

Title: Lung Cancer Stigma: A Concept with consequences for patients

ABSTRACT

Background: Patients with lung cancer (LC) report lower quality of life (QoL) and higher levels of psychological distress compared to other cancer populations. Lung cancer stigma (LCS) may in part explain these findings. **Aim:** We investigated the prevalence of patient-perceived lung cancer stigma (LCS) and its relationships to symptom burden/severity, depression, and deficits in health-related quality of life (HR-QoL). **Methods:** In this descriptive, observational and cross-sectional study, 201 participants were sent questionnaires. These included The Cataldo Lung Cancer Stigma Scale (CLCSS); the Lung Cancer Symptom Scale; the Centre for Epidemiologic Studies-Depression Scale; and the Quality of Life Inventory. **Results:** Participants were on average 69 years old, 52% women, 95% ever smokers, and 18.5% current smokers. The mean total CLCSS score was 53.1 (SD=14.1; range=31-94). LCS was significantly correlated with younger age ($p<0.001$), greater social deprivation ($p<0.05$), being unemployed ($p<0.001$), depression ($p<0.001$), symptom burden ($p<0.001$), and HR-QoL deficits ($p<0.001$). Symptom burden explained 18% of variance in LCS ($p<0.001$). LCS explained 8.5% and 14.3% of the variance in depression ($p<0.001$) and HR-QoL ($p<0.001$), respectively. **Conclusion:** Patients with lung cancer are vulnerable to LCS. Symptom burden can directly contribute to greater perceived LCS. Greater perceived LCS can be directly related to greater levels of depression and lower HR-QoL. A tailored approach is required to screen for LCS and implement interventions to enhance the psycho-social well-being of patients with perceived LCS.

Key words: health-related stigma, clinical care, cancer support, oncology, psychological well-being

AUTHOR CONTRIBUTION

All authors had full access to the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Conceptualization, R.M., R.M., J.C., J.P.; Methodology, R.M., J.C.,; Investigation, L.L., J.M., R.M.,; Formal Analysis, G.K., L.L.,; Resources, J.M., R.M.; Writing

- Original Draft, L.L, G.K.; Writing - Review & Editing, R.M., R.M., J.M., J.C.; Visualization, G.K., L.L.; Supervision, R.M.; Funding Acquisition, R.M.

For Peer Review

INTRODUCTION

Compared to patients with a history of other cancers, patients with lung cancer (LC) are more likely to report only fair or poor health, and exhibit significant psychological problems (Hewitt, Rowland, & Yancik, 2003). Psychological morbidity has been associated with increased symptom burden and lack of social support (Sullivan et al., 2016), being the precursor of poor health-related quality of life (HR-QoL) and increased risk for mortality (Satin, Linden, & Phillips, 2009). Specific to lung cancer, up to 55% of patients may meet the criteria for clinical depression (Cataldo & Brodsky, 2013). In addition, the association between depression and mortality is stronger among patients exhibiting more symptoms and those who report less social support (Sullivan et al., 2016).

Psychological morbidity in patients with lung cancer may have its origins in perceived lung cancer stigma (LCS). In his classic work about stigma, Goffman (2009) defined stigma as “an attribute that is deeply discrediting”. This can result in patients feeling unjustly blamed for their illness and particularly stigmatised because the disease is so strongly associated with smoking (Chapple, Ziebland, & McPherson, 2004; Sasco, Secretan, & Straif, 2004). Blame has often been cited as a major stressor of having lung cancer (Marlow, Waller, & Wardle, 2010; Taylor et al., 2008). Indeed, patients with lung cancer are more likely to report internal causal attributions for their cancer than patients with breast or prostate cancer (Else-Quest, LoConte, Schiller, & Hyde, 2009). Previous US-based research has demonstrated a link between LCS and poor patient outcomes. Specifically, LCS was associated with greater depressive symptomatology (Brown Johnson, Brodsky, & Cataldo, 2014; Cataldo, Slaughter, Jahan, Pongquan, & Hwang, 2011; Gonzalez & Jacobsen, 2012), poorer HR-QoL (Cataldo et al., 2011), and higher symptom severity (Cataldo & Brodsky, 2013). Furthermore, LCS was found to account for unique and significant variability of 5%, 1.2% and 1.3% in depression (Gonzalez & Jacobsen, 2012), HR-QoL (Brown Johnson et al., 2014), and symptom severity (Cataldo & Brodsky, 2013), respectively.

