Depression and suicidality in COPD: understandable reaction or independent disorders?

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ABSTRACT Both depression and chronic obstructive pulmonary disease (COPD) are prevalent, severe and often comorbid disorders. There is a risk of undertreatment for depression in patients with COPD as depressive symptoms, including suicidal tendencies, can erroneously be conceptualised as an understandable reaction to COPD and not as signs of an independent depressive disorder. In this context, the comorbidity rates of COPD and depression, the risk of suicidal behaviour in patients with COPD, and the evidence base for pharmaco- and psychotherapy in these patients are reviewed.

Because symptoms of depression and COPD overlap it remains unclear how far the prevalence of major depression in COPD exceeds that in the general population. The suicide risk appears to be increased in COPD. Methodological studies providing evidence for the antidepressant efficacy of antidepressants or psychotherapy in patients with COPD are lacking. Recommendations for clinicians on how to separate depression from an understandable reaction to COPD are provided.

Given the profound effects of depression on quality of life, life expectancy, COPD prognosis and suicide risk it is important to carefully diagnose and treat depression in patients with COPD according to national guidelines.

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Introduction

Both chronic obstructive pulmonary disease (COPD) and major depressive disorder are prevalent, severe and often comorbid disorders whose outstanding and increasing medical and health policy importance is well documented [1]. The 1-year prevalence of major depressive disorder is ~6.9% in the general population [2]. Therefore, comorbidity with COPD should be a frequently expected clinical problem [3]. In this case there is the risk of undertreatment for depression because depressive symptoms, including suicidal tendencies, can erroneously be conceptualised as an understandable reaction to COPD and not as signs of an independent depressive disorder (diagnostic criteria are shown in table 1), which has to be treated according to guidelines. However, the suffering associated with major depression as well as the risks, including suicide risk [5], require careful diagnosis because effective treatments are available.

In randomised controlled trials (RCTs) the mean effect sizes of antidepressants in major depression were ~0.30 for acute treatment and ~0.60 for relapse prevention, which are comparable to what was found in other areas of medicine [6]. Unless shown otherwise, antidepressant treatments can be expected to be effective in depression with somatic comorbidities. However, evidence for the efficacy of antidepressant treatments would be stronger when specifically shown in patients with comorbid depression and COPD. Therefore, the aims of this review are to: 1) review and critically discuss whether the risk of major depression is increased in patients with COPD; 2) review the risk of suicidal behaviour in patients with COPD; 3) give a critical overview of the evidence for efficacy of pharmaco- and psychotherapy in depressed patients with COPD, based on available reviews and more recent studies [7–11]; and 4) provide practical recommendations concerning the diagnosis of and treatment for depression in patients with COPD.

Risk of major depression in patients with COPD

If COPD is the cause for depression, the comorbidity rates should be higher than what can be expected by chance. However, when interpreting studies on comorbidity rates the methodological problems have to be taken into account. There is a considerable symptom overlap between COPD and major depression, leading to the risk of over-diagnosing depression in epidemiological studies. At the same time, in routine clinical care, the symptom overlap might increase the risk of not recognising a depressive episode in patients with COPD.

TABLE 1 Diagnostic criteria for major depressive disorder[#]

Diagnostic criteria	Description
A	Five or more of the symptoms listed below have to be present during the same 14-day period implying a change from previous functioning, at least one of them being either depressed mood or loss of interest or pleasure (Caveat: it is not allowed to include symptoms that can be clearly attributed to other medical conditions): Depressed mood most of the day and nearly every day Markedly diminished pleasure or interest in (almost) all activities most of the day and nearly every day Significant loss of weight (when not dieting) or gain of weight, or decreased or increased appetite nearly every day In- or hypersomnia nearly every day Psychomotor retardation or agitation nearly every day Loss of energy or fatigue nearly every day Feelings to be worthless or inappropriate or excessive guilt nearly every day Diminished ability to concentrate or think, or indecisiveness, nearly every day Recurrent thoughts of death, suicidal ideation without specific plans to commit suicide, or an attempted suicide, or a specific plan for committing suicide
B	Symptoms lead to clinically relevant distress or impairment regarding occupational, social, or other important areas of functioning
C	The episode cannot be attributed to the physiological effects of a drug or other medical conditions
D	The presence of the major depressive episode cannot be better explained by schizophrenia, schizophreniform disorder, schizoaffective disorder, delusional disorder, or other schizophrenia spectrum and other psychotic disorders
E	A manic or hypomanic episode has never been present

[#]: Summary of the diagonostic criteria according to the Diagnostic and Statistical Manual of Mental Disorders 5th Edn [4].

