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Title: A systematic review and meta-analysis of studies comparing burden from lung cancer and chronic obstructive pulmonary disease (COPD)

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Abstract

Background

hronic obstructive pulmonary disease (COPD) and lung cancer are both life-limiting diseases that confer burden in the form of symptoms and impacts on functioning and quality of life. Comparing burden between these diseases is of interest to determine whether people with COPD require improved access to Specialist Palliative Care. Access should be based on needs rather than diagnosis or prognosis but is limited for people with COPD compared to lung cancer.

Aim

To synthesise research comparing burden from COPD and lung cancer to estimate relative need for Specialist Palliative Care.

Design

A systematic review was conducted of observational quantitative studies published in English peer-reviewed journals comparing burden from COPD and lung cancer (PROSPERO CRD42018108819). No limits were placed on disease stage. Meta-analyses were performed where studies used the same measure; otherwise, synthesis used a narrative approach. Risk of bias was assessed using the Agency for Healthcare Research and Quality tool.

Data sources

Electronic databases were searched in September 2019.

Results

Of 790 articles returned, 13 were included, reporting 11 studies. Risk of bias was generally moderate. Except for pain, burden tended to be at least as substantial from COPD as lung cancer, with breathlessness and impacts on functioning being even worse. Longitudinal studies suggest that people with COPD live with burden for longer.

Conclusion

Efforts should be made to ensure that access to Specialist Palliative Care is commensurate with COPD's substantial and long-lasting burden. Future research should clarify whether managing burden in COPD and lung cancer requires different approaches.

Keywords

Chronic obstructive pulmonary disease (COPD); lung cancer; symptoms; functioning; quality of life; systematic review

Key statements

What is already known about the topic

- Chronic obstructive pulmonary disease (COPD) and lung cancer are both life-limiting diseases that confer burden in the form of symptoms and impacts on functioning and quality of life.

- People with COPD are less likely to access Specialist Palliative Care than those with lung cancer, despite consensus that this should be based on needs rather than diagnosis or prognosis.

What this paper adds

- This systematic review shows that – with the exception of pain - most aspects of burden tend to be at least as substantial from COPD as from lung cancer, and breathlessness and impairments in functioning may be significantly worse.
- Longitudinal studies suggest that people with COPD often live with burden for longer.

Implications for practice, theory, or policy.

- Increased efforts should be made to ensure that people with COPD access Specialist Palliative Care to assist with managing their disease burden.
- Future research is needed to understand interactions between different levels of burden and other factors in each diagnostic group to inform disease-specific management approaches.

Introduction

Lung cancer and chronic obstructive pulmonary disease (COPD) have much in common. Both are lung diseases that affect adults mostly in mid to later life and are among the most common smoking-related causes of death globally (1). Both diseases cause significant burden in the form of symptoms and adverse impacts on functioning and quality of life (2, 3).

Disease burden and its measurement by means of patient-reported outcomes has been taxonomised within an influential model by Wilson and Cleary (1995) (4). This model delineates four 'levels' of outcome based on their more 'proximal' or 'distal' relationship to biological/physiological variables associated with disease and treatment, namely: symptoms, functioning, general health perceptions, and overall quality of life. More distal outcomes are assumed to be determined by flow-on effects from proximal problems, with mediation by personality and environmental factors such as social support.

The pathophysiologies of lung cancer and COPD both centre on the lungs but differ with regard to trajectory, treatment and prognosis. In their advanced stages, both diseases share respiratory symptoms of breathlessness and cough, with breathlessness being the most common and burdensome, especially in COPD (5, 6). Studies have demonstrated associations between symptoms, functioning and quality of life that are consistent with symptoms having flow-on impacts to other aspects of burden, as posited by the Wilson and Cleary model (7, 8).

People with lung cancer and COPD differ substantially in terms of access to Specialist Palliative Care. Specialist Palliative Care is a relatively recent sub-specialty of medicine that provides interdisciplinary care across settings to optimise quality of life and mitigate suffering among people with life-limiting illness (9). Available data suggest that people with COPD may be at least four times less likely to be referred to Specialist Palliative Care compared to people with lung cancer (10, 11). A large scale study across 14 countries (N=5,568,827) found that people with COPD were also less likely than those with lung cancer to die at home or in a palliative care institution, and more likely to die in a hospital or a nursing home (12). Smaller studies from the United States and Taiwan have found that people with COPD are also more likely to access aggressive but clinically futile care at the end of life, including admission to intensive care, ventilation, tube feeding and attempted cardiopulmonary resuscitation (13, 14).

While, historically, Specialist Palliative Care has focused largely on people with cancer in the last weeks or even days before death, contemporary referral criteria are based on need for *"early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual"* (15) at any stage after it is recognised that the person has a life-limiting illness, and regardless of diagnosis. There is a concern that people with COPD may be less likely than people with lung cancer to be referred to Specialist Palliative Care, not because they have lesser need, but because clinicians have been slow to move to a needs- rather than diagnosis-/prognosis-based model for referral (12, 16-18), driving inequality in Specialist Palliative Care access (19). These concerns are consistent with a review of comparative studies, which concluded that COPD confers as much,

if not greater, burden than lung cancer, and over a longer period (20). However, this review was not systematic and may, therefore, have been subject to bias in terms of study selection and synthesis.

The current authors set out to systematically review the evidence comparing burden from lung cancer and COPD to provide a more definitive answer to the research question, '*is burden from COPD in terms of symptoms and adverse impacts on functioning and quality of life as substantial as from lung cancer*'?

Methods

A systematic review protocol was registered in the PROSPERO prospective international register of systematic reviews (CRD42018108819) and is reported in accordance with the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) statement (21).

Eligibility criteria

To be eligible, articles needed to report studies comparing burden from COPD and lung cancer in the context of usual care and published in an English-language, peer-reviewed journal. We excluded studies describing burden in one patient group only because of reduced validity in comparing samples not drawn from the same population or using data for secondary analysis. No limits were set for stage of disease. Studies needed to be quantitative and observational but could be cross-sectional or longitudinal. While qualitative studies provide in-depth insights into lived experience of disease, the current review focused on estimates derived from standardised quantitative measures to facilitate comparisons between diagnostic

groups. No restrictions were set for date of publication. Measures of burden were defined and classified according to Wilson and Cleary's (1995) model of patient reported outcomes (4). Functioning measures were considered to include those of performance status or activities of daily living.

Information sources

The electronic databases Medline, Cumulative Index to Nursing and Allied Health (CINAHL) and PsycINFO were searched in September 2018 and updated in September 2019. These databases were chosen as the most extensive repositories of published research in the disciplines of medicine, nursing/allied health and psychology respectively. The reference lists of the previous non-systematic review (20) and included articles were hand searched for further relevant articles. Where necessary, article authors were contacted by email to request additional summary data to enable meta-analysis.

Search

Search terms were developed through a preliminary search of Medline in consultation with a university librarian. Subject headings and keywords related to lung cancer or COPD combined with breathlessness, performance status and functioning, and quality of life (see Supplementary Table 1). Symptom-related search terms were limited to breathlessness because this is the symptom most often referred to as common between lung cancer and COPD. Databases were searched from their earliest records, and results limited to English language and humans.

Study Selection

Articles returned from database searches were imported into EndNote (version X8). Initially, two researchers (TL and ASM) independently screened the titles/abstracts of 10% of articles against eligibility criteria, each obtaining full-texts as required to decide inclusion/exclusion. After finding >95% agreement, screening for the remaining articles was continued by one reviewer alone (ASM).

Data collection and items

A single reviewer (ASM) extracted data using an MS Excel proforma, with random checks conducted by a second reviewer (TL). Data items included author, year of publication, country, setting, study design, aims, sample characteristics (size, diagnoses, stage of disease, age and gender), outcome measures, results and author conclusions.

Risk of bias in individual studies

To assess risk of bias, we used a version of the Agency for Healthcare Research and Quality (AHRQ) tool (22) that was adapted for observational studies comparing two groups (23). This tool assessed: selection bias (uniformity of inclusion/exclusion criteria and comparability of groups on confounding variables); performance bias (definition of disease groups using standardised systems); detection bias (validity of outcome assessment, and control of confounding variables); and attrition bias (handling of missing data). Each study was appraised for bias by two researchers working independently (TL and ASM), who then discussed to reach consensus on any disagreements, with access to a third reviewer (JP) adjudicating as required.

