences between men and women in treatment gain, neither in Study 1 nor Study 2, as other literature points to gender differences in outcomes of PR and smoking cessation programmes (Aryal, Diaz-Guzman, & Mannino, 2013).

Contrary to our hypotheses, the participants in Study 2 who attended more MBCT sessions did not appear to benefit more from the intervention than participants who attended fewer sessions. Also, shorter duration of treatment was (statistically near-significantly) associated with larger effects of psychosocial intervention on both psychological and physical outcomes in Study 1. These results speak against a dose-response effect, which is otherwise commonly observed in psychosocial intervention (Hansen, Lambert, & Forman, 2002). However, there are multiple possible explanations as to why participants do not show up for MBCT sessions (e.g., perception of sufficient treatment gain; perceived difficulties in relation to the intervention (Harrison et al., 2017); travel issues (Keating et al., 2011)), and also numerous possible ways of interpreting the smaller effect observed for interventions of longer duration (e.g., repetition/overstimulation (Doxsee & Kivlighan, 1994; Lieberman, Yalom, & Miles, 1973); natural deterioration of COPD-patients' physical and psychological condition over time (Viegi et al., 2007); regression towards the mean due to relatively longer follow-up time). Therefore, robust conclusions concerning the role of attendance rate and treatment duration

cannot be made on the basis of the results of the present dissertation, and it is not possible to determine "how much therapy is enough" (Hansen et al., 2002) based on the present findings.

3.1.4 Tele-based MBCT in COPD

Poor study uptake (52% inclusion rate) and low attendance rates (4.0 out of 8 sessions) were seen for face-to-face MBCT in Study 2, which is an issue reflecting a general problem with adherence to outpatient interventions in COPD (Blackstock et al., 2016). Despite the fact that attendance rate did not appear to moderate the effect of MBCT on psychological distress in Study 2, it cannot be ruled out that increased availability of MBCT and in-session attendance may improve outcomes of MBCT in COPD (Malpass et al., 2015). Though not claiming to make any contribution to evidence on efficacy, the results of Study 3 showed tele-delivered MBCT to be a feasible intervention for improving attendance rates in COPD. Quantitatively, average attendance rates were high (7.5 out of 8 sessions) as were satisfaction levels, measured by a number of single items (see Figure 5, p. 34). Moreover, a tendency for mean levels of psychological distress and physical health status impairment to be reduced after the intervention was observed. Moreover, the average reported quality of the therapeutic working alliance in Study 3 (WAI: mean=68.88, SD=10.72) was comparable to ratings in face-to-face MBCT in Study 2 (WAI: mean=63.67, SD=13.63), using the same instructor. Although therapeutic working alliance did not appear to statistically significantly moderate the effect of MBCT on psychological distress in Study 2, it has been described as important for determining the feasibility of tele-based psychosocial intervention (Guise, Anderson, & Wiig, 2014). The quantitative findings of Study 3 generally converge with the results of a review of web-based MBIs in various physical health conditions (Toivonen et al., 2017). Here it is concluded that interventions appear particularly helpful when they are tailored for specific symptoms, which was true for the intervention applied in Study 3. However, it should be mentioned that the uptake rate of Tele-MBCT in Study 3 was remarkably low (17%). This finding should, however, be interpreted in the light of patients being recruited after having already taken part as control participants in Study 2, which was a comprehensive study with frequent, comprehensive questionnaires and a long follow-up period.

Qualitative results of Study 3 indicated that participants experienced a change in relating to unpleasant symptoms which encompassed aspects of attentional flexibility, taking a pause and acceptance of difficult thought and feelings. These themes resonates well with the results of a qualitative study of face-to-face MBCT in COPD and asthma (Malpass et al., 2015) where patients applied an accepting mode of response to difficulties, including the realisation of what was and what was not within their

power to change. Instead of fighting against episodes of breathlessness or low mood, participants learned how to respond wisely, for example, by 'stepping back' from difficulty or by taking a pause, which was also described by participants in Study 3. With regards to the practical aspects of attendance, the tele-based delivery of MBCT in Study 3 seemed to accommodate participants' need for planning as well as their willingness and ability to participate. This finding is in line with a study of tele-delivered MBCT in cancer (Compen et al., 2017) in which completing the intervention in a home environment and not having to travel was appreciated. However, in the study by Compen et al., the intervention was delivered asynchronously, which may limit the comparability with Study 3 of the present dissertation where Tele-MBCT was delivered synchronously. In contrast to the quantitative findings, the qualitative findings of Study 3 suggest that the tele-based format could negatively influence the personal contact with the instructor and between fellow participants, thereby possibly reducing trust and feelings of safety. Specifically, there was an emphasis on technical problems as interfering with the therapeutic relationship, which is in line with findings from other studies (Radhakrishnan, Xie, Berkley, & Kim, 2016). On the other hand, qualitative results of Study 3 also reveal positive influences of the tele-based format on relational aspects, including more efficient management of group dynamics.

In summary, Study 3 reveals both advantages and disadvantages of tele-MBCT within the areas of clinical change, attendance and therapeutic working alliance/relational aspects, the most crucial disadvantages being related to a low uptake rate and negative interference of technical issues for building a trusting and safe therapeutic 'distal' environment.

3.2 Limitations, clinical implications and future research

The studies included in the present dissertation have several methodological strengths. Study 1 was based on a meta-analytic approach including examination of publication bias. Study 2 was a cluster-randomised controlled trial applying a statistical method that takes missing data into account. Study 3 integrated quantitative with qualitative methodologies in the exploration of participants' experiences of a new and relatively unexplored intervention (synchronously delivered tele-MBCT) in COPD. However, there are a number of limitations that should be considered when interpreting the findings with the purpose of understanding how they could be applied in clinical practice and what is called for in future studies.

3.2.1 Categorised intervention types and combined outcomes

Study 1 takes a broader approach to psychosocial intervention in COPD, compared to other reviews (see Table 2, p. 8), by also including mind-body types of psychosocial intervention. The positive effects of psychosocial intervention on physical outcomes and QoL, which is in contrast with the results of other reviews (see Table 2, p. 8), appear to be driven primarily by the inclusion of mind-body interventions in which there is a stronger focus on physical aspects than in intervention types predominantly applying a psychological focus (e.g., CBT). Consequently it can be argued that the classification of mind-body type interventions as 'psychosocial', and the subsequent combination of interventions with widely varying contents, can lead to a summary effect that ignores possibly important differences across studies – a problem which is commonly referred to as 'mixing apples and oranges' (Sharpe, 1997). Meanwhile, the subsequent exploration of reasons for heterogeneity, e.g., the moderating effect of categories of intervention types (i.e, CBT versus mind-body), can be said to justify the general approach of Study 1 by casting light over the specific effects of CBT versus mind-body approaches (Borenstein, Hedges, Higgins, & Rothstein, 2009). Yet, heterogeneity statistics in moderator analyses remain large and statistically significant (i.e., CBT effects for psychological outcomes: I^2=53.6, p=0.028; mind-body effects for physical outcomes: I^2=77.0, p=0.001), suggesting that other variables than the ones explored, e.g., attrition rates, baseline levels of psychological distress and/or anxiety, etc., may account for the diversity in results.

Moreover, the specific outcomes of the studies included in Study 1 are combined in the overall categories of psychological and physical outcomes, respectively. Not all included studies reported data on each outcome category of interest, and the instruments used to measure psychological and physical outcomes were diverse. This was also the case for QoL instruments, with some studies using disease-specific and others using generic outcome measures. Again, the 'apples and oranges'-critique can be applied. To some extent, Study 2 and Study 3 also follow this approach by using combined measures of psychological distress (the HADS total scale, overarching the more specific symptoms of anxiety and depression) and physical health status (the CAT, overarching the more specific symptoms of dyspnea, cough, sputum etc.). This approach can be said to compromise the precision and specificity of results, as the studies were not hypothesis-driven by the expected efficacy of MBCT on a more narrow outcome of interest. As psychosocial intervention – and especially MBCT – in COPD is a relatively unexplored field, Study 2 and Study 3 were designed for a more general exploration of outcomes that could potentially be improved by such interventions. Additional analyses of efficacy on specific outcomes in Study 2 throw some degree of light over the more fine-grained patterns of

change, but in the future, more hypothesis-driven studies, designed for the detection of efficacy on more specific outcomes, e.g., anxiety, depression, dyspnea etc., are needed with the purpose of further validating the proposed model of change in MBCT for COPD.

Implications for clinical practice and future research: Psychosocial intervention, including physically oriented mind-body interventions, have the potential for improving both psychological and physical outcomes in COPD, albeit there is substantial heterogeneity in results which should be further investigated in future studies. Despite this cautionary note, it appears appropriate to recommend delivering psychosocial intervention alongside the medical treatment pathway. Concerning specific types of psychosocial intervention, clinicians could consider offering CBT if the primary purpose is to relieve psychological outcomes, and mind-body interventions with the purpose of relieving physical outcomes. While, the relatively broad outcomes applied in Study 2 limits the specificity of results, additional analyses suggest that MBCT should primarily be considered for relieving symptoms of depression, not anxiety, which is indeed the purpose of the original MBCT programme (Segal et al., 2013). Future studies should be designed with the purpose of detecting face-to-face or tele-delivered MBCT's effects on more specific outcomes, e.g., (panic) anxiety, depression and dyspnea.

3.2.2 Power, sample size and attrition

A considerable limitation of Study 2 is the limited sample size and the consequent lack of statistical power in the estimation of effects on primary outcomes. For example, the only statistically near-significant effect of MBCT on physical health status may be explained by the smaller-than-projected sample size. It should also be noted that a larger sample size for analyses of potential moderators would minimise the risk of Type II error. The small enrolment rate could perhaps be due to the fact that not all patients eligible for PR reported clinically significant levels of psychological distress, i.e., average baseline HADS total score in Study 2 was 13.72 (SD=7.67), which is below the clinical threshold value (≥15) for the HADS total (determined in a sample of oncology/heamatology out patients (Clover, Carter, MacKinnon, & Adams, 2009) and a sample of lung cancer patients (Schellekens et al., 2016)). Perhaps a certain proportion of eligible patients did not feel a need for psychosocial intervention, ("I suppose if I was sicker, I might need it" (Chan & Lehto, 2016)), or there may be an discrepancy between felt need (a need is felt by the subject) and expressed need (a felt need is turned into action by seeking or receiving help), as had previously been found for behavioural intervention in the COPD population (Kendall et al., 2015).

In Study 3, only 17% accepted the invitation to receive tele-MBCT. The majority of the declining participants (64%) did not wish to receive neither face-to-face nor tele-based MBCT at the time of recruitment. From a conservative point of view, the low inclusion rate could ultimately question the feasibility of tele-MBCT, i.e., what is the purpose of delivering an intervention that only a minority of eligible patients are willing to receive (Zernicke et al., 2014)? However, it should be noted that participants in Study 3 might not be representative of the general COPD population, since they were recruited from the control arm of a Study 2, which applied frequent, comprehensive questionnaires and a long follow-up period. Moreover, with a sample size of eight, and based on a different methodological paradigm (Ekeland, Bowes, & Flottorp, 2011), questions regarding generalisability and representativeness cannot be answered on the basis of Study 3 and larger studies in samples representative of the COPD population are needed.

Dropout rates of Study 2 were high in both the intervention and the control arm. This is a general issue in COPD research and practice where adherence rates are generally poor (Blackstock et al., 2016). Dropout, however, was balanced across treatment arms and did not appear, as supported by our sensitivity analyses, to compromise the robustness of the results. More encouragingly, no participants dropped out of Study 3. Aspects of attrition were not assessed in Study 1, which can be subjected to critique as differences in attrition rates could potentially explain heterogeneity of study findings.

Implications for clinical practice and future research: Due to a limited sample size in Study 2, the trustworthiness of MBCT's effect on physical health status is limited. Patients with stronger expressed need for psychosocial intervention may be more ready to the take-up of MBCT, and including patients on the basis of clinically relevant baseline levels of psychological distress should be considered in future studies. However, there are numerous possible reasons for low uptake and high attrition rates in psychosocial intervention, and this area could therefore be explored more inductively in qualitative studies.

3.2.3 Competing control groups and treatment fidelity

In Study 1, only 9 out of 20 studies (5 out of 8 studies in the updated literature search, see Table 3, p. 27) included active control conditions matching the experimental condition in non-specific factors (e.g., structure, social interaction, education about illness, attention from healthcare professionals) with the purpose of directly assessing the assumed active ingredients. None of these studies included a *competing* psychosocial intervention with the purpose of testing the superiority or non-inferiority

of the intervention applied in the experimental condition (Lesaffre, 2008). The same was true for Study 2 where participants in the control arm did not receive a competing psychosocial component as an add-on to the PR programme. The lack of a competing control group means that it remains unknown whether the same, or even better results could have been obtained by adding another type of psychosocial intervention (e.g., CBT) to PR in the control arm. That having been said, participants in the control condition did receive an active intervention, i.e., PR, which somewhat strengthens the validity of the findings compared to other studies including a wait-list control condition.

Moreover, limiting the validity of results, MBCT treatment fidelity in Study 2 was not systematically assessed. The Mindfulness-Based Interventions–Teaching Assessment Criteria (MBI:TAC) is a comprehensive and validated assessment tool that has shown high validity in its capability of determining teaching integrity (adherence, differentiation and competence) in MBCT and MBSR protocols (Crane et al., 2013). The omission of such a tool in Study 2 ultimately raises the question if the intervention that was delivered *was,* in fact, MBCT. This issue is further complicated by Study 2's application of a newly adapted treatment manual, which impeded prolonged training and experience prior to initiation of the study. Moreover, a single instructor was responsible for delivering the MBCT programme, which can be said to limit the generalisability of the findings (e.g., would the intervention be as effective if other instructors delivered it?) especially when therapeutic working alliance appeared to be a statistically near-significant moderator of the effect of MBCT on psychological distress. Perhaps higher variability in ratings of the therapeutic working alliance through the inclusion of several MBCT instructors could have yielded different results on primary outcomes in Study 2. Also, in Study 3, treatment fidelity can be further questioned due to the adding of the extra 'layer of complexity' which is the tele-based *modality* (e.g., can the intervention still be characterised as MBCT when delivered at a distance via tele-monitors?). This issue can be explored in future efficacy trials and qualitative studies comparing face-to-face and tele-delivered MBCT.

Implications for clinical practice and future research: While Study 2 suggest that MBCT is efficacious in reducing psychological distress in COPD, it was not designed to test whether MBCT is superior to other treatments. Moreover, there is no documentation of treatment fidelity, and other mindfulness-instructors delivering treatment might have yielded difference results. This, altogether, limits the validity of the findings, and future studies should therefore consider including a competing and/or attention control condition as well as formal assessment of treatment fidelity and a multiple-instructor design.

3.2.4 Maintenance of effect

In Study 1, the available data do not allow for any conclusions regarding the long-term maintenance of the effect, as the majority of included studies did not collect or present follow-up data in their analysis. In Study 2, treatment effects appeared to last up to six months after the termination of the intervention, but longer follow-up periods are needed, as it may take longer than six months for patients to implement profound life style changes, which can be considered a goal of both PR (i.e., more physically active in daily life) and MBCT (i.e., more mindful in daily life) (Parsons et al., 2017).

Despite not aiming to assess efficacy, the inclusion of longitudinal data-collection in Study 3 could have been informative with the purpose of assessing change in patients' experiences and integration of aspects of MBCT in everyday life. For example, in Malpass et al.'s (2015) qualitative study of COPD- and asthma patients' experiences of MBCT, participants were interviewed two months after the termination of the 8-week intervention programme with the purpose of exploring whether their perceived changes in breathlessness, activity, low mood or anxiety had been sustained over time and independently of the weekly input of the group context and instructor.

Implications for clinical practice and future research: The clinical relevance of the results of Studies 1-3 of the present dissertation is limited by the relatively short duration of data collection, and future studies investigating interventions inviting to prolonged dedication and lifestyle changes should assess the long(er)-term effect. The application of longitudinal qualitative methodology is relevant for the purpose of understanding the complexities of tele-delivered intervention, and future studies could consider exploring the transition from tele-delivery during the 8-week programme to using skills learned in therapy without tele-aid. On a more general level, it should be underscored that there is currently a methodological gap in tele-healthcare ranging from the lack of larger controlled (cost-effectiveness) trials to undeveloped use of qualitative methods and implementation research (Ekeland et al., 2011; Wade & Smith, 2017)

4 Conclusion

The findings of Studies 1-3 of the present PhD dissertation suggest that:

1) Psychosocial intervention is efficacious for improving the combination of psychological outcomes (i.e., anxiety and depression) and, based on updated preliminary results, the combination of physical outcomes (i.e., dyspnea, exercise capacity, fatigue and lung function) in COPD.
2) MBCT as an add-on to PR is efficacious for reducing psychological distress in COPD. Furthermore, there are tentative results to suggest that MBCT may also be efficacious for improving physical health status impairment (statistically near-significant results) and preventing an increase in inflammatory processes.
3) Age moderates the effect of MBCT on psychological distress, with younger age predicting larger treatment gains.
4) Increases in self-compassion is a statistically significant mediator of reductions in psychological distress after MBCT.
5) Tele-delivered MBCT appears feasible for improving attendance rates in COPD, and future trials testing the efficacy of Tele-MBCT should consider including analyses of potential mediators and moderators of the effect as well as careful monitoring of attendance and adverse events.

In spite of these results, limitations of the studies exist and several questions of relevance to clinical practice still needs to be scientifically explored, for example: *Whom should we treat?* Can the results of the present dissertation be informative in other respiratory conditions (e.g., lung cancer, idiopathic pulmonary fibrosis (IPF), asthma)? *For what?* Should we consider focusing more narrowly on COPD-patients with a comorbid clinical diagnosis of anxiety and/or depression? *With what?* What psychosocial intervention programme is superior in comparison with other effective intervention programmes and what are the active ingredients of psychosocial intervention programmes in COPD? *And when?* When in the illness and treatment trajectory are COPD-patients most in need of and receptive to psychosocial treatment? And should it be delivered as an add-on to pulmonary rehabilitation or as a stand-alone?

All the potential pitfalls and unanswered questions taken into account, a broader conclusion remains and is articulated by the editor of the *European Respiratory Journal*:

> *”In conclusion, it becomes increasingly clear that the approach to the chronically or persistently dyspnoeic patients needs to be multifaceted, multidisciplinary and multidimensional: in other words holistic […] In this perspective, it is important to integrate the care of the mind in the care of dyspnoea, and therefore to treat the person as a whole and not only his/her lungs or his/her brain. In other words, consider chronic or persistent breathlessness not only as a syndrome, but, in the end, as a self-contained all-encompassing condition warranting our undivided and “primary” attention.”* (Similowski, 2018, p. 3)

It is my hope, that of all that the present dissertation has tried to communicate, this is the conclusion that will be passed on to the doctors, nurses, physiotherapists and psychologists facing people who are suffering from COPD and who, like all of us, strive for – and deserve – the relief of suffering.

English summary

In addition to the debilitating physical consequences of the disease, patients with chronic obstructive pulmonary disease (COPD) report considerable levels of psychological distress in the form of anxiety and depression symptoms. The aims of the present dissertation are 1) to summarise the existing evidence for the efficacy of psychosocial intervention in improving psychological and physical outcomes, 2) to evaluate the efficacy of a specific psychosocial intervention programme, namely COPD-adapted mindfulness-based cognitive therapy (MBCT), on psychological distress and physical health status in COPD, as well as to explore potential mediators (what works?) and moderators (for whom?) of the effect, and 3) to explore the clinical feasibility of a tele-delivered version of MBCT.

Paper 1 reports the results of a systematic review and meta-analysis investigating the efficacy of psychosocial intervention for psychological and physical outcomes in COPD. Results showed overall psychosocial intervention to be efficacious for improving psychological outcomes. Additional analyses of individual types of psychosocial intervention indicated that cognitive behavioural therapy (CBT) was mainly effective for improving psychological outcomes, whereas mind-body interventions were most effective for improving physical outcomes.

Paper 2 describes findings from a cluster randomised controlled trial of MBCT as an add-on to a standardised pulmonary rehabilitation (PR) programme in COPD. The results showed that MBCT+PR compared to a PR-only control group had positive and clinically relevant effects on psychological distress, i.e., anxiety and depression symptoms combined. Moreover, exploratory analyses suggested that MBCT may prevent an increase in COPD-related inflammation, indicated by increased levels of the pro-inflammatory cytokine of TNF-α in the control group, but not in the intervention group. The effect of MBCT on psychological distress appeared to be facilitated by increased self-compassion, and relatively younger participants seemed to benefit most from MBCT.

In Paper 3 the clinical feasibility of tele-delivered MBCT (Tele-MBCT) for patients with COPD is explored, using a mixed-methods design. Quantitative results revealed that participants attended an average of 7.5 out of 8 sessions of Tele-MBCT. After Tele-MBCT, statistically non-significant improvements of psychological distress and physical health status were observed. Moreover, participants' ratings of the therapeutic working alliance mid-way through the intervention were comparable to ratings in face-to-face MBCT. Qualitative data supports the quantitative findings by revealing that the tele-based format appeared to accommodate participants' planning difficulties and promoted their

ability and wish to participate. However, participant narratives also suggested the tele-based format to be a barrier to developing a trusting and safe therapeutic environment. Additionally, participant narratives about clinical outcomes focused on changes in how to relate to unpleasant sensations, i.e., through attentional flexibility, taking a pause and acceptance of difficult thoughts and feelings.

In summary, psychosocial intervention in general appears as an efficacious intervention for improving psychological outcomes in COPD. More specifically, MBCT may be an efficacious add-on to PR with the purpose of reducing psychological distress in COPD, seemingly by facilitating increases in self-compassion. Relatively younger COPD-patients may experience greater gain from MBCT in comparison with relatively older patients. With the purpose of overcoming low attendance levels of face-to-face MBCT, Tele-MBCT may be a feasible alternative. Future trials testing the efficacy of Tele-MBCT on psychological distress and physical health status in COPD should consider include analyses of potential mediators and moderators of the effect as well as careful monitoring of attendance and adverse events.

Danish summary

I tillæg til sygdommens invaliderende fysiske symptomer oplever mange patienter med kronisk obstruktiv lungesygdom (KOL) betydelig psykologisk belastning i form af angst og depression. Denne afhandlings formål er 1) at sammenfatte den eksisterende evidens for effekten af psykosocial intervention på psykologiske og fysiske variable ved KOL, 2) at afprøve effekten af et specifikt psykologisk behandlingsprogram – mindfulness-baseret kognitiv terapi (MBKT) – på psykologisk belastning og fysisk helbredsstatus blandt patienter med KOL, samt at undersøge mulige mediatorer (hvad virker?) og moderatorer (for hvem?), og slutteligt 3) at undersøge den kliniske gennemførbarhed af en tele-leveret udgave af MBKT for KOL-patienter.

Artikel 1 rapporterer resultaterne af en systematisk litteraturgennemgang og meta-analyse, der undersøger effekten af psykosocial intervention på psykologiske og fysiske variable ved KOL. Resultaterne viste, at psykosocial intervention overordnet set var effektiv med henblik på at forbedre psykologiske variable. Yderligere analyser af individuelle typer af psykosocial intervention indikerede at kognitiv adfærdsterapi (KAT) hovedsageligt forbedrede psykologiske variable, mens mind-body interventioner primært var effektive til en forbedring af fysiske variable.

Artikel 2 beskriver fundene fra en klynge-randomiseret kontrolleret undersøgelse af MBKT som tillæg til et standardiseret lungerehabiliteringsprogram (LR) blandt KOL-patienter. Resultaterne viste en positiv og klinisk relevant effekt af MBKT+LR på psykologisk belastning (kombinationen af angst og depressionssymptomer) i sammenligning med en kontrolgruppe, der kun modtog LR. Derudover tyder resultaterne på, at MBKT forhindrede en stigning i inflammation, siden der var et øget niveau af det pro-inflammatoriske cytokine TNF-α i kontrolgruppen efter behandlingen, men ikke i gruppen, der havde modtaget MBKT. Effekten af MBKT på psykologisk belastning så ud til at blive afstedkommet af en stigning i selv-medfølelse, og relativt yngre deltagere fik mest ud af MBKT.

I Artikel 3 undersøges den kliniske gennemførbarhed af tele-leveret MBKT (Tele-MBKT) for patienter med KOL ved at anvende et mixed-methods design. De kvantitative resultater afslørede at deltagerne i gennemsnit deltog i 7,5 ud af 8 Tele-MBKT-sessioner. Efter Tele-MBKT viste der sig at være statistisk ikke-signifikante forbedringer af psykologisk belastning og fysisk helbredsstatus. Ydermere var deltagernes vurdering af den terapeutiske alliance halvvejs gennem interventionen sammenlignelig med vurderinger af den terapeutisk alliance i ansigt-til-ansigt MBKT. De kvalitative data understøttede de kvantitative fund ved at afsløre at det tele-baserede format tilsyneladende imødekom

deltagerne behov for planlægning og fremmede deres evne til og ønske om at deltage. Dog tydede deltagernes fortællinger også på, at det tele-baserede format kunne være en barriere for at udvikle en tillidsfuld og tryg terapeutisk atmosfære. Derudover fokuserede deltagerfortællingerne vedrørende behandlingsudbytte på forandringer i, hvordan man kan forholde sig til ubehagelige fornemmelser, herunder gennem opmærksomhedsfleksibilitet, at tage en pause og accept af vanskelige tanker og følelser.

Sammenfattende ser det ud til, at psykosocial intervention generelt set er effektiv med henblik på at forbedre psykologiske variable ved KOL. På et mere specifikt plan er MBKT angiveligt et effektivt tillæg til LR med det formål at reducere psykologisk belastning, hvilket tilsyneladende sker gennem en øgning af selv-medfølelse. Relativt yngre KOL-patienter ser ud til at få et bedre udbytte af MBKT sammenlignet med relativt ældre patienter. Med det formål at afhjælpe lave tilstedeværelsesrater i ansigt-til-ansigt MBKT er Tele-MBKT et gennemførbart alternativ. Fremtidige studier, der har til formal at afprøve effekten af Tele-MBKT på psykologisk belastning og fysisk helbredsstatus ved KOL, bør overveje at analysere mulige mediatorer og moderatorer såvel som at monitorere tilstede-værelse og utilsigtede hændelser.

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References

Aalderen, J. R., Breukers, W. J., Reuzel, R. P. B., & Speckens, A. E. M. (2012). The Role of the Teacher in Mindfulness-Based Approaches: A Qualitative Study. *Mindfulness*, *5*(2), 170–178.

Addy, K. B. E. (2007). The treatment of depression and anxiety within the context of chronic obstructive pulmonary disease. *Clinical Case Studies*, *6*(5), 383–393.

Adeloye, D., Chua, S., Lee, C., Basquill, C., Papana, A., Theodoratou, E., … Rudan, I. (2015). Global and regional estimates of COPD prevalence: Systematic review and meta–analysis. *Journal of Global Health*, *5*(2).

Agusti, A. (2007). Systemic Effects of Chronic Obstructive Pulmonary Disease: What We Know and What We Don't Know (but Should). *Proceedings of the American Thoracic Society*, *4*(7), 522–525.

Al-shair, K., Kolsum, U., Dockry, R., Morris, J., Singh, D., & Vestbo, J. (2011). Biomarkers of systemic inflammation and depression and fatigue in moderate clinically stable COPD. *Respiratory Research*, *12*, 3. https://doi.org/10.1186/1465-9921-12-3

Allinson, J. P., Hardy, R., Donaldson, G. C., Shaheen, S. O., Kuh, D., & Wedzicha, J. A. (2017). Combined impact of smoking and early-life exposures on adult lung function trajectories. *American Journal of Respiratory and Critical Care Medicine*, *196*(8), 1021–1030.

Alsubaie, M., Abbott, R., Dunn, B., Dickens, C., Keil, T. F., Henley, W., & Kuyken, W. (2017). Mechanisms of action in mindfulness-based cognitive therapy (MBCT) and mindfulness-based stress reduction (MBSR) in people with physical and/or psychological conditions: A systematic review. *Clinical Psychology Review*, *55*, 74–91.

Andersen, I. C., Thomsen, T. G., Bruun, P., Bødtger, U., & Hounsgaard, L. (2017). The experience of being a participant in one's own care at discharge and at home, following a severe acute exacerbation in chronic obstructive pulmonary disease: a longitudinal study. *International Journal of Qualitative Studies on Health and Well-Being*, *12*, 13719994. https://doi.org/10.1080/17482631.2017.1371994

Aryal, S., Diaz-Guzman, E., & Mannino, D. M. (2013). COPD and gender differences: An update. *Translational Research*, *162*(4), 208–218.

Atlantis, E., Fahey, P., Cochrane, B., & Smith, S. (2013). Bidirectional associations between clinically relevant depression or anxiety and COPD: A systematic review and meta-analysis. *Chest*, *144*(3), 766–777.

Baer, R. A. (2003). Mindfulness training as a clinical intervention: A conceptual and empirical review. *Clinical Psychology Science & Practice, 10*, 125–143.

Baer, R. A., Smith, G. T., Hopkins, J., Krietemeyer, J., & Toney, L. (2006). Using self-report assessment methods to explore facets of mindfulness. *Assessment, 13*(1), 27–45.

Bailey, P. H. (2004). The dyspnea-anxiety-dyspnea cycle - COPD patients' stories of breathlessness: "It's scary /when you can't breathe." *Qualitative Health Research*, *14*(6), 760–778.

Bandura, A. (1977). Self-efficacy: Toward a unifying theory of behavioral change. *Psychological Review*, *84*(2), 191–215.

Baraniak, A., & Sheffield, D. (2011). The efficacy of psychologically based interventions to improve anxiety, depression and quality of life in COPD: A systematic review and meta-analysis. *Patient Education and Counseling*, *83*, 29–36.

Barnes, P. J. (2008). The cytokine network in asthma and chronic obstructive pulmonary disease. *Journal of Clinical Investigation, 118*(11), 3546–3556.

Barnes, P. J., & Celli, B. R. (2009). Systemic manifestations and comorbidities of COPD. *European Respiratory Journal*, *33*(5), 1165–1185.

Bartley, T. (2012). *Mindfulness-based cognitive therapy for cancer*. Oxford: Wiley-Blackwell.

Bathoorn, E., Liesker, J. J. W., Postma, D. S., Koëter, G. H., van der Toorn, M., van der Heide, S., … Kerstjens, H. A. M. (2009). Change in inflammation in out-patient COPD patients from stable phase to a subsequent exacerbation. *International Journal of Chronic Obstructive Pulmonary Disease, 4*, 101–109.

Batink, T., Peeters, F., Geschwind, N., van Os, J., & Wichers, M. (2013). How does MBCT for depression work? Studying cognitive and affective mediation pathways. *PLoS ONE, 8*(8), e72778. https://doi.org/10.1371/journal.pone.0072778

Beck, A. T. (2008). The evolution of the cognitive model of depression and its neurobiological correlates. *The American Journal of Psychiatry*, *165*(8), 969–977.

Bestall, J. C., Paul, E. A., Garrod, R., Garnham, R., Jones, P. W., & Wedzicha, J. A. (1999). Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. *Thorax*, *54*(7), 581–586.

Bhowmik, A., Seemungal, T. A. R., Sapsford, R. J., & Wedzicha, J. A. (2000). Relation of sputum inflammatory markers to symptoms and lung function changes in COPD exacerbations. *Thorax*, *55*, 114–120.

Blackstock, F. C., ZuWallack, R., Nici, L., & Lareau, S. C. (2016). Why don't our COPD patients listen to us? The enigma of nonadherence. *Annals of the American Thoracic Society*, *13*(3), 317–323.

Bock, K., Bendstrup, E., Hilberg, O., & Løkke, A. (2017). Screening tools for evaluation of depression in Chronic Obstructive Pulmonary Disease (COPD). A systematic review. *European Clinical Respiratory Journal*, *4*(1), 1332931. https://doi.org/10.1080/20018525.2017.1332931

Bodhi, B. (2011). What does mindfulness really mean? A canonical perspective. *Contemporary Buddhism*, *12*(1), 19–39.

Borenstein, M., Hedges, L. V, Higgins, J. P. T., & Rothstein, H. R. (2009). Criticisms of meta-analysis. In *Introduction to Meta-Analysis* (pp. 377–387). West Sussex: John Wiley & Sons, Ltd.

Bouchard, S., Dumoulin, S., Michaud, M., & Gougeon, V. (2011). Telepresence experienced in videoconference varies according to emotions involved in videoconference sessions. *Annual Review of Cybertherapy and Telemedicine*, *9*, 104–107.

Bove, D. G., Lomborg, K., Jensen, A. K., Overgaard, D., Lindhardt, B., & Midtgaard, J. (2016). Efficacy of a minimal home-based psychoeducative intervention in patients with advanced COPD: A randomised controlled trial. *Respiratory Medicine*, *121*, 109–116.

Bove, D. G., Overgaard, D., Lomborg, K., Lindhardt, B. Ø., & Midtgaard, J. (2015). Efficacy of a minimal home-based psychoeducative intervention versus usual care for managing anxiety and

dyspnoea in patients with severe chronic obstructive pulmonary disease: a randomised controlled trial protocol. *BMJ Open*, *5*(7), e008031. https://doi.org/10.1136/bmjopen-2015-008031

Bruggeman Everts, F. Z., van der Lee, M. L., & de Jager Meezenbroek, E. (2015). Web-based individual Mindfulness-Based Cognitive Therapy for cancer-related fatigue: A pilot study. *Internet Interventions*, *2*(2), 200–213.

Cafarella, P. A., Effing, T. W., Usmani, Z.-A., & Frith, P. A. (2012). Treatments for anxiety and depression in patients with chronic obstructive pulmonary disease: a literature review. *Respirology*, *17*(4), 627–638.

Carmody, J., & Baer, R. A. (2009). How long does a Mindfulness-Based Stress Reduction program need to be? A review of class contact hours and effect sizes for psychological distress. *Journal of Clinical Psychology*, *65*, 627–638.

Chan, R. R., Giardino, N., & Larson, J. L. (2015). A pilot study: mindfulness meditation intervention in COPD. *International Journal of Chronic Obstructive Pulmonary Disease*, *10*, 445–454.

Chan, R. R., & Lehto, R. H. (2016). The experience of learning meditation and mind/body practices in the COPD population. *Explore*, *12*(3), 171–179.

Clark, D. M. (1986). A cognitive approach to panic. *Behaviour Research and Therapy*, *24*(4), 461–470.

Clark, N. M., Dodge, J. A., Partridge, M. R., & Martinez, F. J. (2009). Focusing on outcomes: Making the most of COPD interventions. *International Journal of Chronic Obstructive Pulmonary Disease*, *4*, 61–77.

Clini, E. M., & Ambrosino, N. (2008). Nonpharmacological treatment and relief of symptoms in COPD. *European Respiratory Journal*, *32*(1), 218–228.

Clover, K., Carter, G. L., MacKinnon, A., & Adams, C. (2009). Is my patient suffering clinically significant emotional distress? Demonstration of a probabilities approach to evaluating algorithms for screening for distress. *Supportive Care in Cancer*, *17*(12), 1455–1462.

Compen, F. R., Bisseling, E. M., Schellekens, M. P. J., Jansen, E. T. M., Lee, M. L. Vander, & Speckens, A. E. M. (2017). Mindfulness-Based Cognitive therapy Tor cancer patients delivered via internet: Qualitative study of patient and therapist barriers and facilitators. *Journal of Medical Internet Research*, *19*(12), e407. https://doi.org/10.2196/jmir.7783

Copas, J., & Shi, J. Q. (2000). Meta-analysis, funnel plots and sensitivity analysis. *Biostatistics*, *1*(3), 247–262.

Coventry, P. A., Bower, P., Keyworth, C., Kenning, C., Knopp, J., Garrett, C., … Dickens, C. (2013). The effect of complex interventions on depression and anxiety in chronic obstructive pulmonary disease: Systematic review and meta-analysis. *PloS One*, *8*(4), e60532. https://doi.org/10.1371/journal.pone.0060532

Coventry, P. A., & Gellatly, J. L. (2008). Improving outcomes for COPD patients with mild-to-moderate anxiety and depression: A systematic review of cognitive behavioural therapy. *British Journal of Health Psychology*, *13*, 381–400.

Crane, R. S., Brewer, J., Feldman, C., Kabat-Zinn, J., Santorelli, S., Williams, J. M. G., & Kuyken, W. (2017). What defines mindfulness-based programs? The warp and the weft. *Psychological Medicine*, *47*(6), 990–999.

Crane, R. S., Eames, C., Kuyken, W., Hastings, R. P., Williams, J. M. G., Bartley, T., … Surawy, C. (2013). Development and validation of the Mindfulness-Based Interventions - Teaching Assessment Criteria (MBI:TAC). *Assessment*, *20*(6), 681–688.

Davidson, R. J., Kabat-Zinn, J., Schumacher, J., Rosenkranz, M., Muller, D., Santorelli, S. F., … Sheridan, J. F. (2003). Alterations in brain and immune function produced by mindfulness meditation. *Psychosomatic Medicine*, *65*(4), 564–570.

de Godoy, D. V., de Godoy, R. F., Becker, B., Vaccari, P. F., Michelli, M., Teixeira, P. J. Z., & Palombini, B. C. (2005). The effect of psychotherapy provided as part of a pulmonary rehabilitation program for the treatment of patients with chronic obstructive pulmonary disease. *Jornal Brasileiro de Pneumologia*, *31*(6), 499–505.

de Godoy, D. V, & de Godoy, R. F. (2003). A randomized controlled trial of the effect of psychotherapy on anxiety and depression in chronic obstructive pulmonary disease. *Archives*

of Physical Medicine and Rehabilitation, *84*(8), 1154–1157.

de Silva, D. (2011). *Helping people help themselves: A review of the evidence considering whether it is worthwhile to support self-management*. *The Health Foundation*. London. Retrieved from https://www.health.org.uk/publication/evidence-helping-people-help-themselves

Deb, A., & Sambamoorthi, U. (2016). Depression treatment patterns among adults with chronic obstructive pulmonary disease and depression. *Current Medical Research and Opinion*, *33*(2), 201–208.