Major depression and COPD have different key symptoms that are relevant for diagnosis (major depression: depressed mood, loss of interest or pleasure, feelings of excessive guilt and suicidal thoughts [4]; COPD: cough symptoms, sputum production, or dyspnoea indicating airflow limitation [12]). However, both disorders are frequently associated with poor physical activity, withdrawal, anhedonia, fatigue, loss of energy, poor appetite, sleep disturbances and difficulties regarding concentration [13]. The use of standardised clinical interviews for the diagnosis of depressive disorders in patients with COPD count symptoms independent of the overall symptom configuration, thus, leading to high comorbidity rates [14]. Furthermore, direct symptom observations by the clinical assessor, such as psychomotor retardation, are of minor relevance for standardised clinical interviews and cannot be utilised in telephone interviews. In addition, the terminology used in the diagnostic procedure is flawed by mixing up quite different disturbances. ''Fatigue'' and ''lack of energy'', which are among the most frequent complaints and symptoms in patients with COPD [15], are too vague to be useful. The term fatigue is used by patients and clinicians for a syndrome associated with increased daytime sleepiness and short sleep onset latencies as found in many nondepressed COPD patients. However, it is also used to describe a syndrome with decreased sleepiness and prolonged sleep onset latencies, as typically found in patients with major depression [16, 17].

Prevalence of depression in patients with COPD

To date, three systematic reviews have focused on whether patients with COPD have an abnormally high prevalence of depression [3, 18, 19].

In the first review, based on four studies [18], the point prevalence of depression in COPD showed a large range from 7% to 42%. In two out of the four studies reviewed the point prevalence of depression in COPD patients was significantly higher than that of the controls [20, 21]. Therefore, the authors could not confirm the hypothesis of an abnormally high risk for depression in COPD patients [18].

Based on more recent findings, a second review [19] ascertained a significantly higher prevalence of depressive symptoms in patients with COPD (24.6%) than in the controls (11.7%). Depression was assessed by a variety of methods in each of the studies; five studies used self-report measures and three studies physician-rated measures. Interestingly, the prevalence of depression was not associated with the severity of COPD (*i.e.* mean forced expiratory volume in 1 s).

However, the aforementioned reviews [18, 19] did not allow conclusions to be drawn about the prevalence of depressive disorders, because of methodological limitations regarding the assessment of depression. Instead of diagnostic interviews only questionnaires were used. It should be noted that questionnaires are only supportive tools suitable for case-finding and diagnosis of major depression requires a face-to-face interview with the patient.

Similarly, a recent meta-analysis suggested that COPD consistently elevated the risk of depression, with the relative risk being 1.69 [3]. Moreover, the risk of COPD outcomes (COPD exacerbation or incidence of emphysema or chronic bronchitis) was consistently increased by depression (relative risk 1.43) [3].

In addition, 18 more recent studies were identified (table 2). Due to different populations and depression rating scales, there is a wide range in the prevalence of depressive symptoms. In this context it is also of interest to note that the depression risk was not related to the lung function [34] and the objectively measured severity of COPD [19].

Overall, COPD does not seem to be a major cause of depression. The somewhat higher prevalence figures for depression in COPD might be explained to a large degree by the symptom overlap. This interpretation is supported by the fact that in depression COPD is not more prevalent than in the general population (2.83% [40] *versus* 4–10% [41]).

Suicidality in patients with COPD

The link between COPD and suicidality has been rarely investigated. According to a Swedish national cohort study [42], COPD was significantly and independently associated with an elevated suicide risk. In a recent epidemiological study [43], the link between COPD and suicidal ideation and suicide attempts was analysed. Whereas 27.2% of the COPD patients stated that they had seriously thought about committing suicide this was the case in only 19.6% of subjects without COPD. The corresponding odds ratio (1.74) was significant. The difference between these two groups regarding a self-reported lifetime history of suicide attempts was even more pronounced and significant (15.0% for COPD patients, 6.6% for subjects without COPD; OR=2.29). According to a large case–control study [44] the relative risk of suicide was significantly elevated among patients with COPD compared with patients without major chronic illnesses (3.1% *versus* 1.9%, respectively; OR=1.80).