Synthesis of results

A meta-analysis was conducted where data were available on the same outcome measure from two or more studies. Where studies were prospective, baseline data were selected for inclusion in meta-analyses. Random effects models were used to allow for the possibility that between-study differences varied according to differences in sample characteristics (24). Summary measures were mean differences between disease groups with 95% confidence intervals (CIs). Heterogeneity was estimated using the Cochrane I^2 statistic, and interpreted according to the Cochrane Handbook of Systematic Reviews as follows: 0% to 40% unimportant, 30% to 60% moderate, 50% to 90%: substantial, and 75% to 100% considerable heterogeneity (25).

Where data were unavailable to conduct a meta-analysis, synthesis used a narrative approach based on methods described by Popay et al. (2006) (26). We followed these authors in recognising that 'vote counting' the number of studies favouring each group can be a useful first step in synthesis provided that results are interpreted with acknowledgement that studies are unlikely to deserve equal 'weight' due to differences in reliability of estimates and risk of bias. Results for symptoms, functioning, health perceptions and quality of life were grouped according to whether: 1) all available studies exclusively found them to be worse in one disease group than the other; 2) all available studies either found them to be worse in one disease or found no difference; 3) studies sometimes found them to be worse in one disease group but in other studies vice-versa, or 4) no available study found a significant difference. For aspects of burden found to be equivocal, a narrative exploration was

conducted of differences in study characteristics and risk of bias that might explain why studies differed in their results. As well as statistical differences, narrative synthesis was concerned with whether between-group differences were clinically important. To standardise measurement across measures, a rule of thumb was adopted of 0.5 standard deviation (SD) for comparisons of mean scores (27). An exception was made for the Karnofsky Performance Scale (KPS) (28) measure of functioning, which is scored in increments of 10 (e.g. 20, 30) rather than single units. To be regarded as a clinically important difference on the KPS, a between-group mean difference of at least 10 points was required to suggest an average disparity of one or more category.

Results

Six hundred and seventy-one articles were returned by searches, of which 270 required full-text retrieval and 13 met inclusion criteria, reporting 11 studies (see Figure 1) (13, 14, 29-39). Articles were excluded based on title/abstract alone because they were not research, did not focus on disease burden, or did not compare lung cancer with COPD. Bausewein et al. (2010a, 2010b) (29, 30) and Weingaertner et al. (2014, 2015) (31, 32) each reported a single German study in two articles. An article by Habraken et al. (2009) (34) reported new data both separately and in combination with data from a previous study that shared some of the same team members by Gore et al. (2000) (33). The current review considered original data from each of these studies separately.

Figure 1 about here

Study characteristics

Included articles were published between 2000 and 2017. Five of the studies were conducted in Europe (29-35), two in the USA (13, 36), and one in each of Australia (39), China (38), Taiwan (14) and Japan (37). Collectively, the samples included a greater number of people with lung cancer (n=2,694) than COPD (n=1,899), due in large part to the Australian study, which included 1,081 people with lung cancer but only 199 with COPD (39). The COPD group in the Australian study also included people with other respiratory diseases, and the numbers with each type of disease were not reported. While data were reported from this study for samples with secondary as well as primary lung cancer, we focused on the group with primary lung cancer in our synthesis. In the other 10 studies, lung cancer samples were smaller than or equal to COPD in all studies apart from two (36, 38).

Age and gender characteristics were similar between groups in all studies that reported these except three (14, 36, 37), one of which had significantly more men with COPD (37) and two of which had significantly older COPD samples (14, 36). Only the two US studies reported data on ethnicity, both of which included >80% Caucasian participants (13, 36). Disease groups were most commonly staged using the tumour, node and metastasis (TNM) staging for lung cancer (40) and Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria for COPD (41). Table 1 summarises the characteristics of each included study.

Table 1 about here

Results of individual studies

The measures used by each of the 11 studies to compare lung cancer with COPD and related results are detailed in Supplementary Table 2. Collectively, studies measured a wide range of domains of burden, assessing all levels of Wilson and Cleary's (1995) model (4).

Risk of bias within studies

The main sources of bias arose from inconsistency in eligibility criteria across disease groups and less than optimal control for confounding variables. Studies by Bausewein et al. (2010a, 2010b) (29, 30) and Weingaertner et al. (2014, 2015) (31, 32) were rated as lowest risk of bias overall, although were also two of the smaller studies in terms of sample size (N=109 and N=82 respectively). Results from risk of bias assessment are summarised in Table 2.

Table 2 about here

Synthesis of results

Table 3 summarises results from vote counting for each domain of burden (i.e. the numbers of studies finding COPD or lung cancer to be worse, or no significant difference). The numbers of studies finding burden to be worse in COPD than lung cancer were generally higher than vice-versa, with the notable exception of pain, which was found to be worse in lung cancer in 5/8 studies.

Table 3 about here

An exploration of equivocal results is presented for each level of burden as follows. Across measures, there were no discernible patterns in results according to sample size or risk of bias. The studies that most consistently found significant differences were mid-ranking in risk of bias and small to moderately sized (33, 35, 38).

Symptoms

Breathlessness (or dyspnoea/shortness of breath/chest tightness) was among the most commonly measured symptom, and was found either to be worse in COPD or not significantly different. A German study by Bausewein et al. (2010a, 2010b) (29, 30) found results to be mixed on the Memorial Symptom Assessment Scale Short Form (MSAS-SF) (42) versus Modified Borg Dyspnea Scale (MBS) (43). Bausewein et al. found the proportion with shortness of breath and severity of distress due to breathlessness to be higher in COPD than lung cancer on the MSAS-SF, but found no significant difference on the MBS. A meta-analysis of the MBS that included Bausewein et al.'s study and another German study by Weingaertner et al. (2014, 2015) (31, 32) found the overall difference between people with lung cancer compared with COPD also to be non-significant, but with substantial heterogeneity (-0.71, 95% CIs -1.98 to 0.56, I^2 79%) (Figure 2). Compared to Weingaertner et al.'s study and some others that found breathlessness to be worse in COPD, Bausewein et al.'s sample included a lower proportion of COPD patients with GOLD stage IV versus III disease as well as a higher proportion of lung cancer patients with metastatic disease, and a lower proportion of male patients. However, these differences were not always consistent, and reporting of disease stage varied.

Figure 2 about here

The study by Bausewein et al. (2010a) was one of three longitudinal studies that tracked breathlessness and/or distress up until death and identified these symptoms to worsen later in the lung cancer than COPD trajectories (29, 31, 39). One of these longitudinal studies was the only one that enabled assessment of between-group differences in breathlessness in terms of clinical importance; breathlessness was worse in COPD to a clinically important extent (≥ 0.5 SD) at all three timepoints (39). The study by Bausewein et al. (2010a) identified individual variations in breathlessness corresponding to four different patterns: fluctuation, increasing, stable and decreasing breathlessness (29). While people with lung cancer differed from people with COPD regarding the relative frequency of these patterns, all four patterns were observed in both groups.

Bausewein et al.'s (2010a, 2010b) (29, 30) results on the Hospital Anxiety and Depression Scale (HADS) (44) were typical of studies measuring anxiety and depression in finding there to be no significant between-group differences. This finding was upheld even when combined in meta-analyses with a UK study by Gore et al. (2000) (33) that found both anxiety and depression to be significantly worse in COPD (anxiety -1.80, 95% CIs -6.41 to 2.80; depression -1.03, 95% CIs -4.86 to 2.70) (Figure 2). Gore et al.'s lung cancer sample differed from Bausewein et al.'s in terms of being mostly (72%) men and having received palliative care radiotherapy over the last 12 months in 80% of cases. It was less clear what might have led other studies to differ from the majority by finding depression to be worse in COPD (34, 35) or anxiety to be worse in lung cancer (13), and between-group differences in

these studies were either mixed (13, 34) or less than the 0.5 SD taken to suggest a clinically important difference (35).