Health-related stigma is a culturally derived phenomenon (Van Brakel, 2006). Therefore, it is important to understand the effects of perceived LCS in a **UK sample to inform healthcare providers**

of the needs of their patients with the intention to develop support pathways for these patients. To date, studies that quantify LCS is limited to studies from the USA, and Australia (Brown & Cataldo, 2013; Brown Johnson et al., 2014; Cataldo & Brodsky, 2013; Cataldo, Jahan, & Pongquan, 2012; Chambers, Baade, et al., 2015; Rose et al., 2018). No research has been conducted in the United Kingdom to explore LCS and its relationship with symptom burden/severity, depression, and HR-QoL. Investigating and understanding these relationships is a necessary first step to facilitate the development of possible targeted LCS interventions. This study aimed to address this existing gap in knowledge in the UK as follows.

Aims and Hypothesis

Our aim was to investigate the prevalence of patient-perceived LCS, and the role of LCS as a covariate of symptom severity and/or burden, depression and HR-QoL.

We aimed to address the following research questions:

1. What is the prevalence and are the characteristics of perceived LCS in LC patients in Scotland?
2. What are the effects of lung cancer symptom severity and/or burden on perceived LCS, controlling for patient socio-demographic characteristics and clinical variables?
3. What are the effects of perceived LCS on depression, controlling for patient socio-demographic characteristics and clinical variables?
4. What are the effects of perceived LCS on HR-QoL, controlling for patient socio-demographic characteristics and clinical variables?

We specifically hypothesised that greater symptom burden and/or severity would be adversely related to greater perceived LCS. In turn, greater perceived LCS would be associated with greater levels of depression and lower HR-QoL.

METHODS

Study design and setting

We conducted a descriptive, observational, cross-sectional study. We recruited a convenience sample of patients with lung cancer from two NHS Health Boards in Scotland, and within these Boards, recruitment took place at six regional hospitals. Reporting of the study was guided by the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement (Von Elm et al., 2014).

Eligibility criteria

Potential participants had to be: (a) aged ≥ 18 years; (b) have a clinical diagnosis of lung cancer; (c) able to understand study information; and (d) be physically and psychologically fit to participate as deemed by a member of the healthcare team. We excluded patients unable to meet any of the above criteria.

Procedures

The study received a favourable ethical opinion from the [*Name of ethical committee to be inserted here*]. (Ref 14/EE/1099). Health professionals identified potential participants during routinely scheduled clinic visits. They briefly outlined the purposes of the study and provided a study pack which contained the patient information sheet, a consent form to be contacted for research interviews (details reported elsewhere), self-reported questionnaires, and a stamped envelope to return the completed pack anonymously to the researcher. Completion of the questionnaires acted as study consent. If the patient did not return the study packs within 14 days, a reminder letter was sent.

Outcome measures

Cataldo Lung Cancer Stigma Scale (CLCSS). The CLCSS is a valid and reliable measure to assess the experiences of stigma (Cataldo et al., 2011). It comprises 31 items and four subscales (stigma and shame, social isolation, discrimination, and smoking) that are rated on a 4-point Likert scale ('strongly disagree', 'disagree', 'agree', 'strongly agree'). A higher score indicates greater experience of stigma (possible score range 31-124). Cronbach's alpha was 0.93. Construct validity was demonstrated with expected relationships with depression in our study as well as other studies (Cataldo et al, 2011, Gonzalez & Jacobson, 2012).

Lung Cancer Symptom Scale (henceforth 'LC symptom scale'). The LC symptom scale measures the severity of lung cancer specific symptoms, and has demonstrated good reliability and content validity (Hollen et al., 2005). The scale has 9 items (rated from 0-100), that measure symptoms, symptom burden and symptom severity. Higher scores indicate greater symptom severity. Cronbach's alpha was 0.84.