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TABLE 2 Prevalence of depressive symptoms/disorders in chronic obstructive pulmonary disease (COPD) patients reported in studies published from 2011 to 2013

First author [ref.]	Assessment tools	Patients	Prevalence of depression %
De [22]	PHQ-9	100 consecutively recruited Indian patients with stable COPD	72
Hayashi [23]	HADS-D	80 outpatients and 51 inpatients suffering from stable COPD in Japan	40.5
Goodwin [24]	CIDI diagnosis of major depression	147 COPD patients (self report) in the USA	24.8
Joo [25]	Standardised questionnaires on comorbidities associated with COPD	354 COPD patients (subsample of 9744 subjects from the Korean population)	COPD: 18.7; non-COPD: 17.4
Loerbroks [26]	GDS-15 sum score ⩾4 points	7995 COPD patients from a large population sample from southern China	22.9
Lou [27]	HADS-D ⩾8 points	1100 outpatients with COPD from China and 1100 healthy controls	COPD: 35.7; controls: 7.2
Marinho [28]	GDS-15	40 elderly COPD patients from Brazil	22.5
Obradovic [29]	HDRS	40 COPD patients from Serbia	20.0
Schnell [30]	Physicians' lifetime diagnosis of depression	995 COPD patients (aged ⩾45 years) from the USA	20.6
Arimura [31]	CES-D score ⩾10 points	52 consecutively recruited and clinically stable COPD patients in the pulmonary departments of five hospitals in Japan	29
Horita [32]	SF-GDS ⩾6 points	84 consecutive, stable COPD outpatients in a Japanese community hospital	38.1
Iguchi [33]	Japanese version of the CES-D sum score ⩾16 points	74 COPD patients from long-term Japanese inpatient rehabilitation facilities	48.6
Lee [34]	PHQ-9 ⩾10 points	803 COPD inpatients from Korea	23.8
Papaioannou [35]	BDI-I sum score ⩾19 points	230 consecutive COPD inpatients in departments of respiratory medicine in two tertiary hospitals in Greece	39.6
Qian [36]	Clinical ICD-9-CM diagnoses of depressive disorders	75 699 US beneficiaries[#] (minimum age 65 years) with a diagnosis of COPD	21.6
Sharma [37]	Global Mental Health Assessment Tool – Primary Care and General Health version	52 consecutive patients with stable COPD attending a respiratory disease clinic in Northern India	COPD: 19.2; controls: 3.4
Warmenhoven [38]	General practitioners' lifetime diagnosis of depressive disorders	982 Dutch patients with COPD, cardiovascular disease and cancer in the last phase of their lives	8.2
Zhang [39]	Face-to-face questionnaire	7597 COPD patients from China	28.3

PHQ-9: patient health questionnaire-9; HADS-D: hospital anxiety and depression scale depression subscale; CIDI: composite international diagnostic interview; GDS-15: geriatric depression scale 15-item version; HDRS: Hamilton depression rating scale; CES-D: Center for Epidemiologic Studies depression scale; SF-GDS: short-form geriatric depression scale; BDI-I: Beck's depression inventory I; ICD-9-CM: international classification of diseases, 9th revision, clinical modification. [#]: persons enrolled in Medicare parts A, B and D in the USA.

Therapeutic strategies for depression in patients with COPD

For four reasons the treatment of depression is important in patients with COPD. 1) Depression in patients with COPD goes along with a markedly reduced quality of life [45, 46], increased healthcare use [47], and an elevated risk of exacerbations and hospitalisations [48]. 2) Effective treatments for depression (antidepressants and psychotherapy) are available [49]. 3) Depression has negative effects on outcomes of pulmonary rehabilitation (especially dyspnoea) in patients with COPD [50]. 4) There is a significant association between depression and lower adherence to treatment in patients with COPD [51].

Effects of antidepressants

Effects of tricyclic antidepressants

Only three double-blind clinical trials were found involving the tricyclic antidepressants (TCAs) doxepin, imipramine (combined with diazepam) and nortriptyline (table 3) [52–54].