Figure 3 about here

As noted above, most studies measuring pain found this to be worse in lung cancer than COPD. The only study that found pain to be worse in COPD was the study by Gore et al. (2000) (33), in which pain in the lung cancer sample may have been substantially managed by palliative radiotherapy.

Sample characteristics may have also been a factor to findings on vitality. The study by Gore et al. (2000) found vitality to be worse in COPD (33), whereas a Dutch study by Habraken et al. (2009) found no between-group differences for this symptom (34). Habraken et al. enrolled disproportionately more people with COPD than with lung cancer (n=82 vs. n=19) and focused on outpatients only, whereas Gore et al. included inpatients as well.

Functioning

Seven studies measured functioning, all of which identified impairments to be worse in COPD, except for the study by Bausewein et al. (2010a/2010b) (29, 30), which again found no difference. A meta-analysis that included this study alongside four others that used the Karnofsky Performance Scale (KPS) (28) found functioning to be significantly better for people with lung cancer than COPD overall (7.64, 95% CIs 3.89 to 11.4, I^2 65%) (Figure 4). However, the 95% CIs of estimates from our meta-

analysis included a (10 point) categorical difference only at the upper end, questioning the clinical importance of the overall estimate.

Figure 4 about here

Differences between the samples of Bausewein et al. (2010a/2010b) and those of Gore et al. (2000) and Weingaertner et al. (2014, 2015) are noted above. Compared with Bausewein et al.'s (2010a/2010b) sample, the Serbian sample of Maric et al. (2016) had more men and a higher proportion of patients with metastatic disease in the lung cancer group. No important differences were observed between Habraken et al.'s (2000) Dutch sample and Bausewein et al.'s (2010a/2010b), but comparisons were hampered by limited and inconsistent reporting. Habraken et al (2000) reported that 23% and 73% of their COPD and lung cancer samples respectively died within a year of data collection, compared to 10% and 62% within 6 months for Bausewein et al. (2010a/2010b).

Studies that used measures of functioning other than the KPS found that patients with COPD compared to lung cancer had greater dependencies on activities of daily living in COPD versus lung cancer on the Katz Activities of Daily Living (13) and were less likely to have high functioning denoted by the Palliative Performance Scale (36). Neither study enabled assessment of clinical importance against the threshold of 0.5 SD.

General health perceptions

Three studies used the Medical Outcomes Study Short Form 36 (SF-36) (45) to measure health perceptions, all of which found these to be less positive in people with COPD than lung cancer (33-35).This scale is based on a single question, namely: “In general, would you say your health is: excellent/very good/good/fair/poor?”. Between-group differences in the two studies that reported scores rather than just p-values (34, 35) were in excess of the (46)0.5 SD assumed to indicate a clinically important difference.

Quality of life

The same three studies reported results on other scales from the SF-36 (47) on quality of life but reported these in ways that precluded a meta-analysis. In all three cases, SF-36 scales either registered lower quality of life in COPD or no significant difference. However, only physical functioning was found to be significantly worse in COPD across all three studies, and differences rarely met criteria for clinical importance where means/SDs were reported.

A Taiwanese study that used the McGill Quality of Life (MQOL) Questionnaire (37) found mixed results, with social support worse in COPD but psychological support worse in lung cancer, and no significant difference on physical symptoms/problems. This study was one of three to measure global or overall quality of life via a single item, all of which found there to be no significant between-group differences (13, 36, 37).

The three studies that used the SF-36 also administered disease-specific quality of life measures, but these could not be compared between groups because measures necessarily differed between lung cancer and COPD (33-35).

Other measures

Measures that could not be readily classified using Wilson and Cleary's (1995) model (4) included sub-scales of the Palliative Outcome Scale (POS) (48) assessing palliative care needs relating to information, sharing feelings, practical matters and a feeling of time being wasted on healthcare appointments, and the Functional Assessment of Chronic Illness Therapy (FACIT) measure of spiritual wellbeing (the FACIT-SP-12) (49). These scales identified no significant differences between groups, except for the POS scale, which found people with lung cancer to fare worse on a scale measuring the degree to which people felt time had been wasted on healthcare appointments.

Discussion

With the notable exception of pain, the current systematic review suggests that most aspects of burden are at least as substantial from COPD as from lung cancer, and that breathlessness and impairments in functioning may be significantly worse. Longitudinal studies indicate that symptoms tend to present later in the lung cancer disease trajectory, suggesting that people with COPD are also likely to live with disease burden for longer (29, 31, 39). These findings confirm and extend those of a non-systematic review published in 2012 (20).

Results from this review are consistent with concerns that people with COPD may be disadvantaged by limited access to Specialist Palliative Care, a specialty specifically aimed at easing burden from life-limiting disease. Research on health professional knowledge, attitudes and beliefs suggests that barriers to Specialist Palliative Care access for people with COPD may stem from difficulties with prognosticating and a commensurate reluctance to discuss end of life care for fear of undermining hope (50, 51). While both COPD and lung cancer are life-limiting, mean survival time from diagnosis is approximately five times longer for people with COPD (30). Symptoms may emerge, present and be interpreted differently for each disease during their respective trajectories. Breathlessness is more insidious in people with COPD and may therefore be less likely to trigger clinical attention compared to the rapid escalation associated with lung cancer towards the end of life (29). Also, pain tends to be less severe and more chronic in COPD compared to lung cancer, and is less well understood in terms of pathophysiology and relationship to other clinical features (52). Pain is assumed by many health professionals to be the main criterion for referring to Specialist Palliative Care (53), and may be the clinical feature most

commonly enabling access for people with lung cancer (54). A survey of Australian and New Zealand Respiratory specialists found that the main reasons they would refer someone with COPD to Specialist Palliative Care included psychosocial and spiritual care, carer support and end of life care (55). Educating health professional about disease burden from COPD and what Specialist Palliative Care can usefully offer to ameliorate this may be needed to support the global shift towards needs-based referral aimed at improving access (12, 16-18).

In addition to barriers to referring patients with COPD to Specialist Palliative Care, it is also worth noting that some services within the specialty may themselves be slow to move to a needs-based model. There is a paucity of research on relevant attitudinal barriers among Specialist Palliative Care clinicians, but a systematic review in 2015 of referral criteria for people with cancer found that prognosis of less than 1 year or even 6 months remained a requirement in some cases (56). Specialist Palliative Care needs to lead the way in aligning access with needs-based rhetoric, advocating for resources to manage the associated increase in caseloads.

The differences in pathophysiology underlying COPD when compared to lung cancer and its influence on their respective trajectories may have implications for how different levels of burden interact and are affected by other factors. Comparative studies suggest that breathlessness is prominent within the symptom profiles for both diseases (29). Breathlessness also has a negative association with functioning of a similar magnitude for both patient groups (31). However, it cannot be assumed that trajectories and associations are due to the same underlying mechanisms for each diagnostic group. One study in our pool identified a relationship between quality

of life and socio-economic factors for people with COPD not found for the lung cancer sample (35), suggesting that unemployment and financial stress may have a greater role as mediating factors in COPD. Other research suggests that reduced work productivity and quality of life are associated with COPD exacerbations (57), perhaps through time spent in hospital and reduced activity from fear of causing a re-occurrence (58). Potential differences of this kind are important because there has been an increasing trend toward delivering the same breathlessness self-management interventions to people regardless of their diagnostic group (59). Further longitudinal research is needed to better understand similarities and differences between pathways to burden in COPD versus lung cancer to inform whether interventional approaches should be targeted based on disease type.

Strengths and Limitations

The systematic approach taken by this review minimised the risk of bias compared to those previous (20). However, a number of limitations should be noted. The most important of these concerns the degree to which COPD and lung cancer are comparable with regard to stage of disease and care received. TNM criteria determine the stage of lung cancer according to degree of metastases, whereas GOLD criteria for COPD define stage based on spirometric criteria and number/severity of exacerbations, as well as, more recently, breathlessness and COPD-specific quality of life. Samples from each group within the same studies were likely to have received different treatments from different services (i.e. Oncology versus Respiratory) even when drawn from the same hospital or community population. There is also likely to be variability between individual services regarding the priority placed on managing symptoms. Most importantly, reporting was limited

on whether participants had received Specialist Palliative Care which, as noted earlier, is more likely for patients with lung cancer than those with COPD. Service factors were seldom reported so could not be controlled for in analyses, and are likely to have contributed to differences in burden. While we sought to address heterogeneity by using a random effects model in our meta-analyses, the capacity of this approach is limited, and the small number of studies available for each comparison may have reduced reliability (60).