Centre for Epidemiologic Studies-Depression Scale (CES-D). The CES-D is a widely used tool to assess depression, with established validity and reliability in a wide range of populations including cancer (Sheehan, Fifield, Reisine, & Tennen, 1995). Twenty items are rated on a 4-point scale. Higher scores indicate greater depression (score range 0-60). Cronbach's alpha was 0.89.

Quality of Life Inventory (QLI). The QLI has four subscales (physical, psychological, social, and spiritual) and consists of 33 items (Ferrell, Wisdom, & Wenzl, 1989). This measure was previously validated with a population with LC (Sarna et al, 2005). Higher scores indicate better HR-QoL (score range 0-10). Cronbach's alpha was 0.91.

We collected self-reported socio-demographic information (e.g. smoking history), and clinical data from case note review, including lung cancer type and stage, presenting symptoms, mode of presentation, date of diagnosis, time since being diagnosed, previous treatment for lung cancer, current management/treatment of lung cancer, and any comorbidities.

Data Analysis

We first investigated the factor structure of the CLCSS in our sample to account for any cultural diversity compared to the original factor structure based on US-based data (Cataldo et al., 2011). Compared to Cataldo et al., 2011 who reported a 4 factor structure (Stigma and Shame, Social Isolation, Discrimination, and Smoking), our analyses resulted in 5 factors (Social Isolation, Smoking, Stigma and Shame, Healthcare provider Stigma, Discrimination) (Table 1). The number of items in the scale per factor are reported in Table 1. (see Supplementary file 1 for details).

Descriptive statistics and graphs were used to analyse CLCSS data. Frequency counts and percentages of responses were generated to describe response patterns and quantify missing data. Total and subscale CLCSS scores were treated as interval-ratio variables and are presented as means, standard deviation and range.

Bivariate associations were explored between socio-demographic characteristics and clinical factors (interval-ratio or categorical), and all patient outcome variables (interval-ratio). Relationships between variables were determined using two samples *t*-test, one-way analysis of variance, or correlation coefficient calculation. Relationships among patient outcome variables were tested through correlation analysis. The functional form of these relationships and any necessary transformations were explored and assumptions of normality checked.

Socio-demographic characteristics and clinical factors statistically significantly associated with patient outcome variables were retained and their effects controlled for in subsequent hierarchical regression modelling to investigate: (a) the effects of lung cancer symptom burden on perceived LCS, and (b) the effects of perceived LCS on depression and HR-QoL after controlling for significant socio-demographic and clinical covariates identified in the previous step. Assumptions relating to the normal distribution of errors and multicollinearity were investigated; no modifications to the analysis were required. Cumulative R^2 and R^2 change (ΔR^2) was reported for each model to indicate the unique contribution of each predictor variable in explaining the variance of each dependent variable. The level of significance was set at 0.05. IBM SPSS (IBM Inc. Chicago, IL) was used for the statistical analysis.

RESULTS

From 368 potential participants approached, 201 (54.6%) returned questionnaire packs. Case notes were accessible and reviewed for 195 participants. The total sample had a mean age of 69.2 ± 9.1 years (range 41-89 years), 52% were women, 63.5% were married/partnered, and 71.2% were in a cohabitating situation (Table 2). Ninety-five percent were ever-smokers, 18.5% current smokers, and 76.9% were quitters. The majority of participants had localised lung cancer (51.9%), non-small cell lung cancer (91.2%), and received surgery alone or in combination with systemic treatment (49.7%).

Prevalence of LCS, symptom severity/burden, depression and HR-QoL deficits

CLCSS score was 53.1 (SD=14.1; Table 1). Perceptions of LCS more frequently reflected eight CLCSS items/statements, endorsed by at least 20% of the sample (**Figure 1**). Most frequently, respondents agreed/strongly agreed that others assumed that lung cancer was caused by smoking even if the patient had stopped smoking years ago (61.7%) or never smoked at all (55.2%). Just over half the respondents 'agreed'/'strongly agreed' that lung cancer is viewed as a self-inflicted disease (51.2%). Eighteen per cent revealed that others had told them that being diagnosed with lung cancer was what they deserved for smoking. One in five respondents agreed that they felt guilty for having lung cancer (20%), and felt the need to hide their lung cancer (20%). Nearly a quarter of participants (23.9%) believed that older people are less likely to be blamed for lung cancer compared to younger ones, that health professionals do not take smoker's cough seriously (26.9%) and that they put off seeking medical help because they were afraid (23.9%).