Dodd, J. W., Hogg, L., Nolan, J., Jefford, H., Grant, A., Lord, V. M., … Hopkinson, N. S. (2011). The COPD assessment test (CAT): Response to pulmonary rehabilitation. A multicentre, prospective study. *Thorax*, *66*(5), 425–429.

Dowd, H., Hogan, M. J., McGuire, B. E., Davis, M. C., Sarma, K. M., Fish, R. A., & Zautra, A. J. (2015). Comparison of an online Mindfulness-based Cognitive Therapy intervention with online pain management psychoeducation. *The Clinical Journal of Pain*, *31*(6), 517–527.

Doxsee, D. J., & Kivlighan, D. M. (1994). Hindering events in interpersonal relations groups for counselor trainees. *Journal of Counseling & Development*, *72*(6), 621–626.

Doyle, C., Bhar, S., Fearn, M., Ames, D., Osborne, D., You, E., … Dunt, D. (2017). The impact of telephone-delivered cognitive behaviour therapy and befriending on mood disorders in people with chronic obstructive pulmonary disease: A randomized controlled trial. *British Journal of Health Psychology*, *22*(3), 542–556.

Duval, S., & Tweedie, R. (2000). Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. *Biometrics*, *56*, 455–463.

Eccleston, C., Fisher, E., Craig, L., Duggan, G. B., Rosser, B. A., & Keogh, E. (2014). Psychological therapies (Internet-delivered) for the management of chronic pain in adults. *Cochrane Database of Systematic Reviews*, *Feb 26*(2), CD010152. https://doi.org/10.1002/14651858.CD010152.pub2

Egger, M., Smith, G. D., Schneider, M., & Minder, C. (1997). Bias in meta-analysis detected by a simple, graphical test. *BMJ*, *315*, 629–634.

Eiser, N., West, C., Evans, S., Jeffers, A., & Quirk, F. (1997). Effects of psychotherapy in moderately severe COPD: a pilot study. *European Respiratory Journal*, *10*(7), 1581–1584.

Eisner, M. D., Blanc, P. D., Yelin, E. H., Sidney, S., Katz, P. P., Ackerson, L., … Iribarren, C. (2008). COPD as a systemic disease: Impact on physical functional limitations. *American Journal of Medicine*, *121*(9), 789–796.

Ekeland, A. G., Bowes, A., & Flottorp, S. (2011). Methodologies for assessing telemedicine: A systematic review of reviews. *International Journal of Medical Informatics*, *81*, 1–11. https://doi.org/10.1016/j.ijmedinf.2011.10.009

Emery, C. F., Schein, R. L., Hauck, E. R., & MacIntyre, N. R. (1998). Psychological and cognitive outcomes of a randomized trial of exercise among patients with chronic obstructive pulmonary disease. *Health Psychology*, *17*(3), 232–240.

Emmelkamp, P. (2011). Effectiveness of cybertherapy in mental health: A critical appraisal. *Annual Review of Cybertherapy and Telemedicine*, *9*, 6–9.

Fabbri, L. M., Luppi, F., Beghé, B., & Rabe, K. F. (2008). Complex chronic comorbidities of COPD. *European Respiratory Journal*, *31*(1), 204–212.

Fabricius, P., Løkke, A., Marott, J. L., Vestbo, J., & Lange, P. (2011). Prevalence of COPD in Copenhagen. *Respiratory Medicine*, *105*(3), 410–417.

Farver-Vestergaard, I., Connor, M. O., Smith, N. C., Løkke, A., Bendstrup, E., & Zachariae, R. (2018). Tele-delivered mindfulness-based cognitive therapy in chronic obstructive pulmonary disease: A mixed-methods feasibility study. *Journal of Telemedicine and Telecare*, [e-pub ahead of print]. https://doi.org/10.1177/1357633X18780563

Farver-Vestergaard, I., Jacobsen, D., & Zachariae, R. (2015). Efficacy of psychosocial interventions on psychological and physical health outcomes in chronic obstructive pulmonary disease: A systematic review and meta-analysis. *Psychotherapy and Psychosomatics*, *84*(1), 37-50.

Farver-Vestergaard, I., O'Toole, M. S., O'Connor, M., Løkke, A., Bendstrup, E., Basdeo, S. A., … Zachariae, R. (2018). Mindfulness-based cognitive therapy in COPD: a cluster randomised controlled trial. *European Respiratory Journal*, *51*(2), 1702082. https://doi.org/10.1183/13993003.02082-2017

Fischer, M. J., Scharloo, M., Abbink, J. J., Thijs-Van Nies, A., Rudolphus, A., Snoei, L., … Kaptein, A. A. (2007). Participation and drop-out in pulmonary rehabilitation: A qualitative analysis of the patient's perspective. *Clinical Rehabilitation*, *21*(3), 212–221.

Fritzsche, A., Clamor, A., & von Leupoldt, A. (2011). Effects of medical and psychological treatment of depression in patients with COPD: A review. *Respiratory Medicine*, *105*(10), 1422–1433.

García-Lizana, F., & Muñoz-Mayorga, I. (2010). What about telepsychiatry? A systematic review. *Primary Care Companion to the Journal of Clinical Psychiatry*, *12*(2), e1–e5. https://doi.org/10.4088/PCC.09m00831whi

Garrod, R., Marshall, J., Barley, E., & Jones, P. W. (2006). Predictors of success and failure in pulmonary rehabilitation. *European Respiratory Journal*, *27*(4), 788–794.

Giacomini, M., Dejean, D., Simeonov, D., & Smith, A. (2012). Experiences of living and dying with COPD: A systematic review and synthesis of the qualitative empirical literature. *Ontario Health Technology Assessment Series*, *12*(13), 1–47.

Gift, A. G., Moore, T., & Soeken, K. (1992). Relaxation to reduce dyspnea and anxiety in COPD patients. *Nursing Research*, *41*(4), 242–246.

Gilbert, P. (2010). *Compassion Focused Therapy: distinctive features*. New York: Taylor & Francis.

GOLD Global Initiative for Chronic Obstructive Pulmonary Disease. (2018). *Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary diease*. Retrieved from https://goldcopd.org/wp-content/uploads/2017/11/GOLD-2018-v6.0-FINAL-revised-20-Nov_WMS.pdf

Goldberg, S. B., Davis, J. M., & Hoyt, W. T. (2013). The role of therapeutic alliance in mindfulness interventions: Therapeutic alliance in mindfulness training for smokers. *Journal of Clinical Psychology*, *69*(9), 936–950.

Goldstein, R. S. (2014). Telemedicine in COPD: Time to pause. *Chest*, *145*(5), 945–949.

Gotink, R. A., Chu, P., Busschbach, J. J. V, Benson, H., Fricchione, G. L., & Hunink, M. G. M.

(2015). Standardised mindfulness-based interventions in healthcare: An overview of systematic reviews and meta-analyses of RCTs. *PLoS ONE*, *10*(4), e0124344. https://doi.org/10.1371/journal.pone.0124344

Gøtzsche, P. C. (2000). Why we need a broad perspective on meta-analysis. *BMJ*, *321*, 585–586.

Grossman, P., Niemann, L., Schmidt, S., & Walach, H. (2004). Mindfulness-based stress reduction and health benefits: A meta-analysis. *Journal of Psychosomatic Research*, *57*(1), 35–43.

Guise, V., Anderson, J., & Wiig, S. (2014). Patient safety risks associated with telecare: a systematic review and narrative synthesis of the literature. *BMC Health Services Research*, *14*, 588. https://doi.org/http://dx.doi.org/10.1186/s12913-014-0588-z

Halpin, D. M. G., Miravitlles, M., Metzdorf, N., & Celli, B. (2017). Impact and prevention of severe exacerbations of COPD: A review of the evidence. *International Journal of COPD*, *12*, 2891–2908.

Hansen, N. B., Lambert, M. J., & Forman, E. M. (2002). The psychotherapy dose-response effect and its implications for treatment delivery services. *Clinical Psychology: Science and Practice*, *9*(3), 329–343.

Harrison, S. L., Lee, A., Goldstein, R. S., & Brooks, D. (2017). Perspectives of healthcare professionals and patients on the application of mindfulness in individuals with chronic obstructive pulmonary disease. *Patient Education and Counseling*, *100*, 337–342.

Harrison, S. L., Lee, A., Janaudis-Ferreira, T., Goldstein, R. S., & Brooks, D. (2016). Mindfulness in people with a respiratory diagnosis: A systematic review. *Patient Education and Counseling*, *99*(3), 348–355.

Hasson, F., Spence, A., Waldron, M., Kernohan, G., McLaughlin, D., Watson, B., & Cochrane, B. (2008). I can not get a breath: experiences of living with advanced chronic obstructive pulmonary disease. *International Journal of Palliative Nursing*, *14*(11), 526–531.

Heinzer, M. M. V., Bish, C., & Detwiler, R. (2003). Acute dyspnea as perceived by patients with chronic obstructive pulmonary disease. *Clinical Nursing Research*, *12*(1), 85–101.

Heslop, K., de Soyza, A., Baker, C., Stenton, S. C., & Burns, G. P. (n.d.). Individualised cognitive

behavior therapy as a treatment for COPD. *Unpublished*.

Holas, P., Michałowski, J., Gaweda, Ł., & Domagała-Kulawik, J. (2017). Agoraphobic avoidance predicts emotional distress and increased physical concerns in chronic obstructive pulmonary disease. *Respiratory Medicine*, *128*, 7–12.

Holmes, E. A., Ghaderi, A., Harmer, C. J., Ramchandani, P. G., Cuijpers, P., Morrison, A. P., … Craske, M. G. (2018). The Lancet Psychiatry Commission on psychological treatments research in tomorrow's science. *The Lancet Psychiatry*, *5*(3), 237–286.

Horton, K. (2008). The use of telecare for people with chronic obstructive pulmonary disease: implications for management. *Nursing*, *16*, 173–180.

Horvath, A. O., & Greenberg, L. S. (1989). Development and validation of the Working Alliance Inventory. *Journal of Counseling Psychology*, *36*(2), 223–233.

Howard, C., & Dupont, S. (2014). 'The COPD breathlessness manual': a randomised controlled trial to test a cognitive-behavioural manual versus information booklets on health service use, mood and health status, in patients with chronic obstructive pulmonary disease. *Primary Care Respiratory Medicine*, *24*, 14076. https://doi.org/10.1038/npjpcrm.2014.76

Hurst, J. R., Vestbo, J., Anzueto, A., Locantore, N., Müllerova, H., Tal-Singer, R., … Wedzicha, J. A. (2010). Susceptibility to exacerbation in chronic obstructive pulmonary disease. *The New England Journal of Medicine*, *363*(12), 1128–1138.

Hynninen, M. J., Bjerke, N., Pallesen, S., Bakke, P. S., & Nordhus, I. H. (2010). A randomized controlled trial of cognitive behavioral therapy for anxiety and depression in COPD. *Respiratory Medicine*, *104*(7), 986–994.

Jadad, A. R., Moore, R. A., Carroll, D., Jenkinson, C., Reynolds, D. J., Gavaghan, D. J., & McQuay, H. J. (1996). Assessing the quality of reports of randomized clinical trials: Is blinding necessary? *Controlled Clinical Trials*, *17*(1), 1–12.

Janssen, D. J., Spruit, M. A., Leue, C., Gijsen, C., Hameleers, H., Schols, J. M., & Wouters, E. F. (2010). Symptoms of anxiety and depression in COPD patients entering pulmonary rehabilitation. *Chronic Respiratory Disease*, *7*(3), 147–157.

Jiang, X., & He, G. (2012). Effects of an uncertainty management intervention on uncertainty, anxiety, depression, and quality of life of chronic obstructive pulmonary disease outpatients. *Research in Nursing & Health*, *35*(4), 409–418.

Johannsen, M., O'Connor, M., O'Toole, M. S., Jensen, A. B., Højris, I., & Zachariae, R. (2016). Efficacy of Mindfulness-Based Cognitive Therapy on Late Post-Treatment Pain in Women Treated for Primary Breast Cancer: A Randomized Controlled Trial. *Journal of Clinical Oncology*, *34*, 3390–3399.

Johnson, J. L., Campbell, A. C., Bowers, M., & Nichol, A.-M. (2007). Understanding the social consequences of chronic obstructive pulmonary disease: the effects of stigma and gender. *Proceedings of the American Thoracic Society*, *4*(8), 680–682.

Jones, P. (2001). Health status measurement in chronic obstructive pulmonary disease. *Thorax*, *56*, 880–887.

Jones, P., Harding, G., Berry, P., Wiklund, I., Chen, W.-H., & Kline Leidy, N. (2009). Development and first validation of the COPD Assessment Test. *European Respiratory Journal*, *34*(3), 648–654.

Jones, P., Miravitlles, M., van der Molen, T., & Kulich, K. (2012). Beyond FEV_1 in COPD: a review of patient-reported outcomes and their measurement. *International Journal of Chronic Obstructive Pulmonary Disease*, *7*, 697–709.

Kabat-Zinn, J. (1990). *Full catastrophe living: Using the wisdom of your mind to face stress, pain and illness*. New York: Dell.

Kabat-Zinn, J. (2006). Mindfulness-Based Interventions in Context: Past, Present, and Future. *Clinical Psychology: Science and Practice*, *10*(2), 144–156.

Kaptein, A. A., Scharloo, M., Fischer, M. J., Snoei, L., Hughes, B. M., Weinman, J., … Rabe, K. F. (2009). 50 years of psychological research on patients with COPD: Road to ruin or highway to heaven? *Respiratory Medicine*, *103*, 3–11.

Kazdin, A. E. (2007). Mediators and mechanisms of change in psychotherapy research. *Annual Review of Clinical Psychology*, *3*, 1–27. https://doi.org/10.1146/annurev.clinpsy.3.022806.091432

Keating, A., Lee, A., & Holland, A. E. (2011). What prevents people with chronic obstructive pulmonary disease from attending pulmonary rehabilitation? A systematic review. *Chronic Respiratory Disease*, *8*(2), 89–99.

Kendall, M., Buckingham, S., Ferguson, S., MacNee, W., Sheikh, A., White, P., … Pinnock, H. (2015). Exploring the concept of need in people with very severe chronic obstructive pulmonary disease: a qualitative study. *BMJ Supportive & Palliative Care*, 1–7. https://doi.org/10.1136/bmjspcare-2015-000904

Kon, S. S. C., Canavan, J. L., Jones, S. E., Nolan, C. M., Clark, A. L., Dickson, M. J., … Man, W. D. C. (2014). Minimum clinically important difference for the COPD Assessment Test: A prospective analysis. *The Lancet Respiratory Medicine*, *2*(3), 195–203.

Kunik, M. E., Braun, U., Stanley, M. A., Wristers, K., Molinari, V., Stoebner, D., & Orengo, C. A. (2001). One session cognitive behavioural therapy for elderly patients with chronic obstructive pulmonary disease. *Psychological Medicine*, *31*(4), 717–723.

Kunik, M. E., Veazey, C., Cully, J. A., Souchek, J., Graham, D. P., Hopko, D., … Stanley, M. A. (2008). COPD education and cognitive behavioral therapy group treatment for clinically significant symptoms of depression and anxiety in COPD patients: A randomized controlled trial. *Psychological Medicine*, *38*(3), 385–396.

Kuyken, W., Watkins, E., Holden, E., White, K., Taylor, R. S., Byford, S., … Dalgleish, T. (2010). How does mindfulness-based cognitive therapy work? *Behaviour Research and Therapy*, *48*(11), 1105–1112.

Lamers, F., Jonkers, C. C. M., Bosma, H., Chavannes, N. H., Knottnerus, J. A., & van Eijk, J. T. (2010). Improving quality of life in depressed COPD patients: Effectiveness of a minimal psychological intervention. *COPD*, *7*(5), 315–322.

Laurin, C., Moullec, G., Bacon, S. L., & Lavoie, K. L. (2011). The impact of psychological distress on exacerbation rates in COPD. *Therapeutic Advances in Respiratory Disease*, *5*, 3–18.

Lesaffre, E. (2008). Superiority, equivalence, and non-inferiority trials. *Bulletin of the NYU Hospital for Joint Diseases*, *66*, 150–154.

Lieberman, M. A., Yalom, I. D., & Miles, M. B. (1973). *Encounter groups: First facts*. New York:

Basic Books.

Lindqvist, G., & Hallberg, L. R.-M. (2010). “Feelings of guilt due to self-inflicted disease”: a grounded theory of suffering from chronic obstructive pulmonary disease (COPD). *Journal of Health Psychology*, *15*(3), 456–466.

Lisansky, D. P., & Clough, D. H. (1996). A cognitive-behavioral self-help educational program for patients with COPD: A pilot study. *Psychotherapy and Psychosomatics*, *65*, 97–101.

Livermore, N., Sharpe, L., & McKenzie, D. (2010). Prevention of panic attacks and panic disorder in COPD. *European Respiratory Journal*, *35*(3), 557–563.

Luk, E., Gorelik, A., Irving, L., & Khan, F. (2017). Effectiveness of cognitive behavioural therapy in a community-based pulmonary rehabilitation programme: A controlled clinical trial. *Journal of Rehabilitation Medicine*, *49*, 264–269.

Lustig, F. (1970). *A study of the effect of a pulmonary rehabilitation program on anxiety, medical orientation, social introversion, attitude toward work and engagement in vocational activities in patients with chronic obstructive pulmonary emphysema (COPD)*. Dissertation. New York.

Malpass, A., Kessler, D., Sharp, D., & Shaw, A. (2015). MBCT for patients with respiratory conditions who experience anxiety and depression: A qualitative study. *Mindfulness*, *6*(5), 1181–1191.

Mannino, D. M., & Buist, A. S. (2007). Global burden of COPD: risk factors, prevalence, and future trends. *Lancet*, *370*, 765–773.

Matera, M. G., Calzetta, L., & Cazzola, M. (2010). TNF-alpha inhibitors in asthma and COPD: We must not throw the baby out with the bath water. *Pulmonary Pharmacology & Therapeutics*, *23*(2), 121–128.

Mathers, C. D., & Loncar, D. (2006). Projections of global mortality and burden of disease from 2002 to 2030. *PLoS Medicine*, *3*(11), 2011–2030.

Maurer, J., Rebbapragada, V., Borson, S., Goldstein, R., Kunik, M. E., Yohannes, A. M., & Hanania, N. A. (2008). Anxiety and Depression in COPD: Current understanding, unanswered questions, and research needs. *Chest*, *134*(4), 43–56.

McCarthy, B., Casey, D., Devane, D., Murphy, K., Murphy, E., & Lacasse, Y. (2015). Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews*, (2), 1–209. https://doi.org/10.1002/14651858.CD003793.pub3.www.cochranelibrary.com

McLean, S., Nurmatov, U., Liu, J. L., Pagliari, C., Car, J., & Sheikh, A. (2012). Telehealthcare for chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews*, *8*, 1–51. https://doi.org/10.1002/14651858.CD007718.pub2

Mularski, R. A., Munjas, B. A., Lorenz, K. A., Sun, S., Robertson, S. J., Schmelzer, W., … Shekelle, P. G. (2009). Randomized controlled trial of mindfulness-based therapy for dyspnea in chronic obstructive lung disease. *Journal of Alternative and Complementary Medicine*, *15*(10), 1083–1090.

Murray, S. A., Kendall, M., Boyd, K., & Sheikh, A. (2005). Illness trajectories and palliative care. *BMJ*, *330*, 1007–1011.

Neff, K. (2003). Self-Compassion: An Alternative Conceptualization of a Healthy Attitude Toward Oneself. *Self and Identity*, *2*(2), 85–101.

O'Donnell, D. E., Banzett, R. B., Carrieri-Kohlman, V., Casaburi, R., Davenport, P. W., Gandevia, S. C., … Webb, K. A. (2007). Pathophysiology of dyspnea in chronic obstructive pulmonary disease. *Proceedings of the American Thoracic Society*, *4*, 145–168.

O'Toole, M. S., Bovbjerg, D. H., Renna, M. E., Lekander, M., Mennin, D. S., & Zachariae, R. (2018). Effects of psychological interventions on systemic levels of inflammatory biomarkers in humans: A systematic review and meta-analysis. *Brain Behavior and Immunity*. [e-pub ahead of print]. https://doi.org/10.1016/j.bbi.2018.04.005

Panagioti, M., Scott, C., Blakemore, A., & Coventry, P. A. (2014). Overview of the prevalence, impact, and management of depression and anxiety in chronic obstructive pulmonary disease. *International Journal of Chronic Obstructive Pulmonary Disease*, *9*, 1289–1306.

Papava, I., Oancea, C., Enatescu, V. R., Bredicean, A. C., Dehelean, L., Romosan, R. S., & Timar, B. (2016). The impact of coping on the somatic and mental status of patients with COPD: A cross-sectional study. *International Journal of COPD*, *11*(1), 1343–1351.

Parsons, C. E., Crane, C., Parsons, L. J., Fjorback, L. O., & Kuyken, W. (2017). Home practice in Mindfulness-Based Cognitive Therapy and Mindfulness-Based Stress Reduction: A systematic review and meta-analysis of participants' mindfulness practice and its association with outcomes. *Behaviour Research and Therapy*, *95*, 29–41.

Perera, W. R., Hurst, J. R., Wilkinson, T. M. a, Sapsford, R. J., Müllerova, H., Donaldson, G. C., & Wedzicha, J. a. (2007). Inflammatory changes, recovery and recurrence at COPD exacerbation. *The European Respiratory Journal*, *29*(3), 527–534.

Perez-Blasco, J., Viguer, P., & Rodrigo, M. F. (2013). Effects of a mindfulness-based intervention on psychological distress, well-being, and maternal self-efficacy in breast-feeding mothers: Results of a pilot study. *Archives of Women's Mental Health*, *16*(3), 227–236.

Perkins-Porras, L., Riaz, M., Okekunle, A., Zhelezna, S., Chakravorty, I., & Ussher, M. (2018). Feasibility study to assess the effect of a brief mindfulness intervention for patients with chronic obstructive pulmonary disease: A randomized controlled trial. *Chronic Respiratory Disease*, 1–11. https://doi.org/10.1177/1479972318766140

Perle, J. G., Langsam, L. C., & Nierenberg, B. (2011). Controversy clarified: An updated review of clinical psychology and tele-health. *Clinical Psychology Review*, *31*(8), 1247–1258.

Piet, J., Würtzen, H., & Zachariae, R. (2012). The effect of mindfulness-based therapy on symptoms of anxiety and depression in adult cancer patients and survivors: a systematic review and meta-analysis. *Journal of Consulting and Clinical Psychology*, *80*(6), 1007–1020.

Plaufcan, M. R., Wamboldt, F. S., & Holm, K. E. (2012). Behavioral and characterological self-blame in chronic obstructive pulmonary disease. *Journal of Psychosomatic Research*, *72*(1), 78–83.

Pooler, A., & Beech, R. (2014). Examining the relationship between anxiety and depression and exacerbations of COPD which result in hospital admission: a systematic review. *International Journal of Chronic Obstructive Pulmonary Disease*, *9*(1), 315–330.

Puhan, M. A., Frey, M., Büchi, S., & Schünemann, H. J. (2008). The minimal important difference of the hospital anxiety and depression scale in patients with chronic obstructive pulmonary disease. *Health and Quality of Life Outcomes*, *6*(1), 46. https://doi.org/10.1186/1477-7525-6-

46

Radhakrishnan, K., Xie, B., Berkley, A., & Kim, M. (2016). Barriers and facilitators for sustainability of tele-homecare programs: A systematic review. *Health Services Research, 51*(1), 48–75.

Ranjita, R., Hankey, A., Nagendra, H. R., & Mohanty, S. (2016). Yoga-based pulmonary rehabilitation for the management of dyspnea in coal miners with chronic obstructive pulmonary disease: A randomized controlled trial. *Journal of Ayurveda and Integrative Medicine*. https://doi.org/10.1016/j.jaim.2015.12.001

Reardon, J. Z., Lareau, S. C., & ZuWallack, R. (2006). Functional Status and Quality of Life in Chronic Obstructive Pulmonary Disease. *American Journal of Medicine, 119*, 32–37.

Rejeski, W. J. (2008). Mindfulness: Reconnecting the body and mind in geriatric medicine and gerontology. *The Gerontologist, 48*(2), 135–141.

Ringbaek, T., Martinez, G., & Lange, P. (2012). A comparison of the assessment of Quality of Life with CAT, CCQ, and SGRQ in COPD patients participating in pulmonary rehabilitation. *COPD, 9*, 12–15.

Riva, G. (2011). Presence, actions and emotions: A theoretical framework. *Annual Review of Cybertherapy and Telemedicine, 9*, 2–5.

Rochester, C. L., Vogiatzis, I., Holland, A. E., Lareau, S. C., Marciniuk, D. D., Puhan, M. A., … Stahlberg, B. (2015). An official American Thoracic Society/European Respiratory Society policy statement: Enhancing implementation, use, and delivery of pulmonary rehabilitation. *American Journal of Respiratory and Critical Care Medicine, 192*(11), 1373–1386.

Rogers, M. A., Lemmen, K., Kramer, R., Mann, J., & Chopra, V. (2017). Internet-Delivered Health Interventions That Work: Systematic Review of Meta-Analyses and Evaluation of Website Availability. *Journal of Medical Internet Research, 19*(3), e90. https://doi.org/10.2196/jmir.7111

Rose, C., Wallace, L., Dickson, R., Ayres, J., Lehman, R., Searle, Y., & Burge, P. S. (2002). The most effective psychologically-based treatments to reduce anxiety and panic in patients with chronic obstructive pulmonary disease (COPD): a systematic review. *Patient Education and*

Counseling, *47*, 311–318.

Rosenkranz, M. a, Davidson, R. J., Maccoon, D. G., Sheridan, J. F., Kalin, N. H., & Lutz, A. (2013). A comparison of mindfulness-based stress reduction and an active control in modulation of neurogenic inflammation. *Brain, Behavior, and Immunity*, *27*(1), 174–184.

Rosser, R., Denford, J., Heslop, A., Kinston, W., Macklin, D., Minty, K., … Guz, A. (1983). Breathlessness and psychiatric morbidity in chronic bronchitis and emphysema: A study of psychotherapeutic management. *Psychological Medicine*, *13*(01), 93–110.

Sassi-Dambron, D. E., Eakin, E. G., Ries, a L., & Kaplan, R. M. (1995). Treatment of dyspnea in COPD: A controlled clinical trial of dyspnea management strategies. *Chest*, *107*(3), 724–729.

Schellekens, M. P. J., van den Hurk, D. G. M., Prins, J. B., Donders, A. R. T., Molema, J., Dekhuijzen, R., … Speckens, A. E. M. (2017). Mindfulness-based stress reduction added to care as usual for lung cancer patients and/or their partners: A multicentre randomized controlled trial. *Psycho-Oncology*, *26*(12), 2118–2126.

Schellekens, M. P. J., van den Hurk, D. G. M., Prins, J. B., Molema, J., van der Drift, M. A., & Speckens, A. E. M. (2016). The suitability of the Hospital Anxiety and Depression Scale, Distress Thermometer and other instruments to screen for psychiatric disorders in both lung cancer patients and their partners. *Journal of Affective Disorders*, *203*, 176–183.

Segal, Z. V, Williams, J. M. G., & Teasdale, J. D. (2002). *Mindfulness-based cognitive therapy for depression*. New York: Guilford Publications.

Segal, Z., Williams, J. M. G., & Teasdale, J. (2013). *Mindfulness-based cognitive therapy for depression*. New York: Guildford Press.

Shahar, B., Britton, W. B., Sbarra, D. A., Figueredo, A. J., & Bootzin, R. R. (2010). Mechanisms of Change in Mindfulness-Based Cognitive Therapy for Depression: Preliminary Evidence from a Randomized Controlled Trial. *International Journal of Cognitive Therapy*, *3*(4), 402–418.

Sharpe, D. (1997). Of apples and oranges, file drawers and garbage: Why validity issues in meta-analysis will not go away. *Clinical Psychology Review*, *17*(8), 881–901. 1f7aa3436fd2&acdnat=1528915974_f018676438453826311 3d111a8eb5df4

Similowski, T. (2018). Treat the lungs, fool the brain and appease the mind: towards holistic care of patients who suffer from chronic respiratory diseases. *European Respiratory Journal*, *51*, 1800316. https://doi.org/10.1183/13993003.00316-2018

Smid, D. E., Franssen, F. M. E., Gonik, M., Miravitlles, M., Casanova, C., Cosio, B. G., … Spruit, M. A. (2017). Redefining Cut-Points for High Symptom Burden of the Global Initiative for Chronic Obstructive Lung Disease Classification in 18,577 Patients With Chronic Obstructive Pulmonary Disease. *Journal of the American Medical Directors Association*, *18*(12), 1097.e11-1097.e24. https://doi.org/10.1016/j.jamda.2017.09.003

Smid, D. E., Franssen, F. M. E., Houben-Wilke, S., Vanfleteren, L. E. G. W., Janssen, D. J. A., Wouters, E. F. M., & Spruit, M. A. (2017). Responsiveness and MCID Estimates for CAT, CCQ, and HADS in Patients With COPD Undergoing Pulmonary Rehabilitation: A Prospective Analysis. *Journal of the American Medical Directors Association*, *18*(1), 53–58.

Smith, S. M. S., Sonego, S., Ketcheson, L., & Larson, J. L. (2014). A review of the effectiveness of psychological interventions used for anxiety and depression in chronic obstructive pulmonary disease. *BMJ Open Respiratory Research*, *1*(1), e000042. https://doi.org/10.1136/bmjresp-2014-000042

Sohanpal, R., Steed, L., Mars, T., & Taylor, S. J. C. (2015). Understanding patient participation behaviour in studies of COPD support programmes such as pulmonary rehabilitation and self-management: a qualitative synthesis with application of theory. *Primary Care Respiratory Medicine*, *25*, 15054. https://doi.org/10.1038/npjpcrm.2015.54

Solomon, B. K., Wilson, K. G., Henderson, P. R., Poulin, P. A., Kowal, J., & McKim, D. A. (2015). A Breathlessness Catastrophizing Scale for chronic obstructive pulmonary disease. *Journal of Psychosomatic Research*, *79*(1), 62–68.

Spijkerman, M. P. J., Pots, W. T. M., & Bohlmeijer, E. T. (2016). Effectiveness of online mindfulness-based interventions in improving mental health: A review and meta-analysis of randomised controlled trials. *Clinical Psychology Review*, *45*, 102–114.

Spinhoven, P., Ormel, J., Sloekers, P. P. A., Kempen, G. I. J. M., Speckens, A. E. M., & Van Hemert, A. M. (1997). A validation study of the Hospital Anxiety and Depression Scale (HADS) in different groups of Dutch subjects. *Psychological Medicine*, *27*, 363–370.

Spruit, M. A., Singh, S. J., Garvey, C., Zu Wallack, R., Nici, L., Rochester, C., … Wouters, E. F. M. (2013). An official American Thoracic Society/European Respiratory Society statement: Key concepts and advances in pulmonary rehabilitation. *American Journal of Respiratory and Critical Care Medicine*, *188*(8), e13–e64. https://doi.org/10.1164/rccm.201309-1634ST

Tasca, G. A., Illing, V., Joyce, A. S., & Ogrodniczuk, J. S. (2009). Three-level multilevel growth models for nested change data: a guide for group treatment researchers. *Psychotherapy Research : Journal of the Society for Psychotherapy Research*, *19*(4–5), 453–461.

Thompson, N. J., Patel, A. H., Selwa, L. M., Stoll, S. C., Begley, C. E., Johnson, E. K., & Fraser, R. T. (2015). Expanding the efficacy of Project UPLIFT: distance delivery of mindfulness-based depression prevention to people with epilepsy. *Journal of Consulting and Clinical Psychology*, *83*(2), 304–313.

Thompson, N. J., Walker, E. R., Obolensky, N., Winning, A., Barmon, C., Diiorio, C., & Compton, M. T. (2010). Distance delivery of mindfulness-based cognitive therapy for depression: project UPLIFT. *Epilepsy & Behavior*, *19*(3), 247–254.

Thyregod, M., & Bødtger, U. (2016). Coherence between self-reported and objectively measured physical activity in patients with chronic obstructive lung disease: a systematic review. *International Journal of COPD*, *11*, 2931–2938.

Toivonen, K. I., Zernicke, K., & Carlson, L. E. (2017). Web-Based Mindfulness Interventions for People With Physical Health Conditions: Systematic Review. *Journal of Medical Internet Research*, *19*(8), e303. https://doi.org/10.2196/jmir.7487

Usmani, Z. A., Carson, K. V, Heslop, K., Esterman, A. J., De Soyza, A., & Smith, B. J. (2017). Psychological therapies for the treatment of anxiety disorders in chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews*, (3). https://doi.org/10.1002/14651858.CD010673.pub2.www.cochranelibrary.com

van Aalderen, J. R., Donders, A. R. T., Giommi, F., Spinhoven, P., Barendregt, H. P., & Speckens, A. E. M. (2012). The efficacy of mindfulness-based cognitive therapy in recurrent depressed patients with and without a current depressive episode: a randomized controlled trial. *Psychological Medicine*, *42*(05), 989–1001.

van der Velden, A. M., Kuyken, W., Wattar, U., Crane, C., Pallesen, K. J., Dahlgaard, J., … Piet, J. (2015). A systematic review of mechanisms of change in mindfulness-based cognitive therapy in the treatment of recurrent major depressive disorder. *Clinical Psychology Review*, *37*, 26–39.

Vanfleteren, L. E. G. W., Spruit, M. A., Groenen, M., Gaffron, S., Van Empel, V. P. M., Bruijnzeel, P. L. B., … Franssen, F. M. E. (2013). Clusters of comorbidities based on validated objective measurements and systemic inflammation in patients with chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine*, *187*(7), 728–735.

Verbeke, G., & Molenberghs, G. (2000). *Linear Mixed Models for Longitudinal Data*. New York: Springer-Verlag.

Vestbo, J., & Lange, P. (2017). Exposure Interaction: A Lifelong Phenomenon with Relevance to Chronic Obstructive Pulmonary Disease. *American Journal of Respiratory and Critical Care Medicine*, *196*(8), 947–948.

Viegi, G., Pistelli, F., Sherrill, D. L., Maio, S., Baldacci, S., & Carrozzi, L. (2007). Definition, epidemiology and natural history of COPD. *The European Respiratory Journal*, *30*(5), 993–1013.

Volpato, E., Banfi, P., Nicolini, A., & Pagnini, F. (2018). A quick relaxation exercise for people with chronic obstructive pulmonary disease: Explorative randomized controlled trial. *Multidisciplinary Respiratory Medicine*, *13*, 1–8. https://doi.org/10.1186/s40248-018-0124-9

Volpato, E., Banfi, P., Rogers, S. M., & Pagnini, F. (2015). Relaxation techniques for people with chronic obstructive pulmonary disease: A systematic review and a meta-analysis. *Evidence-Based Complementary and Alternative Medicine*, 1–22. https://doi.org/10.1155/2015/628365

von Korff, M., Gruman, J., Schaefer, J., Curry, S. J., & Wagner, E. H. (1997). Collaborative management of chronic illness. *Annals of Internal Medicine*, *127*(12), 1097–1102.

von Leupoldt, A. (2017). Treating anxious expectations can improve dyspnoea in patients with COPD. *European Respiratory Journal*, *50*(3), 1701352. https://doi.org/10.1183/13993003.01352-2017

von Leupoldt, A., Fritzsche, A., Trueba, A. F., Meuret, A. E., & Ritz, T. (2012). Behavioral

medicine approaches to chronic obstructive pulmonary disease. *Annals of Behavioral Medicine*, *44*(1), 52–65.

von Leupoldt, A., & Janssens, T. (2016). Could targeting disease specific fear and anxiety improve COPD outcomes? *Expert Review of Respiratory Medicine*, *10*(8), 835–837.

von Leupoldt, A., & Kenn, K. (2013). The psychology of chronic obstructive pulmonary disease. *Current Opinion in Psychiatry*, *26*(5), 458–463.

von Leupoldt, A., Taube, K., Henkhus, M., Dahme, B., & Magnussen, H. (2010). The impact of affective states on the perception of dyspnea in patients with chronic obstructive pulmonary disease. *Biological Psychology*, *84*(1), 129–134.

von Leupoldt, A., Taube, K., Lehmann, K., Fritzsche, A., & Magnussen, H. (2011). The impact of anxiety and depression on outcomes of pulmonary rehabilitation in patients with COPD. *Chest*, *140*(3), 730–736.

Wade, V., & Smith, A. C. (2017). Research methods and methodology in telemedicine. *Journal of Telemedicine and Telecare*, *23*(9), 757–758.

Wedzicha, J. A., & Seemungal, T. A. R. (2007). COPD exacerbations: defining their cause and prevention. *The Lancet*, *370*, 786–796.

Weiner, H. (1988). *Progressive relaxation training in the treatment of chronic obstructive pulmonary disease*. Dissertation. Ohio.

Wigal, K., Creer, T. L., & Kotses, H. (1991). The COPD Self-Efficacy Scale. *Chest*, *99*, 1193–1196.