A further limitation concerns the likelihood that some people in the included studies had both lung cancer and COPD given the relationship between tobacco smoking and both diseases. A systematic review of studies comparing lung cancer prevalence in COPD to controls estimated a summary odds ratio of 6.35 (95% CI: 3.98–10.15) (61). Even the two studies in our pool that tried to exclude people presenting with both diseases (34, 35) are likely to have done so imperfectly given research suggesting that COPD is under-diagnosed in people with lung cancer, perhaps even in the majority of cases (62). Comorbidity of COPD with lung cancer increases burden (63, 64), as well as patients' likelihood of receiving palliative care support (65).

A final limitation concerns the ways in which included studies chose to define and measure burden. Burden-related constructs are often complex and multidimensional, and nomenclature is sometimes inconsistent and/or poorly differentiated. To increase the validity of comparisons, we used an established model for classifying different levels of burden, and confined meta-analyses to studies that used the same measure. This conservative approach had the disadvantage that only a small number of studies could be included in each meta-analysis, ranging from as few as

two studies through to five. Many authors did not report results in a way that enabled assessment of clinical importance as well as statistical significance. Moreover, qualitative research suggests that even constructs that are considered more proximal to the disease, such as breathlessness, may be experienced and interpreted differently by people with lung cancer versus COPD (66). More distal constructs such as quality of life are likely to be subject to a variety of complex factors not measured in the studies. Some, such as self-blame and stigma related to smoking aetiology are experienced by people in both disease groups (67, 68). However, there may be other constructs that are of greater salience for one group or the other. Symptoms experienced by people with lung cancer are likely to be more variable than COPD, depending on the sites of metastasis (5). Limiting our symptom-related search terms to breathlessness may have overlooked studies measuring symptoms that are prevalent in only one disease, thus under-estimating symptom burden from one disease or other.

Limiting inclusion to articles published in English has not been found to lead to significant publication bias in previous research (69). However, when considering the generalisability of results, it is worth noting that studies were conducted in a narrow range of countries and, with the notable exception of the US study by Claessens et al. (2009) (13), had sample sizes of 100 people or less in each disease group.

Conclusion

This systematic review and meta-analysis suggests that most aspects of burden are at least as substantial from COPD as from lung cancer, and that breathlessness and impairments in functioning/ADL are significantly worse. People with COPD are also

likely to live with burden for longer. Given that eligibility for Specialist Palliative Care is defined by needs rather than prognosis, efforts are needed to improve access for people with COPD. Further research is needed to understand the relative pathways underlying disease burden from COPD and lung cancer to establish whether disease-specific approaches are needed to alleviating burden in each case.

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TL, ASM and JP designed and conducted the systematic review. DC, MJ and MB-H assisted with interpretation of results. All authors contributed to writing the manuscript.

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Conflicts of interest

The Authors declare that there is no conflict of interest.

Ethics and consent

Ethics approval was not required for this review.

Data sharing
Data are limited to published articles available within the public domain.

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Table 1: Sample characteristics from 11 studies comparing burden from lung cancer with chronic obstructive pulmonary disease (COPD)

Authors (Year) Country	**Cross-sectional or longitudinal**	**Setting**	**Sample size**		**Stage of disease**		**Age Mean (±SD) or Median/IQR**		**% Male**	
			Lung cancer	COPD	Lung cancer	COPD	Lung cancer	COPD	Lung cancer	COPD
Gore et al (2000) (26) UK	Cross-sectional	Mixed	50	50	Unresectable	FEV1 <0.751 and ≥1 admission for hypercapnic respiratory failure	71.4 (±6.5)	70.5 (±5.5)	72	44
Claessens et al (2000) (8) USA	Longitudinal	Inpatient	939	1008	TNM Stage III/IV	Acute exacerbation of severe COPD	63/no IQR	70/no IQR	62.2	51.3
Habraken et al (2009) (27) Netherlands	Cross-sectional	Outpatient	19	82	TNM Stage IIIb/IV	GOLD Stage III/ IV	69.6 (±6.9)	69.5 (±6.7)	63	66
Bausewein et al. (2010a,b) (4, 23) Germany	Longitudinal	Mixed	49	60	TNM Stage III/IV	GOLD Stage III/IV	63.9 (±9.1)	65.2 (±9.7)	51	48
Currow et al (2010) (32) Australia	Longitudinal	Community	1,081	199	Not specified, but receiving specialist palliative care		Not reported	Not reported	Not reported	Not reported
Taur et al (2012) (31) China	Cross-sectional	Inpatient	129	76	Not indicated	Not indicated	70.0 (±12.2)	79.5 (±7.2)	91.5	98.7
Chou et al (2013) (9) Taiwan	Longitudinal	Inpatient	43	103	Advanced /metastatic defined by no further benefit predicted from anti-	End-stage defined by any of: respiratory failure postintubation, persistent hypoxia, tachycardia or tachypnea after oxygen therapy, unstable hemodynamics with	73.4/59.6-81.9	82.7/77.2-86.9	76.7	73.8

Authors (Year) Country	**Cross-sectional or longitudinal**	**Setting**	**Sample size**		**Stage of disease**		**Age Mean (±SD) or Median/IQR**		**% Male**	
			Lung cancer	COPD	Lung cancer	COPD	Lung cancer	COPD	Lung cancer	COPD
					tumor therapy and suffering from physical, psychosocial or spiritual distress	hypotension, or cachexia with chronic malnutrition				
Weingaertner et al. (2014, 2015) (24, 25) Germany	Longitudinal	Mixed	32	50	TNM Any stage	GOLD Stage III/IV	66.4(+8.2)	67.7(+7.6)	72	58
Wysham et al (2015) (29) USA	Longitudinal	Mixed	152	71	Not indicated	Not indicated	69.5/42.3-89.3	75/51.2-94.7	50	41.5
Maric et al (2016) (28) Serbia	Cross-sectional	Outpatient	100	100	Stage IIIb or IV	GOLD Stage IV	61.3 (±8.97)	63.08 (±9.79)	63	63
Hasegawa et al (2017) (30) Japan	Cross-sectional	Mixed	100	100	Inoperable TNM Stage II/III/IV	GOLD Stage III/IV	66.1 (±10.1)	74.5 (±6.2)	60.3	84.8

FEV1 - forced expiratory volume; GOLD - Global Initiative for Chronic Obstructive Lung Disease; IQR – interquartile range; SD – standard deviation; COPD – chronic obstructive pulmonary disease; TNM – tumour, node, metastasis

Table 2: Risk of bias in 11 studies comparing burden from lung cancer with chronic obstructive pulmonary disease (COPD)

Author (Year) **Country**	**Selection Bias**		**Performance Bias**	**Detection Bias**		**Attrition Bias**
	Uniform inclusion / exclusion criteria	*Control for important confounding and modifying variables*	*Lung cancer and COPD defined for comparison*	*Valid outcomes assessment*	*Confounding variables assessment*	*Missing data handled appropriately*
Gore et al (2000) (26) UK	Y	N	N	Y	N/A	N/A
Claessens et al (2000) (8) USA	N	N	N	Y	N/A	N/A
Habraken et al (2009) (27) Netherlands	Y	N	Y	Y	N/A	N/A
Bausewein et al. (2010a,b) (4, 23) Germany	Y	N	Y	Y	Y	N
Currow et al (2010) (32) Australia	Y	N	N	Y	N	Y
Taur et al (2012) (31) China	N	N	N	Y	N	N/A
Chou et al (2013) (9) Taiwan	Y	N	N	N	N	Y
Weingaertner et al. (2014, 2015) (24, 25) Germany	N	Y	Y	Y	Y	N
Wysham et al (2015) (29) USA	N	N	N	Y	N/A	N/A
Maric et al (2016) (28) Serbia	Y	N	Y	Y	N	N/A
Hasegawa et al (2017) (30) Japan	N	N	Y	Y	N/A	N/A