One study [54] reported a large effect size for nortriptyline (Cohen's d -1.07) compared with placebo [10]; however, as only 30 patients completed the study it was strongly underpowered. Due to even more serious methodological limitations of the remaining studies no firm conclusions can be drawn concerning TCAs in patients with comorbid depression and COPD. In addition, the acceptability of TCAs in this patient group

TABLE 3 Antidepressant drugs in patients with chronic obstructive pulmonary disease (COPD) and depressive disorders: blinded treatment trials with tricyclic antidepressants

Characteristics of the study	Doxepin [52]	Imipramine [53]	Nortriptyline [54]
Study design	Randomised double-blind, placebo-controlled crossover clinical trial	Double-blind clinical trial with recruitment of patients on alternate basis; no placebo control	Randomised double-blind, placebo-controlled clinical trial
Participants	12 outpatients with stage III of COPD and severe depression (9 completed)	54 consecutively recruited patients with all stages of COPD and ''depressive neurosis''	36 inpatients with COPD (stages II–III) and depression according to DSM-III (30 completed)
Interventions	6-week treatment with either doxepin hydrochloride (flexible doses, maximally 25 mg·day^{-1}) or placebo	Imipramine combined with a benzodiazepine (diazepam) plus bronchodilators *versus* bronchodilators alone	12-week treatment with either nortriptyline or placebo (weekly increase of 0.25 mg·kg^{-1} up to 1 mg·kg^{-1} of body weight)
Outcomes	BDI (sum score)	BDI (sum score)	CGI score, HDRS (sum score)
Main results	No significant decrease of depression scores (doxepin: Cohen's d 0.37$^{\#}$; placebo: Cohen's d 0.46$^{\#}$); comparable antidepressive effects (low-middle) for doxepin and placebo	Imipramine-diazepam combination was associated with faster recovery in depressed patients with COPD Diazepam-induced respiratory failure is a serious side-effect	Nortriptyline was significantly superior to placebo (Cohen's d -1.07$^{\#}$ for the difference in reduction of HDRS total scores between nortriptyline and placebo)
Randomisation procedure	No information available	According to a subclassification of patients on alternate basis	By a table of random numbers
Support by manufacturers	No information available	No information available	Yes (partly)
Verified clinical COPD diagnosis	Yes	Yes	Yes
Assessment of depressive episodes in the past/family history of affective disorders/ core symptoms of depression	No	No	No
Assessment of compliance	Yes, by drug monitoring (pill count)	No	Yes, by pill count, nortriptyline serum levels and patients reports

DSM-III: Diagnostic and Statistical Manual of Mental Disorders, 3rd revision; BDI: Beck's depression inventory; CGI: clinical global improvement scale; HDRS: Hamilton depression rating scale. $^{\#}$: effect size as computed for a review [10] on effects of antidepressants and psychotherapy on depression in COPD patients.

is clearly limited by their side-effects (especially anticholinergic and antihistaminergic side-effects such as sedation) [10].

Regarding effects of TCAs on lung function in patients with COPD, neither effects on spirometry [52–54] or on peak expiratory flow rates [53] and respiratory function measured by arterial blood gases [54] have been found.

Effects of selective serotonin reuptake inhibitors

Four selective serotonin reuptake inhibitor (SSRI) trials with sample sizes >10 were detected, examining citalopram, fluoxetine and paroxetine (table 4).

Overall, the available studies did not have the statistical power to detect superiority of SSRI over placebo [55–58]. In addition, the drop-out rates in these trials were high (21–50%), and a variety of depression rating scales was used (table 4) [10], Frustration with multiple medications and the fear of side-effects have been discussed as the reasons for high dropout rates for depressed COPD patients reported in these antidepressant trials [10]. Negative effects of SSRIs on lung function in depressed patients with COPD do not appear to be a major problem. In the case of paroxetine, no significant changes in lung function were found [58]; respiratory symptoms did not worsen and dyspnoea slightly improved [57].

Possible adverse effects of antidepressants on lung function

There are some caveats regarding the interaction between antidepressant drugs and drugs commonly used in COPD (table 5). Whereas there are no principal contraindications of antidepressants in COPD patients, combination of fluvoxamine and St. John's wort with theophylline is contraindicated [61]. Concerning bupropion there is the risk of involuntary overdose, because this substance is also prescribed under a different brand name for the indication of smoking cessation [59].