Williams, M. J., Dalgleish, T., Karl, A., & Kuyken, W. (2014). Examining the factor structures of the Five Facet Mindfulness Questionnaire and the Self-Compassion Scale. *Psychological Assessment*, *26*(2), 407–418.

Worth, H. (1997). Self management in COPD: One step beyond? *Patient Education and Counseling*, *32*, 105–109.

Worth, H., & Dhein, Y. (2004). Does patient education modify behaviour in the management of COPD? *Patient Education and Counseling*, *52*, 267–270.

Yohannes, A. M., & Alexopoulos, G. S. (2014a). Depression and anxiety in patients with COPD. *European Respiratory Review : An Official Journal of the European Respiratory Society*, *23*, 345–349.

Yohannes, A. M., & Alexopoulos, G. S. (2014b). Pharmacological treatment of depression in older patients with chronic obstructive pulmonary disease: Impact on the course of the disease and health outcomes. *Drugs & Aging*. https://doi.org/10.1007/s40266-014-0186-0

Yohannes, A. M., Junkes-Cunha, M., Smith, J., & Vestbo, J. (2017). Management of dyspnea and anxiety in chronic obstructive pulmonary disease: A critical review. *Journal of the American Medical Directors Association*, *18*(12), 1096.e1-1096.e17.

Zachariae, R., Lyby, M. S., Ritterband, L. M., & O'Toole, M. S. (2016). Efficacy of internet-delivered cognitive-behavioral therapy for insomnia - A systematic review and meta-analysis of randomized controlled trials. *Sleep Medicine Reviews*, *30*, 1–10. https://doi.org/10.1016/j.smrv.2015.10.004

Zernicke, K. A., Campbell, T. S., Speca, M., Mccabe-Ruff, K., Flowers, S., & Carlson, L. E. (2014). A randomized wait-list controlled trial of feasibility and efficacy of an online mindfulness-based cancer recovery program: The eTherapy for cancer applying mindfulness trial. *Psychosomatic Medicine*, *76*(4), 257–267.

ZuWallack, R. (2007). How are you doing? What are you doing? Differing perspectives in the assessment of individuals with COPD. *COPD: Journal of Chronic Obstructive Pulmonary Disease*, *4*(3), 293–297.

Zwerink, M., van Der Palen, J., van Der Valk, P., Brusse-Keizer, M., & Effing, T. (2013). Relationship between daily physical activity and exercise capacity in patients with COPD. *Respiratory Medicine*, *107*, 242–248.

Appendices

Appendix A: Paper 1

Appendix B: Paper 2

Appendix C: Paper 3

Appendix D: Mindfulness-based cognitive therapy in chronic obstructive pulmonary disease: adjusted treatment manual

Appendix E: Supplementary material for Paper 3

Appendix F: Declarations of co-authorship (Papers 1-3)

Appendix A: Paper 1

Farver-Vestergaard, I., Jacobsen, D. & Zachariae, R. (2015). Efficacy of psychosocial interventions on psychological and physical health outcomes in chronic obstructive pulmonary disease: a systematic review and meta-analysis. *Psychotherapy and Psychosomatics* 84: 37-50.

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Efficacy of Psychosocial Interventions on Psychological and Physical Health Outcomes in Chronic Obstructive Pulmonary Disease: A Systematic Review and Meta-Analysis

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Key Words

Meta-analysis · Psychosocial intervention · Chronic disease management · Chronic obstructive pulmonary disease

Abstract

Background: Psychosocial intervention has been suggested as a potentially effective supplement to medical treatment in chronic obstructive pulmonary disease (COPD), but no reviews so far have quantified the existing research in terms of both psychological and physical health outcomes. We therefore conducted a systematic review and meta-analysis of controlled trials evaluating the effects of psychosocial interventions on psychological and physical health outcomes in COPD. ***Methods:*** Two independent raters screened 1,491 references for eligibility. Twenty independent studies investigating a total of 1,361 patients were included, assessed for their methodological quality, and subjected to meta-analytic evaluation. ***Results:*** After adjusting for potential publication bias, a statistically significant overall effect was found for psychological (Hedges' g = 0.38, 95% confidence interval, CI = 0.19–0.58; p < 0.001) outcomes. When analyzing individual intervention types, cognitive behavioral therapy appeared to be effective (g = 0.39, CI = 0.15–0.62; p = 0.001) for improving psychological outcomes. In contrast, for physical outcomes, only mind-body interventions (e.g. mindfulness-based therapy, yoga, and relaxation) revealed a statistically significant effect (g = 0.40; CI = 0.01–0.79; p = 0.042). ***Conclusions:*** Taken together, the results lend support to psychosocial intervention as a tool in the management of COPD. However, due to indications of possible publication bias towards positive findings, the results should be interpreted with some caution, and more high quality research is needed.

Introduction

Chronic obstructive pulmonary disease (COPD) involves persistent obstruction of the airways and lung function impairment, and it affects up to about 10% of the population worldwide [1]. The most common physical symptoms of the disease are breathlessness (dyspnea), cough, and excessive sputum production [2], but many patients also experience extrapulmonary physical consequences such as systemic inflammation, nutritional abnormalities, and muscoloskeletal dysfunction, resulting in fatigue, low activity level, and poor exercise capacity [3]. In addition to these devastating physical problems, patients with COPD often experience psychological prob-

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lems in the form of symptoms of anxiety and depression [4]. In the research literature, these symptoms are often combined as specific components of overall psychological distress or psychological impairment [5–7]. Furthermore, adding to the confusion, several studies focus on poor health-related quality of life (QoL), which is a multifaceted construct including both physical, psychological, and social function and symptoms [8]. The physical and psychological effects of the disease appear to influence each other significantly, as exemplified by research reporting links between fatigue and QoL [9], psychological distress and exacerbation rates [5], as well as dyspnea and anxiety and depression [10–12]. Psychosocial intervention, defined as intervention programs with a psychosocial aim that does not include the prescription of medications or has a solely physical focus (e.g. acupuncture or massage therapy), could therefore serve as a potentially effective supplement to medical or physically oriented treatment initiatives in COPD.

So far, a number of reviews have summarized the effects of psychosocial interventions on psychological outcomes in COPD. In 2002, Rose et al. [13] published a narrative systematic review of 6 randomized controlled trials (RCTs) evaluating psychological interventions as a means of reducing anxiety and panic, and concluded that the evidence in the area was inconclusive. Later, Coventry and Gellatly [14] conducted a systematic review of 4 studies of cognitive behavioral therapy (CBT) for COPD patients with mild-to-moderate anxiety and depression. They included nonrandomized RCTs (NRCTs) as well as RCTs, but found no conclusive evidence of an effect. More recently, in a comprehensive systematic review and meta-analysis of 9 studies (RCTs as well as noncontrolled studies) by Baraniak and Sheffield [15], the authors noted that psychologically oriented interventions often included aims of improving physical outcomes such as physical functioning, dyspnea and exercise capacity. Despite this, their subsequent meta-analysis only included the psychological outcomes of anxiety, depression, and QoL. Their analysis revealed a medium combined effect size ($r = -0.273$, 95% confidence interval, CI = –0.419 to –0.141) on anxiety only, corresponding to a standardized mean difference (Cohen's d) of 0.57. Clark et al. [16] have contributed with a broader narrative review of nonsystematic reviews, systematic reviews and meta-analyses that included clinical and educational as well as psychosocial interventions. They concluded that behaviorally oriented interventions, in addition to improving psychological outcomes, also have the potential of influencing physical outcomes such as pulmonary function and exercise capacity, but did not further address the efficacy of psychosocial interventions on psychological and physical outcomes. Furthermore, the available reviews generally note the relatively low methodological quality of studies evaluating psychosocial interventions in COPD.

To the best of our knowledge, there has thus not yet been an attempt to systematically and quantitatively evaluate psychosocial interventions in terms of both psychological and physical outcomes in COPD. The objective of the present study was therefore to contribute to the evidence base by conducting a systematic review and meta-analysis of the efficacy of psychosocial interventions on relevant psychological as well as physical outcomes in COPD. In addition, it was explored whether some types of psychosocial interventions (e.g. CBT that focuses on altering maladaptive links between thinking and behavior patterns [17] or mind-body interventions that focus on the bidirectional relationship of mind and body as the mediator of change such as for example mindfulness-based therapy, meditative yoga or relaxation [18]) are more effective than others and to what degree the effects are related to the methodological quality of the studies.

Methods

The present study was protocol based and conducted in accordance with the PICO approach [19] and the PRISMA recommendations for reporting systematic reviews and meta-analyses [20].

Search Strategy

We conducted a systematic review using a key word-based search in the electronic databases of PubMed, PsychINFO, Embase, Web of Science, Cochrane Library and CINAHL. Relevant MeSH terms of all databases were included in the search. Key words related to the population ('COPD' OR 'chronic obstructive pulmonary disease' OR 'chronic obstructive lung disease' OR 'chronic obstructive airway disease' OR 'chronic obstructive respiratory disease' OR 'chronic bronchitis' OR 'emphysema') were combined with key words related to the intervention ('psychological intervention*' OR 'psychosocial intervention*' OR 'psychotherap*' OR 'psychoeducation*' OR 'psycho-education*' OR 'behavi*ral therap*' OR 'cognitive therap*' OR 'mindfulness*' OR 'relaxation*' OR 'meditation' OR 'imagery' OR 'hypnos*') and outcomes ('depressi*' OR 'anxiet*' OR 'panic' OR 'quality of life' OR 'mental health' OR 'health status' OR 'physical activity' OR 'exercise' OR 'pulmonary function' OR 'lung function' OR 'symptom level' OR 'breathlessness' OR 'dyspnea' OR 'fatigue'). The search was conducted independently by the first and the second author (I.F.-V. and D.J.) for the period from database inception to March 2014.

Selection Procedure and Data Extraction

Only English-language reports published in peer-reviewed journals were considered eligible for the present study. Eligible

studies were those that evaluated individual-, or group-based psychosocial interventions aimed at improving psychological and/or physical outcomes for adult patients with a COPD diagnosis. Concerning study design and comparison, only trials with a control group were included. Papers were excluded if the focus was on patients with comorbid physical conditions or if the intervention did not involve a psychosocial component. For example, interventions in the form of pulmonary rehabilitation or self-management programs were excluded unless a substantial part of the program was explicitly characterized as being psychosocial, e.g. mind-body exercises such as meditative yoga, or counseling with elements of CBT or analytical therapy. In addition, reports focusing on interventions with a physical focus, such as acupuncture or massage therapy, or on complementary and alternative treatments, e.g. energy healing or music therapy, were generally excluded. However, certain complementary and alternative interventions were included if they primarily consisted of psychosocial components that had a broader biopsychosocial purpose, e.g. relaxation, guided imagery or meditation.

In the first round of assessment, the authors I.F.-V. and D.J. independently removed duplicates and screened the titles and abstracts of the identified references with the purpose of excluding irrelevant studies. In the second round of assessment, full texts of the remaining references were read and ineligible reports were excluded on the basis of the criteria described above and the reasons for exclusion registered. Disagreements and uncertainties were discussed with the third author (R.Z.) until a negotiated conclusion was reached.

Using the Microsoft Access software, a database was designed with the specific purpose of managing the data of the present study. Data from the included studies were extracted independently and cross-checked by I.F.-V. and D.J. Any disagreements were resolved by negotiation with R.Z. When there was disagreement on one or more of the criteria included in the quality assessment, the paper was re-examined closely, the initial reason for disagreement discussed, and a negotiated conclusion reached.

Quality Assessment

Study quality was assessed using the criteria of Jadad et al. [21], a tool to evaluate methodological quality, e.g. use and description of randomization and blinding procedures and description of dropout rates (score range: 0–13). Five additional quality criteria were specifically developed for the present study (inclusion of an active control group, pre-post data, any attempts of blinding of patients and/or researchers, use of standardized and reliable outcome measures), yielding a revised Jadad total quality score (range: 0–18). Quality ratings were not used as weights when calculating aggregated effect sizes (ESs), as this is discouraged due to risk of inducing bias [22]. Instead, associations between ESs and study quality were explored with meta-ANOVAs and metaregression.

Heterogeneity

Heterogeneity was explored using Q and I^2 statistics. Heterogeneity tests are aimed at determining whether results reflect genuine between-study differences (heterogeneity), or whether the variation is due to random error (homogeneity) [23]. Due to the generally low statistical power of heterogeneity tests, a p value ≤0.10 was used to determine significant heterogeneity [24]. The I^2 quantity provides a measure of the degree of inconsistency by estimating the amount of variance in a pooled ES that can be accounted for by heterogeneity in the sample of studies and is not influenced by the number of studies (K) [25]. An I^2 value of 0% indicates no observed heterogeneity. Values of 25, 50, and 75% are considered low, moderate and high, respectively.

Computing ESs

Hedges' g was used as the standardized ES. Hedges' g is a variation of Cohen's d [26] correcting for possible bias due to small sample size [27]. They both provide an estimate of the standardized mean difference, but whereas d pools the variances using n for each sample, g uses n – 1 for each sample. ESs were computed using pre- and postintervention means or medians and their standard deviations or ranges. In case of missing data, we attempted to contact the authors, asking them to provide this information. Pooled ESs were weighted by the inverse standard error, taking into account the precision of each study. A random effect model was used in all analyses. For readers more familiar with r (the effect size correlation) as an indicator of effect, the corresponding r has also been included in the text.

Analytical Strategy

First, pooled overall ESs for the effect of psychosocial interventions on psychological and physical outcomes were calculated. If the results indicated study heterogeneity, possible between-study differences in ESs were explored by comparing the ESs of studies according to the following study characteristics: active versus passive control, intervention type, methodological quality, treatment duration, number of sessions, age, gender and lung function at baseline. This was done with either meta-ANOVA or metaregression.

The calculations were conducted with Comprehensive Meta-Analysis, Version 2 (www.meta-analysis.com), SPSS-20 (www.ibm.com/software/analytics/spss/) and various formulas in Microsoft Excel.

Publication Bias

Publication bias, a widespread problem when conducting meta-analyses [28], was evaluated with funnel plots, Egger's method, and by calculating fail-safe numbers [29, 30]. A funnel plot is a graphic illustration of study ESs in relation to study size or precision. Egger's test provides a statistic for the skewness of results [31]. Calculation of fail-safe numbers is aimed at achieving an indication of the number of unpublished studies with null findings that would reduce the result to statistical nonsignificance ($p > 0.05$). It has been suggested that a reasonable level is achieved if the fail-safe number exceeds $5K + 10$ (K = number of studies in the meta-analysis) [32]. If the results were suggestive of publication bias, an adjusted ES was calculated using the trim and fill method of Duval and Tweedie [33], which imputes ESs of missing studies and recalculates the ES accordingly.

Results

The study selection process with reasons for exclusion is described in the PRISMA flow diagram shown in figure 1. The initial search yielded 1,491 articles, out of which

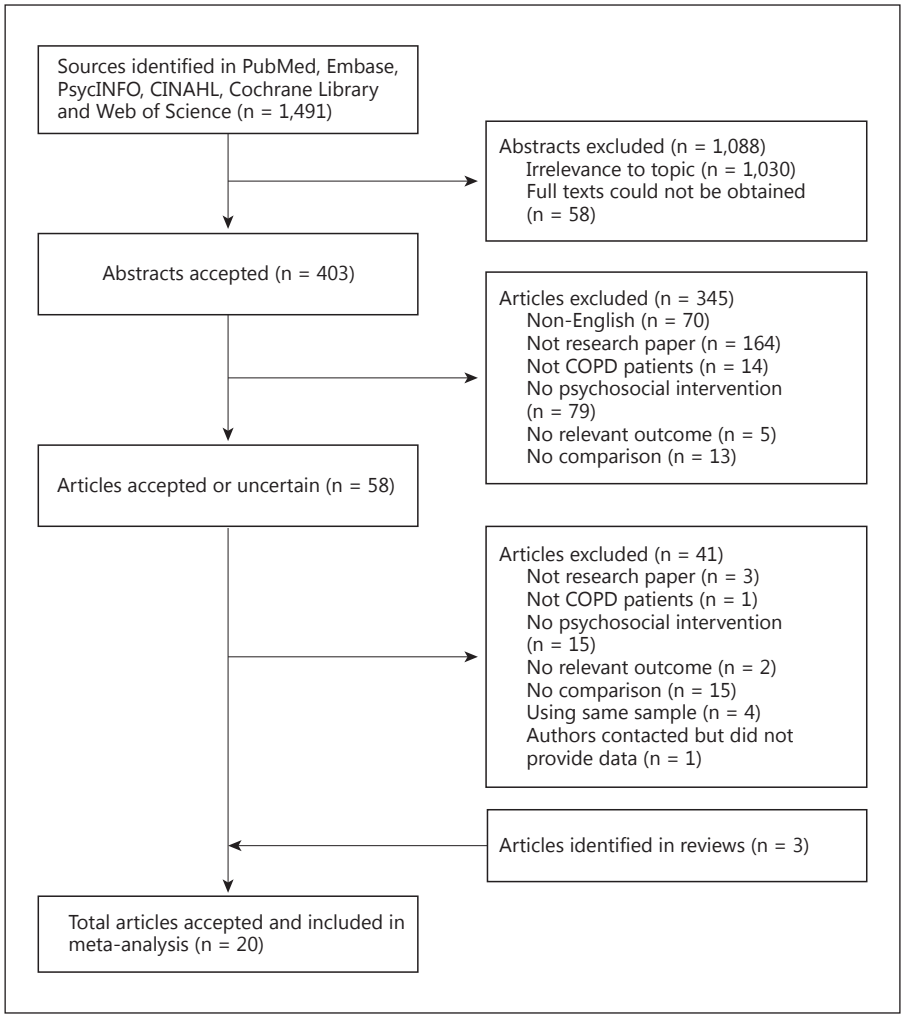

Fig. 1. PRISMA flowchart of the study selection procedure.

403 articles were read in full during the second round of assessment. The authors I.F.-V. and D.J. initially disagreed on 102 (25%) articles (interrater agreement: 0.50; kappa statistic). Keeping in mind the broad and complex nature of the field of behavioral intervention, disagreements were most often a result of different initial assumptions of whether certain complex behavioral interventions could be classified as psychosocial intervention. The specific criteria and final inclusion of the individual studies were thus negotiated, and the third author, R.Z., took part in the discussion concerning 58 of the articles selected in the first round. After excluding 41 further articles, 3 additional articles were included on the basis of a screening of other systematic reviews on the subject [13–15]. The authors of 2 papers with missing data (control group data and SDs, respectively) provided the requested data after they had been contacted. The author of a third paper with missing data (means and SD for all outcomes relevant for the purpose of the present study) was unable to provide the data, and the study was therefore excluded. A final total of 20 individual research papers describing results of 20 independent studies published from 1983 to 2012 were included in the study and subjected to meta-analytic evaluation.

Study Characteristics

The characteristics of the included studies are summarized in table 1. The 20 studies had investigated a total of 1,565 COPD patients (mean percentage of women: 35.1) and analyzed final data for 1,361 participants. Six hundred and eighty-three subjects received psychosocial intervention, 394 took part in an intervention that could not be classified as psychosocial (active control group), and 284 received care as usual (passive control group).

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Table 1. Study characteristics

Author	Year	Study design	Sample size and COPD severity at baseline	Mean age, years (% women)	Groups	Intervention type (category)	Number of sessions and treatment duration, weeks	Physical outcome measure(s)	Psychological outcome measure(s)	Quality of life outcome measure	Jadad quality score	Jadad-revised quality score
(1) Rosser et al. [36]	1983	RCT	65 (22) –	66 (33.8)	(1) PC (17/12) (2) Analytic psychotherapy (16/10)	Analytic	8 (8)	(1) Lung function: spirometry	–	–	9	12
(2) Gift et al. [45]	1992	RCT	26 (26) M: 54.0	67 (69.2)	(1) AC (relaxation without guiding) (13/13) (2) Guided relaxation (13/13)	Mind-body	4 (4)	(1) Lung function: Wright peak flow meter (2) Dyspnea: VAS	(1) Anxiety: SAI	–	6	9
(3) Sassi-Dambron et al. [46]	1995	RCT	98 (89) M: 50.0	67.4 (44.9)	(1) AC (health education) (51/43) (2) Health education, relaxation and stress management (47/46)	Mind-body	6 (6)	(1) Dyspnea: VAS (2) Exercise capacity: 6MWT	(1) Anxiety: SAI (2) Depression: CES-D	QWB	9	12
(4) Eiser et al. [47]	1997	NRCT	20 (20) P: 100% severe	72.2 (60.0)	(1) PC (8/8) (2) CBT (12/12)	CBT	6 (6)	(1) Lung function: spirometry (2) Dyspnea: VAS (3) Exercise capacity: 6MWT	–	SGRQ	5	7
(5) Emery et al. [34]	1998	RCT	79 (48) M: 42.0	66.6 (53.2)	(1) PC (25/25) (2) Stress management, CBT format (25/23)	CBT	63 (10)	(1) Lung function: spirometry	(1) Anxiety: SAI (2) Depression: CES-D	SIP	9	11
(6) Kunik et al. [48]	2001	RCT	56 (48) –	71.3 (17.0)	(1) AC (COPD education) (29/27) (2) CBT (24/21)	CBT	1 (1)	(1) Exercise capacity: 6MWT	(1) Anxiety: BAI (2) Depression: GDS	SF-36	10	14
(7) De Godoy et al. [35]	2005	RCT	49 (30) M: 34.0	– (27.0)	(1) PC (14/14) (2) CBT and logotherapy techniques (16/16)	CBT	24 (12)	(1) Exercise capacity: distance walked-weight product	(1) Anxiety: BAI (2) Depression: BDI	SGRQ	7	10
(8) Kheirabadi et al. [49]	2008	RCT	42 (42) –	56.4 (31.0)	(1) PC (21/21) (2) Psychoeducation and behavior therapy (21/21)	Behavioral	8 (8)	(1) Lung function: CCQ symptoms subscale	–	CCQ	7	9
(9) Kunik et al. [50]	2008	RCT	238 (235) M: 46.0	66.3 (3.8)	(1) AC (COPD education) (120/119) (2) CBT (118/116)	CBT	8 (8)	(1) Dyspnea: CRQ dyspnea subscale (2) Exercise capacity: 6MWT (3) Fatigue: CRQ fatigue subscale	(1) Anxiety: BAI (2) Depression: BDI	SF-36	10	13
(10) Donesky-Cuenco et al. [51]	2009	RCT	41 (29) M: 47.7	69.9 (72.4)	(1) PC (21/15) (2) Yoga meditation (20/14)	Mind-body	24 (12)	(1) Dyspnea: CRQ dyspnea subscale (2) Lung function: spirometry (3) Exercise capacity: 6MWT (4) Fatigue: CRQ fatigue subscale	(1) Anxiety: SAI state subscale (2) Depression: CES-D	SF-36	9	11
(11) Mularski et al. [52]	2009	RCT	86 (86) P: 64% severe	67.4 (0.0)	(1) AC (support groups) (42/42) (2) Mindfulness-based breathing therapy (44/44)	Mind-body	8 (8)	(1) Lung function: MSAS (2) Dyspnea: VAS (3) Exercise capacity: 6MWT	–	SGRQ	10	13
(12) Singh et al. [53]	2009	RCT	72 (64) M: 51.5	63.0 (30.0)	(1) AC (relaxation without music) (36/32) (2) Music therapy and relaxation (36/32)	Mind-body	2 (1)	(1) Lung function: respiratory rate (2) Dyspnea: VAS	(1) Anxiety: SAI-state subscale	–	9	13
(13) Hynninen et al. [54]	2010	RCT	51 (51) M: 58.8	61.0 (51.0)	(1) PC (26/26) (2) CBT (25/25)	CBT	7 (7)	(1) Fatigue: PSQI	(1) Anxiety: BAI (2) Depression: BDI	SGRQ	8	10
(14) Lamers et al. [55]	2010	RCT	187 (187) –	71.0 (40.0)	(1) PC (91/91) (2) CBT and self-management elements (96/96)	CBT	4 (12)	–	(1) Anxiety: SCL-90 anxiety subscale (2) Depression: BDI	SGRQ	10	13
(15) Livermore et al. [56]	2010	RCT	41 (41) M: 54.1	73.4 (56.1)	(1) PC (20/20) (2) CBT (21/21)	CBT	4 (4)	–	(1) Anxiety: HADS anxiety subscale (2) Depression: HADS depression subscale	SGRQ	11	14
(16) Yeh et al. [57]	2010	RCT	10 (10) M: 50.0	66.0 (40.0)	(1) PC (5/5) (2) Tai chi meditative exercise (5/5)	Mind-body	24 (12)	(1) Lung function: spirometry (2) Dyspnea: CRQ dyspnea subscale (3) Exercise capacity: 6MWT (4) Fatigue: CRQ fatigue subscale	(1) Depression: CES-D	CRQ	10	13
(17) Chan et al. [37]	2011	RCT	206 (139) P: 43% severe	73.0 (8.7)	(1) AC (breathing techniques and walking exercise) (69/69) (2) Tai chi meditative exercise (70/70)	Mind-body	24 (12)	(1) Lung function: spirometry (2) Dyspnea: Borg scale (3) Exercise capacity: 6MWT (4) Fatigue: Borg scale	–	–	10	14

Table 1 (continued)

Author	Year	Study design	Sample size and COPD severity at baseline	Mean age, years (% women)	Groups	Intervention type (category)	Number of sessions and treatment duration, weeks	Physical outcome measure(s)	Psychological outcome measure(s)	Quality of life outcome measure	Jadad quality score	Jadad-revised quality score
(18) Kapella et al. [58]	2011	RCT	18 (18) M: 60.5	62.5 (22.2)	(1) AC (wellness education) (9/9) (2) CBT for insomnia (9/9)	CBT	6 (6)	(1) Fatigue: PSQI	(1) Anxiety: POMS anxiety subscale (2) Depression: POMS depression subscale	FPI	9	12
(19) Ng et al. [59]	2011	RCT	80 (80) M: 36.9	72.4 (11.2)	(1) AC (breathing techniques and walking exercise) (40/40) (2) Qigong meditative exercise (40/40)	Mind-body	4 (4)	(1) Exercise capacity: 6MWT	–	SF-36	11	15
(20) Jiang and He [60]	2012	RCT	100 (96) P: 39% severe	65.0 (30.2)	(1) PC (50/47) (2) Uncertainty management, cognitive and behavioral strategies (50/49)	CBT	4 (4)	–	(1) Anxiety: SAI -state subscale (2) Depression: HADS depression subscale	SF-36	11	14

Sample size: reported total sample size, with final sample size used in evaluation of effect on outcomes in parentheses; COPD severity: percent predicted forced expiratory volume per second reported as mean (M) or percentage (P) in the category 'severe'; mean age with percentage of women in parentheses; groups: number assigned/number in final analysis; AC = active control; PC = passive control; mind-body = relaxation, mindfulness, meditative yoga, qigong or tai chi; physical outcome measures: 6MWT = 6-min walk test [61], Borg Scale [62], CRQ = Chronic Respiratory Questionnaire [63], MSAS = Memorial Symptom Assessment Scale [64], PSQI = Pittsburgh Sleep Quality Index [65], respiratory rate (number of chest wall or abdomen rise and fall movements per minute [53]), spirometry [66], VAS = visual analog scale [67]; psychological outcome measures: BAI = Beck Anxiety Inventory [68], BDI = Beck Depression Inventory [69], CES-D = Center for Epidemiological Studies Depression scale [70], GDS = Geriatric Depression Scale [71], HADS = Hospital Anxiety and Depression Scale [72], POMS = Profile of Mood States [73], SAI = Spielberger Anxiety Inventory [74], SCL-90 = Symptom Checklist-90 [75]; QoL outcome measures: CCQ = Clinical COPD Questionnaire [76], CRQ = Chronic Respiratory Questionnaire [63], FPI = Functional Performance Inventory [77], SF-36 = 36-item Short Form Health Survey [78], SGRQ = Saint George's Respiratory Questionnaire [79], SIP = Sickness Impact Profile [80], QWB = Quality of Well-Being Scale [81]; Jadad study quality score with a range from 0 to 13; total study quality score: modified Jadad score with additional study quality indicators with a range from 0 to 18.

The mean age ranged from 56.4 to 73.4 years, and the mean baseline lung function varied from 34.0 to 60.5% predicted forced expiratory volume per second. Study sample sizes ranged from 10 to 238 (mean number: 78.2). A total of 19 studies were RCTs with the remaining study presenting data from an NRCT. The majority of interventions could be classified as either CBT (10 studies) or mind-body interventions (8 studies; e.g. mindfulness-based therapy, yoga, and relaxation). The 2 remaining interventions were analytical and behavioral therapy, respectively. The number of treatment sessions varied from 1 to 63 (mean: 12.0 sessions) and stretched over 1–12 weeks (mean: 7.3 weeks).

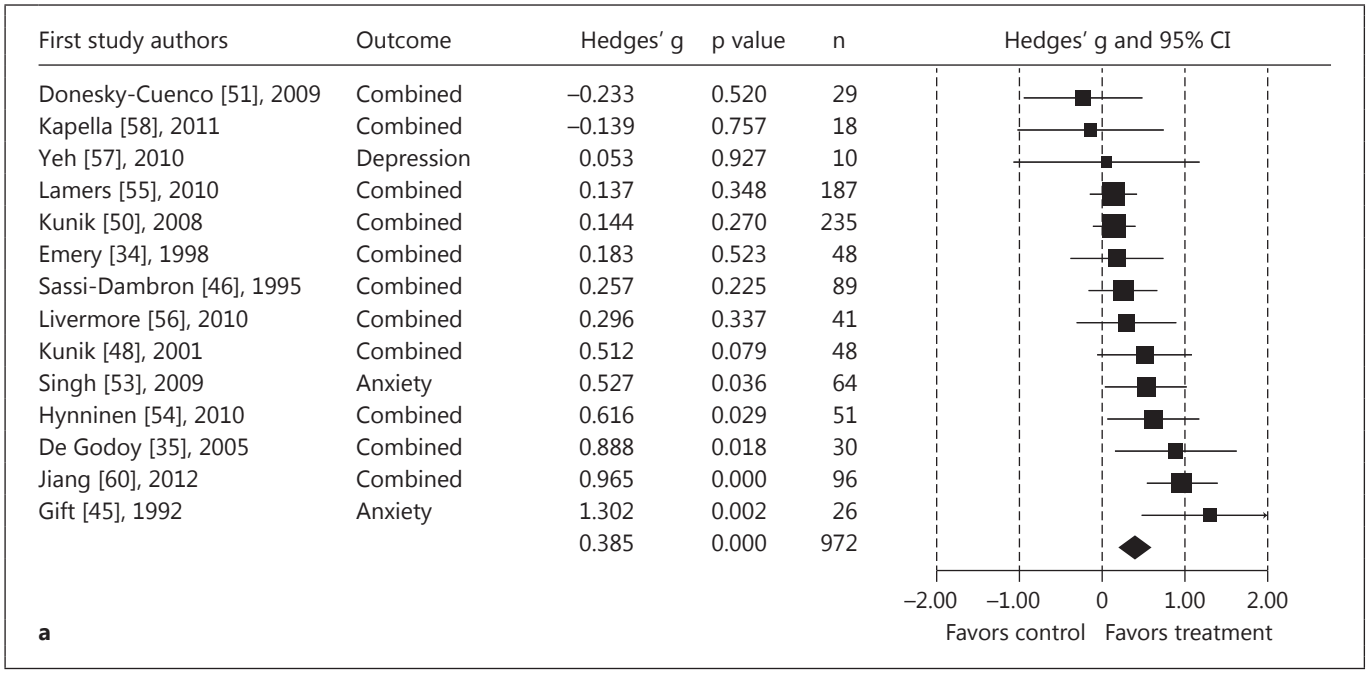
Three studies [34–36] included more than 2 group conditions, and data from conditions that made it impossible to isolate the effect of the psychosocial intervention (e.g. comprehensive pulmonary rehabilitation programs with psychosocial elements) were excluded. One study [37] included both an active and a passive control group, and only the active group was used as comparison.

Across the included studies, 14 studies reported data on the psychological outcomes of anxiety and depression, frequently assessed in parallel by the Hospital Anxiety and Depression Scale or separately by the Spielberger Anxiety Inventory or Beck Anxiety Inventory to measure anxiety, and the Beck Depression Inventory or the Center for Epidemiological Studies Depression Scale to measure depression. Seventeen studies reported data on physical health outcomes such as lung function, dyspnea, exercise capacity and fatigue, most often assessed with spirometry (forced expiratory volume per second), visual analog scales, the 6-min Walking Test and the Pittsburgh Sleep Quality Index, respectively. Sixteen studies reported data on QoL, most often measured with the disease-specific Saint George's Respiratory Questionnaire, the Chronic Respiratory Questionnaire or the generic instrument Short Form Health Survey.

The Jadad quality score of the included studies ranged from 5 to 11 (mean score = 9.00; SD = 1.65), and the Jadad revised score from 7 to 15 (mean score = 11.95; SD = 2.09). The interrater agreement ratio for the individual Jadad items ranged from 0.70 to 1 with kappa scores (adjusting for chance agreement) ranging from 0.32 to 0.80.

Main Effects

The results of the meta-analyses are summarized in table 2 and illustrated with Forrest plots (fig. 2). As the QoL construct includes both psychological and physical domains, a combined ES for QoL was calculated sepa-



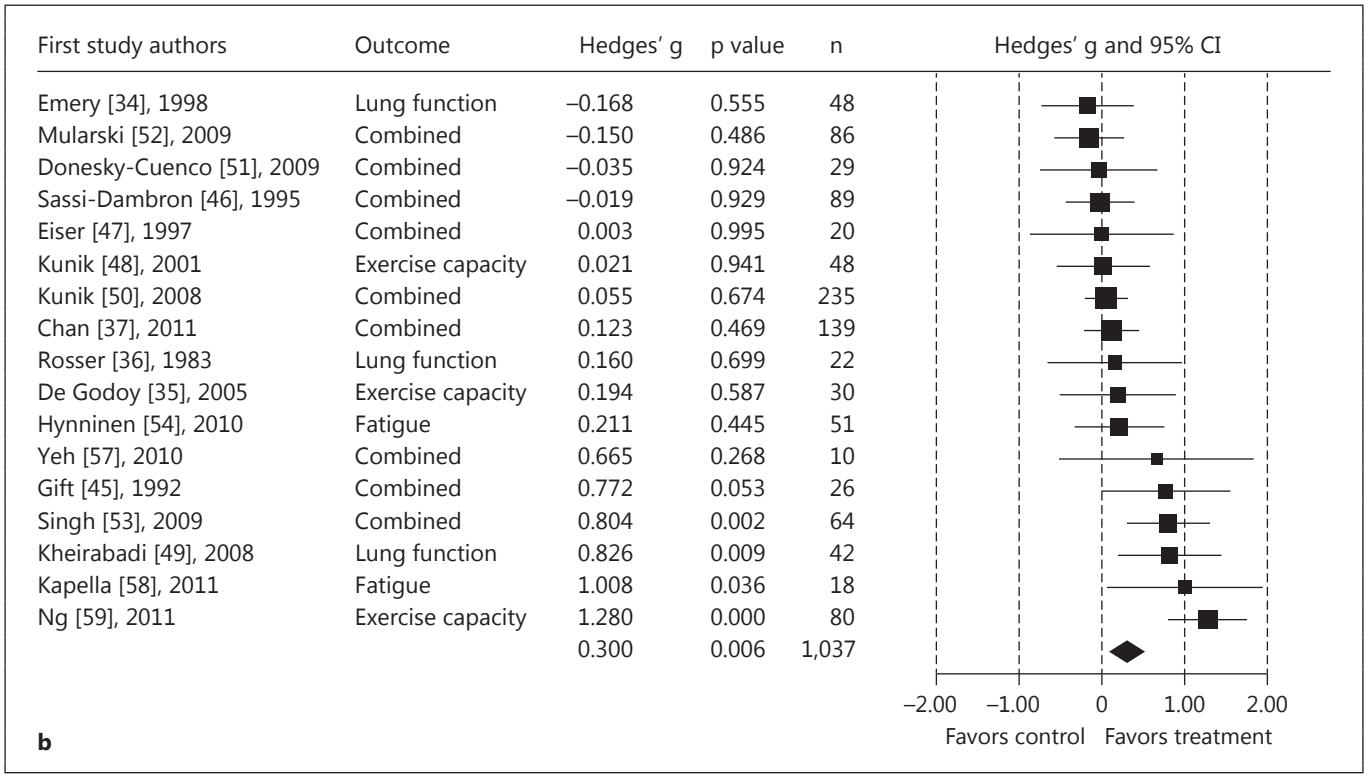
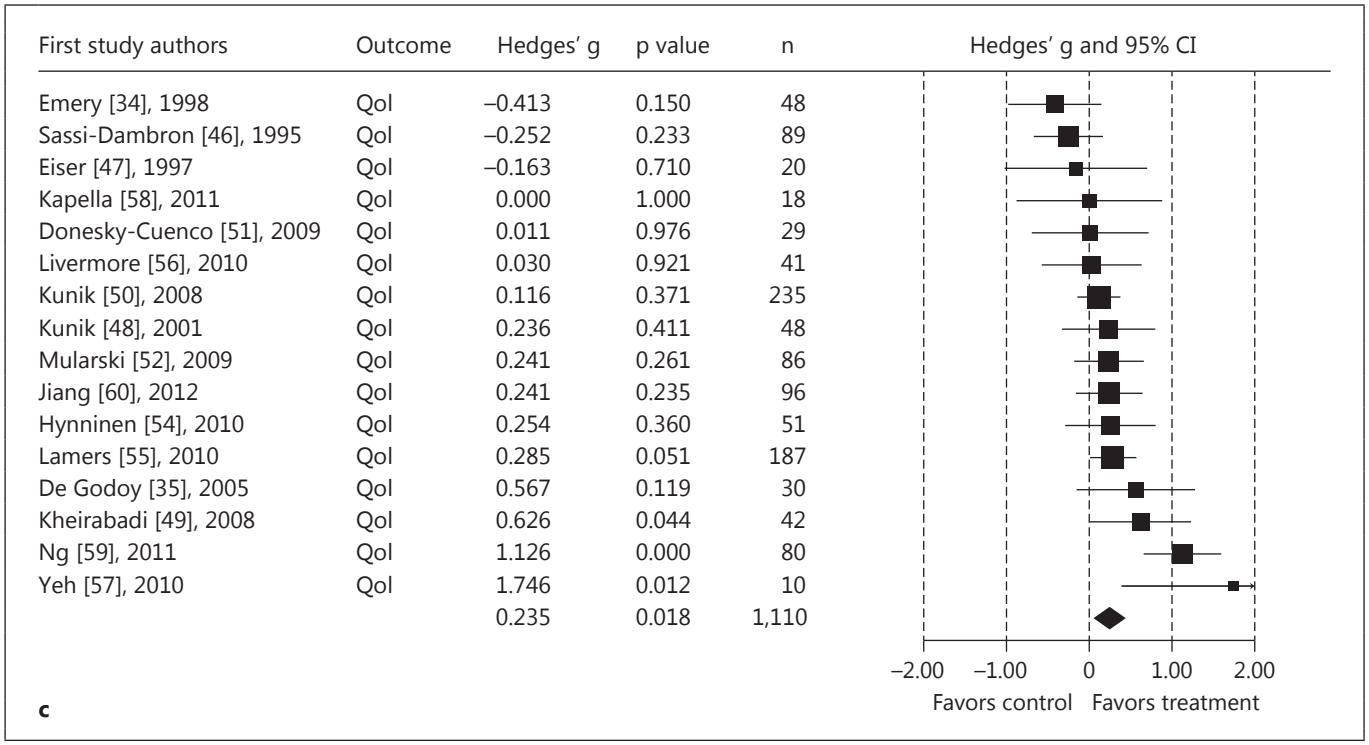


Fig. 2. Combined effect sizes (Hedges' g; random effect model) of psychosocial interventions on psychological (**a**), physical (**b**) and QoL outcomes (**c**) in studies of COPD patients.