N = No, criterion not met; N/A – not applicable; Y – Yes, criterion met

Table 3: Number of studies finding various domains of burden to be worse in COPD compared to lung cancer, vice-versa, or no significant difference

Level of burden	**Construct**	**Number of studies**			
		Worse in COPD	**Worse in lung cancer**	**No difference**	**Total***
Symptoms	Anxiety	1	0	3	4
	Depression	1	0	1	2
	Mood	0	1	1	1
	Distress	0	0	2	2
	Suicide risk	1	0	1	1
	Feeling sad	0	0	1	1
	Nervousness	0	0	1	1
	Irritability	0	0	1	1
	Worrying	0	0	1	1
	Feeling anxious or worried	0	1	0	1
	Family anxious	0	1	0	1
	Life worthwhile	0	0	1	1
	Feeling good	1	0	0	1
	Pain	1	6	3	9
	Breathlessness	6	0	5	9
	Shortness of breath	2	0	1	3
	Chest tightness	1	0	0	1
	Cough	0	1	2	3
	Dysphagia	0	0	1	1
	Dry mouth	1	0	0	1
	Fatigue	0	2	3	4
	Lack of energy	0	0	1	1
	Vitality	1	0	1	2
	Lack of strength/weakness	0	0	2	2
	Feeling drowsy/ difficulty sleeping	0	1	1	1
	Insomnia	1	1	0	2
	Poor appetite/anorexia	0	1	3	4
	Weight loss	0	0	1	1
	Nausea	0	1	1	2
	Abdominal distention	0	1	0	1
	Feeling bloated	1	0	0	1
	Constipation	1	1	0	2
	Diarrhoea	0	0	1	1
	Urine retention	1	0	0	1
	Sweats	0	0	1	1
	Changes in skin	1	0	0	1
	Pressure sores	0	1	0	1
	Oedema	1	0	0	1
	Delirium	0	1	0	1
	Numbness in hands/feet	0	0	1	1
	Thirst	1	0	0	1
	“I don’t look like myself”	0	0	1	1

Level of burden	Construct	Number of studies			
		Worse in COPD	Worse in lung cancer	No difference	Total*
	Problems with sexual activity	0	1	0	1
	Symptoms other than pain and breathlessness	0	1	0	1
	Total number of symptoms	0	0	1	1
	Mean severity of all symptoms	1	0	0	1
	Average frequency and distress caused by all MSAS symptoms	0	0	1	1
	Average frequency of four psychological symptoms and distress associated from six physical symptoms	0	0	1	1
	Average of distress associated with 12 physical symptoms	0	0	1	1
Functioning	Performance status or activities of daily living	7	0	1	8
Health perceptions	General health perceptions	3	0	0	3
Quality of life	Social support	1	0	0	1
	Psychological support	0	1	0	1
	Role emotional	1	0	2	3
	Mental health	2	0	1	3
	Mental component summary	1	0	0	1
	Physical symptoms/problems	0	0	1	1
	Role physical	1	0	2	3
	Physical functioning	3	0	0	3
	Physical component summary	1	0	0	1
	Social functioning	2	0	1	3
	Overall quality of life score (SF-36)	1	0	0	1
	General/global quality of life (single item)	0	0	3	3
Other measures	Spiritual wellbeing	0	0	1	1
	Existential issues	0	0	1	1
	Palliative care needs	0	1	2	2

* Some studies yielded results reported in more than one column; COPD = chronic obstructive pulmonary disease.

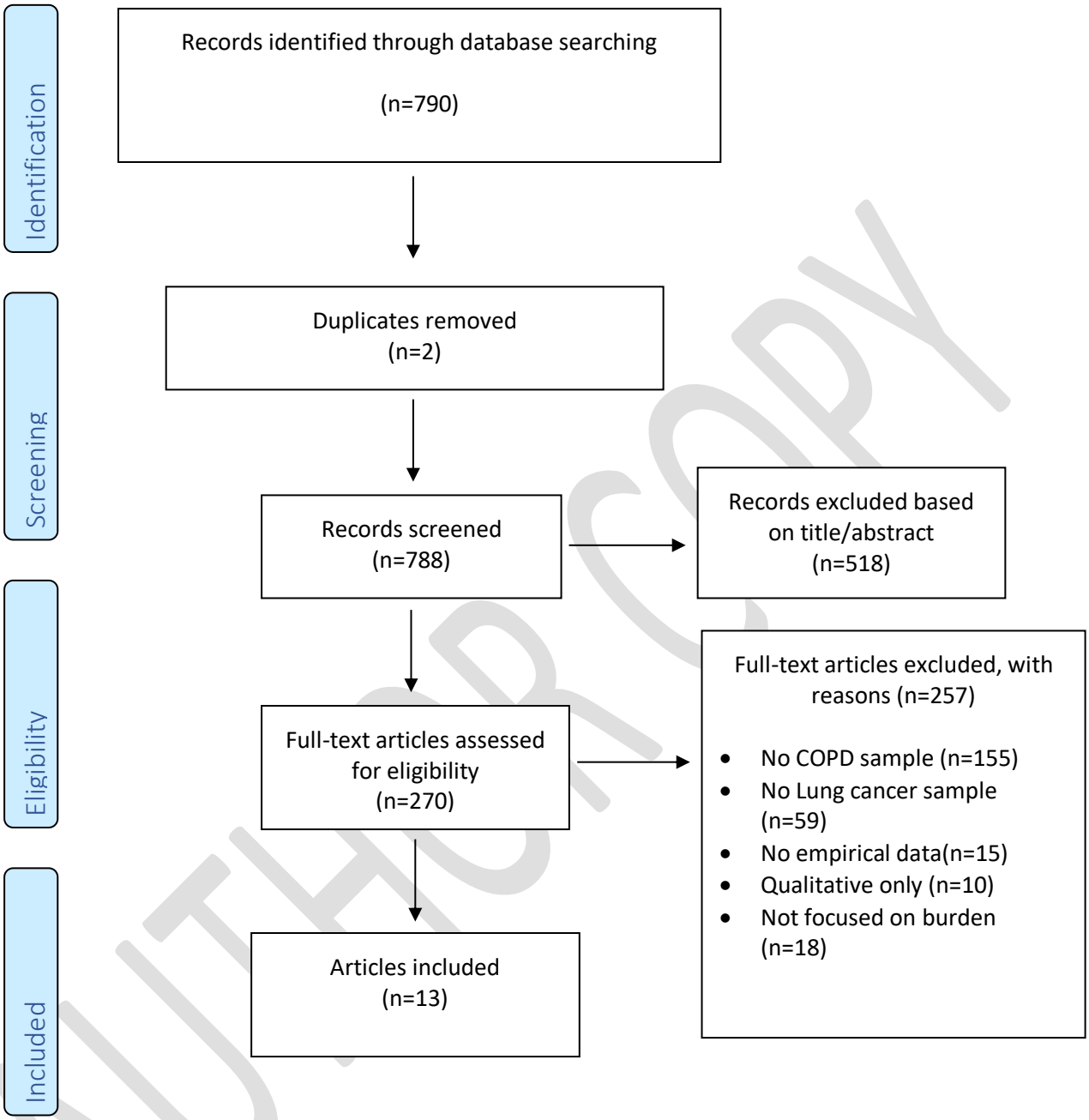

Figure 1. Flowchart showing the numbers of articles screened and included.

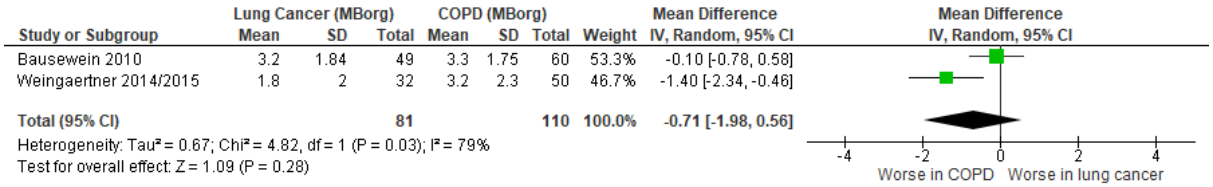

Figure 2: Meta-analysis of results from two studies comparing the Modified Borg Dyspnea Scale in people with lung cancer and people with chronic obstructive pulmonary disease (COPD).