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TABLE 4 Antidepressant drugs in patients with chronic obstructive pulmonary disease (COPD) and depressive disorders: blinded treatment trials with selective serotonin reuptake inhibitors

Study characteristics	Citalopram [55]	Fluoxetine [56]	Paroxetine [57]	Paroxetine [58]
Study design	Randomised, double-blind, placebo-controlled clinical trial	Single-blinded, open clinical trial	Randomised, double-blind, placebo-controlled clinical trial	Randomised, double-blind, placebo-controlled clinical trial
Participants	27 adult COPD patients with BDI sum scores of ⩾15 points without severe depression (19 completed)	57 COPD outpatients (stages II–III) and depression according to GMS scores (⩾3) (7 completed)	23 COPD outpatients (mean stage III) and a GDS sum score of ⩾11 points (15 completed)	28 COPD outpatients (stages II–III) and depressive disorders according to ICD-10 criteria
Interventions	12-week treatment with citalopram (20 mg·day^{-1}; increase to 40 mg at week 6, if tolerated) or placebo	6-month treatment with fluoxetine (20 mg·day^{-1})	12-week treatment with paroxetine (2 patients: 10 mg·day^{-1}; 6 patients: 20 mg·day^{-1}) or placebo	6-week treatment with paroxetine (20 mg·day^{-1}) or placebo; then, unblinded application of paroxetine (20 mg·day^{-1}) for 3 months
Outcomes	Response to treatment at weeks 6 and 12 as assessed by the HDRS	Sum scores for the MADRS at baseline, 6 weeks and 3 months	Sum scores in the GDS at final follow-up (in regular cases week 12)	Sum scores in the HADS, BDI, MADRS and SGRQ; 6-min walk test
Main results	No significant group difference, but stronger antidepressant effects of citalopram in cases of mild-to-moderate depression	4 out of 7 who completed also responded to fluoxetine, 5 patients dropped out due to adverse side-effects of fluoxetine	Significant antidepressant effects of paroxetine (in contrast to placebo); no significant group difference in GDS outcome	No significant group difference after 6 weeks; significant improvement after 3 months (HADS-D: Cohen's d 1.33#)
Randomisation method	No information available	No	Random numbers table	No information available
Manufacturer support	No information available	No information available	No	No information available
Verified COPD diagnosis	No information available	Yes	Yes	Yes
Depressive episodes in the past	No information available	Yes, previous diagnosis for depression led to exclusion	No	Yes, previous diagnosis for depression led to exclusion
Family history of affective disorders	No information available	No information available	No	No
Assessment of core symptoms of depression	No	No	No	No
Compliance assessment	No information available	No information available	Yes, by pill count	Yes, by pill count

BDI: Beck's depression inventory; GDS: geriatric depression screening scale; GMS: geriatric mental state schedule; ICD-10: international classification of diseases, 10th revision; HDRS: Hamilton depression rating scale; MADRS: Montgomery–Asberg depression rating scale; HADS: hospital anxiety and depression scale; SGRQ: St George's Respiratory Questionnaire; HADS-D: HADS depression subscale. #: effect sizes as computed for a review by FRITZSCHE *et al.* [10] on effects of antidepressants and psychotherapy on depression in COPD patients.

Treatment for suicidal or psychotic major depression in COPD patients can require the use of antipsychotics. Typical and atypical antipsychotics are often combined with antidepressants in the treatment of patients with psychotic major depression. Some atypical antipsychotics have an antidepressant effect on their own and are used without additional antidepressants in the treatment of major depression. So far, adverse effects of typical and atypical antipsychotics in COPD patients have not been reported.

Effects of psychotherapy

The efficacy of cognitive and behavioural interventions for depression in patients with COPD (especially cognitive behavioural therapy (CBT)) was well summarised in a recent review [10]. Six RCTs were available.

CBT was associated with a significant reduction of depressive symptoms in patients with COPD in the majority of studies. However, no strong conclusions can be drawn because a publication bias is probable. Moreover, depressive symptoms also strongly decrease in the placebo arms of the RCTs. Whether these improvements are larger than those in the control condition is important. To date, only one study found

TABLE 5 Adverse interactions between antidepressants and drugs commonly used in patients with chronic obstructive pulmonary disease (COPD)

Drug	Antidepressant drugs to avoid	Antidepressant drugs recommended
Drugs containing bupropion (typically administered for smoking cessation in patients with COPD)	Bupropion	Any other antidepressant drugs (*e.g.* other SSRIs)
Inhaled bronchodilators (*e.g.* ipratropium, salbutamol)	No antidepressant drug is specifically contraindicated	Any
Theophylline	Fluvoxamine (due to inhibition of theophylline metabolism) St. John's wort (due to increased theophylline metabolism)	Any other antidepressant drugs (*e.g.* other SSRIs)
Corticosteroids (*e.g.* beclomethasone, prednisolone)	No antidepressant drug is specifically contraindicated	Any
Leukotriene antagonists (*e.g.* montelukast)	No antidepressant drug is specifically contraindicated	Any

SSRI: selective serotonin reuptake inhibitor. Further details can be found in [59, 60].