(For figure 2c see next page.)



c

2

rately. Combining the ESs in the 2 overall categories of psychological and physical outcomes, regardless of individual study characteristics, yielded statistically significant ESs for both categories [psychological: Hedges' g = 0.39 (corresponding to r = 0.19), p < 0.001; physical: g = 0.30 (r = 0.15), p = 0.006], in both cases corresponding to a small effect [26]. The fail-safe number for psychological outcomes (K = 90) exceeded the criterion (K = 80) [32], suggesting a robust effect. This was not the case for the physical outcomes fail-safe number (K = 64; criterion K = 95). When exploring indicators of publication bias, the funnel plots for both outcome categories appeared skewed and Egger's test indicated the possibility of bias in favor of larger published positive ESs. When imputing missing ESs with the trim and fill method [33], the resulting adjusted pooled ES was smaller but remained statistically significant for the psychological outcome category. This was not the case for physical outcomes. With respect to specific outcomes, the combined ESs for anxiety, depression, dyspnea and QoL (g = 0.24–0.45, r = 0.12–0.22) all reached statistical significance (p = 0.001–0.047). The combined ES (g = 0.25, r = 0.12) for exercise capacity was near-significant (p = 0.069), whereas the combined ESs for fatigue and lung function did not reach statistical significance.

Associations between ES and Study Characteristics

As the *Q* statistics for both psychological and physical outcomes were statistically significant (p = 0.017, <0.001) and the I^2 statistic indicated low to moderate heterogeneity, we explored possible sources of heterogeneity and analyzed whether the ESs varied according to between-study differences in study design (active versus passive control), intervention type (CBT versus mind-body), sample characteristics (age; gender; lung function at baseline), intervention length (number of sessions; treatment duration) and methodological quality (quality scores).

Study Design

The pooled ESs for the active and passive control group studies are shown in table 2. With respect to psychological outcomes, the ES's were similar, and the between-group difference did not reach statistical significance. For the physical outcomes, the combined ES was smaller for passive control than active control studies, but again, the between-group difference did not reach statistical significance.

Intervention Type

The combined ESs of studies examining the effects of CBT and mind-body interventions are shown in table 2.

Table 2. Effects of psychological intervention on psychological and physical outcomes in COPD patients

	Sample size		Heterogeneity[a]				Global ESs			Fail-safe numbers[c]	Criterion[d]
	K	n	Q	d.f.	p	I^2	Hedges' g[b]	95% CI	p		
(A) Main effects											
Psychological (anxiety + depression)	14	972	26.0	13	0.017	49.9	0.39	0.19 – 0.58	<0.001	90	80
Psychological adj. for publication bias[e]	(15)	–	–	–	–	–	0.38	0.19 – 0.58	–	–	–
Physical (dyspnea + exercise capacity + fatigue + lung function)	17	1,037	42.2	16	<0.001	62.1	0.30	0.08 – 0.52	0.006	64	95
Physical adj. for publication bias[e]	(19)	–	–	–	–	–	0.20	–0.05 – 0.44	–	–	–
Anxiety	13	962	46.3	12	<0.000	74.1	0.45	0.18 – 0.72	0.001	108	75
Depression	12	882	13.1	11	0.286	16.2	0.26	0.11 – 0.42	0.001	30	70
Dyspnea	9	698	19.7	8	0.011	59.5	0.27	0.00 – 0.53	0.047	15	55
Dyspnea adj. for publication bias[e]	(10)	–	–	–	–	–	0.20	–0.08 – 0.48	–	–	–
Exercise capacity	10	766	26.8	9	0.002	66.4	0.25	–0.02 – 0.52	0.069	–	–
Fatigue	6	482	9.7	5	0.083	48.7	0.13	–0.17 – 0.42	0.411	–	–
Lung function	10	486	19.9	9	0.018	54.9	0.14	–0.14 – 0.43	0.320	–	–
QoL	16	1,110	34.3	15	0.003	56.3	0.24	0.04 – 0.43	0.018	42	90
(B) Moderation analysis: study design (active vs. passive control)											
Psychological (active control)	6	480	9.5	5	0.092	47.1	0.37	0.09 – 0.65	0.010	15	40
Psychological (passive control)	8	492	16.2	7	0.023	56.8	0.39	0.09 – 0.69	0.010	24	50
Between groups[f]	14	972	0.09	1	0.928	–	–	–	–	–	–
Physical (active control)	9	785	35.3	8	0.001	77.3	0.37	0.05 – 0.69	0.022	35	55
Physical (passive control)	8	252	6.8	7	0.446	0.0	0.20	–0.04 – 0.45	0.105	–	50
Between groups[f]	17	1,037	0.70	1	0.404	–	–	–	–	–	–
(C) Moderation analysis: intervention type (CBT vs. mind–body)											
Psychological (CBT)	9	754	17.2	8	0.028	53.6	0.39	0.15 – 0.62	0.001	43	55
Psychological (mind-body)	5	218	8.7	4	0.070	53.8	0.38	–0.05 – 0.81	0.081	–	–
Between groups[f]	14	972	0.0	1	0.971	–	–	–	–	–	–
Physical (CBT)	7	450	4.9	6	0.552	0.0	0.09	–0.10 – 0.27	0.345	–	45
Physical (mind-body)	8	523	30.4	7	0.001	77.0	0.40	0.01 – 0.79	0.042	26	50
Between groups[f]	15	973	2.0	1	0.153	–	–	–	–	–	–

K indicates number of published studies; K in parentheses (K) indicates number of published studies + number of imputed studies; d.f. = degrees of freedom.

[a] Q statistic: p values <0.1 taken to suggest heterogeneity. I^2 statistic: 0% (no heterogeneity), 25% (low heterogeneity), 50% (moderate heterogeneity), 75% (high heterogeneity).

[b] ES = Hedges' g. Standardized mean difference, adjusting for small sample bias. A positive value indicates an effect size in the hypothesized direction, i.e. reduced distress or relative smaller increase in distress in the intervention group. To ensure independency, if a study reported results for more than 1 measure, the ESs were combined (mean), ensuring that only 1 ES per study was used in the calculation.

[c] Number of nonsignificant studies that would bring the p value to nonsignificant ($p > 0.05$).

[d] A fail-safe number exceeding the criterion ($5 \times k + 10$) indicates a robust result [32].

[e] If analyses indicated the possibility of publication bias, missing studies were imputed and an adjusted ES rate calculated [33].

[f] Meta-ANOVA (between-study comparisons).

For psychological outcomes, CBT and mind-body yielded similar ESs [g = 0.39 (r = 0.19) and g = 0.38 (r = 0.19)]. However, only CBT reached statistical significance, whereas mind-body interventions were near-significant (p = 0.081). For physical outcomes, only mind-body interventions yielded a statistically significant ES of g = 0.40 (r = 0.20). In comparison, the ES for CBT for physical outcomes was small (g = 0.09, r = 0.05) and statistically nonsignificant. The difference between the effects of CBT versus mind-body interventions, however, did not reach statistical significance. Insufficient power for tests of moderation is a well-known problem in meta-analysis [38]. Following the suggestions of Hedges and Pigott [38], we therefore conducted a post hoc power analysis, revealing a statistical power of the between-group comparison of CBT and mind-body interventions for physical outcomes of only 0.30.

As only mind-body interventions appeared to be effective for the combined physical outcomes, the effects of mind-body intervention for each of the individual physical outcomes were analyzed. A statistically significant effect of mind-body intervention was found for dyspnea [g = 0.38 (K = 7), CI = 0.04–0.71, p = 0.028]. The remaining effect sizes did not reach statistical significance (g =

Table 3. Moderation analyses: results of metaregression analyses

Dependent variable	Independent variable	K	β[a]	95% CI	p
Psychological (anxiety + depression)	Study quality (Jadad)	13	–0.10	–0.26–0.06	0.219
	Study quality (revised Jadad)	13	–0.05	–0.70–2.59	0.491
	Treatment duration	13	–0.06	–0.12–0.00	0.054[b]
	Number of sessions	13	–0.00	–0.02–0.01	0.552
	Mean age	12	–0.03	–0.08–0.02	0.197
	Percent women	13	0.00	–0.01–0.01	0.873
	Mean FEV1%	10	0.01	–0.02–0.04	0.576
Physical (dyspnea + exercise capacity + fatigue + lung function)	Study quality (Jadad)	16	0.00	–0.15–0.15	0.972
	Study quality (revised Jadad)	16	0.03	–0.09–0.14	0.655
	Treatment duration	16	–0.05	–0.11–0.00	0.066[b]
	Number of sessions	16	–0.01	–0.02–0.00	0.114
	Mean age	15	–0.02	–0.07–0.03	0.364
	Percent women	16	0.00	–0.01–0.01	0.819
	Mean FEV1%	10	0.01	–0.04–0.05	0.754

FEV1% = Percent forced expiratory volume per second.
[a] Mixed effects regression: unrestricted maximum likelihood.
[b] Near-significant ($p < 0.10$).

–0.02 to 0.33; K = 3–6; p = 0.146–0.951). No effects of CBT were found for any of the individual physical outcomes (no further data shown). When comparing effect sizes between mind-body therapies and CBT for the individual physical outcomes, mind-body therapies yielded larger effect sizes than CBT for dyspnea (g = 0.38 vs. 0.01), lung function (0.15 vs. –0.24), and exercise capacity (0.33 vs. 0.08), whereas the results for fatigue appeared to favor CBT (–0.02 vs. 0.26). None of the differences reached statistical significance, however (no further data shown).

Sample Characteristics, Intervention Length and Study Quality

As shown in table 3, we conducted 2 metaregression analyses (unrestricted maximum likelihood) with the Jadad quality score, the Jadad revised quality score, treatment duration, number of sessions, mean age, percent women, and mean predicted forced expiratory volume per second as the predictor variables and ESs for the combined psychological and physical outcome categories as dependent variables. In both analyses, only treatment duration reached near-significance (psychological: p = 0.054; physical: p = 0.066), with negative regression slopes (psychological: B = –0.06; physical: B = –0.05) indicating that longer treatment duration was associated with smaller ESs for psychological and physical outcomes. Furthermore, we compared the average duration and number of sessions of CBT and mind-body interventions. The results indicated that mind-body intervention had longer duration (7.2 weeks, SD = 3.9) and included more sessions (18.8, SD = 20.0) than CBT (6.0, SD = 3.0, and 10.5, SD = 16.0). However, the differences did not reach statistical significance (p = 0.41 and 0.25).

Discussion

The results initially revealed statistically significant effects of psychosocial interventions on both psychological (g = 0.39, r = 0.19) and physical (g = 0.30, r = 0.15) outcomes in COPD patients when compared with passive (care as usual) or active control groups. The effect size for psychological outcomes remained relatively stable and statistically significant after adjusting for possible publication bias, whereas the effect size for physical outcomes was reduced (g = 0.20, r = 0.10) and became only near-significant. Our findings are in contrast to the results of another relatively recent meta-analysis by Baraniak and Sheffield [15], where only anxiety was improved by psychologically based interventions in COPD. A possible explanation for the inconsistent findings could be that the quantity of published research in the area has grown over the years since Baraniak and Sheffield conducted their

review. Thus, coupled with the fact that we also included psychosocial mind-body interventions, the results of the present study were based on data from a larger combined sample of COPD patients. Also, in the present study, we have statistically adjusted for possible publication bias, which Baraniak and Sheffield reckoned was a problem for the interpretation of their results, thereby giving way for a more precise ES estimate.

As the construct of QoL is a multifaceted and relatively incongruently defined construct [39], we found it inappropriate to include it in either the psychological or the physical overall outcome category. The results revealed a statistically significant, but small, effect on QoL, giving further support to the notion that psychosocial intervention may improve outcomes that involve both the psychological and the physical domain of COPD. However, researchers conducting future meta-analyses should be aware of the possible pitfalls of combining data from studies defining QoL differently.

Regarding the effects of the different types of psychosocial intervention being used with COPD patients, the moderation analyses showed that only CBT, but not mind-body interventions, significantly improved psychological outcomes. For the physical outcomes, the opposite result was found. Here, only the results for mind-body interventions reached statistical significance. When exploring effects on the individual types of physical outcomes, mind-body interventions had larger, albeit nonsignificant, effects on dyspnea, exercise capacity, and lung function, whereas the effect on fatigue was nonsignificant in the opposite direction. Our findings could be interpreted as supporting previous speculations [15, 40] that ruminative thinking and avoidance, the primary focus of CBT, are often associated with the characteristic and noteworthy physical symptoms in COPD. Consequently, subjecting symptoms such as dyspnea to the exposure techniques often used in CBT could in the best case be ineffective and, in the worst case, harmful. In contrast, mind-body interventions explicitly take into account the co-influencing aspects of physical and psychological issues in COPD and hold a primary focus on physical sensations, rather than on psychological, i.e. cognitive and emotional, processes, as the therapeutic gateway towards change [41]. However, it should here be noted that the precision of the estimated effect sizes of intervention types in the present study may be limited, as indicated by the relatively broad confidence intervals. In addition, the results of our post hoc power analysis suggest that more studies are needed to confirm this preliminary conclusion.

With the purpose of minimizing costs, psychosocial interventions are often delivered alongside other behavioral treatment initiatives such as pulmonary rehabilitation programs (most often including health education and physical exercise). Exploring directly whether this mode of delivery influences the effect of the psychosocial interventions lay outside the scope of the present study. However, the results failed to find any difference in ESs between the studies that included an active control group and those that did not (passive control group). This could indicate that receiving other behavioral treatments (e.g. disease-specific or general health education, breathing and walking exercise, and support groups) simultaneously does not compromise the effect of psychosocial intervention. On the other hand, whether psychosocial intervention moderates, e.g. boosts or reduces, the effects of other behavioral and medical treatment regimens still needs to be explored.

Surprisingly, the near-significant results of our metaregression analysis indicated that overall, irrespective of the type of intervention, longer treatment duration may reduce the effect of psychological intervention. One possible explanation for this inverse relationship could be the natural deterioration of the chronic patients' psychological and physical condition over time – especially prevalent for smokers [42]. Another explanation could be the tedium of longer interventions or overstimulation, which are long-discussed challenges in the psychotherapy process [43, 44]. However, as a third possible explanation, the lesser effects of longer interventions could also be due to the relatively longer follow-up time, which might cause a loss of novelty and regression toward the mean. The finding that longer duration was associated with smaller, rather than larger, ESs also suggests that the – nonsignificant – finding of longer duration of mind-body interventions compared to CBTs does not explain the larger ESs found for physical outcomes for mind-body interventions compared to CBT. Further studies are needed to identify the optimal type and duration of psychosocial interventions for various outcomes in COPD.

The present study is the first to quantify the effect of psychosocial interventions on psychological as well as physical outcomes in COPD. It has several strengths in that it is based on rigorous methodological procedures and instruments (i.e. protocol-based inclusion with two independent reviewers, comprehensive methodological quality ratings and adjustment for publication bias) and includes only controlled studies, which substantially increases the likelihood that changes in postintervention scores can be attributed to the intervention and not to

other potentially confounding variables. Moreover, the present study includes mind-body interventions, which have generally been ignored in reviews of psychological intervention in COPD so far, even though they form a type of psychosocial intervention that has become a subject of increased popularity and evidence in the health care research literature over the last few decades [41]. Among the limitations are that the available data do not allow for any conclusions as to the long-term maintenance of the effect, as the majority of included studies did not present follow-up data in their analysis. Furthermore, not all included studies reported data on each outcome category of interest, and the instruments used to measure psychological and physical outcomes were diverse. This was also the case for QoL instruments, with some studies using disease-specific and others using generic outcome measures.

Conclusions

The results of this methodologically thorough systematic review and meta-analysis suggest that psychosocial interventions, including physically oriented mind-body interventions, have the potential for improving both psychological and physical outcomes in COPD. It should be noted, however, that our findings of possible publication bias towards studies reporting larger and positive ESs may question the robustness of the effect found for physical outcomes. Despite this cautionary note, based on the overall results, it appears appropriate to recommend delivering psychosocial intervention alongside the already established medical treatment pathway. Concerning specific types of psychosocial intervention, clinicians could consider offering CBT if the primary purpose is to relieve psychological health outcomes, and mind-body interventions with the primary purpose of relieving physical health outcomes. However, clinicians, researchers and policy makers should be aware that, due to statistical power issues and the possible tendency towards publishing positive and significant findings, the robustness of the results presented here cannot be fully ensured and should therefore be interpreted with some caution.

Disclosure Statement

The authors declare that they have no conflict of interest.

References

1 Rycroft CE, Heyes A, Lanza L, Becker K: Epidemiology of chronic obstructive pulmonary disease: a literature review. Int J COPD 2012; 7:457–494.
2 Rabe KF, Hurd S, Anzueto A, Barnes PJ, Buist SA, Calverley P, Fukuchi Y, Jenkins C, Rodriguez-Roisin R, van Weel C, Zielinski J: Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med 2007;176:532–555.
3 Agustí AGN: Systemic effects of chronic obstructive pulmonary disease. Proc Am Thorac Soc 2005;2:367–370.
4 Hynninen KMJ, Breitve MH, Wiborg AB, Pallesen S, Nordhus IH: Psychological characteristics of patients with chronic obstructive pulmonary disease: a review. J Psychosom Res 2005;59:429–443.
5 Laurin C, Moullec G, Bacon SL, Lavoie KL: The impact of psychological distress on exacerbation rates in COPD. Ther Adv Respir Dis 2011;5:3–18.
6 Yohannes AM, Baldwin RC, Connolly MJ: Depression and anxiety in elderly patients with chronic obstructive pulmonary disease. Age Ageing 2006;35:457–459.
7 Cafarella PA, Effing TW, Usmani Z-A, Frith PA: Treatments for anxiety and depression in patients with chronic obstructive pulmonary disease: a literature review. Respirology 2012; 17:627–638.
8 Anderson KL: The effect of chronic obstructive pulmonary disease on quality of life. Res Nurs Health 1995;18:547–556.
9 Breslin E, van der Schans C, Breukink S, Meek P, Mercer K, Volz W, Louie S: Perception of fatigue and quality of life in patients with COPD. Chest 1998;114:958–964.
10 Borge CR, Wahl AK, Moum T: Association of breathlessness with multiple symptoms in chronic obstructive pulmonary disease. J Adv Nurs 2010;66:2688–2700.
11 Bailey PH: The dyspnea-anxiety-dyspnea cycle – COPD patients' stories of breathlessness: 'It's scary when you can't breathe'. Qual Health Res 2004;14:760–778.
12 De Voogd JN, Sanderman R, Postema K, van Sonderen E, Wempe JB: Relationship between anxiety and dyspnea on exertion in patients with chronic obstructive pulmonary disease. Anxiety Stress Coping 2011;24:439–449.
13 Rose C, Wallace L, Dickson R, Ayres J, Lehman R, Searle Y, Burge PS: The most effective psychologically based treatments to reduce anxiety and panic in patients with chronic obstructive pulmonary disease (COPD): a systematic review. Patient Educ Couns 2002;47: 311–318.
14 Coventry PA, Gellatly JL: Improving outcomes for COPD patients with mild-to-moderate anxiety and depression: a systematic review of cognitive behavioural therapy. Br J Health Psychol 2008;13:381–400.
15 Baraniak A, Sheffield D: The efficacy of psychologically based interventions to improve anxiety, depression and quality of life in COPD: a systematic review and meta-analysis. Patient Educ Couns 2011;83:29–36.
16 Clark NM, Dodge JA, Partridge MR, Martinez FJ: Focusing on outcomes: making the most of COPD interventions. Int J COPD 2009;4: 61–77.
17 Dobson KS (ed): Handbook of Cognitive-Behavioral Therapies. New York, Guilford Press, 2010.
18 Barrows KA, Jacobs BP: Mind-body medicine: an introduction and review of the literature. Med Clin North Am 2002;86:11–31.

19 Sackett DL, Richardson WS, Rosenberg W, Haynes RB: Evidence-Based Medicine: How to Practice and Teach EBM. New York, Churchill Livingston, 1997.
20 Moher D, Liberati A, Tetzlaff J, Altman DG: Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol 2009;62:1006–1012.
21 Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJM, Gavaghan DJ, McQuay HJ: Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials 1996;17:1–12.
22 Greenland S, O'Rourke K: On the bias produced by quality scores in meta-analysis, and a hierarchical view of proposed solutions. Biostatistics 2001;2:463–471.
23 Sterne JAC, Egger M, Moher D: Addressing reporting biases; in Higgins JPT, Green S (eds): Cochrane Handbook for Systematic Reviews of Intervention, ed 5.0.1. The Cochrane Collaboration, 2008. www.cochrane-handbook.org.
24 Poole C, Greenland S: Random-effects meta-analyses are not always conservative. Am J Epidemiol 1999;150:469–475.
25 Higgins JPT, Thompson SG, Deeks JJ, Altman DG: Measuring inconsistency in meta-analyses. BMJ 2003;327:557–560.
26 Cohen J: Statistical Power Analysis for the Behavioral Sciences, ed 2. Hillsdale, Erlbaum, 1988.
27 Hedges L, Olkin I: Statistical Methods for Meta-Analysis. New York, Academic Press, 1985.
28 Ioannidis JPA, Trikalinos TA: The appropriateness of asymmetry tests for publication bias in meta-analyses: a large survey. Can Med Assoc J 2007;176:1091–1096.
29 Copas J, Shi JQ: Meta-analysis, funnel plots and sensitivity analysis. Biostatistics 2000;1:247–262.
30 Deeks JJ, Macaskill P, Irwig L: The performance of tests of publication bias and other sample size effects in systematic reviews of diagnostic test accuracy was assessed. J Clin Epidemiol 2005;58:882–893.
31 Egger M, Smith GD, Schneider M, Minder C: Bias in meta-analysis detected by a simple, graphical test. BMJ 1997;315:629–634.
32 Rosenthal R: The file drawer problem and tolerance for null results. Psychol Bull 1979;86:638–641.
33 Duval S, Tweedie R: Trim and fill: a simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. Biometrics 2000;56:455–463.
34 Emery CF, Schein RL, Hauck ER, MacIntyre NR: Psychological and cognitive outcomes of a randomized trial of exercise among patients with chronic obstructive pulmonary disease. Health Psychol 1998;17:232–240.
35 De Godoy DV, de Godoy RF, Becker B, Vaccari PF, Michelli M, Teixeira PJZ, Palombini BC: The effect of psychotherapy provided as part of a pulmonary rehabilitation program for the treatment of patients with chronic obstructive pulmonary disease. J Bras Pneumol 2005;31:499–505.
36 Rosser R, Denford J, Heslop A, Kinston W, Macklin D, Minty K, Moynihan C, Muir B, Rein L, Guz A: Breathlessness and psychiatric morbidity in chronic bronchitis and emphysema: a study of psychotherapeutic management. Psychol Med 1983;13:93–110.
37 Chan AWK, Lee A, Suen LKP, Tam WWS: Tai chi qigong improves lung functions and activity tolerance in COPD clients: a single blind, randomized controlled trial. Complement Ther Med 2011;19:3–11.
38 Hedges LV, Pigott TD: The power of statistical tests for moderators in meta-analysis. Psychol Methods 2004;9:426–445.
39 Jones P, Miravitlles M, van der Molen T, Kulich K: Beyond FEV1 in COPD: a review of patient-reported outcomes and their measurement. Int J COPD 2012;7:697–709.
40 Coventry PA, Bower P, Keyworth C, Kenning C, Knopp J, Garrett C, Hind D, Malpass A, Dickens C: The effect of complex interventions on depression and anxiety in chronic obstructive pulmonary disease: systematic review and meta-analysis. PloS One 2013;8:e60532.
41 Barrows KA, Jacobs BP: Mind-body medicine: an introduction and review of the literature. Med Clin North Am 2002;86:11–31.
42 Viegi G, Pistelli F, Sherrill DL, Maio S, Baldacci S, Carrozzi L: Definition, epidemiology and natural history of COPD. Eur Respir J 2007;30:993–1013.
43 Lieberman MA, Yalom ID, Miles MB: Encounter Groups: First Facts. New York, Basic Books, 1973.
44 Doxsee DJ, Kivlighan DM: Hindering events in interpersonal relations groups for counselor trainees. J Couns Dev 1994;72:621–626.
45 Gift AG, Moore T, Soeken K: Relaxation to reduce dyspnea and anxiety in COPD patients. Nurs Res 1992;41:242–246.
46 Sassi-Dambron DE, Eakin EG, Ries AL, Kaplan RM: Treatment of dyspnea in COPD: a controlled clinical trial of dyspnea management strategies. Chest 1995;107:724–729.
47 Eiser N, West C, Evans S, Jeffers A, Quirk F: Effects of psychotherapy in moderately severe COPD: a pilot study. Eur Respir J 1997;10:1581–1584.
48 Kunik ME, Braun U, Stanley MA., Wristers K, Molinari V, Stoebner D, Orengo CA: One session cognitive behavioural therapy for elderly patients with chronic obstructive pulmonary disease. Psychol Med 2001;31:717–723.
49 Kheirabadi GR, Keypour M, Attaran N, Bagherian R, Peza M: Effect of add-on 'self-management and behavior modification' education on severity of COPD. Tanaffos 2008;7:23–30.
50 Kunik ME, Veazey C, Cully JA, Souchek J, Graham DP, Hopko D, Carter R, Sharafkhaneh A, Goepfert EJ, Wray N, Stanley MA: COPD education and cognitive behavioral therapy group treatment for clinically significant symptoms of depression and anxiety in COPD patients: a randomized controlled trial. Psychol Med 2008;38:385–396.
51 Donesky-Cuenco D, Nguyen HQ, Paul S, Carrieri-Kohlman V: Yoga therapy decreases dyspnea-related distress and improves functional performance in people with chronic obstructive pulmonary disease: a pilot study. J Altern Complem Med 2009;15:225–234.
52 Mularski RA, Munjas BA, Lorenz KA, Sun S, Robertson SJ, Schmelzer W, Kim AC, Shekelle PG: Randomized controlled trial of mindfulness-based therapy for dyspnea in chronic obstructive lung disease. J Altern Complem Med 2009;15:1083–1090.
53 Singh VP, Rao V, Prem V, Sahoo RC, Keshav Pai K: Comparison of the effectiveness of music and progressive muscle relaxation for anxiety in COPD: a randomized controlled pilot study. Chron Respir Dis 2009;6:209–216.
54 Hynninen MJ, Bjerke N, Pallesen S, Bakke PS, Nordhus IH: A randomized controlled trial of cognitive behavioral therapy for anxiety and depression in COPD. Respir Med 2010;104:986–994.
55 Lamers F, Jonkers CCM, Bosma H, Chavannes NH, Knottnerus JA, van Eijk JT: Improving quality of life in depressed COPD patients: effectiveness of a minimal psychological intervention. COPD 2010;7:315–322.
56 Livermore N, Sharpe L, McKenzie D: Prevention of panic attacks and panic disorder in COPD. Eur Respir J 2010;35:557–563.
57 Yeh GY, Roberts DH, Wayne PM, Davis RB, Quilty MT, Phillips RS: Tai chi exercise for patients with chronic obstructive pulmonary disease: a pilot study. Respir Care 2010;55:1475–1482.
58 Kapella MC, Herdegen JJ, Perlis ML, Shaver JL, Larson JL, Law JA, Carley DW: Cognitive behavioral therapy for insomnia comorbid with COPD is feasible with preliminary evidence of positive sleep and fatigue effects. Int J COPD 2011;6:625–635.
59 Ng BHP, Tsang HWH, Jones AYM, So CT, Mok TYW: Functional and psychosocial effects of health qigong in patients with COPD: a randomized controlled trial. J Altern Complem Med 2011;17:243–251.
60 Jiang X, He G: Effects of an uncertainty management intervention on uncertainty, anxiety, depression, and quality of life of chronic obstructive pulmonary disease outpatients. Res Nurs Health 2012;35:409–418.
61 American Thoracic Society: ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med 2002;166:111–117.
62 Borg GAV: Psychophysical bases of perceived exertion. Med Sci Sports Exerc 1982;14:377–381.

63 Guyatt GH, Berman LB, Townsend M, Pugsley SO, Chambers LW: A measure of quality of life for clinical trials in chronic lung disease. Thorax 1987;42:773–778.
64 Portenoy RK, Thaler HT, Kornblith AB, Lepore JM, Friedlander-Klar H, Kiyasu E, Sobel K, Coyle N, Kemeny N, Norton L, Scher H: The Memorial Symptom Assessment Scale: an instrument for the evaluation of symptom prevalence, characteristics and distress. Eur J Cancer 1994;30A:1326–1336.
65 Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ: The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatr Res 1989;28:193–213.
66 Qaseem A, Wilt TJ, Weinberger SE, Hanania NA, Criner G, van der Molen T, Marciniuk DD, Denberg T, Schünemann H, Wedzicha W, MacDonald R, Shekelle P: Diagnosis and management of stable chronic obstructive pulmonary disease: a clinical practice guideline update from the American College of Physicians, American College of Chest Physicians, American Thoracic Society, and European Respiratory Society. Ann Intern Med 2011;155:179–192.
67 Gift AG: Visual analogue scales: measurement of subjective phenomena. Nurs Res 1989;38:286–288.
68 Beck AT, Steer RA: Beck Anxiety Inventory Manual. San Antonio, Psychological Corporation, Harcourt Brace & Co, 1993.
69 Beck AT, Ward CH, Mendelsohn M, Mock J, Erbaugh J: An inventory for measuring depression. Arch Gen Psychiatry 1961;4:561–571.
70 Radloff LS: The CES-D scale: a self-report depression scale for research in the general population. Appl Psychol Meas 1977;1:385–401.
71 Stiles PG, McGarrahan JF: The Geriatric Depression Scale: a comprehensive review. J Clin Geropsychol 1998;4:89–110.
72 Zigmond AS, Snaith RP: The Hospital Anxiety and Depression Scale. Acta Psychiatr Scand 1983;67:570–579.
73 McNair D, Lorr M, Droppleman M: The Profile of Mood States. San Diego, Educational and Industrial Testing Service, 1992.
74 Spielberger L: STAI Manual. Palo Alto, Psychologists Consultants Press, 1983.
75 Derogatis LR: Symptom Checklist-90 Manual. Baltimore, Johns Hopkins University Press, 1977.
76 Van der Molen T, Willemse BWM, Schokker S, ten Hacken NHT, Postma DS, Juniper EF: Development, validity and responsiveness of the Clinical COPD Questionnaire. Health Qual Life Outcomes 2003;1:13.
77 Leidy NK: Psychometric properties of the functional performance inventory in patients with chronic obstructive pulmonary disease. Nurs Res 1999;48:20–28.
78 Ware JE: SF-36 Health Survey: Manual and Interpretation Guide. Boston, Health Institute, New England Medical Center, 1933.
79 Meguro M, Barley EA, Spencer S, Jones PW: Development and validation of an improved, COPD-specific version of the St George Respiratory Questionnaire. Chest 2007;132:456–463.
80 Bergner M, Bobbitt RA, Carter WB, Gilson BS: The Sickness Impact Profile: development and final revision of a health status measure. Med Care 1981;19:787–805.
81 Kaplan RM, Anderson JP: The quality of well-being scale: rationale for a single quality of life index; in Walker SR, Rosser RM (eds): Quality of Life: Assessment and Application. London, MTP Press, 1988, pp 51–77.

Appendix B: Paper 2

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Mindfulness-based cognitive therapy in COPD: a cluster randomised controlled trial

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ABSTRACT A considerable proportion of patients with chronic obstructive pulmonary disease (COPD) entering pulmonary rehabilitation (PR) report psychological distress, which is often accompanied by poor physical health status. Mindfulness-based cognitive therapy (MBCT) has been shown to improve psychological and physical outcomes in other chronic diseases. We therefore evaluated the efficacy of MBCT as an add-on to a standard PR programme in COPD.

COPD patients eligible for PR were cluster randomised to receive either an 8-week, group-based MBCT programme as an add-on to an 8-week PR programme (n=39), or PR alone (n=45). The primary outcomes of psychological distress and physical health status impairment were measured with the Hospital Anxiety and Depression Scale (HADS) and the COPD Assessment Test (CAT) before randomisation (T1), mid- (T2) and post-intervention (T3), and at 3 (T4) and 6 (T5) months' follow-up .

A statistically significant time×arm effect was found for the HADS (Cohen's d=0.62, 95% CIs (d)=0.18–1.06, p=0.010). The treatment effect on the CAT failed to reach statistical significance (d=0.42, 95% CIs (d)=−0.06–0.90, p=0.061).

MBCT showed a statistically significant and durable effect on psychological distress, indicating that MBCT may be an efficacious add-on to standard PR programmes in COPD.

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This trial was pre-registered at ClinicalTrials.gov (number NCT02042976).

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Introduction

A considerable proportion of patients with chronic obstructive pulmonary disease (COPD) entering pulmonary rehabilitation (PR) report clinically significant levels of psychological distress in the form of anxiety (32%) and depression (27%) [1]. Psychological distress is often undertreated in COPD, and is associated with poor physical outcomes, including physical health status impairment, low physical activity levels and inflammation [2, 3]. The efficacy of psychopharmacological treatment in COPD is limited and patients are often reluctant to take additional medication [4, 5]. Psychosocial intervention has been suggested as an alternative or complementary treatment strategy for reducing psychological distress and physical impairment [3, 6]. This approach is supported by a recent meta-analysis of controlled trials of psychosocial interventions showing reduced psychological distress in COPD, particularly when interventions included cognitive elements [7]. Additionally, another recent meta-analysis [8] indicates that relaxation and meditative techniques have the potential to improve both physical and psychological outcomes in COPD. Taken together, psychosocial interventions that combine cognitive and meditative elements may be effective in improving both psychological and physical outcomes in COPD.

Mindfulness-based cognitive therapy (MBCT) [9] is a group-based intervention that integrates mindfulness meditation with elements of cognitive behavioural therapy. MBCT aims to assist the patient in recognising maladaptive cognitions, emotions and bodily sensations, and relating to them in a non-judgemental and compassionate manner. In contrast to another popular mindfulness-based intervention, mindfulness-based stress reduction, which primarily consists of meditative elements, the combination of cognitive therapy and meditative training in MBCT may be a helpful approach to reduce the self-blaming, catastrophising cognitions and misinterpretations of bodily sensations (*e.g.* breathlessness) that have been linked to patterns of anxiety, demobilisation and depression in COPD [10, 11]. MBCT has been shown to improve psychological and physical outcomes in other chronic diseases [12], and it could also be effective in COPD. To date, only two studies of relatively limited methodological quality, *i.e.* a small pilot study [13] and a randomised controlled trial with a gender-biased sample [14], have explored the efficacy of mindfulness-based intervention in COPD. The effects found for respiratory rate, emotional function [13], dyspnoea and health-related quality of life [14] did not reach statistical significance or were in the opposite of the expected direction. Both studies used mindfulness-based stress reduction, and no studies so far have explored the efficacy of MBCT in COPD.