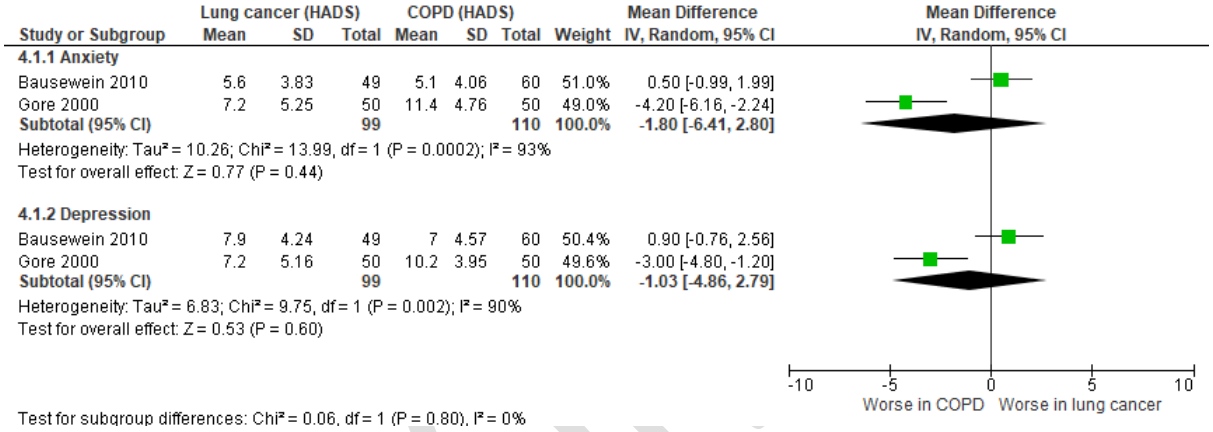

Figure 3: Meta-analysis of results from two studies comparing the Hospital Anxiety and Depression Scale (HADS) in people with lung cancer and people with chronic obstructive pulmonary disease (COPD)

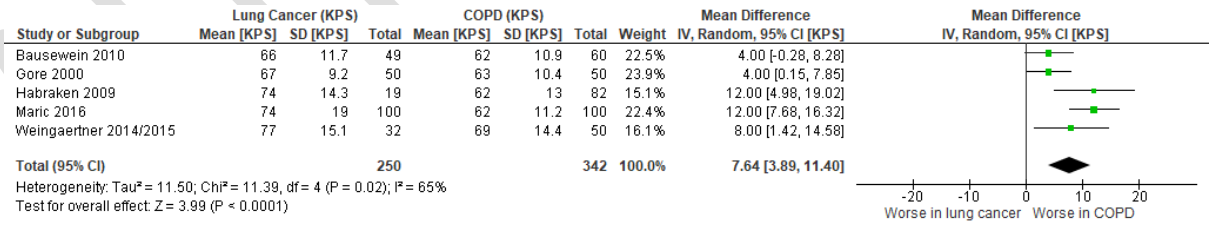

Figure 4: Meta-analysis of results from 5 studies comparing Karnofsky Performance Status in people with lung cancer and people with chronic obstructive pulmonary disease (COPD)

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Supplementary Table 2: Results from 11 studies comparing burden from lung cancer with chronic obstructive pulmonary disease (COPD)

Level	Construct	Measure	Article	Worse in COPD	Worse in lung cancer	No significant difference
Symptoms	Anxiety/ depression	HADS	(33)	Mean (SD) depression in lung cancer vs COPD: 7.22 (5.16) vs 10.18 (3.95), p<0.01 Mean (SD) anxiety in lung cancer vs COPD: 7.20 (5.25) vs 11.44 (4.76), p<0.0001 Proportions with clinically relevant scores on either scale: 52% lung cancer vs 90% COPD		
			(34)	Proportion of clinically significant depression: 32% vs 49%, (no p-value reported)		Median (IQR) anxiety: 7(4-10) vs 6 (3-10), p=0.641 Median (IQR) depression: 6 (4-9) vs 7 (4-11), p=0.228 Proportion of clinically significant anxiety: 42% vs 42 %, (p-value not reported)
			(29)			No statistically significant difference (p>0.01)
			(30)			No p values reported. Graphs suggest 25% have suggestive/probable anxiety and almost 50% have suggestive/probable depression in both groups
	Depression	BDI	(35)	Mean (SD): 17.04 (10.07) vs 20.19 (10.54), p=0.032		
		MSDS	(36)			No statistically significant difference in proportions with lung cancer vs COPD reporting depression

Level	Construct	Measure	Article	Worse in COPD	Worse in lung cancer	No significant difference
	Mood	POMS	(13)		Median (25th, 75th percentile), anxiety in people dying within 2 months: 1.33 (0.67, 2.00) vs 1.17 (0.67, 2.67), p-value not reported.	Median (25th, 75th percentile) anxiety in all people: 0.83 (0.17-1.50) vs 0.83 (0.33, 1.67), p-value not reported Depressive affect in all people, median (25th, 75th percentile): 0.38 (0.00, 1.13) vs 0.38 (0.00, 1.00), p-value not reported.
	Distress	DT	(31)			Mean (SD, range) of symptom distress: 4.5 (2.3, 0-10) vs 4.6 (2.4 0-10), p=0.77
		MSAS-PSYC	(30)			Average distress associated with six psychological symptoms in lung cancer vs COPD: 1.1 (range 0-3.4) vs 1.3 (range 0.1-3.5), p=0.36
	Suicide risk	Suicide risk screening	(38)			Proportion (%) of people with moderate to high levels of symptom (reported as not significant, no value given): Suicidal thoughts: 18 (14.0%) vs 18 (23.7%), Negative thoughts: 23 (17.8%) vs 20 (26.3%), Behavioural symptoms: 18 (14.0%) vs 13 (17.1%)
		Suicide tendency scale	(38)	Mean (SD) of suicide tendency score: 2.5 (0.3) vs 2.6 (0.4), (p value not reported)		
	Feeling sad	MSAS-SF	(30)			28 (57%) vs 23 (38%), p=0.05
	Nervousness	MSAS-SF	(30)			23 (48%) vs 35 (59%), p=0.24
	Irritability	MSAS-SF	(30)			23 (47%) vs 23 (38%), p=0.82
	Worrying	MSAS-SF	(30)			32 (65%) vs 39 (67%), p=0.83
	Feeling anxious or worried	POS	(30)		Median 1 vs 0.5 (p=0.01)	

Level	Construct	Measure	Article	Worse in COPD	Worse in lung cancer	No significant difference
	Family anxious	POS	(30)		Median 3 vs 2 (p=0.01)	
	Life worthwhile	POS	(30)			Median 0 vs 1 (p=0.56)
	Feeling good	POS	(30)	Median 1 vs 0 (p=0.05)		
	Pain	Ad hoc measure - interview	(13)		Proportions with severe pain*: 27% lung cancer vs 17% COPD (p=.002)	Proportions of people dying within 2 months with severe pain**: 35% lung cancer vs 28% COPD (p=>0.05)
		MSDS	(36)			Moderate to severe pain: 51% vs 38%, p=0.08 Number of people reporting pain as a symptom, p>0.05
		MSAS-SF	(30)		Pain 34 (69%) vs 26 (43%), p=0.01	
		MSDS	(38)		Pain mean 3.96 vs 2.43 (textual description that difference was significant)	
		MQOL	(37)		Pain 20.6% vs 6.0% (no p value given but significance assumed)	
		SF-36	(34)			Bodily pain: 74 (41-80) vs 62 (41-100), p=0.559
		SF-36	(33)	p≤0.05		
		SF-36	(35)		Bodily pain: 54.72 (34.57%) vs 67.90 (33.15%), p=0.006	
		POS	(30)		Median 1 vs 3 (p=0.00)	
	Breathlessness	Ad hoc measure - interview	(13)	Proportions with severe breathlessness*: 26% lung cancer vs 48% COPD (p=.001)		Proportions of people dying within 2 months with severe breathlessness: 46% lung cancer vs 60% COPD (p>0.05)