Symptom burden and symptom severity were low (mean: 31.1, 21.9) (Table 3). Shortness of breath and fatigue were on average reported as the most severe symptoms, followed by appetite loss and cough. Over half (55.2%) of respondents met the criteria for clinical depression (score >16). HR-QoL was moderate to good on average.

Relationships among study variables

Positive correlations were demonstrated with depression, symptom burden, and all lung cancer symptoms except for appetite loss (Table 4). A moderate-to-strong negative correlation of perceived LCS with overall HR-QoL and all HR-QoL sub-domains was found.

Negative correlations between LCS scores and sociodemographic variables were found with age, (Table 4). Positive correlations with LCS scores were observed for unemployed/homemaker status, and deprivation index. Although not statistically significant, current smokers reported on average greater perceived LCS than people who were not currently smokers.

We identified significant relationships of higher levels of depression with younger age, female gender, living alone, being unemployed or homemaker, having a low annual income, being a smoking non-quitter or a current smoker, lower HR-QoL and higher symptom burden (Table 4).

Significant relationships of poorer HR-QoL with younger age, being unemployed or a homemaker, being a smoking quitter or a current smoker, being symptomatic prior to lung cancer diagnosis, having received radiotherapy, higher depression levels, and higher symptom burden were found.

Symptom burden as a predictor of greater perceived LCS

Accounting for the effects of age, employment status and social deprivation, hierarchical regression showed that the overall regression model of the second step was statistically significant with 18% of the variance in symptom burden being explained, $F(4, 174)=9.24, p<0.001$. More details are shown in Table 5. Incremental R^2 for symptom burden was significant ($\Delta R^2=0.05$).

Perceived LCS as a predictor of greater patient depression

Accounting for the effects of covariates, hierarchical regression showed that the overall regression model of the third step was statistically significant with 22% of the variance in depression being explained, $F(8, 138)=4.96, p<0.001$ (Table 6). Socio-demographic characteristics explained 12.1% ($p=0.006$) of the total variance in depression, clinical factors explained 1.8% ($p>0.05$), and perceived

LCS contributed uniquely and significantly explaining 8.5% ($p < 0.001$) of the total variance in depression.

Perceived LCS as a predictor of lower patient HR-QoL

Accounting for the effects of covariates, hierarchical regression showed that the overall regression model of the third step was statistically significant with 35% of the variance in HR-QoL being explained, $F(6, 174) = 15.36$, $p < 0.001$ (Table 6). Socio-demographic characteristics explained 14.4% ($p < 0.001$), clinical factors explained 5.9% ($p = 0.005$), and perceived LCS contributed uniquely and significantly explaining 14.3% ($p < 0.001$) of the total variance in HR-QoL.

DISCUSSION

These findings support our hypotheses that greater perceived LCS can be directly associated with greater levels of depression and lower HR-QoL among patients with a lung cancer diagnosis. Moreover, we were able to confirm that symptom burden (but not symptom severity) can directly contribute to greater perceived LCS. These observations have clear implications for clinical practice and research.

As in previous research (Brown Johnson, Brodsky, & Cataldo, 2014; Cataldo, Jahan, & Pongquan, 2012; Lebel et al., 2013), analysis of CLCSS scores indicated that patients with lung cancer are vulnerable to stigmatisation after diagnosis, although in this study, mean LCS scores were below the mid-range of the scale. Other studies have shown CLCSS scores of 75-102 (vs 53.1 in this study) (Brown Johnson et al., 2014; Cataldo & Brodsky, 2013; Cataldo et al., 2012). This observation may indicate that the perceived LCS was generally low in this study's sample. Low scores were also reported in two Australian samples of lung cancer patients with scores ranging from 52-55 (Rose et al., 2018; Chambers et al., 2015) and one American sample with a mean stigma score of 68 (Carter-Harris et al., 2014). In these samples patients had a confirmed diagnosis of lung cancer and were either recruited via oncology clinics (Rose et al., 2018; Carter-Harris et al., 2014) or local support groups (Chambers et al., 2015). The participants in studies with high stigma scores recruited a

convenience sample via online cancer support websites, which could have influenced the LCS score because those participants may not be a typical lung cancer population.