CBT to have stronger antidepressant effects in COPD patients than standard care [62]. Other studies including one with a waiting list as the control group failed to find significant effects. In line with these findings, a recent meta-analysis revealed only small, nonsignificant effects of CBT on self-reported symptoms of depression in COPD patients [63]. In comparison to COPD education, CBT has been shown to have a comparable antidepressant effect [64].

Practical consequences

Keeping in mind the symptom overlap for depression and COPD, it is likely that COPD-related symptoms add to the number of symptoms required to formally diagnose a depressive disorder, thereby leading to an overestimation of the prevalence of depression in COPD patients. This bias could explain the increased prevalence of depression in patients with COPD reported in some of the epidemiological studies. Possibly, without this bias, the depression prevalence in COPD patients would not be much higher than that expected by chance. This would argue against COPD being a strong causal factor in the pathogenesis of depression. This view is supported by the findings that depression prevalence is not related to the severity of COPD [19] and that in patients with major depression the prevalence of COPD is even lower than in the general population [40].

The independence of depression from COPD is further supported by the fact that 23% of these patients had already experienced depressive episodes before the onset of COPD [65]. This reasoning underlines that caution is required when interpreting depression mainly as an understandable reaction to COPD, even when the patients themselves name COPD as the reason for their despair. This raises the question of how clinicians can separate a normal psychological reaction to severe COPD from a major depression. The following criteria and depression-specific symptoms are helpful in everyday practice in identifying the presence of a major depression: feelings of guilt (''I am a burden for my family''); profound anhedonia (''even when my grandchild visits me, I cannot enjoy it''); emotional numbness (''I can feel no feelings at all, not even grief, as if I am dead''); high inner tension (''…as if I am always on edge''); difficulties in relaxing and falling asleep (exhausted, but not sleepy); earlier depressive episodes; positive family history of affective disorders; suicidal tendencies; and delusional depression (typically delusions of guilt or wrong doing, delusion of poverty or hypochondriacal delusion).

Care has to be taken not to oversee an acute risk of suicide. An active exploration is necessary in every patient with a relevant depressive syndrome.

Concerning pharmacotherapy for depression it has to be concluded that there is sufficient evidence neither for the efficacy of antidepressants in depressed patients with COPD nor for the lack of efficacy. Therefore, until shown to the contrary, it has to be assumed that antidepressants are effective in this subgroup of patients as they are in patients without COPD. Because of the less problematic side-effect profile and the safety in overdose SSRIs should be preferred to TCAs. According to most guidelines antidepressants should be offered, especially in patients with moderate-to-severe depression. In this context, it has to be emphasised that antidepressants have to be prescribed when a depressive disorder is fully diagnosed in order to avoid their overprescription. According to the diagnostic criteria for major depression (table 1) symptoms which

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might be sufficiently explained by COPD (*e.g.* sleep problems) in a patient should not be used additionally as a symptom for diagnosing comorbid major depression.

In view of the fact that >50% of patients with COPD and an even higher percentage of patients with major depression suffer from sleep problems [66], hypnotics such as benzodiazepines might be considered as a treatment option. Indeed, benzodiazepines were effective in ameliorating quality of sleep in this patient group [67]. However, the well-known risk of drug dependence forbids the long-term use of these drugs. In addition, several case reports and case series have reported adverse pulmonary events associated with benzodiazepines in COPD patients [68], although this is not confirmed by all studies [69].

Concerning the efficacy of psychotherapy of depression in COPD no convincing evidence has been provided to date. However, since there are no reasons to assume a lack of efficacy for psychotherapy in these patients, treatment according to guidelines has to be provided. CBT is the psychotherapy with the best evidence for efficacy in patients with major depression [70]. In line with this, the recently published COPD-specific UK National Institute for Health and Care Excellence guidelines recommend "identifying and managing anxiety and depression" [60].

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