The aim of the present study was therefore to test the efficacy of MBCT as an add-on to a standard PR programme in improving the primary outcomes of psychological distress and physical health status impairment in COPD. Our secondary hypotheses were that MBCT would lead to heightened activity levels measured by accelerometers and reduction of the expression of the inflammatory cytokines interleukin (IL)-6, IL-8, tumour necrosis factor alpha (TNF-α) and IL-17E. These cytokines have previously been shown to be induced by psychological distress [15]; they play a role in COPD pathology [16] and are reduced with mindfulness-based intervention [17]. Additionally, we explored the possible moderating effects of age, gender, MBCT attendance rate and patients' perception of the therapeutic working alliance, together with the potential mediating effects of mindfulness, self-compassion, breathlessness catastrophising and COPD-specific self-efficacy.

Methods

The study was a cluster randomised controlled trial conducted at Aarhus University Hospital, Denmark, with the intervention arm receiving MBCT as an add-on to a standard PR programme (MBCT+PR) and the active control arm receiving PR only. PR classes were group based and served as units of randomisation. The cluster randomised design was chosen to avoid the risk of contamination bias if individual patients attending the same PR group were randomised to the MBCT+PR and PR-only arms, respectively. As all outcomes were relevant to and reported by individual patients, study objectives pertain to the individual level. Ethics approval was obtained from the Central Denmark Region Committee on Health Research Ethics (number 1-10-72-253-13) and the trial was pre-registered at ClinicalTrials.gov (number NCT02042976).

Participants

COPD patients referred to PR at Aarhus University Hospital from February 2014 to January 2016 were invited to take part in the study. At the cluster level, all PR groups held at Aarhus University Hospital after the study initiation date were eligible for inclusion. At the individual patient level, inclusion criteria were 1) a spirometry-confirmed (forced expiratory volume in 1 s <50%) COPD diagnosis together with a Medical Research Council dyspnoea score of ⩾3 and 2) physical capability to attend the exercise component of PR. Exclusion criteria were 1) a comorbid diagnosis of stroke, dementia or unstable coronary heart disease and 2) an inability to speak or understand Danish. After receiving written and oral information and providing written consent, patients completed the first questionnaire package. Patients

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were then allocated to a PR group (cluster), which was then randomised following the procedure described below.

Randomisation and blinding

PR groups were cluster randomised to either MBCT-PR or PR only. A random allocation sequence of 12 units, corresponding to the planned number of PR groups to be enrolled in the study, was generated by an independent researcher prior to data collection using Power and Sample Size Software (PASS), v.12 (NCSS, Kaysville, UT, USA). Researchers and clinicians involved in patient recruitment were blind to the allocation sequence, which was kept secure. Owing to the nature of psychosocial interventions, patient blinding could not be maintained throughout the intervention, and 2–7 days before the first session of a new PR group, information about the study arm allocation of that particular PR group was provided to patients, research assistants and clinicians.

Treatment arms

The standardised MBCT programme tested in the present study included one 30- to 60-min individual telephone interview followed by eight weekly 105-min group sessions of meditation and educational cognitive exercises. The programme was originally developed to prevent relapse in previously depressed individuals [9]. An adapted treatment manual was developed and piloted with a group of four COPD patients prior to initiation of the present trial (overview in table 1; complete manual in supplementary material). This resulted in four COPD-specific modifications: 1) focus on the heartbeat, the blood flow and the feet's contact with the ground as a means of meditational stabilisation instead of the breath, 2) reduced length and intensity of meditation exercises and home practice, 3) reduced complexity of cognitive exercises and 4) exclusion of the whole-day retreat. The intervention was conducted by a clinical psychologist (I. Farver-Vestergaard). Group sizes varied from three to 13 depending on the number of consenting patients assigned to the respective PR group. Weekly hand-outs and an audio compact disc with meditation exercises were provided to each patient for between-session practice.

The PR programme consisted of two weekly sessions over an 8-week period. One weekly session lasted 90 min, with physical exercise only. The other weekly session lasted 150 min and included physical exercise and disease- and lifestyle-oriented education. The programme followed the guidelines of the American Thoracic Society and the European Respiratory Society [18].

In the MBCT+PR arm, MBCT was added to the PR programme after each of the eight weekly 90-min sessions.

Measures

Primary outcome measures

Psychological distress was assessed using the Hospital Anxiety and Depression Scale (HADS) [19]. Total scores range from 0 to 42 with higher scores representing higher levels of psychological distress. Internal consistency (Cronbach's α) was 0.82 in the present sample [20]. The COPD Assessment Test (CAT) [21] was used to assess physical health status impairment. Total scores range from 0 to 40 with higher scores representing higher levels of physical health status impairment. The measure has shown satisfactory psychometric properties (α=0.92) [22]. Data were collected pre- (T1), mid- (4 weeks after first session) (T2) and post intervention (8 weeks after first session) (T3) as well as at 3 (T4) and 6 months (T5) after the final session.

Secondary outcome measures

Daily physical activity was measured with triaxial accelerometers (ActiGraph Monitor wGT3X-BT) carried around the waist for two periods of 7 days (T1 and T3). The accelerometers stored data at 80 Hz with 10 s epochs (ActiLife Analysis Software, Maribo Medico, Maribo, Denmark). Data were considered valid if the wear time was $\geqslant$10 h per day for $\geqslant$4 days [23]. The average mid-day (10:00–16:00 h) activity level was calculated for each patient at T1 and T3 and expressed as vector magnitude counts per minute (VMcpm, the vectorial sum of activity in the three orthogonal directions measured over a 1-min period) [24]. For analyses of inflammatory cytokines, whole blood samples were collected in 6-mL tubes (PAXgene) at T1 and T3. RT-PCR was carried out as previously described [25], using the following primers: TNF-α (Hs01113624_g1), IL-6 (Hs01075666_m1), IL-8 (Hs00174103-m1), IL-17E (Hs03044841_m1) and 18 s (Hs03003631_g1).

Moderators

Age and gender were registered at T1. The number of MBCT sessions attended was registered for each patient in the MBCT+PR arm at T3. Patients' individual perceptions of the therapeutic working alliance

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TABLE 1 Overview of the chronic obstructive pulmonary disease-specific mindfulness-based cognitive therapy programme

Session	Theme	Mindfulness exercises	Cognitive exercises	Home work
1	"Awareness and automatic pilot"	"The raisin exercise"; "The body scan"		"The body scan" every day; mindfulness of a routine activity
2	"Living in our heads"	"Awareness of the heartbeat and the blood flow"	"Thoughts and feelings exercise" (noticing connection between thoughts and emotional states); introduction of "the pleasant experiences calendar" (monitoring daily activities and their effects on thoughts, emotions and bodily sensations)	"Awareness of the heartbeat and the blood flow" every day; mindfulness of a routine activity; complete "the pleasant experiences calendar"
3	"Gathering the scattered mind"	"Awareness of the heartbeat, blood flow and body"; "The 3-min breathing space"; "Mindful stretching"	Review of "the pleasant experiences calendar"; introduction of "the unpleasant experiences calendar" (monitoring daily activities and their effects on thoughts, emotions and bodily sensations)	"Mindful stretching" every day; "the 3-min breathing space" 3 pre-scheduled times per day; complete "the unpleasant experiences calendar"
4	"Recognising aversion"	"Awareness of the heartbeat, blood flow, body, sounds and thoughts"; "the 3-min breathing space"	Review of "the unpleasant experiences calendar"; "automatic thoughts exercise" (noticing negative automatic thoughts and their effects on emotions and bodily sensations, and knowing when to do a 3-min breathing space)	"Awareness of the heartbeat, blood flow, body, sounds and thoughts" every day; "the 3-min breathing space" every time something uncomfortable happens
5	"Allowing/letting be"	"Being with the difficult"; "Walking meditation"; "the 3-min breathing space"		"Being with the difficult" every day; "the 3-min breathing space" every time something uncomfortable happens
6	"Thoughts are not facts"	"Awareness of thought and the emotional reaction"; "the 3-min breathing space"	"Mood, thoughts and alternative viewpoints exercise" (our mood can influence how we think about/ interpret a situation); "My personal warning system" (noticing personal signals of bad mood and anxiety)	Mindfulness exercise of own choice every day; "the 3-min breathing space" every time something uncomfortable happens"; complete "my personal warning system"
7	"How can I best take care of myself?"	"Awareness of spontaneous reactions of body, emotions, thoughts"; "the 3-min breathing space"	Review of "the personal warning system"; "Activities and mood exercise" (noticing connections between daily activities and mood); introduction of "the action plan" (a personal plan how to best schedule activities when emotions threaten to overwhelm"	Use the mindfulness exercises that you are planning to use after the programme has ended; complete the personal "action plan"
8	"Maintaining and extending new learning"	"The body scan"	Review of "the action plan"	-

The complete manual can be found in the supplementary material.

was assessed with the Working Alliance Inventory (WAI) [26] at T2, and patients were asked to keep a diary of frequency and duration of meditation practice between sessions.

Mediators

Mindfulness (Five-Facet Mindfulness Questionnaire (FFMQ) [27]), self-compassion (Self-Compassion Scale (SCS) [28]), breathlessness catastrophising (Breathlessness Catastrophizing Scale (BCS) [29]) and COPD-specific self-efficacy (COPD Self-Efficacy Scale (CSES) [30]) were measured at all time points. FFMQ total scores consisted of four out of five facets [31].

Statistical analysis

A priori sample size calculations indicated that 2×56 patients would be sufficient to detect an average 3-point reduction in CAT scores after PR with 80% statistical power (two-sided alpha, 5%) [32]. In

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addition, the chosen sample size would also allow for detection of a between-group minimal clinically important difference in HADS scores over time of 20% [20] with a statistical power of 78%. Missing items were substituted with the patient's average response on the remaining scale items, if the patient had completed ⩾50% of the items [33].

Mixed linear models (MLMs) were chosen to compare MBCT+PR and PR only over time on the primary outcome variables and the secondary outcome variable of activity level, based on the intent-to-treat sample. We specified both two- (time nested within individuals) and three-level models (time nested within individuals nested within clusters). Owing to non-convergence of the models, the final models were specified with only two levels. However, there was no time×cluster differences over time on primary outcomes (HADS, p=0.799; CAT, p=0.209). Time was entered as a log-transformation of the time points (*i.e.*, 1–5 [34]). An intervention effect was indicated by a statistically significant two-way interaction between the arm and the time. Treatment moderators were explored as either two-way interaction terms (time×moderator) in the MBCT+PR arm only – when measures were only available in the MBCT+PR arm (*i.e.*, attendance rate and working alliance) – or three-way interaction terms (time×arm×moderator) when measures were available in both arms (*i.e.*, gender and age). Effect sizes were expressed as Cohen's *d* derived from the *F*-test calculated as $d=2^{*}\sqrt{(F/\mathrm{df})}$ [35]. All MLMs were estimated with the maximum likelihood method.

In case of a detected effect of MBCT+PR, the FFMQ, the SCS, the BCS and the CSES were explored as mediators in time-lagged analyses [36] where the mediator at time_x predicted the outcome at time_{x+1}, controlling for the outcome variable at time_x and the mediator at time_{x-1}. In case of a significant result, the reverse pattern was also explored in order to test for reciprocal relations. These analyses were conducted on the MBCT+PR group only, where five observation points were available.

Statistical analyses of the fold change in cytokine mRNA expression levels were carried out using Graph Pad software version 6. Two-way ANOVAs were used to compare cytokine mRNA fold change values in the MBCT+PR and PR-only arms from T1 to T3. We also examined correlations between the change in mRNA cytokine expression levels and the change in HADS scores from T1 to T3.

The statistical analyses were conducted with IBM SPSS statistics version 24 and Stata version 14.

Results

Participant characteristics

From February 20, 2014, to January 15, 2016, 84 out of 161 patients assessed for eligibility (52%) in 12 clusters consented to participate in the trial (figure 1). 60 patients declined participation (37%) and 17 were ineligible (11%). 14 patients from the intent-to-treat population withdrew from the study, and 12 patients failed to return questionnaires after two unanswered telephone reminders. Eligible patients who declined participation in the study (n=60) did not differ statistically significantly from participants in terms of gender, but were statistically significantly older (mean age 71.9 years *versus* 67.2 years, p=0.002). Average PR attendance did not differ significantly between the MBCT+PR (mean=10.7 sessions) and PR only (mean=10.0 sessions) arms (p=0.434), and was generally similar to the attendance rate reported in an evaluation of the PR service at Aarhus University Hospital, with 55 patients out of 120 completing the programme (unpublished data).

Baseline characteristics are shown in table 2. The treatment arms were well balanced with regard to demographics, clinical characteristics, outcome variables and cluster characteristics, the only exception being use of complementary and alternative medicine over the last year. At baseline, 27.4% of the total sample had clinically significant anxiety levels (⩾10 points on the HADS anxiety subscale) and 19% had clinically significant depressive symptoms (⩾10 points on the HADS depression subscale).

Primary outcomes

Means and standard deviations for the primary outcomes across all time points are shown in table 3 together with the effects. No main effect of time was found for the HADS (Cohen's *d*=0.13, p=0.616) or the CAT (*d*=0.16, p=0.293). In contrast, a statistically significant time×arm effect was found for the HADS, corresponding to a medium effect size (*d*=0.62). The effect for the CAT was smaller and did not reach statistical significance. When adjusting the results for multiple comparison with the Benjamini–Hochberg correction, the effect on the HADS remained statistically significant. Two types of sensitivity analyses were then performed for this significant result. First, when analysing the possible association of HADS scores at baseline with subsequent study dropout with logistic regression, no effect was found (p=0.932). In addition, when testing the robustness of the observed effect on the HADS with an MLM with the last observation carried forward for study dropouts, the effect remained significant (*d*=0.53, p=0.021).

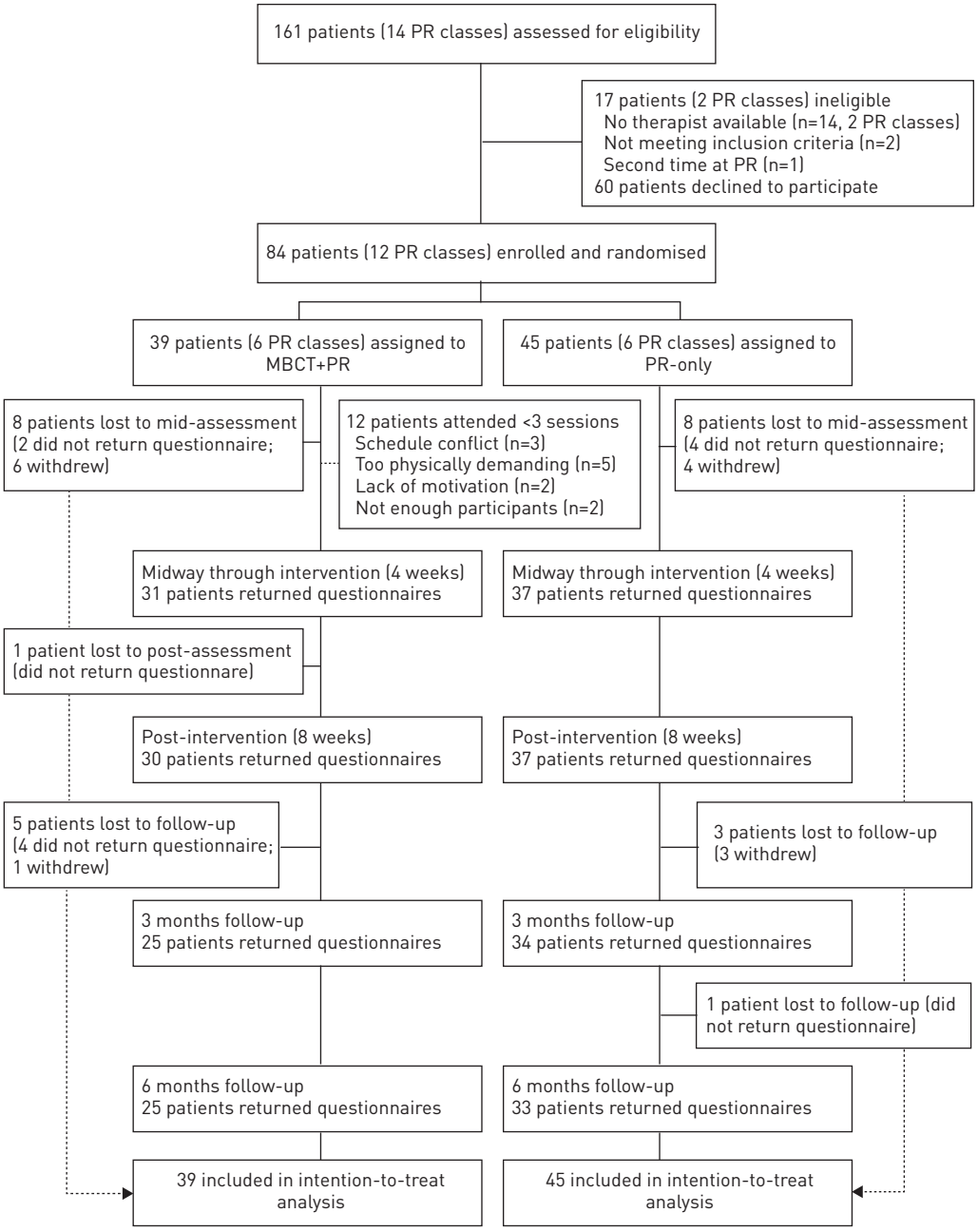

FIGURE 1 Trial profile. MBCT: mindfulness-based cognitive therapy; PR: pulmonary rehabilitation.

Intra-cluster correlation coefficients were 0.02 and 0.21 for the HADS and the CAT, respectively. Supplementary analyses of the HADS depression and anxiety subscales showed a statistically significant time×arm effect on depression, but not anxiety (table 3).

Secondary outcomes

A statistically significant increase in TNF-α mRNA from T1 to T3 was found in the PR-only arm, but TNF-α remained unchanged in the MBCT+PR arm (figure 2). The between-arm differences did not reach statistical significance. No statistically significant changes were found in IL-6 and IL-8 mRNA from T1 to T3. IL-17E mRNA was not detectable in the peripheral blood of any patients at any time point analysed and was therefore not subjected to statistical analysis. Correlations between changes in TNF-α, IL-6 and IL-8 mRNA and change in HADS scores were 0.03, 0.05 and 0.008 for MBCT+PR (n=19) and 0.0053, 0.08 and 0.08 for PR only (n=19). Supplementary analyses of the frequency of hospitalisations (p=0.213)

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TABLE 2 Baseline characteristics of the intention-to-treat population

	Total (n=84)	Intervention (n=39)	Control (n=45)	p-value[#]
Age years	67.2±7.74	66.67±8.03	67.67±7.54	0.558
Gender				0.449
Women	48 (57.1%)	24 (61.5%)	24 (53.3%)	
Men	36 (42.9%)	15 (38.5%)	21 (46.7%)	
Marital status (n=82)				0.673
Married/cohabiting	40 (48.8%)	19 (51.4%)	21 (46.7%)	
Single/widow(er)	42 (51.2%)	18 (48.6%)	24 (53.3%)	
Educational level (n=81)				0.986
Lower (<2 years of further education)	61 (75.3%)	28 (75.7%)	33 (75.0%)	
Medium (2–4 years of further education)	18 (22.2%)	8 (21.6%)	10 (22.7%)	
Long (⩾5 years of further education)	2 (2.5%)	1 (2.7%)	1 (2.3%)	
Occupational status (n=80)				0.928
Full- or part-time work	4 (5.0%)	2 (5.6%)	2 (4.5%)	
Unemployed	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Retired	72 (90.0%)	32 (88.9%)	40 (90.9%)	
Sick leave	4 (5.0%)	2 (5.6%)	2 (4.5%)	
Attitude towards psychotherapy	3.58±1.07	3.55±1.26	3.61±0.92	0.824
Use of psychological support during the last year (n=82)				0.559
Yes	13 (15.9%)	5 (13.5%)	8 (17.8%)	
No	69 (84.1%)	32 (86.5%)	37 (82.2%)	
Use of CAM treatment during the last year (n=79)				0.042
Yes	18 (22.8%)	4 (11.8%)	14 (31.1%)	
No	61 (77.2%)	30 (88.2%)	31 (68.9%)	
Knowledge about mindfulness (n=79)				0.527
Yes	22 (27.8%)	11 (31.4%)	11 (25.0%)	
No	57 (72.2%)	24 (68.6%)	33 (75.0%)	
FEV_1 (% predicted)	37.74±11.76	37.50±12.09	37.94±11.62	0.872
MRC	3.59±0.86	3.56±0.89	3.63±0.84	0.744
BMI	25.75±6.70	25.88±7.25	25.63±6.29	0.893
Comorbidity				
Cancer (n=83)	10 (12.0%)	6 (15.8%)	4 (8.9%)	0.336
Heart condition (n=83)	38 (45.8%)	18 (47.4%)	20 (44.4%)	0.790
Osteoporosis (n=83)	37 (44.6%)	15 (39.5%)	22 (48.9%)	0.390
Smoking (n=81)				0.807
Yes	23 (28.4%)	11 (29.7%)	12 (27.7%)	
No	58 (71.6%)	26 (70.3%)	32 (72.3%)	
Type of treatment				
ICS (n=82)	70 (85.4%)	31 (83.8%)	39 (86.7%)	0.713
LABA (n=82)	77 (93.9%)	35 (94.6%)	42 (93.3%)	0.812
LAMA (n=82)	80 (97.6%)	35 (94.6%)	45 (100.0%)	0.114
PDE4 inhibitors (n=82)	10 (12.2%)	4 (10.8%)	6 (13.3%)	0.728
Home oxygen use (n=81)	4 (4.9%)	2 (5.6%)	2 (4.4%)	0.819
Antidepressant and/or anxiolytic drug treatment during the last year (n=84)	19 (22.6%)	10 (25.6%)	9 (20.0%)	0.538
CAT total (n=71)	19.06±7.08	19.40±7.21	18.80±7.07	0.729
HADS total (n=82)	13.72±7.67	14.04±7.65	13.46±7.77	0.737
Activity level VMcpm (n=62)	389.70 ±166.82	397.11±144.68	382.75±187.29	0.738
IL-6 (n=38)	1.59±1.57	1.54±1.67	1.84±1.53	0.840
IL-8 (n=38)	1.48±1.90	1.10±2.28	1.40±1.48	0.660
TNF-α (n=38)	0.96±0.50	0.84±0.35	1.08±0.60	0.210
Number of PR group (clusters)	12	6	6	
PR group (cluster) size	7.00±2.73	6.50±1.87	7.5±3.51	0.552

Data are presented as mean±SD or n (%). CAM: complementary and alternative medicine; FEV_1: forced expiratory volume in 1 s; MRC: Medical Research Council dyspnoea score; BMI: body mass index; ICS: inhaled corticosteroids. LABA: long-acting β2-agonists; LAMA: long-acting muscarinic antagonists; PDE4: phosphodiesterase 4; CAT: COPD Assessment Test; HADS: Hospital Anxiety and Depression Scale; VMcpm: vector magnitude counts per minute; IL: interleukin; TNF: tumour necrosis factor; PR: pulmonary rehabiliation. [#]: independent samples t-tests for continuous variables, Chi-squared tests for categorical variables.

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TABLE 3 Primary outcomes and effect

	Baseline		Mid-intervention		Post-intervention		3 month follow-up		6 month follow-up	
	MBCT+PR	PR	MBCT+PR	PR	MBCT+PR	PR	MBCT+PR	PR	MBCT+PR	PR
HADS										
Mean±SD	14.04±7.65	13.46±7.77	13.18±7.20	13.71±6.66	12.13±7.08	14.18±8.24	12.08±6.21	15.34±6.95	12.46±5.72	14.74±8.26
N	37	45	30	36	30	37	24	33	25	33
	Time × arm interaction: F=6.9, p=0.010; Cohen's *d*=0.62; 95% CI (*d*)= 0.18–1.06									
CAT										
Mean±SD	19.40±7.21	18.80±7.07	21.38±5.77	21.09±6.15	18.55±7.19	17.39±4.95	19.25±5.94	21.47±6.21	19.30±6.17	20.55±7.18
N	30	41	31	35	20	18	25	34	25	33
	Time × arm interaction: F=3.6; p=0.061; Cohen's *d*=0.42; 95% CI (*d*)= −0.06–0.90									
Supplementary analyses										
HADS-D										
Mean±SD	6.32±3.67	5.90±4.10	5.78±3.57	5.91±3.47	5.33±3.77	6.26±4.60	5.42±3.98	7.17±3.93	5.45±3.03	6.76±4.82
N	37	45	30	36	30	37	24	33	25	33
	Time × arm interaction: F=7.1; p=0.009; Cohen's *d*=0.51; 95% CI (*d*)= 0.07–0.95									
HADS-A										
Mean±SD	7.72±4.72	7.57±4.12	7.40±4.22	8.09±4.17	6.80±3.86	7.92±4.16	6.67±2.81	8.17±3.60	7.01±3.44	7.99±4.21
N	37	45	30	37	30	37	24	33	25	33
	Time × arm interaction: F=2.3; p=0.136; Cohen's *d*=0.26; 95% CI (*d*)= −0.18–0.70									

MBCT: mindfulness-based cognitive therapy; PR: pulmonary rehabilitation; HADS: Hospital Anxiety and Depression Scale total score; CAT: COPD Assessment Test; HADS-A: HADS anxiety subscore; HADS-D: HADS depression subscore.

and exacerbations (p=0.904) indicated no statistically significant time×arm effects at T5. The effect on activity level did not reach statistical significance.

Moderators

A moderating effect of age was found for the effect on the HADS (F=4.3, p=0.040; d=0.38), indicating a better outcome for younger patients. The moderating effects of gender (d=0.31, p=0.096), the WAI (d=0.83, p=0.072) and attendance rate (d=0.19, p=0.579) did not reach statistical significance. Only three patients in the MBCT+PR arm completed meditation practice diaries, and the data were therefore not subjected to statistical analysis.

Mediators

Changes in self-compassion (SCS) significantly preceded changes in HADS scores (table 4). The reverse pattern was not significant, (B=0.20, p=0.227). Changes in the FFMQ, the BCS and the CSES were not significant predictors of subsequent change in the HADS.

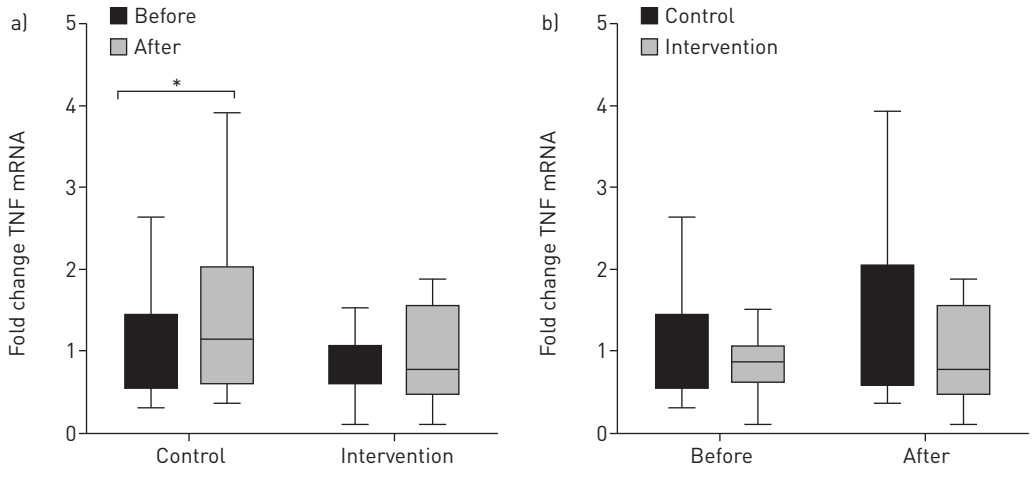

FIGURE 2 Tumour necrosis factor (TNF)-α mRNA fold change. *: p<0.05.

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TABLE 4 Mediators of the effect on Hospital Anxiety and Depression Scale total score

	Baseline		Mid-intervention		Post-intervention		3 month follow-up		6 month follow-up	
	MBCT+PR	PR	MBCT+PR	PR	MBCT+PR	PR	MBCT+PR	PR	MBCT+PR	PR
FFMQ										
Mean±SD	102.51±11.64	104.49±14.68	101.40±14.29	103.52±13.71	107.31±12.84	103.53±12.43	106.77±12.47	102.57±13.46	107.43±14.11	104.65±14.03
N	33	41	30	32	29	35	25	32	24	31
	Time-lagged analysis: B=0.05, p=0.424, 95% CIs (B)= −0.07–0.17									
SCS										
Mean±SD	39.53±5.46	40.22±6.09	39.00±7.26	38.58±5.15	40.36±5.87	39.13±5.15	41.13±6.16	39.00±6.42	39.78±5.92	38.16±5.94
N	34	37	25	33	25	32	24	29	23	31
	Time-lagged analysis: B=0.24, p=0.035, 95% CIs (B)=0.02–0.46									
BCS										
Mean±SD	26.35±13.39	22.04±11.63	22.93±12.36	22.24±10.24	19.34±11.96	21.64±10.25	17.77±10.23	22.91±12.19	18.52±10.69	22.66±13.22
N	37	42	30	34	30	36	25	32	24	32
	Time-lagged analysis: B=0.01, p=0.878), 95% CIs (B)= −0.12–0.14									
CSES										
Mean±SD	90.72±23.94	92.05±22.57	91.10±23.16	93.97±23.30	95.52±27.03	94.53±22.53	95.04±28.16	90.44±22.84	91.32±27.46	91.86±23.24
N	32	41	25	33	27	33	24	32	24	32
	Time-lagged analysis: B=0.03, p=0.337, 95% CIs (B)= −0.03–0.08									

MBCT: mindfulness-based cognitive therapy; PR: pulmonary rehabilitation; FFMQ: Five-Facet Mindfulness Questionnaire, range: 31 (low mindfulness) to 155 (high); SCS: Self Compassion Scale, range: 12 (low self compassion) to 60 (high); BCS: Breathlessness Catastrophizing Scale, range: 0 (low catastrophising) to 52 (high); CSES: COPD Self Efficacy Scale, range: 34 (low self-efficacy) to 170 (high).

Discussion

Our main findings indicated that MBCT as an add-on to PR led to a clinically relevant reduction (1.5 points [20]) in psychological distress in COPD (d=0.62). The effect size was larger than the previously found pooled effect size for psychosocial intervention in COPD (Hedges' g=0.38) [7], and was maintained 6 months after termination of the 8-week intervention period. Our results are in disagreement with the earlier studies of mindfulness-based interventions, which found no statistically significant effects on the psychological outcomes of anxiety and perceived stress in COPD [13, 14]. Additional analyses suggested that MBCT relieved psychological distress primarily by reducing symptoms of depression rather than anxiety, which may explain the null findings in earlier studies. Furthermore, the interventions evaluated in earlier studies did not include cognitive elements, and combining elements from mind–body interventions and cognitive behavioural therapy in the MBCT programme for COPD may therefore be more effective than mindfulness meditation only [7]. Our results should be interpreted with caution, as a psychological control component was not added to the PR programme in the control arm (PR only). A statistical trend-wise effect was observed for physical health status impairment (d=0.42, p=0.061). This effect did not reach a clinically relevant level (a 2.0 point reduction [22]), but was, however, similar to the pooled effect size previously found for effects of mind–body interventions on physical outcomes in COPD (g=0.40) [7]. The statistically near-significant effect for this outcome could therefore possibly be explained by the smaller than planned sample size obtained within the time-frame of the present study. There was no effect of time across treatment arms, which was unexpected, as both arms received a standard PR programme previously shown to reduce psychological distress and physical health status impairment [18]. A possible explanation could be that PR prevented a worsening of outcomes, which could otherwise have been the result of the progressive disease of COPD. As PR is part of standard COPD care, it would have been unethical to include a study arm that did not receive PR.

A statistically significant increase in TNF-α from before to after treatment was found in the PR-only control arm, but no changes were observed in MBCT+PR participants. This could indicate that MBCT prevented the exacerbation of TNF-α-mediated inflammation over time. In correspondence with our findings, mindfulness practice has previously been shown to be associated with larger reductions in TNF-α after stress induction in healthy individuals [17]. This specific cytokine is believed to play a role in lung diseases, and inhibiting TNF-α has been proposed as a relevant therapeutic target in inflammatory diseases [37]. Adverse side effects of pharmacological TNF-α inhibitors such as pain and diarrhoea are common in COPD, suggesting the potential relevance of MBCT as an alternative in inflammation control [37]. No effects were found for the remaining inflammatory markers of IL-6, IL-8 and IL-17E. Our use of peripheral blood cells as a biological source of pro-inflammatory cytokine, as opposed to cells from the lung microenvironment, might explain the lack of mRNA expression of these specific cytokines. Examination of tissue resections or bronchoalveolar lavage fluid could perhaps have yielded different results. Our results should therefore be considered preliminary and require further examination in future studies.

No statistically significant effect of the intervention was found for patients' activity levels as measured with accelerometers. In addition to the possibility of insufficient statistical power for this secondary variable, another explanation could be that it takes more than 8 weeks of training for patients to implement the complex behaviour changes needed to observe changes in their average physical activity level [18]. Longer follow-up periods could thus be relevant for activity monitoring in future studies.

Our additional results suggest that age moderates the effect of MBCT on psychological distress, with MBCT appearing to be more effective for younger COPD patients. This is in line with a review stating that younger COPD patients may be more adept at learning the skills and tools taught in psychosocial intervention [38]. This finding may guide clinicians when referring patients to MBCT. The moderating effects of gender, MBCT attendance rate and therapeutic working alliance did not reach statistical significance. The non-significant effect of gender differs from the results reported in the COPD literature of gender differences in medical and behavioural treatment adherence and outcomes [39]. Concerning MBCT attendance, the reasons for non-attendance may vary, including perception of sufficient treatment gain or perceived difficulties in relation to the intervention, which could explain the lack of a moderating effect. We attempted to assess the frequency of home practice, but the number of completed home practice diaries in the present sample was insufficient. Taking the large effect size of therapeutic working alliance into account (d=0.83), the non-significant result for this moderator could be due to the relatively limited number of patients in the MBCT+PR arm (n=39).

The results of our exploratory mediational analyses suggest that the effect of MBCT on psychological distress may be facilitated through increased levels of self-compassion. Our finding suggests that stimulating a non-judgemental attitude through mindfulness meditation and cognitive exercises may be efficacious in relieving psychological distress in COPD, a disease where feelings of smoking-related self-blame and stigma are highly prevalent and associated with depression [40]. However, other potential mechanisms driving the effect of MBCT in COPD cannot be excluded, and future research should implement more assessment points, *e.g.* at every session, in order to capture more fine-grained dynamics of change.

The present study has several strengths, including a randomised design and a long-term (6 month) follow-up. However, a number of limitations should also be noted. First, as an attention control condition was not added to the PR programme in the PR-only arm, we cannot rule out that additional attention from healthcare professionals may have boosted the effect in the MBCT+PR arm. On the other hand, the validity of our findings is supported by controls receiving an active intervention previously shown to be effective [18]. Second, because of a lower inclusion rate than expected, the final sample size was smaller than projected, which could explain the statistically non-significant effect (p=0.061) found for physical health status impairment. The limited enrolment rate could perhaps be due to that not all patients eligible for PR reported clinically significant levels of psychological distress. Third, patients who declined participation in the study were older than participating patients, which could limit the external validity of our results. Fourth, attrition rates were high in both the intervention and the control arm. This is a general issue in COPD research and practice where compliance rates generally are poor [41]. Dropout, however, was balanced across treatment arms and did not appear, as supported by our sensitivity analyses, to compromise the robustness of the results. Finally, the single-site design with only one MBCT instructor and one team of PR providers may limit the generalisability of the results. Taken together, to increase validity of the results, future multi-site trials including larger samples and attention control arms are recommended.