Level	Construct	Measure	Article	Worse in COPD	Worse in lung cancer	No significant difference
		MBS	(31)	Number (%) with breathlessness: 24 (75%) vs 48 (96%), p=0.005 Number (%) with continuous breathlessness: 7 (22%) vs 26 (52%), p=0.007 Number (%)with severe breathlessness: 3 (9%) vs 16 (32%)		
		MBS	(32)	Total number (%) of episodes of breathlessness: 189 (100%) vs 403 (100%), p<0.001 Mean (SD) Borg score: 4.2 vs 6.2, p<0.001 Number (%) severe Borg scores, (≥5): 4.2 (1.9%) vs 6.2 (2.1), p<0.001 Median (range) of breathlessness episodes (min): 5.0 (0.3-120 minutes) vs 7.0 (0.02-600 minutes), p=0.002 Percentage of breathlessness episodes: ≤5 min: 62.5% vs 50.0%, p=0.001 ≤10 min (cumulative): 79.9% vs 69.1%, p=0.003 ≤20 min (cumulative): 95.7% vs 86.5%, p=0.001 Timing of breathlessness episodes: Only during the day: 96.7% vs 74.0%, p<0.001		Frequency of breathlessness episodes: >3 per day: 19.1% vs 24% 1-3 per day: 55.5% vs 47.7% Weekly: 24.3% vs 27.3%. No p-value
		MBS	(29)			No statistically significant difference (p value not reported)
		MSDS	(36)			41% vs 54%, p=0.08

Level	Construct	Measure	Article	Worse in COPD	Worse in lung cancer	No significant difference
		MSAS-SF	(30)	Number and proportion with each symptom with lung cancer vs COPD: Shortness of breath: 42 (86%) vs 58 (97%), p=0.04 Severity of breathlessness in lung cancer vs COPD: median 3 (range 0-7) vs median 3 (range 0-10) Score (range) of distress due to breathlessness with lung cancer vs COPD: 3.2 (range 0-4) vs 4 (range 0-4), p=0.01		
		Modified MRC Dyspnea Scale	(34)	Median (IQR) for lung cancer 2.0 (1.0-3.0) vs for COPD 4.0 (4.0-5.0) (p<0.05)		
			(37)			Proportion scoring 0 or 1: 58.7% vs 45.4%, p=0.21 Proportion scoring ≥2: 41.2% vs 54.5%, p=0.21
		SAS	(39)	Mean (SD) breathlessness severity for lung cancer vs COPD at 3 time points (days before death): T1 (60-53): 3.1 (2.6) vs 5.0 (3.0) T2 (30-23): 3.6 (2.7) vs 5.2 (2.8) T3 (7-0): 4.4 (2.5) vs 5.8 (2.8)		
	Shortness of breath	MSDS	(38)	Mean severity of symptoms (0-10): shortness of breath: 3.59 vs 4.56		
		MQOL	(37)	Proportions with lung cancer vs COPD who have symptoms: shortness of breath 11.1% vs 57.5% (p=.000001)		
		POS	(30)		Median 2 vs 2 (p=0.18)	
	Chest tightness	MSDS	(38)	Mean severity of symptoms (0-10): Chest tightness: 2.82 vs 3.32		
	Cough	MSAS-SF	(30)			Cough: 38 (78%) vs 37 (62%), p=0.07
		MSDS	(38)		Mean severity of symptoms (0-10) Cough: 3.51 vs 2.79	

Level	Construct	Measure	Article	Worse in COPD	Worse in lung cancer	No significant difference
		MQOL	(37)			Cough 1.5% vs 6.0%;
	Dysphagia	MSDS	(36)			No statistically significant difference in proportions with lung cancer vs COPD reporting
	Dry mouth	MSAS-SF	(30)	32 (65%) vs 51 (85%), p=0.02		
	Fatigue	MSDS	(36)			No statistically significant difference in proportions with lung cancer vs COPD reporting
		MSDS	(38)		Mean severity of symptoms (0-10): 3.36 vs 2.97	
		MQOL	(37)		Tiredness 8 (12.6%) vs 4 (12.1%)	(Trouble sleeping) 11 (17.4%) vs 1 (3.0%), p>0.05
		MSAS-SF	(30)			(Trouble sleeping) 25% vs 33%, p=0.68
	Lack of energy	MSAS-SF	(30)			Lack of energy: 41 (84%) vs 58 (97%), p=0.14
	Vitality	SF-36	(34)			Median (IQR): 40 (20-65) vs 40 (29-60), p=0.927
		SF-36	(33)	p≤0.05		
	Lack of strength/weakness	MSDS	(38)			Lack of strength, weakness: 3.13 vs 2.84, p>0.05
		MQOL symptom scales$	(37)			4.7% vs 15.1%, p>0.05
	Feeling drowsy/ difficulty sleeping	MSAS-SF	(30)		Feeling drowsy 43 (87%) vs 41 (68%), p=0.02	Difficulty in sleeping 25 (51%) vs 33 (55%), p=0.68
	Insomnia	MSDS	(38)		Mean severity of smptoms (0-10): 4.11 vs 3.59	
		MSDS	(36)	People with lung cancer were more likely to experience insomnia (p<0.005)		

Level	Construct	Measure	Article	Worse in COPD	Worse in lung cancer	No significant difference
	Poor appetite/anorexia	MSDS	(38)		Mean severity of symptoms (0-10): 3.13 vs 2.72	
		MQOL symptom scales[$]	(37)			17.4% vs 3%, p>0.05
		MSAS-SF	(30)			Lack of appetite: 36 (74%) vs 24 (40%), p=0.00
		MSDS	(36)			No statistically significant difference.
	Weight loss	MSAS-SF	(30)			27 (56%) vs 23 (38%), p=0.62
	Nausea	MSDS	(36)		People with lung cancer were more likely to experience nausea (p<0.005)	
		MQOL symptom scales[$]	(37)			6.3% vs 0%, p>0.05
	Abdominal distention	MSDS	(38)		3.39 vs 3.11	
	Feeling bloated	MSAS-SF	(30)	15 (31%) vs 31 (52%), p=0.03		
	Constipation	MSDS	(38)	3.19 vs 4.46		
		MQOL symptom scales[$]	(37)		Proportions with lung cancer vs COPD who have symptoms: constipation 22.2% vs 0.0%	
	Diarrhoea	MQOL symptom scales[$]	(37)			6.3% vs 0%, p>0.05
	Urine retention	Ad hoc five point scale, nurse rated	(14)	68.2% vs 36.7%, p=0.048.		
	Sweats	MSAS-SF	(30)			19 (39%) vs 30 (51%), p=0.21
	Changes in skin	MSAS-SF	(30)	Changes in skin: 17 (35%) vs 35 (60%), p=0.01		

Level	Construct	Measure	Article	Worse in COPD	Worse in lung cancer	No significant difference
	Pressure sores	Ad hoc five point scale, nurse rated	Chou (2013)		Median severity score: 3 vs 2, p=0.017	
	Oedema	Ad hoc five point scale, nurse rated	(14)	95.5% vs 46.7%, p<0.001		
	Delirium	Ad hoc five point scale, nurse rated	(14)		46.7% vs 13.6%, p=0.017	
	Numbness in hands/feet	MSAS-SF	(Bausewein, Booth, Gysels, Kühnbach, et al., 2010)	Numbness in hands/feet	MSAS-SF	(Bausewein, Booth, Gysels, Kühnbach, et al., 2010)
	Thirst	MSDS	(38)	(Score out of 10) 3.13 vs 3.48		
	"I don't look like myself"	MSAS-SF	(30)			26 (53%) vs 29 (48%), p=0.62
	Problems with sex				28 (58%) vs 19 (32%), p=0.01	
	Symptoms other than pain and breathlessness	POS	(30)		Median 1 vs 0 (p=0.01)	
	Total number of symptoms	Ad hoc five point scale, nurse rated	(14)			Median (25th, 75th percentile) number of symptoms in lung cancer vs COPD: 10.0 (8.0, 12.0) vs 10.0 (8.0-13.0), p=0.666
	Mean severity of all symptoms	MSDS	(38)	Mean (median, range) severity of all symptoms: 24.31 (25, 1-92) vs 26.17 (21.5, 2-73)		
	Average frequency and distress caused by all MSAS symptoms	TMSAS	(30)			Average frequency and distress caused by all 32 MSAS symptoms in lung cancer vs COPD: 1.1 (range 0-2.7) vs 1.2 (0.3-2.5), p=0.73