Rose et al. (2018) suggested that the LCS scores were low due to their sample being newly diagnosed with lung cancer. However, our sample was diagnosed on average 2.6 years prior to study participation. It could be suggested that gender may contribute to the findings of different scores of stigma as those studies with higher scores had a higher proportion of women (Brown Johnson et al., 2014; Cataldo & Brodsky, 2013; Cataldo et al., 2012). However, an Australian study that reported lower stigma scores had a higher proportion of men (Rose et al., 2018) and another study with an Australian sample had a higher proportion of women (Chambers et al., 2015). Both genders were evenly presented in this study making gender a less likely explanation. One factor that studies with lower stigma score had in common is the age of participants. In these studies, including the present study, participants' mean age was 65-69 years (Rose et al., 2018; Chambers et al., 2015).

However, this observation should be interpreted with caution, as there is no consensus on what is low or high stigma using the CLCSS. It may also indicate that participants with high levels of perceived LCS did not return their questionnaires. A recent study validated a new LCS tool to establish cut-off values to identify patients with clinically meaningful LCS (Ostroff et al., 2019). They found a value of 37.5 (possible range of 25-125) and above to be clinically meaningful. The evidence is clear that perceived stigma is associated with poorer psychological well-being and therefore it is important that these patients receive intervention. Patients who only score high on a few items of the CLCSS resulting in an overall low score are still expressing perceptions of stigma. Thus, a lower score should also be recognised and those patients should be offered intervention. It is therefore important to establish a meaningful cut-point to identify patients in need for support. Future research could explore the cut-off points for the CLCSS which are clinically relevant for patients with LC.

Findings for the role of LCS as predictor for depression, and poorer HR-QoL in patients with lung cancer are consistent with the literature (Brown Johnson et al., 2014; Gonzalez & Jacobsen, 2012). Greater scores of stigma were predictive of higher levels of depression and poorer HR-QoL. This

population has been found to exhibit poorer psychological well-being than other cancer populations (Zabora, BrintzenhofeSzoc, Curbow, Hooker, & Piantadosi, 2001). The present findings assist in the identification of contributing factors to this high depressive symptomatology. Although only 8.5% of the variance in depression was explained by perceived LCS, this significant finding gives credence to the notion that the social implications and adverse social experiences of living with lung cancer can well build on patients' feelings of low mood. It is possible that the longer patients live with perceived LCS, the greater the chances for them developing chronic depression.

In addition to depression, we found that perceived LCS uniquely contributed to poorer HR-QoL. Further research is warranted to investigate a mediation path that leads from perceived LCS to depression and subsequently to HR-QoL, and investigate possible additional mediators such as social anxiety. Indeed, anxiety has previously been found to be related to higher levels of stigma (Brown Johnson et al., 2014; Cataldo & Brodsky, 2013). Anxiety as an additional stressor could further negatively affect health and increase the risk for stress-related illnesses (Link & Phelan, 2006).

Attempting to identify the actual onset of perceived LCS, we identified a significant relationship between symptom burden and perceived LCS. Overt symptoms, such as cough, dyspnoea or haemoptysis may interfere with social interactions and lead to overt or covert reactions from others that may trigger experiences of LCS in patients with lung cancer. These relationships warrant future investigation. Interestingly, symptom severity did not make a significant contribution to perceived LCS over and above symptom burden. This may indicate that even mild symptoms, when manifested during social interactions and in everyday life (e.g. cough, dyspnoea), can be seen as a source of LCS for patients with lung cancer (Maguire, Stoddart, Flowers, McPhelim, & Kearney, 2014). These relationships have not been explored previously in people with lung cancer, but these findings may partly explain the higher perceived stigma in this group of patients compared to other cancers (Marlow, Waller, & Wardle, 2015).