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References

1 Janssen DJ, Spruit MA, Leue C, *et al.* Symptoms of anxiety and depression in COPD patients entering pulmonary rehabilitation. *Chron Respir Dis* 2010; 7: 147–157.
2 Pumar MI, Gray CR, Walsh JR, *et al.* Anxiety and depression: important psychological comorbidities of COPD. *J Thorac Dis* 2014; 6: 1615–1631.
3 Yohannes AM, Alexopoulos GS. Depression and anxiety in patients with COPD. *Eur Respir Rev* 2014; 23: 345–349.
4 Fritzsche A, Clamor A, von Leupoldt A. Effects of medical and psychological treatment of depression in patients with COPD: a review. *Respir Med* 2011; 105: 1422–1433.

https://doi.org/10.1183/13993003.02082-2017

5 Yohannes AM, Alexopoulos GS. Pharmacological treatment of depression in older patients with chronic obstructive pulmonary disease: impact on the course of the disease and health outcomes. *Drugs Aging* 2014; 31: 483–492.
6 von Leupoldt A, Janssens T. Could targeting disease specific fear and anxiety improve COPD outcomes? *Expert Rev Respir Med* 2016; 10: 835–837.
7 Farver-Vestergaard I, Jacobsen D, Zachariae R. Efficacy of psychosocial interventions on psychological and physical health outcomes in chronic obstructive pulmonary disease: a systematic review and meta-analysis. *Psychother Psychosom* 2015; 84: 37–50.
8 Volpato E, Banfi P, Rogers SM, *et al.* Relaxation techniques for people with chronic obstructive pulmonary disease : a systematic review and a meta-analysis. *Evid-Based Complementary Altern Med* 2015: 1–22.
9 Segal Z, Williams JMG, Teasdale J. Mindfulness-based cognitive therapy for depression. New York, Guildford Press, 2013.
10 Moore MC, Zebb BJ. The catastrophic misinterpretation of physiological distress. *Behav Res Ther* 1999; 37: 1105–1118.
11 Livermore N, Sharpe L, McKenzie D. Catastrophic interpretations and anxiety sensitivity as predictors of panic-spectrum psychopathology in chronic obstructive pulmonary disease. *J Psychosom Res* 2012; 72: 388–392.
12 Gotink RA, Chu P, Busschbach JJ V, *et al.* Standardised mindfulness-based interventions in healthcare: An overview of systematic reviews and meta-analyses of RCTs. *PLoS One* 2015; 10: 1–17.
13 Chan RR, Giardino N, Larson JL. A pilot study: mindfulness meditation intervention in COPD. *Int J Chron Obstruct Pulmon Dis* 2015; 10: 445–454.
14 Mularski RA, Munjas BA, Lorenz KA, *et al.* Randomized controlled trial of mindfulness-based therapy for dyspnea in chronic obstructive lung disease. *J Altern Complement Med* 2009; 15: 1083–1090.
15 Dowlati Y, Herrmann N, Swardfager W, *et al.* A meta-analysis of cytokines in major depression. *Biol Psychiatry* 2010; 67: 446–457.
16 Cazzola M, MacNee W, Martinez FJ, *et al.* Outcomes for COPD pharmacological trials: from lung function to biomarkers. *Eur Respir J* 2008; 31: 416–468.
17 Rosenkranz MA, Davidson RJ, Maccoon DG, *et al.* A comparison of mindfulness-based stress reduction and an active control in modulation of neurogenic inflammation. *Brain Behav Immun* 2013; 27: 174–184.
18 Spruit MA, Singh SJ, Garvey C, *et al.* An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation. *Am J Respir Crit Care Med* 2013; 188: e13–e64.
19 Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand* 1983; 67: 361–370.
20 Puhan MA, Frey M, Büchi S, *et al.* The minimal important difference of the hospital anxiety and depression scale in patients with chronic obstructive pulmonary disease. *Health Qual Life Outcomes* 2008; 6: 46.
21 Jones PW, Harding G, Berry P, *et al.* Development and first validation of the COPD Assessment Test. *Eur Respir J* 2009; 34: 648–654.
22 Kon SSC, Canavan JL, Jones SE, *et al.* Minimum clinically important difference for the COPD Assessment Test: a prospective analysis. *Lancet Respir Med* 2014; 2: 195–203.
23 Friis AL. Dietary beetroot juice – effects on physical performance in COPD patients: a randomized controlled crossover trial. *Int J COPD* 2017; 12: 1765–1773.
24 Hecht A, Ma S, Porszasz J, *et al.* Methodology for using long-term accelerometry monitoring to describe daily activity patterns in COPD. *COPD* 2009; 6: 121–129.
25 Basdeo SA, Kelly S, O'Connell K, *et al.* Increased expression of Tbet in CD4(+) T cells from clinically isolated syndrome patients at high risk of conversion to clinically definite MS. *Springerplus* 2016; 5: 779.
26 Tracey TJ, Kokotovic AM. Factor structure of the Working Alliance Inventory. *Psychol Assess* 1989; 1: 207–210.
27 Baer RA, Smith GT, Hopkins J, *et al.* Using self-report assessment methods to explore facets of mindfulness. *Assessment* 2006; 13: 27–45.
28 Raes F, Pommier E, Neff KD, *et al.* Construction and factorial validation of a short form of the Self-Compassion Scale. *Clin Psychol Psychother* 2011; 18: 250–255.
29 Solomon BK, Wilson KG, Henderson PR, *et al.* A breathlessness catastrophizing scale for chronic obstructive pulmonary disease. *J Psychosom Res* 2015; 79: 62–68.
30 Emme C, Mortensen EL, Rydahl-Hansen S, *et al.* Danish version of "The COPD self-efficacy scale": Translation and psychometric properties. *Scand J Caring Sci* 2012; 26: 615–623.
31 Williams MJ, Dalgleish T, Karl A, *et al.* Examining the factor structures of the Five Facet Mindfulness Questionnaire and the Self-Compassion Scale. *Psychol Assess* 2014; 26: 407–418.
32 Dodd JW, Hogg L, Nolan J, *et al.* The COPD Assessment Test (CAT): response to pulmonary rehabilitation. A multicentre, prospective study. *Thorax* 2011; 66: 425–429.
33 Schafer JL, Graham JW. Missing data: our view of the state of the art. *Psychol Methods* 2002; 7: 147–177.
34 Tasca GA, Illing V, Joyce AS, *et al.* Three-level multilevel growth models for nested change data: a guide for group treatment researchers. *Psychother Res* 2009; 19: 453–461.
35 Verbeke G, Molenberghs G. Linear Mixed Models for Longitudinal Data. New York, Springer-Verlag, 2000.
36 Pek J, Hoyle RH. On the (in)validity of tests of simple mediation: threats and solutions. *Soc Personal Psychol Compass* 2016; 10: 150–163.
37 Matera MG, Calzetta L, Cazzola M. TNF-alpha inhibitors in asthma and COPD: we must not throw the baby out with the bath water. *Pulm Pharmacol Ther* 2010; 23: 121–128.
38 Coventry PA, Gellatly JL. Improving outcomes for COPD patients with mild-to-moderate anxiety and depression: A systematic review of cognitive behavioural therapy. *Br J Health Psychol* 2008; 13: 381–400.
39 Aryal S, Diaz-Guzman E, Mannino DM. COPD and gender differences: an update. *Transl Res* 2013; 162: 208–218.
40 Plaufcan MR, Wamboldt FS, Holm KE. Behavioral and characterological self-blame in chronic obstructive pulmonary disease. *J Psychosom Res* 2012; 72: 78–83.
41 Blackstock FC, ZuWallack R, Nici L, *et al.* Why don't our COPD patients listen to us? The enigma of nonadherence. *Ann Am Thorac Soc* 2016; 13: 317–323.

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Appendix C: Paper 3

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Tele-delivered mindfulness-based cognitive therapy in chronic obstructive pulmonary disease: A mixed-methods feasibility study

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Abstract

Introduction: Mindfulness-based cognitive therapy has been shown to reduce psychological distress in chronic obstructive pulmonary disease, but uptake and attendance rates of hospital-based, face-to-face mindfulness-based cognitive therapy are low. The present mixed-methods study evaluates the clinical feasibility of home-based, tele-delivered mindfulness-based cognitive therapy in chronic obstructive pulmonary disease.

Methods: Eight patients with chronic obstructive pulmonary disease (mean age: 72.6 years; 50% female) received a standardised eight-week mindfulness-based cognitive therapy programme delivered via home-based video-conferences in groups of four. Feasibility in relation to (a) clinical change, (b) attendance and (c) instructor-patient working alliance were evaluated with questionnaires and semi-structured interviews.

Results: Statistically non-significant reductions in psychological distress (Cohen's $d = 0.504$; $p = 0.399$) and physical health status impairment ($d = 0.743$; $p = 0.156$) were observed from pre- to post-intervention. Participant narratives about clinical outcomes focused on changes in how to relate to unpleasant sensations, i.e. through attentional flexibility, taking a pause and acceptance. The average attendance rate was 7.5 (standard deviation = 0.8) out of eight sessions and no participants dropped out. The tele-based format appeared to accommodate participants' planning difficulties and promoted their ability and wish to participate. Although participant narratives suggested the tele-based format to be a barrier to developing a trusting and safe therapeutic environment, working alliance questionnaire scores were comparable to those found for face-to-face mindfulness-based cognitive therapy.

Discussion: The preliminary results indicate that tele-delivered mindfulness-based cognitive therapy is a clinically feasible intervention in chronic obstructive pulmonary disease. Future large-scale, randomised controlled trials testing its efficacy on the outcomes of psychological distress and physical health status should include analyses of potential mediators and moderators of the effect as well as and careful monitoring of attendance and adverse events.

Keywords

Telecare, mixed-methods design, chronic obstructive pulmonary disease, psychological distress, physical health status

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Introduction

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide.[1] In addition to physical symptoms such as breathlessness, cough and excessive mucus production, patients often report high levels of psychological distress.[2] COPD patients experiencing psychological distress typically also report poor physical health status as well as frequent use of acute healthcare services,[3] indicating a need for efficacious interventions for reducing psychological distress in this patient group.[4]

Mindfulness is 'the awareness that emerges through paying attention on purpose, in the present moment, and nonjudgmentally to the unfolding of experience moment by moment' (p. 145).[5] Stimulating this form of awareness through regular meditation practice has been shown to reduce psychological distress and relieve physical symptoms in cancer and chronic pain patients.[6,7]

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Mindfulness-based cognitive therapy (MBCT) is a manualised eight-week, group-based psychological intervention combining mindfulness meditation with elements from cognitive behavioural therapy (CBT).[8] MBCT has recently shown to reduce psychological distress in COPD in a randomised controlled trial with face-to-face MBCT delivered as an addition to a standardised pulmonary rehabilitation (PR) programme.[9] Unfortunately, as is often seen for behavioural interventions in COPD,[10] uptake and attendance rates were low (52% inclusion rate; mean number of MBCT sessions attended = 4.0 (standard deviation (SD) = 2.74)). Among the reasons for COPD patients' non-attendance are activity limitations, travel issues and costs.[10] Similar issues are seen in other physical health conditions, and synchronous and asynchronous tele-based delivery of MBCT (tele-MBCT) has shown to be feasible in chronic diseases such as cancer, chronic pain and irritable bowel syndrome.[11,12] While asynchronous, self-directed intervention types may be challenging for the present generation of COPD patients (i.e. elderly population with relatively limited computer skills),[13] synchronous, facilitated tele-delivered medical consultations and PR programmes, in which healthcare professionals and patients communicate through a videoconference device, have been shown to be feasible and acceptable in COPD.[14,15] To date, however, little is known about the clinical feasibility of tele-delivered psychological interventions in COPD.

Using videoconferencing to deliver psychological intervention has received increasing empirical support, with the available studies indicating high levels of patient satisfaction.[16] Yet, the field is still in its infancy, and concerns have been raised that tele-delivered psychological interventions could negatively impact the development of a productive therapeutic working alliance and complicate procedures for taking clinical responsibility of patients at a distance.[17] Moreover, additional issues have been raised regarding technology-mediated presence, e.g. whether technology-mediated experiences evoke the same bodily, emotional and cognitive dynamics as a real experience and how this may influence clinical outcomes. Furthermore, little is known about individual variation in the experience of, and responses to, technology-mediated environments.[18,19] Therefore, in addition to quantitative assessments of changes in pre-specified clinical parameters (i.e. psychological distress and physical health status), it is relevant to qualitatively explore individual patients' experiences with receiving and engaging in tele-MBCT with the overall purpose of evaluating its clinical feasibility and identifying relevant design issues for future efficacy trials.

Based on this background, the aim of the present study was to evaluate the clinical feasibility of tele-MBCT in COPD using a mixed-methods design to: (a) measure pre-post-intervention clinical change in psychological distress and physical health status; (b) monitor drop-out rate and attendance rates (number of tele-MBCT sessions attended); (c) measure the participants' perception of the therapeutic working alliance during the intervention and (d) explore the participants' individual experiences with receiving tele-MBCT.

Specifically, a 'convergent parallel' type of design[20] was applied, with quantitative and qualitative data collected independently and then analysed to contribute to the understanding of the same particular phenomenon.

Methods

The methodology and reporting of the present study has been subjected to a comprehensive critical appraisal using instruments for evaluating mixed-methods research good reporting of a mixed methods study (GRAMMS) assessment of reporting;[21] Sale and Brazil's assessment of methodology[22] (see Supplementary Material File S1)).

Patients with a spirometry-confirmed (forced expiratory volume in one second <50%) COPD diagnosis were invited to take part in the present feasibility study. The participants were recruited from the control group of a larger study.[9] After having provided informed consent, and after having completed a baseline questionnaire package, a touch-screen computer for conducting videoconsultation (EWII Telecare, Odense, Denmark) was installed in the participants' homes and a brief individual test call from the MBCT instructor was made. As part of the test call, the MBCT instructor and each participant settled on a convenient date and time for an individual pre-intervention clinical interview (see below). All participants were then invited to take part in eight group-based, videoconference sessions, constituting the tele-MBCT intervention described in the following. The touch-screen computers were removed after termination of the tele-MBCT intervention, followed by participants completing post-intervention questionnaires and taking part in individual qualitative research interviews.

Intervention

The tele-MBCT intervention was based on the manualised MBCT programme[23] originally developed to prevent relapse in major depression and adjusted to meet the needs of COPD-patients.[9] Tele-MBCT was comprised of an initial 30–60 min individual interview followed by eight weekly 120-minute group sessions of meditation, mindfulness movement activities and cognitive exercises. Participants were encouraged to practice mindfulness meditation individually at home between sessions for an approximate duration of 20–30 min per day. The eight sessions were led by a clinical psychologist (IF-V). Weekly handouts and an audio compact disc (CD) with meditation and mindful movement exercises were sent by post to each participant prior to the first tele-MBCT group session. For further details concerning the intervention content, see Farver-Vestergaard et al.[9]

Since participants were recruited from an elderly sample (mean age of the mother sample = 67.2 years)[9]

we did not expect all participants to have their own computer. Therefore, the tele-MBCT intervention was delivered via touch-screen computers installed in the participants' homes prior to the first session. The computers had integrated camera, speaker and microphone, allowing each participant to see, hear and speak to the instructor and the other participants. The instructor operated a provider station to make a group call to all participants prior to each session and to terminate the call after each session. The instructor contacted service providers in instances of technical issues.

Quantitative evaluation

The clinical parameters of psychological distress and physical health status impairment were assessed pre- and post-intervention. Psychological distress was assessed with the Hospital Anxiety and Depression Scale (HADS).[24] Its 14 items yield a total score ranging from 0–42, with higher scores representing higher levels of distress. Physical health status impairment was measured with the COPD Assessment Test (CAT).[25] This consists of eight items resulting in a total score ranging from 0–40, with higher scores representing higher levels of impairment. Both questionnaires have shown satisfactory psychometric properties in COPD (HADS Cronbach's $\alpha = 0.82$; CAT $\alpha = 0.92$).[9]

For each individual participant, the total number of MBCT sessions (0–8) attended as well as the potential wish to withdraw from the intervention were registered. Average attendance and drop-out rates for the whole sample were computed.

Between session four and five, participants completed the Working Alliance Inventory (WAI),[26] measuring their perceptions of the therapeutic instructor-patient working alliance. Total scores range from 12–84 with higher scores representing a better alliance.

Paired *t*-tests were performed to explore changes in HADS and CAT scores after tele-MBCT.

Qualitative evaluation

Semi-structured qualitative interviews were conducted with all participants immediately after completion of the tele-MBCT programme either in the participant's own home or via telephone (the interview guide is shown in Supplementary Material File S2). Interviews were conducted by a research assistant (NCS) with a background in psychology and experience within the field of psychological intervention in COPD. All interviews were transcribed verbatim by a second research assistant. The analysis was based on the thematic analysis framework.[27] The six iterative phases of analysis started with a thorough and detail-oriented reading of research interviews and moved gradually towards a condensed understanding of the data through the identification and definition of themes. The initial coding of data was based on an inductive approach, but as the analysis moved towards the definition of themes, it took a more deductive approach with focus on areas of the data that complemented the quantitative evaluation (i.e. clinical change, attendance and working alliance). In this approach we sought to provide as balanced an account of experiences as possible by actively seeking conflicting utterances under a given theme. The analysis was primarily carried out by the first author (IF-V), supplemented with discussions with the interviewer (NCS) and other colleagues.[28] During the analytical process, a reflective logbook was kept, using the NVivo software (NVivo, Version 11.3.0.773; QSR, 1999–2016).

Results

In the period from February–May 2016, a total of eight out of 47 invited COPD patients (17%) were enrolled in the study and allocated to two treatment groups of four participants each (reasons for non-participation: eight patients preferred face-to-face MBCT; 25 patients were not interested in receiving any form of MBCT at the time of recruitment; six patients did not respond to our telephone calls). The individual participant and total sample characteristics at baseline, as well as HADS, CAT and WAI scores are shown in Table 1. Three participants (numbers 2, 3 and 5) reported a pre-to-post treatment reduction of the HADS score, while an increase was observed in two participants (number 1 and 7). Five participants reported a reduction of the CAT score after Tele-MBCT (number 1, 4, 5, 6 and 7), while two participants reported an increase (number 2 and 8).

Quantitative results

On average, a medium (Cohen's $d = 0.50$), but statistically non-significant reduction in HADS scores was observed from pre- to post-intervention ($t(7) = 0.90$, $p = 0.399$). Likewise, a medium ($d = 0.74$), non-significant reduction in CAT scores was seen from pre- to post-intervention ($t(7) = 1.587$, $p = 0.156$).The average attendance rate was 7.5 (SD = 0.8) out of eight sessions, and no participants dropped out. The average WAI score assessed between session four and five was 68.88 (SD = 10.72).

Qualitative results

The themes emerging from the qualitative analysis complement the quantitative data by relating to (a) clinical change, (b) attendance and (c) working alliance.

Theme 1: Changes in relating to unpleasant symptoms. When asked about what they had gained from the intervention, participants generally described a change in how they related to unpleasant psychological symptoms and physical sensations from before to after the intervention. Three prominent areas of change were identified: First, several participants described an experience of increased attentional flexibility (Table 2, Quote 1), including an improved

Table 1. Individual participant and total sample characteristics.

Participant no.	Gender	Age	Work	FEV1% predicted	HADS total pre	HADS total post	HADS change	CAT total pre	CAT total post	CAT change	WAI total midway
1	Male	71	Retired	34	8	9	1	20	14	–6	71
2	Male	79	Retired	43	17	15	–2	25	26	1	69
3	Female	76	Retired	49	20	17	–3	23	23	0	60
4	Male	78	Retired	46	13	13	0	16	13	–3	76
5	Female	85	Retired	54	35	23	–12	22	21	–1	84
6	Male	60	Full-time	27	18	18	0	19	15	–4	79
7	Female	76	Retired	33	11	15	4	19	18	–1	54
8	Female	56	Retired	19	5	5	0	19	21	2	58
Total sample	50% women	M = 72.6 SD = 9.9	87.5% retired	M = 38.1 SD = 11.9	M = 15.9 SD = 9.3	M = 14.4 SD = 5.5	MD = 1.5 95% CI = –2.45–5.45	M = 20.4 SD = 2.8	M = 18.9 SD = 4.6	MD = 1.5 CI = –0.73–3.73	M = 68.88 SD = 10.72

CAT: COPD Assessment Test; COPD: chronic obstructive pulmonary disease; CI: confidence interval; FEV1% predicted: forced expiratory volume in one second, percentage of predicted value in age-matched normative sample; HADS: Hospital Anxiety and Depression Scale; M: mean; MD: mean difference; SD: standard deviation; WAI: Working Alliance Inventory.

capability of being aware of both positive and negative aspects of life (Table 2, Quote 2). Second, taking a pause – physically and mentally – is another example of changes in ways of relating to unpleasant experiences (Table 2, Quote 3). Third, a number of participants mentioned increased acceptance as a new way of dealing with unpleasant sensations (Table 2, Quote 4). Not all participants reported changes right away. One participant stated: 'I'm feeling as I've felt all along' (Participant 3). Later in the interview, however, this participant described that the intervention had made her aware of the importance of pausing before action: 'It [tele-MBCT] taught me a whole lot about not just reacting straight away. Take a moment to make sure that your head agrees with your response'.

Theme 2: Practical aspects of attendance. In relation to attendance, the participants described a number of practical benefits related to the tele-delivered format of the intervention. Most participants experienced the home-based format and the associated reduction of travel burden, positively. First, the tele-based format appeared to make planning of the day easier, which was perceived by several participants as a very important aspect when attending a large number of treatment sessions (Table 2, Quote 5). Second, a few participants expressed that the home-based format had a positive influence on their choice to participate in the intervention at all, and one participant declared that without the tele-based format, she would not have been able to take part at all (Table 2, Quote 6).

Theme 3: Relational aspects. Finally, the tele-based intervention also appeared to influence the relational aspects of taking part in the intervention sessions. Negative influences of the tele-based format mentioned included an experience of a reduced and disturbed personal contact with the other participants and the instructor, often caused by technical problems (i.e. disruption due to an unstable video connection). According to some participants, this led to difficulties in creating an atmosphere of trust and safety, which in turn was perceived as a barrier to the willingness to disclose certain personal experiences and feelings (Table 2, Quote 7). One participant expressed the need for a hotline for participants who are left alone with their worries and concerns, each time the video-consultation was, timely or untimely, disconnected. In spite of these negative influences on the quality of participating in the sessions, most participants reported that, over time, the personal contact with fellow participants and the instructor developed into a warm, respectful and caring relationship (Table 2, Quote 8). Among the positive influences mentioned were that the tele-based format demanded more intense management of the group dynamics, which led to increased concentration – something several participants felt was lacking in face-to-face interventions they had attended (Table 2, Quote 9). Moreover, the tele-based format used in the present study did not allow groups of more than four participants plus the instructor, and several participants mentioned that this allowed more time to address the issues of each participant, which was perceived positively (Table 2, Quote 10).

Discussion

The present study is among the first to evaluate the clinical feasibility of a tele-delivered psychological intervention in COPD, using a mixed-methods design. Overall, the quantitative study results are concerned with three areas: (a) clinical change, (b) attendance and (c) working alliance, with the qualitative data on participant experiences complementing and expanding on the quantitative results.

Clinical change

The results of the quantitative evaluation indicated that, for psychological distress, an average reduction of

Table 2. Qualitative themes and subthemes with supporting data extracts from semi-structured interviews.

Theme	Subtheme	Quote (participant no.)
Changes in relating to unpleasant symptoms	Attentional flexibility	Quote #1 Participant: *I think I forget about it [the physical pain]. I don't think it goes away. I just think you forget about it.* Interviewer: *Maybe you direct your attention towards something else?* Participant: *That is my sensation, anyway. Because it is there all the time, the pain* (Participant 2).
		Quote #2 *This is about awareness, and awareness is certainly good. And having an awareness of both positive and negative situations – that is what it is all about. You have to be aware of both. [. . .] If one cannot see neither the positive nor the negative, then life will be shitty. Quite frankly* (Participant 1).
	Taking a pause	Quote #3 *And then I have gotten some tools. And exercises. And a method for sitting down and immersing oneself, regardless of whether it's to do with a pause. [. . .] I think I may have used that beforehand, because I get so short of breath, that my body needs a break. That is one of the only things, that I had to learn the hard way. And that's why I think that it's a good think to participate in a course like this where you can talk about it. [. . .] It [mindfulness practice] makes people slow down. For me it's purely physical. Pulse and system, but also lungs. The lung system. While what she's doing, that's awareness, you know soothing the mind* (Participant 8).
	Acceptance	Quote #4 *It is really nice that she [the instructor] says that now you have to lie down and you can't keep the thoughts away and that's completely alright, too. I can almost hear her say that it's okay. That has been lovely, and I really take that with me onwards* (Participant 7).
Practical aspects of attendance	Need for planning	Quote #5 *The advantage [of the tele-based format] was that you didn't have to leave the house at 10 am. [With tele-MBCT] the days started out nice and quietly. And then you could have lunch on time* (Participant 3).
	Willingness and ability to participate	Quote #6 *And I have been glad that it is home-based. Otherwise I wouldn't have been able to participate. So I would not have participated, if it had not been via the tele-monitor. [. . .] But I wanted to participate just as much as those people, who are still able to run around and play ball up against the walls and stuff like that. I just can't do that. And they [respiratory clinic] are not good at creating courses for people like me, who are too ill* (Participant 8).
Relational aspects	Negative aspects of tele-based format	Quote #7 Participant: *But opening up has been difficult. I only opened up 90%.* Interviewer: *Would it have been easier to completely open up, if you were sitting across from each other?* Participant: *Yes, I think I would get it all out then. And that has been a big thing for me.* Interviewer: *Is it because it makes you feel safer to physically sit across from a person?* *Participant: I think so. You'll be quick to figure out if it is someone you trust and if the chemistry is there* (Participant 5).
	Positive aspects of tele-based format	Quote #8 *Also gradually, as the session moved forward, then it was as if we really knew each other. As time passed. [. . .] That was amazing that you could get so close when other people were there. To expose yourself, when total strangers were listening* (Participant 2).
		Quote #9 *It is my experience that when you meet via the tele-monitor, [. . .] there is more respect for when the instructor says something than when you meet in person. When you meet in person people talk. But that is a normal interaction-thing. That if you feel like the instructor isn't saying something, that capture your attention, then you can spent the time whispering to your neighbour. You can't do that here. [. . .] People exhibit a different discipline and that means that you can be more effective in a 'distal learning universe' than if you meet in person* (Participant 8).
		Quote #10 *Well the upside of using the tele-monitor and of not being more people than we were, were that if someone raised their hand they got to say something. And it was not like the same people talked all the time, which is often the case on courses like these. There can be people who talk more and longer than others. But here it's limited. Also because we only were four. Then you can say something quickly. [. . .] And if you have a comment. You get to say that quicker as well, than in courses were you are face to face because such courses would probably include more people* (Participant 7).

1.5 points on the HADS was seen after tele-MBCT, representing a clinically relevant improvement (minimal clinically important difference (MCID) for the HADS = 1.5 points).[29] The average improvement corresponds to a medium effect size (Cohen's $d = 0.50$). Concerning physical health status, the average reduction of 1.5 points of the CAT score did not exceed the suggested MCID of two points.[30] However, the magnitude of the average improvement was medium-to-large ($d = 0.74$). For both outcomes, the differences failed to reach statistical significance, which is likely due to the small number of participants included in the present feasibility study. Looking at individual participants' change scores after tele-MBCT, only three participants reported improvements of HADS scores, and the average improvement described above appeared to be driven by a single participant (Participant 5) reporting a considerably large improvement. Five individual participants reported an improvement in CAT scores after the intervention and there were no apparent outliers. Summing up observations across individuals, it appears that it was not the same participants who experienced improvements both in psychological distress and physical health status. Moreover, individual participants with relatively high levels of psychological distress at baseline tended to report post-treatment improvements in HADS scores. In contrast, individual participants who reported improvement of physical health status after the intervention had relatively low levels of CAT scores before the intervention. Based on these findings, future efficacy studies should consider taking baseline levels of psychological distress and physical health status into account when including patients. When considering the qualitative results, participant narratives focused on changes in how they related to psychological and physical concerns and symptoms. Changes included (a) attentional flexibility, which also encompassed a broader awareness of both positive and negative aspects of life, (b) pausing and improved pacing of physical and mental activities and (c) increased acceptance of difficult thoughts and feelings. The ability to pause has previously been described as an important facet of optimal COPD management,[31] and attentional flexibility and acceptance are inherent concepts in the theory of how mindfulness-based intervention achieves its outcomes.[32] While this could be taken as suggesting that the participants may have learned to interpret their experiences through the narrative of mindfulness intervention, the accounts obtained in the present study may also provide indications of possible mechanisms of change to be tested further through mediational analyses in larger trials.

Attendance

The average attendance rate was considerably higher in the present study (7.5 out of eight sessions) than in a recently published randomised controlled trial (RCT) of face-to-face delivered MBCT (4.0 out of eight sessions).[9] Complementing these findings, the qualitative results suggest that the tele-based format met the participants' needs for being able to plan their day and improved their ability and willingness to participate, which resonates with the findings of a qualitative study of tele-delivered MBCT in cancer.[12] It is unknown, however, whether higher attendance rates in itself leads to improved outcomes. Reasons for non-attendance may vary, including perceptions of insufficient treatment gains or negative attitudes towards the intervention. Furthermore, adherence between sessions (e.g. engaging in home practice; integrating mindfulness in everyday life activities) may be more important for intervention outcomes than the number of attended treatment sessions.[23] Future studies should supplement measures of session attendance with between-session adherence to home practice as well as registering reasons for non-attendance. The inclusion rate of the present study was relatively low (17%). This finding should, however, be interpreted in the light of patients being recruited after having already participated in a RCT with frequent (five measurement points), comprehensive questionnaires and a long follow-up period (six months).[9]

Working alliance

The average perception of the therapeutic alliance in the present study (WAI: mean = 68.88, SD = 10.72) was comparable to the results obtained in an RCT of face-to-face MBCT using the same instructor as in the present study (WAI: mean = 63.67, SD = 13.63).[9] This finding supports the feasibility of tele-MBCT, as non-specific factors such as the working alliance have been suggested to be as important in technology-delivered interventions as in face-to-face therapy.[17] The qualitative results of the present study complement these findings by indicating that the tele-based format could negatively influence the personal contact with the instructor and between fellow participants, thereby possibly reducing trust and feelings of safety. Similar concerns related to issues of confidentiality and the impersonal nature of tele-based interaction have previously been reported.[12,33] It has been recommended that ethical and safety procedures should be considered and thoroughly described in future studies, e.g. by including face-to-face clinical interviews and monitoring of adverse events.[17,34] Moreover, participant narratives emphasised technical problems as interfering with the therapeutic relationship, which is in line with findings from other studies.[35] Technological issues should therefore be monitored and explored in more detail in future studies, e.g. paying special attention to patients living in remote areas where Internet connectivity may be relatively poor.

On the other hand, participants in the present study also reported positive influences of the tele-based format on relational aspects, including more efficient management of the group dynamics. Taken together, whether positively or negatively, the tele-based format appears to

influence relational aspects, which may in turn influence outcomes. Future studies are therefore recommended to explore the influence of relational aspects, e.g. by including measures such as the Distance Communication Comfort Scale.[36] In the longer term, as new generations are aging, the COPD population will be predominated by people who are more adept in tele-based communication, and relational aspects of tele-delivered psychological intervention may perhaps become less of an issue.[37]

Limitations

As this was a feasibility study, certain limitations should be taken into account when interpreting the results. First, due to the small sample size, the statistical power and precision is limited, and change scores (pre-post quantitative data) should not be interpreted as an indicator of treatment effect, but rather as a clinical summary of a number of individual cases. Second, the participants were a convenience sample recruited from the control arm of a larger randomised trial testing the efficacy of face-to-face MBCT,[9] and the participants in the present study may therefore have had a more positive attitude towards psychological intervention than COPD patients in general. Third, a control group was not included and we cannot, therefore, be certain whether similar changes over time could have occurred spontaneously. Fourth, questionnaire contents might have influenced participant narratives in the subsequent interview.

Perspectives

The results of the present study suggest that tele-MBCT could be a clinically feasible intervention in COPD. Future, large-scale randomised controlled trials are needed to explore the efficacy of tele-MBCT on the outcomes of psychological distress and physical health status in COPD. Based on the present findings, future studies could preferably include (a) inclusion criteria related to baseline levels of psychological distress and physical health status, (b) mediational analyses of MBCT-related factors, e.g. attentional flexibility and acceptance, and moderating influences of tele-related factors, e.g. distance communication and tele-presence, (c) monitoring of session attendance and between-session adherence as well as underlying reasons for (non-)attendance and (d) careful consideration and description of ethical and safety procedures. Finally, and on a more general level, the question of cost-effectiveness of telehealth in COPD remains unanswered,[15,38] and is of crucial relevance for the implementation of tele-delivered interventions such as tele-MBCT.[33] Therefore, future trials could be improved by including comprehensive short- and long-term health economic analyses, as well as delivering the intervention via a desktop-based application as a less costly alternative to the touch-screen computers installed in patients' homes for the purpose of the present study.

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Supplementary Material

Supplementary material is available for this article online.

References

1. From the Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2017. Available at: http://goldcopd.org.
2. Von Leupoldt A and Kenn K. The psychology of chronic obstructive pulmonary disease. *Curr Opin Psychiatry* 2013; 26: 458–463.
3. Pumar MI, Gray CR, Walsh JR, et al. Anxiety and depression: Important psychological comorbidities of COPD. *J Thorac Dis* 2014; 6: 1615–1631.
4. von Leupoldt A and Janssens T. Could targeting disease specific fear and anxiety improve COPD outcomes? *Expert Rev Respir Med* 2016; 10: 835–837.
5. Kabat-Zinn J. Mindfulness-based interventions in context: Past, present, and future. *Clin Psychol Sci Pract* 2006; 10: 144–156.
6. Johannsen M, O'Connor M, O'Toole MS, et al. Efficacy of mindfulness-based cognitive therapy on late post-treatment pain in women treated for primary breast cancer: A randomized controlled trial. *J Clin Oncol* 2016; 34: 3390–3399.
7. Piet J, Würtzen H and Zachariae R. The effect of mindfulness-based therapy on symptoms of anxiety and depression in adult cancer patients and survivors: A systematic review and meta-analysis. *J Consult Clin Psychol* 2012; 80: 1007–1020.
8. Beck JS. *Cognitive behavior therapy*. New York: The Guilford Press, 2011.
9. Farver-Vestergaard I, O'Toole MS, O'Connor M, et al. Mindfulness-based cognitive therapy in COPD: A cluster randomised controlled trial. *Eur Respir J* 2018; 51: 1702082.

10. Blackstock FC, ZuWallack R, Nici L, et al. Why don't our COPD patients listen to us? The enigma of nonadherence. *Ann Am Thorac Soc*. Epub ahead of print 16 February 2016; 13: 317–323.
11. Toivonen KI, Zernicke K and Carlson LE. Web-based mindfulness interventions for people with physical health conditions: Systematic review. *J Med Internet Res* 2017; 19: e303.
12. Compen FR, Bisseling EM, Schellekens MPJ, et al. Mindfulness-based cognitive therapy for cancer patients delivered via Internet: Qualitative study of patient and therapist barriers and facilitators. *J Med Internet Res* 2017; 19: 1–19.
13. Horton K. The use of telecare for people with chronic obstructive pulmonary disease: Implications for management. *Nursing* 2008; 16: 173–180.
14. McLean S, Nurmatov U, Liu JL, et al. Telehealthcare for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2012; 8: 1–51.
15. Goldstein RS. Telemedicine in COPD: Time to pause. *Chest* 2014; 145: 945–949.
16. García-Lizana F and Muñoz-Mayorga I. What about telepsychiatry? A systematic review. *Prim Care Companion J Clin Psychiatry* 2010; 12. DOI: 10.4088/PCC.09m00831whi.
17. Emmelkamp P. Effectiveness of cybertherapy in mental health: A critical appraisal. *Annu Rev Cybertherapy Telemed* 2011; 9: 6–9.
18. Riva G. Presence, actions and emotions: A theoretical framework. *Annu Rev Cybertherapy Telemed* 2011; 9: 2–5.
19. Bouchard S, Dumoulin S, Michaud M, et al. Telepresence experienced in videoconference varies according to emotions involved in videoconference sessions. *Annu Rev Cybertherapy Telemed* 2011; 9: 104–107.
20. Caffery LJ, Martin-Khan M and Wade V. Mixed methods for telehealth research. *J Telemed Telecare* 2017; 23: 764–769.
21. O'Cathain A, Murphy E and Nicholl J. The quality of mixed methods studies in health services research. *J Health Serv Res Policy* 2008; 13: 92–98.
22. Sale J and Brazil K. A strategy to identify critical appraisal criteria for primary mixed methods research. *Qual Quant* 2004; 38: 351–365.
23. Segal Z, Williams JMG and Teasdale J. *Mindfulness-based cognitive therapy for depression*. New York: Guildford Press, 2013.
24. Zigmond AS and Snaith RP. The Hospital Anxiety And Depression Scale. *Acta Psychiatr Scand* 1983; 67: 361–370.
25. Jones PW, Harding G, Berry P, et al. Development and first validation of the COPD Assessment Test. *Eur Respir J* 2009; 34: 648–654.
26. Tracey TJ and Kokotovic AM. Factor structure of the Working Alliance Inventory. *Psychol Assess* 1989; 1: 207–210.
27. Braun V and Clarke V. Using thematic analysis in psychology. *Qual Res Psychol* 2006; 3: 77–101.
28. Cutcliffe JR. Reconsidering reflexivity: Introducing the case for intellectual entrepreneurship. *Qual Health Res* 2003; 13: 136–148.
29. Puhan MA, Frey M, Büchi S, et al. The minimal important difference of the hospital anxiety and depression scale in patients with chronic obstructive pulmonary disease. *Health Qual Life Outcomes* 2008; 6: 46.
30. Kon SSC, Canavan JL, Jones SE, et al. Minimum clinically important difference for the COPD Assessment Test: A prospective analysis. *Lancet Respir Med* 2014; 2: 195–203.
31. Lomborg K and Kirkevold M. Curtailing: Handling the complexity of body care in people hospitalized with severe COPD. *Scand J Caring Sci* 2005; 19: 148–156.
32. Williams JMG. Mindfulness and psychological process. *Emotion* 2010; 10: 1–7.
33. Monnier J, Knapp RG and Frueh BC. Recent advances in telepsychiatry: An updated review. *Psychiatr Serv* 2003; 54: 1604–1609.
34. Guise V, Anderson J and Wiig S. Patient safety risks associated with telecare: A systematic review and narrative synthesis of the literature. *BMC Health Serv Res* 2014; 14: 588.
35. Radhakrishnan K, Xie B, Berkley A, et al. Barriers and facilitators for sustainability of tele-homecare programs: A systematic review. *Health Serv Res* 2016; 51: 48–75.
36. Schneider PL. Mediators of distance communication technologies in psychotherapy: Development of a measure, https://www.studio5d.com/paul/research/DCCS.html (1999, accessed 1 June 2018).
37. Heinzelmann PJ, Lugn NE and Kvedar JC. Telemedicine in the future. *J Telemed Telecare* 2005; 11: 384–390.
38. Udsen FW, Hejlesen O and Ehlers LH. A systematic review of the cost and cost-effectiveness of telehealth for patients suffering from chronic obstructive pulmonary disease. *J Telemed Telecare* 2014; 20: 212–220.