Level	Construct	Measure	Article	Worse in COPD	Worse in lung cancer	No significant difference
	Average frequency of four psychological symptoms and distress associated from six physical symptoms	MSAS-GDI	(30)			Average frequency of four psychological symptoms and distress associated from six physical symptoms in lung cancer vs COPD: 1.6 (range 0-3.3) vs 1.4 (0.1-3.3), p=0.13
	Average of distress associated with 12 physical symptoms	MSAS-PHYS	(30)			Average of distress associated with 12 physical symptoms in lung cancer vs COPD: 1.5 (range0-3.4) vs 1.1 (0.1-2.5), p=0.05
Functioning	Performance status/ADL	KPS	(33)	Mean (SD) of KPS: 66.9 (9.2) vs 62.5 (10.4), p=<0.05		
			(34)	Mean (SD) for lung cancer 74.2 (14.3) vs for COPD 62.0 (13.0) (p<0.05)		
			(29)			Mean (SD) for lung cancer 66 (11.7) vs for COPD 62 (10.9), p=0.11 (Sig Lev 5%)
			(31)	Mean (SD, range): 80.0 (13.7, 40-90) vs 69.4 (14.3, 30-90), p=0.001		
			(35)	73.5 ±19.0 vs 61.0 ± 11.2, p=0.001		
		EADL Scale	(33)	Mean (SD) of EADL limitation: 9.4 (4.1) vs 11.3 (4.2), p<0.05		
				Proportion who are house-bound: 36% vs 82% (no p-value reported)		
				Proportion who are chair-bound: 10% vs 36%, (no p-value reported)		
		KADL	(13)	Mean ADL dependencies:1.46 vs 1.63, p=0.004		
		GARS	(34)	Median (IQR) of ADL: 12 (11-17) vs 18 (15-22), p<0.001		
				Median (IQR) of IADL: 12 (9-17) vs 16 (13-19), p=0.006		

Level	Construct	Measure	Article	Worse in COPD	Worse in lung cancer	No significant difference
		PPS	(36)	Low score (%): 14.1% vs 21.6%, p=0.026 Medium score (%): 56.3% vs 64.9%, p=0.026 High scores (%): 29.7% vs 13.5%, p=0.009		
Health perceptions	General health perceptions	SF-36	(34)	Median (IQR): 30 (20-42) vs 21 (14-35), p=0.03		
			(33)	p≤0.05		
			(35)	Mean (SD): 42.29 (19.96) vs 25.44 (15.23) 0.001		
QOL	Social support	MQOL	(37)	Median (IQR) 7.5 (6.5-9.0) vs 5.5 (3.5-8.0), p=0.002		
	Psychological support	MQOL	(37)		Median (IQR) 6.0 (5.0-8.6) vs 8.0 (6.0-9.5), p=0.01	
	Role emotional	SF-36	(34)			Median (IQR): 33 (0-100) vs 50 (0-100), p=0.309
			(33)			p>0.05
			(35)	Mean (SD): 41.33 (46.21) vs 27.67 (41.86), p=0.03		
	Mental Health	SF-36	(34)			Median (IQR): 72 (40-80) vs 68 (48-80), p=0.651
			(33)	p≤0.05		
		SF-36	(35)	Mean (SD): 57.68 (23.21) vs 47.84 (22.08) p=0.002		
	Mental Component	SF-36	(35)	Mean (SD): 47.93 (26.10) vs 36.07 (20.79), p=0.001		
	Physical symptoms and problems	MQOL	(37)			Median (IQR) 5.3 (4.0-7.1) vs 5.0 (3.8-5.8), p=0.34
	Role physical	SF-36	(34)			Median (IQR): 0 (0-25), vs 0 (0-0), p=0.452

Level	Construct	Measure	Article	Worse in COPD	Worse in lung cancer	No significant difference
			(33)			p>0.05
			(35)	12.25 (25.99) vs 3.00 (10.22), p=0.001		
	Physical functioning	SF-36	(35)	Median (IQR): 42.90 (29.60) vs 22.40 (22.55), p=0.001		
			(33)	p≤0.05		
			(34)	Median (IQR): 50 (25-75) vs 10 (0-25), p<0.001		
	Physical component summary	SF-36	(35)	Median (IQR): 38.04 (21.60) vs 29.69 (14.35), p=0.001		
	Social functioning	SF-36	(34)			Median (IQR): 63 (25-75) vs 38 (25-75), p=0.374
			(33)	p≤0.05		
			(35)	Mean (SD): 51.12 (35.31) vs 39.37 (30.27), p=0.012		
	Overall quality of life score	SF-36	(35)	Mean (SD): 42.98 (21.26) vs 32.88 (15.61), p=0.001		
	General/global QOL	Ad hoc measure	(36)			General QOL item p=0.37 Poor QOL (%): 25.0% vs 15.5% Fair QOL (%): 51.9% vs 58.6% Good QOL (%): 23.1% vs 25.0%
		MQOL	(37)			Median (IQR): 5.0 (4.0-6.7) vs 5.0 (5.0-8.0), p=0.13
		Ad hoc five point scale, nurse rated	(13)			Median: 4 vs 4, p=0.058

Level	Construct	Measure	Article	Worse in COPD	Worse in lung cancer	No significant difference
Other	Spiritual wellbeing	FACIT-SP-12	(37)			Median (IQR) of total FACIT-SP-12: 26 (21-36.2) vs 27 (16.0-38.0), p=0.81 Meaning and Peace domain: 18 (15.0-24.0) vs 18 (10.2-25.5), p=0.56 Faith domain: 8 (6.0-11.0) vs 8 (4.0-14.0), p=0.66
	Existential issues	MQOL				Median (IQR): 6.5 (5.0-7.8), p=0.07
	Palliative care needs	POS	(31)			Overall scores were similar between disease groups (p value not reported)
			(30)		Median total POS 11 vs 8 (p=0.02); total POS plus 12 vs 10 (p=0.03); wasted time 0 vs 0 (p=0.00)	Median information score 0 vs 0 (p=0.05); sharing feelings 0 vs 0 (p=0.93); practical matters (0 vs 0 (p=0.49)

* results for patient report; ** results for surrogate report; $=chi-square calculated from data reported in article; ADL – Activities of Daily Living; BDI - Beck Depression inventory; COPD – Chronic Obstructive Pulmonary Disease; DT – Distress Thermometer; EADL – Extended Activities of Daily Living; EORTC QLQ-LC13 – European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (Lung Cancer); FACIT-SP-12 – Functional Assessment of Chronic Illness Therapy – Spiritual Wellbeing, 12 item scale; GARS - Groningen Activities of Daily Living Restriction Scale; HADS - Hospital anxiety and depression scale; IQR – Interquartile range; KADL – Katz Activities of Daily Living; KPS – Karnofsky Performance Scale; MBS - Modified Borg Dyspnea Scale; MQOL – McGill Quality of Life; MRC – Medical Research Council; MSAS-GDI - Memorial Symptom Assessment Scale, Global Distress Index; MSAS-Psyc – Memorial Symptom Assessment Scale, Psychological symptoms; MSAS-SF – Memorial Symptom Assessment Scale, Short form; MSDS – McGill Symptom Distress Scale (?); POMS – Profile of mood states; PPS Palliative Performance Scale; QOL – Quality of life; SAS – Symptom Assessment Scale; SD – Standard deviation; SF-36 – Medical Outcomes Scale Short Form 36; SGRQ – St George's Respiratory Questionnaire (COPD specific); TMSAS – Total Memorial Symptom Assessment Scale; vs - versus.