Appendix D: MBCT in COPD – Adjusted treatment manual

"Mindfulness-based cognitive therapy in chronic obstructive pulmonary disease: Adjusted treatment manual" by Ingeborg Farver-Vestergaard. Published as supplementary material to Paper 2.

Unit for Psychooncology and Health Psychology - Aarhus University and Aarhus University Hospital

Mindfulness-based cognitive therapy in chronic obstructive pulmonary disease

Adjusted treatment manual based on ”Mindfulness-based cognitive therapy for depression” by Segal, Teasdale and Williams

Ingeborg Farver-Vestergaard

Contents

Note

This adapted manual should not be considered a "stand-alone", and can only be read a supplement to the original treatment manual developed by Segal, Williams and Teasdale (2013).

References

Bartley, T. (2012). *Mindfulness-based cognitive therapy for cancer*. Oxford: Wiley-Blackwell.

Kabat-Zinn, J. (1990). *Full catastrophe living: Using the wisdom of your mind to face stress, pain and illness*. New York: Dell.

Remen, R. N. (1996). *Kitchen table wisdom: Stories that heal.* New York: Riverhead Books.

Segal, Z., Williams, J. M. G., & Teasdale, J. (2013). *Mindfulness-based cognitive therapy for depression*. New York: Guildford Press.

Sessions agendas

Session 1 – ”Awareness and automatic pilot”

THEME

On automatic pilot, it is easy to drift into ”doing” mode and negative thought patterns concerning the negative in life (e.g. the COPD diagnosis, breathlessness, guilt etc.) that can tip us into vicious cycles of anxiety, breathlessness, inactivity, bad mood etc. Habitual doing mode also robs us of our potential for living life more fully. We can transform our experience by *intentionally* paying attention to it in particular ways (”being” mode). We begin to practice stepping out of automatic pilot by paying attention intentionally (mindfully) to eating, to the sensations of the body and to aspects of everyday practice.

AGENDA

1. **Welcome: INTRODUCE THE ELEMENTS OF THE COURSE: EXERCISES, INQUIRY, TEACHING, HOMEWORK (draw parallels to physical exercise, fx it’s difficult to explain how to do it, you have to learn it by doing it)**
   Underscore the intention/compassion: e.g. we often take care of our close ones, also on days where we don’t really feel like doing what it takes – we need to practice doing so in relation to ourselves as well. I will do as much as I can as teacher, but you have to do the most yourselves. Therefore it is very important that you come to the training, and that you do your homework. In the beginning ”you don’t have to like it, you just have to do it” (Jon Kabat-Zinn).

   The teacher(s) introduces him-/herself

2. **Ground rules:** Turn off your cell phone
   No breaks, so feel free to go to the toilet etc. whenever
   Confidentiality

3. **Discuss in pairs**: a) What do you think ”mindfulness” is? b) What do you hope to gain from this course? → **in class**: people share their thoughts and the teacher link to the theme of the session if relevant.

4. **“The raisin exercise”** + inquiry

5. **“The body scan”** + inquiry (Remember to say before the guiding that it is okay to cough during the exercise. People can choose whether want to sit up or lay down on a mat)

6. **Distribute CDs and programs** and explain how to use the CD and program for home pratice

7. **Home practice assignment**- “The body scan” every day + mindfulness of a routine activity

8. **Discuss in pairs**: a) timing of home practice, b) what obstacles may arise, c) how to deal with them (can be left out if there is not enough time)

PLANNING AND PREPARATION

- Raisins to distribute during the raisin exercise
- CDs and programs
- Meditation bells
- Attendance list
- Write the title of the session on the blackboard, but not until the theme comes up in inquiry or class discussion.

Deviations from the original MBCT program

- The participants do not introduce themselves: The participants know each other already, because the MBCT program is an add-on to their rehabilitation program.
- Be very specific: The participants need the information and guidings to be very specific. So keep that in mind when teaching and guiding. For example, use only the word ”awake” as the opposition of ”falling asleep”, not the more abstract use of the word as synonymous to ”alert” or ”attentive”.

Session 2 – "Living in our heads"

THEME

In doing mode we "know about" our experience only indirectly, conceptually, through thought. This means we can easily get lost in negative thought patterns (rumination) and worry. Mindfulness of the body provides an opportunity to explore a new way of knowing directly, intuitively – "experientially". Experiential knowing is a way to be aware of unpleasant experiences without getting lost in negative thought patterns. Already, most participants will be experiencing some difficulties in their practice. These difficulties offer precious opportunities to practice letting go of thinking and to connect with direct awareness of the body. Three themes should be introduced 1) from doing- to being-mode (Body scan home practice and Awareness of heartbeat and blood flow exercise), 2) become aware of barriers (via inquiry/feedback), 3) become aware of negative thought patterns (via inquire/feedback and "Walking down the street"-exercise)

AGENDA

1. **Sitting meditation part 1 "Awareness of the heartbeat and the blood flow"** + inquiry (Remember to say before the guiding that it is okay to cough during the exercise)

2. **Home practice review** (body scan, mindful routine activity)

3. **"Thoughts and feelings exercise" ("Walking down the street")** – see page 7 + cognitive diamond (p. 8)

4. **Introduce the "Pleasant experiences calendar" (See Handouts section)**: let one or two of the participants give a few examples and go through them on the blackboard, to make sure everybody has understood how to do it at home during the following week.

5. **Home practice assignment** (underscore the importance of home practice)
    - Sitting meditation part 1 "Awareness of the heartbeat and the blood flow": every day
    - Complete the "Pleasant experiences calendar" (See handouts section)
    - Mindfulness of a routine activity

PLANNING AND PREPARATION

- Bring copies of the Pleasant Experiences Calendar

THOUGHTS AND FEELINGS EXERCISE (”WALKING DOWN THE STREET”)

1. This exercise is a little different from the mindfulness exercises you already know from the CD. But I will invite you to take a comfortable, upright position. Close your eyes and imagine the following scenario:

> ”You are walking down the street,… and on the other side of the street you see some-
>
> Body you know… You smile and wave… The person doesn’t react and walks by”

2. Bring awareness to your experience right now:
   What are you **thinking** of?

   What **feelings** arise?

   Are there any **body sensations**?

   What do you feel like **doing**?

3. Now open your eyes.

4. And I will ask you to describe your reactions in this exercise: What thoughts came up (or maybe pictures in your head)? What feelings? What happened in your body? Were there anything you felt like doing?

5. Write the reactions of the participants on the blackboard as they speak. Use the cognitive diamond as the framework on the board.

Let the participants sum up the meaning with the exercise themselves by asking for example:

”What do we make of this?” ”What do you think the point of doing this exercise is?”

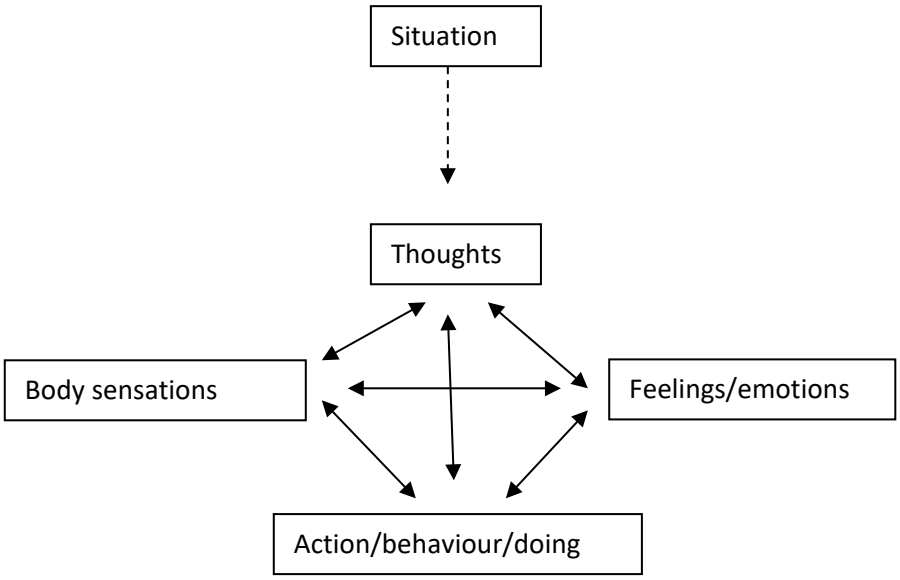
- Make sure you validate all that is being said.
- If possible, draw parrallels to the theme, and make sure the participants understand it (be very clear and concrete, the less complicated the better)

The key message of the exercise:

The same (objective) situation can result in many different thoughts, interpretations and therefore also many different feelings/emotions, body sensations and actions/behaviour. Thoughts, feelings/emotions, body sensations and behaviour is closely connected and are influencing each other all the time.

> Thoughts about a situation are often automatic, and we are often not aware of them.
>
> Nevertheless they influence what we feel and what we do.

THE COGNITIVE DIAMOND:



Deviations from the original MBCT program

- Awareness of the blood flow instead of the breath. The breath and breathing is often the trigger of frustration and anxiety in this group. Therefore it is inappropriate and deviant from the purpose of the MBCT-program to use the breath as ”an anchor” to ”gather the scattered mind”. The blod flow is (like the breath) another physical mechanism that is with us all the time.
  That having been said, it is important that the breath is not ignored or problematised. We focus on the breath during this program as we would focus on any other uncomfortable thought or body sensation (bring awareness to it -> accept –> let it go -> gather focus around the blood flow/grounding/body)
- The Body scan is not guided in this session, due to the fact that too many elements introduced in one session is too much for these participants to handle. But make sure the experience from the Body scan home work is shared properly in class (linking to this session’s theme)
- The Body scan is not part of the home work for this week. The complexity of having many different elements as part of the home work is to difficult for these participants to handle.
- The cognitive diamond can be used as a model to sum up the participants’ experiences from the ”Walking down the street” exercise. It is a relatively simple model, which is ideal for this group.
- The example in the Pleasant Experience Calendar is changed so it corresponds to everyday life of these participants.

Session 3 – "Gathering the scattered mind"

THEME

The mind is often scattered and lost in thought because it is working away in the background to complete unfinished tasks and strive for future goals. Instead, we need to find a way to intentionally "come back" to the here and now. The blood flow and the body offer and ever-present focus on which we can reconnect with mindful presence, gather and settle the mind, and ease ourselves from doing into being. Classic problem solving (by thinking) often does not help when it comes to feelings/emotions – and breathlessness.

AGENDA

1. **Sitting meditation part 1 and 2 "Awareness of heartbeat, blood flow and body**" (awareness of blood flow and body →how to respond to intense physical sensations) + inquiry

2. **Home practice review**
   (Sitting meditation part 1 "Awareness of heartbeat and blood flow", mindfulness of routine activity)

   Review the Pleasant Experiences Calender→ <u>the participants share and the teacher sum up on the blackboard</u>

3. **Read "Surprised by meaning" in *Kitchen table wisdom (Remen (1996))*** (as an example of focusing on the here and now, noticing positive experiences) + interpretation (let the participants give their interpretation →link to the theme)

4. **The 3-minute "breathing space**" + inquiry (if there is enough time: how can we plan our day to do the breathing space three times per day) Focus on how the breathing space can be used to get as much out of positive experiences as possible.

5. **"Mindful stretching"**(REMEMBER: it is important to be aware of and respect the limit of your body – draw parallels to the physical training in the rehabilitation program) + inquiry

6. **Unpleasant experiences calendar** (See handouts section): let one or two of the participants give a few examples and go through them on the blackboard, to make sure everybody has understood how to do it.

7. **Home practice assignment**
   - "Mindful stretching" every day
   - Unpleasant experiences calendar
   - "3 minute breathing space" 3 times per day on pre-scheduled times.

PLANNING AND PREPARATION

- Bring copies of the Unpleasant Experiences Calendar
- Bring the book "Kitchen table wisdom" by Rachel N. Remen (1996)

Deviations from the original MBCT program

- Awareness of the heartbeat and blood flow instead of the breath. The breath and breathing is often the trigger of frustration and anxiety in this group. Therefore it is inappropriate and deviant from the purpose of the MBCT-program to use the breath as ”an anchor” to ”gather the scattered mind”. The blod flow is (like the breath) another physical mechanism that is with us all the time. That having been said, it is important that the breath is not ignored or problematised. We focus on the breath during this program as we would focus on any other uncomfortable thought or body sensation (bring awareness to it -> accept –> let it go -> gather focus around the blood flow/grounding/body)
- Reading stories: These participants need as many examples/illustrations of the program as possible. Reading stories that deliver the message of the program is helpful. Stories from the book ”Kitchen Table Wisdom” by Rachel N. Remen are read to the participants at selected sessions throughout the program.
- Mindful stretching: the exercise has been altered to fit the bodily condition of these participants (see manuscript)
- The 3-minute breathing space: the overall format of this exercise is the same as in the original program, but the content has been changes in step 2: The focus is on the feet’s connection to the ground instead of the breath.

Session 4 – "Recognizing aversion"

THEME
The skill of "coming back" needs to be complemented by seeing more clearly what "takes us away" into doing, rumination, mind wandering and worry. We being the experiential investigation of *"aversion"*, the mind's habitual reaction to unpleasant feelings and sensations, driven by the need not to have these experiences, which is at the root of emotional suffering in relation to a chronic illness. Mindfulness offers a way of staying present by giving another way to view things: It helps us take a wider perspective and relate differently to experience.

Be aware that we have a tendency to want the pleasant and avoid the unpleasant; mindfulness is an alternative to *both* of these tendencies.

AGENDA

1. **Sitting meditation part 1, 2 and 3 "Awareness of blood flow, body, sounds and thoughts"** + inquiry

2. **Home practice review** (Mindful stretching; 3-min breathing space x3)
   Review the Unpleasant Experiences Calendar → the participants share and the teacher sum up on the blackboard (draw parrallels to the automatic thoughts that can arise ("**Automatic thoughts exercise**") -> "when you are in a bad mood, how often do these thoughts arise?" + "when you are in a good mood, how often do these thougths arise?"

3. **"3-min breathing space" (p. 11)** (introduce it this time as a pause when something uncomfortable happens) + inquiry. The exercise illustrates that it is a good way to follow up on uncomfortable experiences (because it follows the discussion of the Unpleasant Experiences Calendar)

4. **Home practice assignment**
   - Sitting meditation part 1, 2 and 3 every day.
   - 3-min breathing space (everytime something uncomfortable happens).

AUTOMATIC THOUGHTS EXERCISE

Examples of "Automatic thoughts" (follow-up on Unpleasant Experiences Calendar if relevant)

1. "Why can't I ever succeed?"
2. "I'm so disappointed in myself"
3. "Nothing feels good anymore"
4. "I can't get started"
5. "I feel so helpless"

Can you recognize any of these thoughts from your own life? Which ones?

- When you are in a bad mood, how often do these thoughts arise? How much do you believe them/how convincing are they?
- When you are in a good mood, how often do these thoughts arise? How much do you believe them/how convincing are they?

Summing up on Automatic thoughts exercise: When we are challenged physically and mentally, it is normal to have these thoughts at times. And on days where we feel low, thoughts like these often feel like ”the truth” about us. But these thought are actually symptoms of bad mood or anxiousness, just like a high temperature is a symptom of flu. Becoming aware, through mindfulness, that they are just ”the voice of a bad mood/anxiety speaking” allows us to step back from them and begin to choose whether to take them seriously or not. THE MEANING IS NOT TO IGNORE THE THOUGHTS, BUT TO BE AWARE OF THEM IN ANOTHER WAY THAT THE ONE WE ARE USED TO. Perhaps, in fact, we can learn to simply notice them, acknowledge their presence, and let them go. You can do a 3-min breathing space when becoming aware of negative thoughts. (Guide a breathing space in class to illustrate your point)

Deviations from the original MBCT program

- “Walking meditation” is moved to session 5. Walking often result in breathing difficulties among the participants (draw parallels to physical exercises in the rehabilitation program). Therefore it is relevant to introduce the walking meditation in session 5, where we begin to focus on being with the difficult.
- The “Automatic thoughts” exercise (which is very depression-specific) is only introduced indirectly as part of the follow-up on Unpleasant Experiences Calendar.
- Do not read the poem “Wild geese”. It is too abstract for these participants.

Session 5 – "Allowing/Letting be"

THEME

Relating differently to unpleasant feelings and sensations – allowing things to be as they already are. We can disempower aversion by intentionally bringing to all experience a sense of "allowing" it to be, just as it is, without judging it or trying to make it different. Such an attitude of acceptance embodies a basic attitude of kindness to experience. From this clear seeing we can choose what, if anything, needs to change. It is important that it is clear that from this session on, we begin to focus on being with the difficult (rather than "just" practicing being mindful).

AGENDA

1. **"Being with the difficult"** (20-30 min)→ inquiry

2. **Home practice review** (sitting meditation part 1, 2 and 3; 3-min breathing space when unpleasant).

3. **Read "The story about the king and his three sons**" (the MBCT-manual, page 269 + interpretation (let the participants give their interpretation →link to the theme)

4. **"Walking meditation"** (see the format of the exercise below "Deviations from the original MBCT program)

5. **"3-min breathing space"** when experiencing something uncomfortable + inquiry

6. **Home practice assignment**
   - "Being with the difficult" meditation every day
   - 3-min breathing space when experiencing something difficult

Deviations from the original MBCT program

- The walking meditation has been moved from session 4 to this session. The instructions are as follows: while walking (first slowly, then faster and faster) bring awareness to **1) sensations in the feet and legs,** then **2) expanding awareness to encompass the whole body**, and then **3) expanding your awareness again to the space around you and your body walking here.** Include this instruction from time to time during the walking meditation: "If your awareness wander, perhaps to you breath, which might have become shorter, then simply notice that this is what is happening, explore the sensations, and then let it go and move your attention back to X" (in the same way as when paying attention to the difficult in the sitting meditation).
- Read the story of the king and his three sons instead of Rumi's poem, which is too abstract for these participants.

Session 6 – "Thoughts are not facts"

THEME

Relating differently to thoughts. We free ourselves from the ruminative doing mode when we clearly see negative moods as passing states of mind, and negative thinking as the distorted products of those mind states. It is enormously liberating to realize that our thoughts are merely thoughts, even the ones that say they are not, and to recognize the contexts out of which they are born. Introduce the negative thoughts funnel (from the original MBCT-manual).

AGENDA

1. **"Sitting meditation part 1, 2 and 3"**. Awareness of blood flow, body, sounds, thoughts and how we relate emotionally to the thoughts that arise + inquiry.

2. **Home practice review** ("Being with the difficult" meditation, 3-min breathing space).

3. **On the blackboard, "John was on his way to school" (the original MBCT-manual, page 299)**: John was on his way to school; He was worried about the math lesson; He was not sure he could control the class again today; It was not part of a janitor's duty. Write each sentence one after another on the blackboard -> interpretation (let the participants give their interpretation →link to the theme)

4. **"Mood, thoughts and alternative viewpoints" exercise** (Our mood/feelings can influence how we think about/interpret a situation, p. 15)

5. **"3-min breathing space"** as the first step when thoughts take over + inquiry. MENTION: daily practice is important to shift from doing- to being-mode (e.g. by taking a 3-min breathing space)

6. **Mention preparation for end of course** – we will start talking about how to use what we have learned when the course is over. Link to next activity.

7. **Discuss "unpleasantness" signals** → discuss in pairs –> share in group (use the negative thought funnel or the cognitive diamond to sum up. (REMEMBER: introduce **"My personal warning system**", (See handouts section)

8. **Home practice assignment**
   Make mindfulness part of your life, a way of life, rather than a short therapeutical intervention. It is a long-term method to improve quality of life and prevent bad mood and anxiety. It is the "everyday-ness" of the training that is important.

    a. Choose whatever meditation you want every day
    b. 3-min breathing space when something uncomfortable arise
    c. Notice warnings of bad mood/anxiety/"unpleasantness" -> fill in "My personal warning system"

”Mood, thoughts and alternative viewpoints” exercise:

1. ”You are feeling down because you’ve just had a quarrel with a friend at a dinner-party. Shortly afterward, you bump into another friend at the party, and he or she rushes off quickly, saying he or she could not stop. What would you think?”

   DISCUSS (USE BLACKBOARD TO NOTE REACTIONS)

2. ”You are feeling happy because you have just been praised for good work you’ve done at the dinner party. Shortly afterward, you bump into another friend at the party, and he or she rushes off quickly, saying he or she could not stop. What would you think?”

   DISCUSS (USE BLACKBOARD TO NOTE REACTIONS)

   interpretation (let the participants give their interpretation →link to the theme)

Deviations from the original MBCT-program

- The content of the ”Mood, thoughts and alternative viewpoints” exercise has been adapted to these participants

Session 7 – "How can I best take care of myself?"

THEME

Using skillful action to take care of ourselves in the face of lowering mood/anxiety etc. We can lift bad mood and anxiousness by intentional skillful action. We can respond more promptly and effectively to lowering mood by learning to recognize our personal pattern of warning signs. After taking a breathing space, we kindly take care of ourselves by acts that give pleasure or a sense of mastery, or provide a clear focus for mindfulness.

AGENDA

1. **"Sitting meditation" part 1, 2 and 3**. Awareness of blood flow, body; noticing how we relate to our experiences through the reactions we have to whatever thoughts, feelings or body sensations arise within the practice, noting their effects and reactions to them, on the body + inquiry.

2. **Home practice review**
   (Choose whatever track on the CD you want every day + **"My personal warning system"** (See handouts section) -> sum up on the blackboard

3. **"Activities and mood exercise"** (See handouts section) (guide it as a meditation practice + the participants fill in the list, see handout for this session) –> the negative thought funnel/exhaustion funnel (p. 359 in the original MBCT manual). REMEMBER: keep the exercise as simple as possible

4. **"The action plan", plan how to best schedule activities for when mood threatens to overwhelm**: introduce the action plan (See handouts section) –> the participants work in pairs -> sum up on blackboard

5. **Remember to tell the participants:** 3-min breathing space as the "first step" before choosing whether to take mindful action. Write on blackboard: 1. becoming aware of what is present? 2. 3-min breathing space 3. choose mindful action (which can also be doing nothing)

6. **"3-min breathing space"** – inquiry

7. **Read: "I never promised you a rose garden" from *Kitchen Table Wisdom (Remen (1996))*** -> interpretation (let the participants give their interpretation →link to the theme)

8. **Home practice assignment**
   a. Select, from all the different forms of practice, a pattern you intend to use on a regular basis
   b. 3-min breathing space when something uncomfortable arise
   c. Fill in the Action Plan (See handouts section)

PREPARATION AND PLANNING

- Bring the book "Kitchen Table Wisdom"
- Bring handouts for the activities exercise

Deviations from the original MBCT-program:

d. The activities exercise has been changed to a more simple version. ”Nourishing” (N) activities are called ”+” activities and ”depleating” (D) activities are called ”-” (minus) activities. The ”mastery” activities are left out.

e. The exhaustion funnel is relatively complex as it is described in the original manual. Therefore, the negative thought spiral can be mentioned, but do not go through all of it explicitly.

Session 8 – "Maintaining and extending new learning"

THEME

Planning a new way of living. Maintaining and extending a more mindful and caring way of being requires clear intention and planning. It is helpful to link intentions for regular mindfulness practice to a personally significant value or positive reason for taking care of oneself. "What have you gotten out of this program?/The most important thing you have learned in this program?"

AGENDA

1. **"The body scan"** + inquiry
2. **Home practice review**: (including warning system and action plan (See handouts section))
3. **Review of the whole course:** what has been learned?
4. **Distribute sheets with the stories that have been read during the program (as mementos of the course):** The participants each mention the most important thing they have gotten out of this course (one word). -> Sum up on blackboard
5. **End of class:** participants wishing each other well

PREPARATION AND PLANNING

- Bring sheets with stories that have been read in class throughout the course

Handouts

Pleasant experiences calendar

Be aware of pleasant event *at the time it is happening*. Use the following questions to focus your awareness on the details of the experience as it is happening. Write it down later.

What was the experience	**How did your body feel, in detail, during this experience?**	**What moods and feelings accompanied this event?**	**What thoughts went through your mind?**	**What thoughts are present when writing this down?**
Example: Heading home after grocery shopping – stopping, hearning a bird sing.	*Lightness across the face, aware of shoulders dropping, uplift of corners of mouth.*	*Relief, pleasure*	*"That's good," "How lovely" "It's so nice to be outside"*	*"It was such a small thing, but I'm glad I noticed it"*
Day 1				
Day 2				
Day 3				
Day 4				
Day 5				
Day 6				

Unpleasant experiences calendar

Be aware of an unpleasant experience *at the time it is happening*. Use these questions to focus your awareness on the details of it as it is happening. Write it down later.

What was the experience?	**How did your body feel, in detail, during this experience?**	**What moods and feelings accompanied this event?**	**What thoughts accompanied this event?**	**What thoughts are in your mind now as you write this down?**
<u>Example:</u> Waiting for the cable company to come out and fix our line. Realize that I am missing an important meeting at work.	*Temples throbbing, tightness in my neck and shoulders, pacing back and forth.*	*Angry, helpless*	*"Is this what they mean by service?" "They don't have to be responsible, they have a monopoly"*	*"I hope I don't have to go through that again soon"*
Day 1				
Day 2				
Day 3				
Day 4				
Day 5				
Day 6				

List of everyday activities

Activities	+ or - ?

A plan for my future mindfulness practice, which I will try out over the next week**.**

Long meditations (e.g. Body Scan or Awareness of Blood Flow and Body"):

Short meditations (e.g. 3-minute breathing space):

"Informal" mindfulness (e.g. mindful eating):

Activities and mood exercise – teacher version

Exercise to explore links between activities and mood

Exercise 1A:

Guiding:

Grounding, ”Close your eyes and bring your attention to what you do over the course of a normal day…

- What is a typical day like for you…? What happens…?

- For example, what happens in the morning…? Perhaps activities such as getting out of bed, dressing, making coffee, having break-fast etc…

- And what happens in the afternoon…? Perhaps activities such as spending time in the garden, meeting friends or family, cleaning the house etc….

- And then what happens in the evening..? Perhaps activities such as cooking dinner, doing the dishes, watching TV, reading a book, go-ing to bed, etc…

Now open you eyes….”

Instruct the participants to write down a list of the activities they do on a normal day (see the list on next page). ”

List of everyday activities

Activities	+ or - ?

After having completed the list of activities…:

1) …mark the activities that lift your mood and gives energy with a ”+”.

2) …mark the activities that lowers your mood and/or takes away energy with a ”-”.

Please note that a certain activity can be both ”+” and ”-”

Exercise 1B:

Ask the participants the following questions and discuss and sum up on the blackboard.

1. What activities have you written down? (-> write them on the board)
2. Are they ”+” or ”-” (-> mark the activities with an ”+” and/or ”-”)
3. How is the balance between the ”+” and ”-” activities?
4. How can you learn to be more aware of the ”+” activities?
5. How can you change things to have more ”+” activities?
6. How can you learn to be more aware of the ”-” activities?
7. How can you change things to make the ”-” fill up less of your day/thoughts/life?
8. How can you best handle the ”-” when they happen or you start thinking about them?

The key thing is to be aware that you only have a certain amount of energy for one day. It is very important that you are aware of your body and mind’s limits. -> that can be done through mindfulness/awareness and compassion/being kind to yourself.

Exercise 2:

Consider how you can use what you have learned in this program in the future. Be realistic.

Make a plan that you can try out over the next week before we meet for the last time:

Long meditations (e.g. the Body Scan or Awareness of Blood Flow and Body):

Short meditations (e.g. 3 min breathing space):

”Informal” mindfulness practice (e.g. mindful eating, mindful routine activity):

Discuss on blackboard.

My personal warning system

This worksheet offers an opportunity to increase your awareness of what happens for you when vicious cycles of anxiety, breathlessness, inactivity, bad mood etc. begin to appear. The aim is, carefully and with curiosity, to investigate the thoughts, feelings, body sensations, and patterns of behavior that tell you that your mood is starting to drop.

What triggers vicious cycles of anxiety, breathlessness, inactivity, bad mood etc. for you?

- Triggers can be external (things that happen to you) or internal (e.g. thoughts, feelings, memories, concerns, body sensations).
- Look out for small triggers as well as large ones – sometimes something that appears quite trivial can spark a vicious spiral.

Are there any old habits of thinking or behavior that might unwittingly keep you stuck in these vicious cycles (e.g. ruminating, trying to suppress or turn away from painful thoughts and feelings and body sensations, struggling with it instead of accepting and exploring it)?

My personal action plan

Last week, you wrote down what are your personal warning signals of vicious cycles of anxiety, breathlessness, inactivity, bad mood etc. On this sheet, we consider how you might skillfully respond when you find yourself in this position.

Ask yourself: In the past, what have you noticed that helped when you were becoming scared, inactive, depressed etc.? How could you respond to the turmoil of thoughts and feelings without adding to it? How can you best care for yourself when something bad happens (e.g. things that would soothe you, activities that might nourish you, people you might contact, small things you could do to respond wisely to distress)?

Now write down suggestions to yourself for an action plan that you can use as a framework for coping, once you or your friends/family have noticed early warning signs (remember to address the frame of mind that you might be in at the time; e.g. “I know you probably will not be keen on the idea but I think that, nonetheless, it is very important that you…”). For example, you might put on a body scan or sitting meditation recording; remind yourself of what you learned during the class that was helpful then; take frequent 3-min breathing spaces etc. It may be helpful to remind yourself that what you need at time of difficulty is no different from what you have already practiced many times throughout this course.

Meditation guides

The Raisin Exercise

[Same guiding as in the original MBCT-program, p. 112-113]

The Body Scan

Durations: approximately 25-30 minutes

1. [Bells]

2. Inviting you to lie down on your bed or a mat on the floor or sit up in a chair where your back can be supported, making yourself comfortable, in a place where you will be warm and undisturbed. Allowing your eyes to close gently. Feeling your feet's contact with the ground, the sensation of contact with something solid, firm, persistent, no matter what else is going on in your body or mind right now.

3. Taking a few moments now to get in touch with the fact that your heart is beating – sensing it directly, perhaps in the chest region, or just imagining the heartbeat. When you are ready, bring your awareness to the physical sensations in your body, especially to the sensations of touch or pressure, where your body makes contact with the floor or bed. Getting a sense of the heart providing blood to the whole of the body – providing softness and warmth, making the body sink a little deeper into the bad or chair.

4. Remind yourself of the intention of this practice. Its aim is not to feel any different, relaxed or calm; this may happen or it may not. Instead, the intention of the practice is, as best you can, to bring awareness to any sensations you detect, as you focus your attention on each part of the body in turn.

5. Now bring your awareness to the physical sensations in the chest area. Noticing what the breath feels like in this moment, without having to change or fix anything. And see if you can also notice the sensations of your heart beating in the chest area – rapidly or slowly, heavily or shallow? Take a few minutes to feel the sensations of your heartbeat.

6. Having connected with the sensations in the chest region, bring the focus or "spotlight" of your awareness down the left leg, into the left foot, and out to the toes of the left foot. Focus on each of the toes of the left foot in turn, bringing a gentle curiosity to investigate the quality of the sensations you find, perhaps noticing the sense of contact between the toes, a sense of tingling, warmth, or no particular sensation.

7. When you are ready, feel or imagine the blood flowing from the heart and down into the abdomen, into the left leg, the left foot, and out to the toes of the left foot. Providing energy, softness and warmth to this area of your body. As best you can, continue this for a few moments, feeling or imagining the blood running all the way from the heart down to your toes – softening, warming. Perhaps feeling the blood flow as a pulse, a tingling, or whatever you are sensing right now. It may be difficult to get the hang of this – just practicing this as best you can, approaching it playfully.

8. Now, when you are ready, let go of awareness of the toes, and bring your awareness to the sensations on the bottom of your left foot – bringing a gentle, investigative awareness to the sole of the foot, the instep, the heel (e.g. noticing the sensations where the heel makes contact with the bed or ground). Experiment with feeling the blood flowing in this area while exploring the sensations of the lower foot.

9. Now allow the awareness to expand into the rest of the foot – to the ankle, the top of the foot, and right into the bones and joints. Then, feeling or imagining how the blood can transport your awareness from the left foot to the lower left leg – the calf, shin, knee, and so on, in turn.

10. Continue to bring awareness, and a gentle curiosity, to the physical sensations in each part of the rest of the body in turn – to the upper left leg, the right toes, right foot, right leg, pelvic area, back, abdomen, chest, fingers, hands, arms, shoulders, neck, head, and face. In each area, as best you can, bring the same

detailed level of awareness and gentle curiosity to the body sensations present. In each area, getting a sense of the blood flowing into the area, providing energy, softness, warmth.

11. When you become aware of tension, or of other intense sensations in a particular part of the body – perhaps uncomfortable sensations related to the breath – you can imagine how the blood flows into these areas, providing exactly what the area needs to restore: energy, softness, warmth.

12. The mind will inevitably wander away from the body from time to time. That is entirely normal. It is what minds do. When you notice it, gently acknowledge it, noticing where the mind has gone off to, and then gently return your attention to the part of the body you intended to focus on.

13. After you have “scanned” the whole body in this way, spend a few minutes being aware of a sense of the body as a whole, and of the blood flowing freely in the body.

14. If you find yourself falling asleep, you might find it helpful to prop your head up with a pillow, open your eyes, or do the practice sitting up rather than lying down.

15. [Bells]

Sitting meditation part 1: Awareness of the heartbeat and the bloodflow

Duration: approximately 10-15 minutes

1. [Bells]

2. Finding a comfortable upright position, sitting on a firm, straight-back chair or a stool. If you use a chair, it is very helpful to sit away from the back of the chair, so that your spine is self-supporting.

3. Allow your back to adapt an erect, dignified and comfortable posture. Place your feet flat on the floor, with your legs uncrossed. Gently closing your eyes.

4. Bringing awareness to the sensations in the body as you are sitting here right now. Perhaps the sensations of contact between your body and the chair, and between your feet and the floor. Feeling your feet's contact with the ground, the sensation of contact with something solid, firm, persistent, no matter what else is going on in your body or mind right now. Spend a minute or two exploring these sensations, just as in the body scan.

5. Now becoming aware of the fact that your heart is beating. Maybe sensing the beating of the heart directly…in the chest region perhaps. Or if you can't feel your heart beating right now, simply knowing that your heart is beating, and being aware of that.

6. The heartbeat is our lifelong companion, and it provides blood, energy, warmth to our bodies all the time – whether we are aware of it or not. The blood flows from the heart and upwards, through shoulders, neck and head. Outwards through arms and hands. Downwards through the abdomen, legs and feet.

7. Now bringing awareness to the sensations of blood flowing through your body.

8. What does the blood flow feel like? Perhaps like a wave through certain areas in your body? Perhaps a throbbing sensation? A fluttering or tingling? Warmth? There is no right way or wrong way to feel. Just curiously exploring what it feels like for you right now.

9. Perhaps you cannot feel the blood flowing in your body right now, and if that is the case, then that's completely fine. Then simply noting "I cannot feel the blood flowing in the body right now".

10. Becoming aware of the changing sensations as the blood flow through your body from moment to moment.

11. Our heart provides fresh and clean blood for our whole body - flowing through the shoulders, neck and head…the arms and hands…the abdomen, legs and feet.

12. And as best you can, letting whatever is present be there. Not having to change or fix anything. Simply sensing or imagining how the heart provides energy, softness and warmth to all areas of the body, moment after moment.

13. Sooner or later you will notice that your mind has been wandering. Thinking, planning. That is not a problem at all, that is what minds do. It is not a mistake or a failure.

14. When you notice that your awareness is no longer on the sensations of blood flowing in your body, gently congratulate yourself – you have come back and are once more aware of your experience! You may

want to acknowledge briefly where the mind has been. The, gently escorting awareness back to a focus on the sensations of blood flowing through your body.

15. Perhaps exploring where in the body you feel the bloodflow most vividly. Maybe that is a throbbing in the head? A tingling in the hands? A wave in the feet or the legs? Or somewhere else.

16. Filling this part of your body with awareness. Exploring the sensations in this area. What does it feel like in this area? Throbbing, jitteriness, warmth? Do the sensations change from moment to moment, or do they stay the same?

17. As best you can, bringing kindness and patience to yourself when you discover that your mind has wandered away. Seeing the mind wandering as an opportunity to get to know your mind better, not a mistake or a failure.

18. Every time your mind wanders, the instruction is simply to notice, acknowledge where your mind went to, and escorting it back to the area of the body where you feel the blood flow most vividly.

19. Remember that the purpose of this exercise is not to get rid of thoughts, but to bring full awareness to whatever is present right now, and to bring back awareness again and again whenever the mind has wandered…Reminding ourselves that no matter what is going on in our lives, our heartbeat is our constant companion, proving energy, softness and warmth.

20. So every time the mind wanders, noticing and escorting the attention back to the area of the body where you feel the bloodflow most vividly.

21. And now, expanding awareness to take in the whole body and the sensations of blood flowing through the whole body. Upwards through shoulders, neck and head. Outwards through arms and hands. Downwards through the abdomen, legs and feet. The blood providing new energy, softness and warmth for the whole body.

22. [Bells]

Sitting meditation part 2 – Awareness of the body

Duration: approximately 10 minutes

1. [Start this meditation with Sitting meditation part 1]

2. While still aware, in the background, of the blood flowing in the body, change your primary focus, so that you become aware of a sense of the body as a whole and of the changing patterns of sensation throughout the body. You may find that you get a sense of the movements of the blood throughout the body; the blood filling up the whole body, reaching all parts and edges.

3. The mind will wander repeatedly away from the body sensations – this is natural, to be expected, and in no way a mistake or failure. Whenever you notice that your awareness has drifted away from sensations in the body, you might want to congratulate yourself; you have "woken up". Gently note where your mind was ("thinking"), and kindly focus your attention back to a sense of your body as a whole.

4. As best you can, keep things simple, gently attending to the actuality of sensations throughout your body from one moment to the next.

5. As you sit, some sensations may be particularly intense, such as pains in the back, knees, or shoulders, or a troubled breath or cough. You may find that awareness is repeatedly drawn to these sensations, and away from your intended focus on the body as a whole. You may want to use these times to experiment with choosing intentionally either to shift posture, or to remain still and bring the focus of awareness into the region of intensity. If you choose to remain still, then, as best you can, explore with gentle and wise attention the detailed pattern of sensations here: What, precisely, do the sensations feel like? Where exactly are they? Do they vary over time or from one part of the region of intensity to another? Not so much thinking about them, as just feeling them. You may want to imagine or feel how the heart is beating fresh blood into this area, providing energy, softness, warmth, just as in the body scan.

6. Whenever you find yourself "carried away" from awareness in the moment by the intensity of physical sensations, or in any other way, remind yourself that you can always reconnect with the here and now by refocusing awareness on the sense of the body as a whole. Once you have gathered yourself in this way, allow the awareness to expand once more, so it includes a sense of sensations throughout the body.

7. And now for the last few moments of this sitting, bringing your attention back to focus on your heart providing fresh blood to the whole of the body. Reminding ourselves that no matter what is going on in our lives, our heartbeat is our constant companion, proving energy, softness and warmth.

8. [Bells]

Sitting meditation part 3 – Awareness of sounds and thoughts

Durations: approximately 10 minutes

1. [Bells]

2. [Start this meditation with Sitting meditation part 1 and 2]

3.-9. [Same guiding as in the original MBCT-program, p. 221-222]

10. If at any time you feel that your mind has become unfocused and scattered, of if it keeps getting repeatedly drawn into the drama of your thinking and imaginings, you may like to notice where this is affecting your body. Often, when we don't like what is happening, we feel a sense of contraction or tightness in the face, shoulders, chest or throat, and a sense of wanting to "push away" our thoughts and feelings. See if you notice any of this going on for you when some intense feelings arise. Then, once you have noticed this, see if it is possible to come back to the sensations of your body as whole and the heart providing fresh, softening, warming blood to the whole of the body. The body is right here, right now, and the body, the feet, have contact with the solid, firm ground – you are *here* right now, no matter what else is going on in your body or mind. Using this focus on the body to anchor and stabilise your awareness.

11. [Bells]

The 3-min breathing space

[Bells]

1. AWARENESS - Observation
”As the first step in the breathing step, becoming aware of what is your experience right now.

What thoughts are here? What feelings…? And the bodily sensations…the breath…? Simply noticing what is here right now, without any judgment.”

2. FOCUSING/GATHERING
”Then, as the second step of the breathing space, gathering attentions around the legs and feet on solid ground.

With your feet on the ground, you are connected to something solid, firm, persistent. You are present right here and right now. No matter what else is happening in your body and mind.”

3. EXPANDING
”And then, as the third step, expanding awareness to take in the whole body sitting or standing here. Sensing how the heart is beating and the blood flowing in the body, providing energy, warmth. Softness and openess. Whatever is present right now… being open to it… it is already here… sensing the blood flowing into it, filling it with energy, softness and warmth.

Perhaps taking this sense of openess and acceptance with you for the remainder of your day”

[Bells]

Mindful stretching

Durations: approximately 25-30 minutes

1. [Bells]

2. Finding a comfortable upright position, sitting on a firm, straight-back chair or a stool. If you use a chair, it is very helpful to sit away from the back of the chair, so that your spine is self-supporting.

3. Allow your back to adapt an erect, dignified and comfortable posture. Place your feet flat on the floor, with your legs uncrossed. Gently closing your eyes.

4. Bringing awareness to the sensations in the body as you are sitting here right now. Perhaps the sensations of contact between your body and the chair, and between your feet and the floor. Spending a minute or two exploring these sensations, just as in the body scan.

5. Throughout this exercises, we will be doing a few stretches. The purpose is to become aware of your body in movement, and to explore your own bodily limits and ”edges” if you like. Becoming aware of your bodily limits without having to cross them. Cultivating a sense of compassion for yourself, taking good care of yourself.

6. So when you are ready, stretching both hands and arms slowly in front of you with the fingers pointing towards the ceiling and the palms facing forward. Holding this stretch while bringing full awareness to the sensations in the arms and hands. Now, give your hands a quick shake and slowly lower the arms and place them in the lap. Spending a few moments experiencing the after effects of this stretch. Sensing how the heart provides blood to the areas that has been activated – a tingling or warmth in the arms and hands perhaps.

7. Now, slowly dropping your head to the side, so that the ear is facing down towards the shoulder. Slowly starting a rolling movement of the head, so that the chin face towards the chest, and further until the opposite ear is pointing towards the opposite shoulder. And then slowly rolling your head forwards again and back where it came from. Continuing like this for a few moments. Slowly. And with full awareness of the sensations in the body, the neck, the head and the shoulders, as you are doing this movement. And now, stretching your neck so the head is in an upright position again, and spending a few moments experiencing the aftereffects of this movement.

8. Then, when you are ready, rolling both shoulders, as if you were to draw circles in the air with them. Slowly, carefully, bringing awareness to the sensations in the body from moment to moment. Then dropping the shoulders. And bringing full awareness to the after effects of this movement.

9. When you are ready, pulling up both shoulders towards the ears, as high as they can get. Fully aware of the sensations. Holding this stretch for a few seconds, bringing awareness to the tense sensations in the shoulders and neck, and then dropping the shoulder quickly and heavily. Being aware of the movement and sensations from moment to moment. Now pulling up both shoulders again, feeling the stretch, and letting go heavily. And then again, repeating the movement: pulling, holding, letting go. Spending now a few moments sensing the after effects of these movements.

10. And now letting your left arm hang alongside the body and the chair and bend your left hand, so that the back of the hand faces upwards, and the palm faces the floor. Sensing the stretch in your arm and hand. Fully aware. From moment to moment. And then letting go, placing the left hand in the lap and shifting to the other arm. The right arm. Alongside the body, bending the right hand and feeling the stretch in the right arm and hand. Letting go of the right hand, placing it in the lap. Spending a few moments being aware of the after affects of this stretch.

11. When you are ready, twisting the upper body (the torso and both arms) to the left, so that your legs and bottom stay where they are, while the upper body is facing left. Pulling and twisting your upper body as far as you can to the left while being fully aware of the sensations and the bodily limits. Explore the sensations of your bodily limits. Perhaps the effect on this movement on your breath – without having to change anything. Now letting go and slowly shifting to the other side. Twisting and pulling the upper body to the right, as far as it can go. All the time being fully aware of your body and its limits and edges. Letting go and facing forwards again, feeling the after effects of this stretch.

12. Then, with full attention, stretch your left leg out in front of you, the heel touching the floor, feeling a stretch on the back of the leg. Again, bringing awareness to the perhaps pretty intense sensations, taking care of yourself, exploring your bodily limits. If you feel like increasing the stretch a bit, leaning forward a bit, feeling the intensivation of the stretch from moment to moment. Taking care of your self. Now letting go of the stretch and switching legs, so your right leg is stretched out in front of your, the heel touching the floor. The food bending upwards, feeling a stretch on the back of your right leg. Perhaps increasing the stretch a bit by bending forwards. Fully aware of the changing sensations from moment to moment. And then letting go of the right leg. Now with both feet firmly on the ground. Sitting here for a few moments, bringing awareness to the after effects of these stretches.

13. Now slowly lifting the left leg and foot a tiny bit from the floor, so that your left foot is hanging a few centimetres from the floor. Aware of the intense sensations in your left leg as you are lifting the leg and foot. Perhaps feeling how your body want to just let go and lower the leg – what does that feel like? And then, when you are ready, lowering the leg and placing the foot firmly back on the floor. Switching now to the right leg, lifting leg and foot from the floor. All the time being aware of the intense sensations. Perhaps how they are intensified from moment to moment. And then when you are ready, letting go and placing your right foot on the floor again. Spending a few moments exploring the after effects of this lift.

14. And now, expanding awareness to the body as a whole, sitting here. What does it feel like in the body after having done all these stretches and movements? Heaviness or lightness, warmth? There is no right way to feel, simply noticing what is here in this very moment. How is the breath after having done these exercises? Rapid or calm breathing – deep or shallow breathing? There is no need to change how the breath is at this moment. Simply noticing. And sensing how the heart is constantly providing fresh blood to the whole of the body. Providing energy, warmth and softening the areas of your body that have just been activated by the stretches and movement.

15. Just sitting here for a few more moments, fully aware of the body as a whole.

16. [Bells]

Inspired by Trish Bartley (2012)

Being with the difficult and working with it through the body

Duration: approximately 15-20 minutes

1. [Bells]

2. [Start this meditation with Sitting meditation part 1]

3. Sit for a few moments, focusing on the sensations of the blood flow, then widening the awareness to take in the body as a whole.

4. While you are sitting, if you notice that your attention keeps being pulled away to unpleasant thoughts or emotions, you can explore something different from what we have been practicing up until now.

5. Until now, when you have been sitting and notice that your mind has wandered, the instruction has been simply to notice where the mind had gone, then gently and firmly escort the attention back to the breath or body, or back to whatever you intended to be focusing on.

6. Now you can explore a different way to respond. Instead of bringing attention back from a thought or feeling, now allow the thought or feeling to *remain* in the mind. Then, shifting the attention into the body, see if you can become aware of any physical sensations in the body that come along with the thought or emotion.

7. Then when you have identified such sensations, deliberately move the focus of attention to the part of the body where these sensations are strongest. Perhaps that is in the chest or throat, or in the abdomen? Imagining that your heart provides fresh blood to this area – softening, warming, opening – just as you practiced in the body scan, not to change the sensations but to explore them, to see them clearly.

8. If there are no difficulties or concerns coming up for you now and you want to explore this new approach, then, if you choose, you might *deliberately bring to mind a difficulty* that is going on in your life at the moment – something you don't mind staying with for a short while. It does not have to be very important or critical, but something that you are aware of as somewhat unpleasant: perhaps a situation where you feel somewhat angry, regretful, or guilty over something that has happened. If nothing comes to mind, perhaps you might choose something from the past, either recent or distant, that once caused unpleasantness.

9. Now, once you have focused on some troubling thought or situation – some worry or intense feeling – allow yourself to take some time to tune in to any physical sensation in the body that the difficulty evokes.

10. See if you are able to note, approach, and investigate inwardly what feelings are arising in your body, becoming mindful of those physical sensations, deliberately directing your focus of attention to the region of the body where the sensations are strongest in a gesture of an embrace, a welcoming.

11. This gesture might include imagining how fresh, warm blood fills up that part of the body, exploring the sensations, watching their intensity shift up and down from one moment to the next.

12. Once your attention has settled on the body sensations and they are vividly present in the field of awareness, unpleasant as they may be, you might try deepening the attitude of acceptance and openness to whatever sensations you are experiencing by saying to yourself from time to time: "It is here now. It is OK to be open to it. Whatever it is, it's already here. Let me open to it." Soften and open to the sensations you become aware of, intentionally letting go of tensing and bracing. Say to yourself: "Softening, Opening".

13. Then see if it is possible to stay with the awareness, exploring these body sensations and your relationship to them, letting them be, allowing them to be just as they are.

14. Remember that, by saying "It's already here" or "It's OK", you are not judging the original situation or saying that everything's fine, but simply helping your awareness, right now, to remain open to the sensations in the body.

15. You do not have to *like* these feelings – it is natural not to want to have them around. You may find it helpful to say to yourself, inwardly, "It's OK not to want these feelings; they're already here; let me be open to them".

16. If your choose, you can also experiment with holding in awareness both the sensations in the body and the feeling of the heart beating fresh blood into that area, moment by moment. Together with the sensations of your feet on the floor – you are in contact with something solid, firm, persistent, no matter what else is going on in your body and mind.

17. And when you notice that the body sensations are no longer pulling your attention to the same degree, simply return 100% to sitting with awareness of the blood flowing in the whole body as the primary object of attention.

18. If, in the next few minutes, no powerful body sensations arise, feel free to try this exercise with any body sensations you notice, even if they have no particular emotional charge.

19. [Bells]

Appendix E: Supplementary material for Paper 3

Assessment of mixed-methods methodology and interview guide. Published as supplementary material to Paper 3.

Critical appraisal criteria for quantitative and qualitative methods (Sale & Brazil, 2004)				
Goals of criteria	**Qualitative methods**	**The present study**	**Quantitative methods**	**The present study**
Truth value (Credibility vs. internal validity)	Triangulation of sources	*This is a mixed-methods study where data come from the sources of questionnaires (quantitative) and semi-structured interviews (qualitative) with the purpose of understanding the same particular phenomenon – in this case, the clinical feasibility of tele-MBCT in COPD.*	Extraneous or confounding variables identified	*Not included*
	Triangulation of methods	*This is a mixed-method study with a "convergent parallel" design* (Caffery, Martin-Khan, & Wade, 2017)*, which means that quantitative and qualitative data are gathered independently and then analysed to contribute to the understanding of the same particular phenomenon – in this case, the clinical feasibility of tele-MBCT in COPD.*	Extraneous or confounding variable(s) or baseline differences controlled for in the analysis	*Not included*
	Triangulation of investigators	*The analysis was primarily carried out by IF-V supplemented with discussions with the interviewer (NCS) and other colleagues*	Statement about comparability of control group to intervention group at baseline	*No control group included*
	Triangulation of theory/perspective	*Not included*	Statement that comparison group was treated equally aside from intervention	*No control group included*
	Peer debriefing	*Not included*	Informed consent stated	*Participants gave informed written consent as part of the larger study from which they are included (see Farver-Vestergaard et al., 2018)*
	Negative case analysis or searching for disconfirming evidence	*In the analysis, we sought to give as balanced an account of experiences as possible by actively seeking conflicting utterances under a given theme.*	Ethical review undertaken	*The larger study from which the sample of the present study is recruited has been approved by the Central Denmark Region Committee on Health Research Ethics (see Farver-Vestergaard et al., 2018)*

	Member checks	*Not included*	Statement that confidentiality protected	*Stated in both oral and written information prior to consent (not included in manuscript)*
	Use of quotations	*In the results sections, exemplifying quotations are given for each theme.*	-	-
	Informed consent stated	*All participants gave informed consent to interview participation, specifically.*	-	-
	Ethical review or human subject review undertaken	*The larger study from which the sample of the present study is recruited has been approved by the Central Denmark Region Committee on Health Research Ethics (see Farver-Vestergaard et al., 2018)*	-	-
	Statement that confidentiality protected	*Stated in both oral and written information prior to consent (not included in manuscript)*	-	-
	Consent procedures described	*Consent procedures were described to all participants in the information material prior to consent (not included in manuscript)*	-	-
Applicability (Transferability/ Fittingness vs. External validity/ Generalisability	Statement of purpose	*The overall purpose of the present mixed-methods study is to evaluate the clinical feasibility of tele-MBCT and to identify focus points for the design of future efficacy trials.*	Statement of purpose	*The overall purpose of the present mixed-methods study is to evaluate the clinical feasibility of tele-MBCT and to identify focus points for the design of future efficacy trials.*
	Statement of research question(s)	*How does individual participants experience taking part in tele-MBCT*	Objective of study explicitly stated or described	*1) measure change in the outcomes of psychological distress and physical health status impairment from pre- to post-intervention,* *2) monitor attendance rates (i.e. number of tele-MBCT sessions attended) and drop-out rate,* *3) measure participants' perceived quality of the therapeutic working alliance mid-way through the intervention,*
	Phenomenon of study stated	*An eight week tele-based psychosocial intervention called tele-delivered mindfulness-based cognitive therapy (tele-MBCT). More specifically, the study explores its clinical feasibility, which naturally includes participants' perceptions.*	Description of intervention if appropriate	*The MBCT intervention is described in detail by Farver-Vestergaard* (Farver-Vestergaard et al., 2018). *The tele-MBCT intervention was delivered via touch-screen computers that were installed in the participants' homes prior to the first session. The computers had integrated camera, speaker and microphone, allowing each patient to see, hear and speak to the other participants and the*

				instructor. The instructor operated a provider station in order to make a group call to all participants prior to each session and to terminate the call after each session. The provider station also had integrated devices enabling the instructor to see, hear and speak to all participants. The instructor contacted service providers directly in instances of technical issues.
	Rationale for the use of qualitative methods	*Concerns are raised that the tele-delivered format could negatively influence the clinical feasibility of specific psychosocial intervention programmes. While the field is still in its infancy, however, clinical parameters of interest have not yet been identified, and there is therefore a need for 'bottom-up' explorations of individual participants' experiences of tele-MBCT.*	Outcome measure(s) defined	*The outcomes of psychological distress and physical health status impairment were measured pre- and post-intervention. Psychological distress was assessed by the Hospital Anxiety and Depression Scale (HADS). Its 14 items yield a total score ranging from 0-42, with higher scores representing higher levels of distress. The questionnaire is validated and frequently used in COPD. Physical health status impairment was measured by the COPD Assessment Test (CAT). It consists of eight items resulting in a total score ranging from 0-40, with higher scores representing higher levels of impairment.*
	Rationale for the tradition within qualitative methods	*Analysis was based on the framework of thematic analysis as described by Braun and Clarke. A realist epistemological approach was taken where an account of explicit meanings across the data set is sought.*	Assessment of outcome blinded	*Questionnaires were labelled with an ID-number, such that questionnaires did not include name or other personal identifiers. (not described in manuscript)*
	Description of study context	*As a response to the relatively low attendance (average: 4 out of 8 treatment sessions) and uptake rates in our randomised controlled trial of hospital-based, face-to-face MBCT (Farver-Vestergaard et al., 2018) we decided to conduct the present feasibility study of a home-based tele-delivered version of the intervention (tele-MBCT).*	Description of setting or conditions under which data collected	*Participants filled in all questionnaires at home. (Not described in manuscript).*
	Statement of how setting was selected	*With the purpose of testing the clinical feasibility of tele-MBCT, the home-based setting was chosen to maximise the ecological validity and clinical relevance of the study.*	Design stated explicitly i.e. case study, cross-sectional study, cohort study, RCT	*Mixed-methods feasibility study.*

	Sampling procedure described	*All control group participants of the larger study previously described (Farver-Vestergaard et al., 2018) were asked to participate in the present feasibility study. Those who did not wish to receive the tele-based version of MBCT were offered face-to-face MBCT instead and, hence, were not part of the present feasibility study.*	Subject recruitment or sampling selection described	*All control group participants of the larger study previously described (Farver-Vestergaard et al., 2018) were asked to participate in the present feasibility study. Those who did not wish to receive the tele-based version of MBCT were offered face-to-face MBCT instead and, hence, were not part of the present feasibility study.*
	Justification or rationale for sampling strategy	*The above sample strategy was chosen primarily for pragmatic reasons.*	Sample randomly selected	*No.*
	Description of participants or informants	*Participant characteristics are described in the manuscript.*	Inclusion and exclusion criteria for subject selection stated explicitly	*Inclusion criteria for the larger study, from which the participants of the present study were included, were 1) a spirometry-confirmed (forced expiratory volume in 1 s < 50%) COPD diagnosis togeather with a Medical Research Council dyspnoea score of ≥3, and 2) physical capability to attend the exercise component of pulmonary rehabilitation at the time of inclusion. Exclusion criteria were 1) a comorbid diagnosis of stroke, dementia or unstable coronary heart disease and 2) an inability to speak or understand Danish.*
	Data gathering procedures described	*Semi-structured qualitative interviews were conducted with all participants immediately after completion of the tele-MBCT programme either in the patients' own home or via telephone. Interviews were conducted by a research assistant (NCS) who had a background in psychology and experience within the field of psychological intervention in COPD.*	Study population defined or described	*Participant characteristics are described in Table 1 in the manuscript.*
	Audiotaping procedures described	*Interviews were recorded and stores safely as mp3 files. Upon storage, they were immediately deleted from the recording device. (Not described in manuscript)*	Source of subjects stated i.e. sampling frame identified	*Sampling frame described in detail by Farver-Vestergaard et al.* (2018) *(not described in manuscript)*
	Transcription procedures described	*All interviews were transcribed verbatim by an independent research assistant.*	Source of controls stated	*No control group included*
	Field note procedures described	*The interviewer (NCS) shared her interview reflections with the first author/analyst (IF-V), who regularly took field notes during the data*	Selection of controls described	*No control group included*

		collection and analysis phases. Notes were managed using Nvivo software. Notes are in Danish and can be obtained upon request. (not included in manuscript)		
	Data analysis described	*The six iterative phases of analysis started with a thorough and detail-oriented reading of research interviews and gradually moved towards a condensed understanding of the data through the definition of themes, as suggested by Braun and Clarke (2006)*	Control or comparison group described	*No control group included (mentioned in the limitations section of the manuscript, p. 10)*
	Coding techniques described	*The initial coding of data was based on an inductive approach, but as the analysis moved towards the definition of themes, it took a more deductive approach where the focus was on areas of the data that supplemented the elements in the quantitative evaluation (i.e., outcomes, attendance rate and working alliance).*	Statement about nonrespondents or dropouts	*Participants completed all questionnaires and there were no dropouts.*
	Data collection to saturation specified	*The interviewer sought saturation by asking follow-up questions such as "can you please tell a bit more about that?" or "is there anything else you want to add?" (not described in manuscript)*	Missing data addressed	*Not relevant.*
	Statement that reflexive journals or logbooks kept	*During the analysis process, a reflective logbook was kept, using the NVivo software.*	Power calculation to assess adequacy of sample size or sample size calculated for adequate power	*Not relevant as this is not an efficacy study, but a study exploring the clinical feasibility of the intervention.*
	Description of raw data	*Interview recordings were securely stored as mp3 files, and deleted after transcription and anonymization. The anonymised transcription raw data was stored and managed, using the Nvivo software. Moreover, in the initial analysis phase* (see Braun & Clarke, 2006)*, transcription*	Statistical procedures referenced or described	*Dependent t tests were performed to estimate the average change of psychological distress (the Hospital Anxiety and Depression Scale) and physical health status impairment (the COPD Assessment Test) post-intervention.*

		raw data was printed on paper to allow for more in-depth familiarising with the data material. (not described in manuscript)		
	-	-	P values stated	*yes*
	-	-	Confidence intervals given for main results	*Confidence intervals for the mean difference in HADS scores from pre- to post-intervention: Mean diff.=1.5, 95% CIs [-2.45 – 5.45]* *Confidence intervals for the mean difference in CAT scores from pre- to post-intervention: Mean diff.=1.5, 95% CIs [-0.73 – 3.73]*
	-	-	Data gathering procedures described	*After having consented to participation in the study, participants received the pre-intervention questionnaire by post. All pre-intervention questionnaires were completed and returned prior to the first tele-MBCT session. Participants completed and returned the Working Alliance Inventory after the fourth sessions if the tele-MBCT (midway). Post-intervention questionnaires were completed and returned immediately after the eighth and final session of tele-MBCT. (manuscript p. 4-5)*
	-	-	Data collection instruments or source of data described	*Pen-and-paper questionnaires*
	-	-	At least one hypothesis stated	
	-	-	Both statistical and clinical significance acknowledged	*The results of the quantitative evaluation indicated that, for psychological distress, an average reduction of 1.5 points on the HADS was seen after tele-MBCT, representing a clinically relevant improvement of the outcome (minimal clinically important difference (MCID) for the HADS=1.5 points). This reduction corresponds to a medium effect size (Cohen's d=0.504). Concerning physical health status, the average reduction of 1.5 points of the CAT did not exceed the MCID of 2 points. However, the magnitude of the effect was moderate to large (d=0.743). For both outcomes, the differences failed to reach statistical significance, which is*

				most likely due to the small number of participants included in the present feasibility study.
Consistency (Dependability vs. Reliability)	External audit of process	*The analysis was primarily carried out by IF-V supplemented with discussions with the interviewer (NCS) and other colleagues.*	Standardisation of observers described	*The primary researcher (IF-V) served both as the MBCT-instructor and the main data analyst. To minimise risk of bias, data were labelled with ID number instead of names or any other person-sensitive data. (not described in manuscript).*
Neutrality (Confirmability vs. Objectivity)	External audit of data and reconstructions of the data	*Both a long version and a short version of the "story" of the thematic analysis* (see Braun & Clarke, 2006)*, was read by and discussed with the interviewer (NCS). Themes were redefined on the basis of other researchers' perspectives. Moreover, data extracts/quotations were translated from Danish to English by three independent research assistants, and a final version was agreed upon. (not described in manuscript)*	-	-
	Bracketing	*Both a long version and a short version of the "story" of the thematic analysis* (see Braun & Clarke, 2006)*, was read by and discussed with the interviewer (NCS). Themes were redefined on the basis of other researchers' perspectives. (not described in manuscript).*	-	-
	Statement of researcher's assumptions or statement of researcher's perspective	*The primary researcher (IF-V) served both as the MBCT-instructor and the main data analyst. To minimise the risk of a narrow perspective, it was decided that another researcher (NCS) should carry out interviews. Whenever the primary researcher (IF-V) noted potential bias, e.g. when translating data extracts from Danish to English, assistance from independent researcher was sought. (not described in manuscript).*	-	-

Reference

Braun, V., & Clarke, V. (2006). Using thematic analysis in psychology. *Qualitative Research in Psychology*, *3*(2), 77–101. https://doi.org/10.1191/1478088706qp063oa

Caffery, L. J., Martin-Khan, M., & Wade, V. (2017). Mixed methods for telehealth research. *Journal of Telemedicine and Telecare*, *23*(9), 764–769.

https://doi.org/10.1177/1357633X16665684

Farver-Vestergaard, I., O'Toole, M. S., O'Connor, M., Løkke, A., Bendstrup, E., Basdeo, S. A., … Zachariae, R. (2018). Mindfulness -based cognitive therapy in COPD: a cluster randomised controlled trial. *European Respiratory Journal*, *51*(2), 1702082. https://doi.org/10.1183/13993003.02082-2017

Sale, J., & Brazil, K. (2004). A strategy to identify critical appraisal criteria for primary mixed methods research. *Quality & Quantity*, *38*(74), 351–365.

Supplementary file S2. Interview guide

Topic	Suggested questions
General experience of the MBCT intervention	- What was it like to take part in the intervention? - What did you get out of taking part?
General experience of using the tele-monitor	- What do you think it would have been like to take part in the intervention face-to-face instead of via the tele-monitor? - Would you have preferred a face-to-face format? - What has been the advantages of using the tele-monitor? - What has been the disadvantages of using the tele-monitor?
Information telephone call	Cue: A few weeks before the intervention started, you received a telephone call from [name of instructor], asking if you were willing to participate and informing you about the tele-based format. - What were your thoughts about the project at that time? - What were your thoughts on having a tele-monitor installed in your home? - What made you consent to participation? - Was there something you would have liked to know or would wish had been different at this point?
Installation of tele-monitor and test-call	Cue: You had a visit from [name of installer], who installed the tele-monitor in your home. Together you made a short test call to [name of instructor] where you settled on a time for the individual pre-class interview. - What was it like to have the tele-monitor installed in your home? - Was there something you would have liked to know or would wish had been different at this point?
Individual pre-class interview via the tele-monitor	Cue: About a week before the group intervention started, you had an individual pre-class interview with [name of instructor] via the tele-monitor (approximately ½ hour]. You told her about yourself and she told you about the MBCT intervention. - What was it like to use the tele-monitor by yourself for the first time? - What was it like to talk to [name of instructor] in this way? - Was there something you would have liked to know or would wish had been different at this point?
MBCT intervention	- What was it like to meet the group via the tele-monitor for the first time? - What was it like to meet for the following sessions? Did anything change over the course of the 8 weeks? - Please describe your relationship with the other participants - Please describe your relationship with [name of instructor] - Was there something you would have liked to know or would wish had been different at this point?
Additional topics	- Who have you told about this project? What do you typically tell them? - How has your spouse (if he/she has one) reacted in relation to this project? - Is there something important about this project that we haven't covered yet? Do you have any questions? - What could we do better for other participants in the future?

Appendix F: Declarations of co-authorship (Papers 1-3)

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Declaration of co-authorship*

Full name of the PhD student: Ingeborg Farver-Vestergaard

This declaration concerns the following article/manuscript:

Title:	Efficacy of psychosocial interventions on psychological and physical health outcomes in chronic obstructive pulmonary disease: A systematic review and meta-analysis
Authors:	Ingeborg Farver-Vestergaard, Dorte Jacobsen & Robert Zachariae

The article/manuscript is: Published ☒ Accepted ☐ Submitted ☐ In preparation ☐

If published, state full reference: Farver-Vestergaard, I., Jacobsen, D., & Zachariae, R. (2015). Efficacy of psychosocial interventions on psychological and physical health outcomes in chronic obstructive pulmonary disease: A systematic review and meta-analysis. *Psychotherapy and Psychosomatics, 84,* 37–50. doi:10.1159/000367635

If accepted or submitted, state journal:

Has the article/manuscript previously been used in other PhD or doctoral dissertations?

No ☒ Yes ☐ If yes, give details:

The PhD student has contributed to the elements of this article/manuscript as follows:

A. Has essentially done all the work
B. Major contribution
C. Equal contribution
D. Minor contribution
E. Not relevant

Element	Extent (A-E)
1. Formulation/identification of the scientific problem	A
2. Planning of the experiments/methodology design and development	B
3. Involvement in the experimental work/clinical studies/data collection	B
4. Interpretation of the results	B
5. Writing of the first draft of the manuscript	A
6. Finalization of the manuscript and submission	B

Signatures of the co-authors

Date	Name	Signature
28/2-2017	Dorte Jacobsen	
28/2-2017	Robert Zachariae	

In case of further co-authors please attach appendix

Date: 28/2-17

*As per policy the co-author statement will be published with the dissertation.

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AARHUS UNIVERSITY

Signature of the PhD student

*As per policy the co-author statement will be published with the dissertation.

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Declaration of co-authorship*

Full name of the PhD student: Ingeborg Farver-Vestergaard

This declaration concerns the following article/manuscript:

Title:	Mindfulness-based cognitive therapy in COPD: a cluster randomised controlled trial
Authors:	Ingeborg Farver-Vestergaard, Mia S. O'Toole, Maja O'Connor, Anders Løkke, Elisabeth Bendstrup, Sharee A. Basdeo, Donal J. Cox, Pádraic J. Dunne, Kai Ruggeri, Frances Early and Robert Zachariae

The article/manuscript is: Published ☒ Accepted ☐ Submitted ☐ In preparation ☐

If published, state full reference: Farver-Vestergaard, I., O'Toole, M. S., O'Connor, M., Løkke, A., Bendstrup, E., Basdeo, S. A., Cox, D. J., Dunne, P. J., Ruggeri, K., Early, F., & Zachariae, R. (2018). Mindfulness-based cognitive therapy in COPD: a cluster randomised controlled trial. *European Respiratory Journal* 51: 1702082

If accepted or submitted, state journal:

Has the article/manuscript previously been used in other PhD or doctoral dissertations?

No ☒ Yes ☐ If yes, give details:

The PhD student has contributed to the elements of this article/manuscript as follows:

A. Has essentially done all the work
B. Major contribution
C. Equal contribution
D. Minor contribution
E. Not relevant

Element	Extent (A-E)
1. Formulation/identification of the scientific problem	A
2. Planning of the experiments/methodology design and development	B
3. Involvement in the experimental work/clinical studies/data collection	B
4. Interpretation of the results	B
5. Writing of the first draft of the manuscript	A
6. Finalization of the manuscript and submission	A

Signatures of the co-authors

Date	Name	Signature
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23.03.18	Anders Løkke	
23.03.18	Elisabeth Bendstrup	
23/4/18	Sharee A. Basdeo	

In case of further co-authors please attach appendix

Date:

*As per policy the co-author statement will be published with the dissertation.

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Signature of the PhD student

Appendix: Further co-authors

Date	Name	Signature
21/4/18	Donal J. Cox	
21-4-18	Pádraic J. Dunne	
2/5/18	Kai Ruggeri	
25/4/18	Frances Early	
16/09/18	Robert Zachariae	

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Declaration of co-authorship*

Full name of the PhD student: Ingeborg Farver-Vestergaard

This declaration concerns the following article/manuscript:

Title:	Tele-delivered mindfulness-based cognitive therapy in chronic obstructive pulmonary disease: A mixed-methods feasibility study
Authors:	Ingeborg Farver-Vestergaard, Maja O'Connor, Nina Coulthard Smith, Anders Løkke, Elisabeth Bendstrup and Robert Zachariae

The article/manuscript is: Published ☐ Accepted ☒ Submitted ☐ In preparation ☐

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If accepted or submitted, state journal: Journal of Telemedicine and Telecare

Has the article/manuscript previously been used in other PhD or doctoral dissertations?

No ☒ Yes ☐ If yes, give details:

The PhD student has contributed to the elements of this article/manuscript as follows:

A. Has essentially done all the work
B. Major contribution
C. Equal contribution
D. Minor contribution
E. Not relevant

Element	Extent (A-E)
1. Formulation/identification of the scientific problem	A
2. Planning of the experiments/methodology design and development	A
3. Involvement in the experimental work/clinical studies/data collection	B
4. Interpretation of the results	B
5. Writing of the first draft of the manuscript	A
6. Finalization of the manuscript and submission	A

Signatures of the co-authors

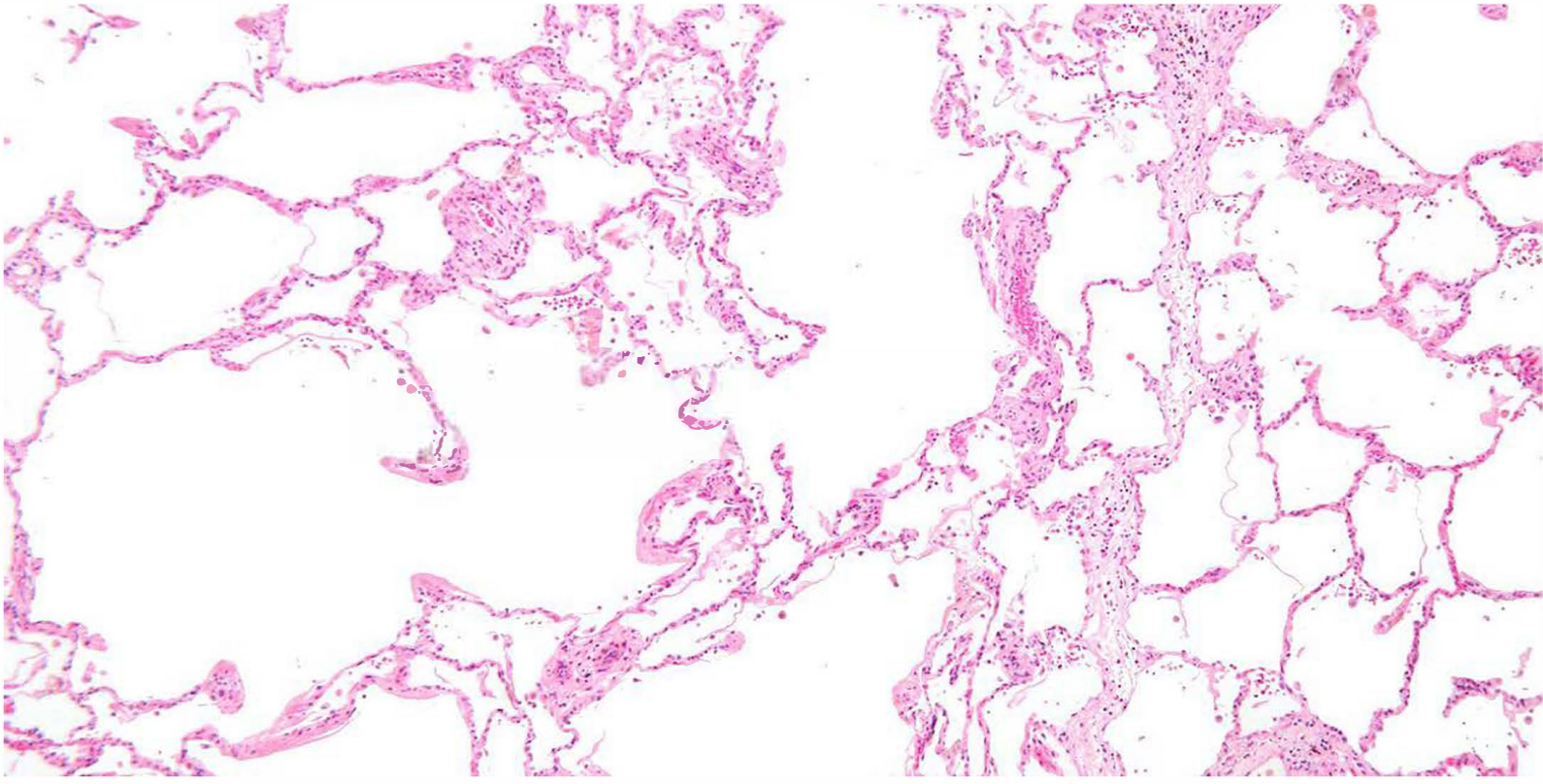
Date	Name	Signature
18.06.18	Maja O'Connor	
18.06.18	Nina Coulthard Smith	
26.06.18	Anders Løkke	
26.06.18	Elisabeth Bendstrup	
26.06.18	Robert Zachariae	

In case of further co-authors please attach appendix

Date: 26.06.18

Signature of the PhD student

*As per policy the co-author statement will be published with the dissertation.



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