Personalised care for patients with lung cancer who **manifest perceived** LCS is required. Our findings indicate that patients with poorer socioeconomic backgrounds have higher levels of LCS. While data

on smoking rates across socioeconomic groups exist (Centers for Disease Control, 2008) the association with LCS has not been demonstrated. Stuber, Galea, and Link (2008) investigated the associations between smoking stigma and educational status. Their findings indicate that better socioeconomic background is associated with higher levels of smoking-related stigma. It is thought that people with social deprivation have more exposure to smoke-free laws (Barbeau, Krieger, & Soobader, 2004) thus leading to higher perceived stigma. Their participants were smokers and non-smokers from New York City neighbourhoods answering a survey about relationships between neighbourhood characteristics and drug use. The design of their study (different measure, sample without LC) may explain the difference to our data. Further investigation of this relationship with LC patients is needed.

We also found that younger patients are more likely to experience LCS. Older participants may feel less stigma due to the social acceptability of smoking when they first started smoking (Chapple et al., 2004). We did not find a significant difference in perceived LCS between current and past smokers or non-smokers. Previous studies also failed to demonstrate a relationship between smoking status and LCS (Cataldo et al., 2012), which is in support of findings from qualitative research where participants reported LCS regardless of smoking status (Chapple et al., 2004). Smoking cigarettes is recognised as the main contributing risk factor for lung cancer, and national and international health policies have targeted the tobacco industry to attempt to reduce the burden of this disease. In doing so, this may have come with a cost; that these health policies lead to experiences of stigma in people diagnosed with lung cancer (Bell, Salmon, Bowers, Bell, & McCullough, 2010; Chapple et al., 2004; Stuber et al., 2008). Thus, it is likely that smoking history is irrelevant for experiences of perceived stigma if people with lung cancer are being queried about their smoking history by strangers, acquaintances or healthcare professionals after a diagnosis (Hamann et al., 2014). However, there is qualitative evidence that smoking history is relevant in the experience of internalized stigma (Hamann et al., 2014). It is likely that the small number of never-smokers in our study contributed to the lack of relationship. Associations between smoking status and depression, however, were significant, and this demonstrates that these patients have a need for care to address psychological morbidities, whether

this is related to the experience of stigma or not. Further research should be considered to investigate the role of smoking and the experience of stigma.

In this study, we, as well as other research groups, have demonstrated that perceived LCS can originate from various sources and take various forms (Brown & Cataldo, 2013; Chapple et al., 2004; Hamann et al., 2014; Lehto, 2014; J. Weiss et al., 2017). Perceived stigma from healthcare professionals can be detrimental, as patients can feel discomfort communicating their symptoms to health professionals, which in turn can lead to delay in presentation, in diagnosis, and in treatment, or even low uptake of treatment (Corner, Hopkinson, & Roffe, 2006; Lehto, 2014; Tod, Craven, & Allmark, 2008). Supportive and empathetic communication is important to promote adherence to treatment (Zolnieriek & DiMatteo, 2009). Furthermore, shame and blame can also lead to high levels of distress and depression amongst family members and partners (Milbury, Badr, & Carmack, 2012; Siminoff, Wilson-Genderson, & Baker, 2010). Therefore, it is important not to exclude family members from such discussions, and to assess for the families'/carers' own perceptions of LCS and how this may impact on their own feelings. It is thus important for health professionals to enter into sensitive discussions with patients and their families to explore the prevalence, nature and chronicity of LCS perceptions.

Currently, interventions to reduce stigma among these patients are lacking, but individual counselling, or group interventions have been suggested to help the stigmatized to protect themselves from the impact of stigma, and reduce their vulnerability to encounters of stigmatization (M. G. Weiss, Ramakrishna, & Somma, 2006). In this group of patients, a combined intervention addressing depressive symptomatology and stigma should be considered because of the relationship between the two. A recent wellness intervention with patients with lung cancer, which was based on Cognitive Behaviour Therapy (CBT), focused on psycho-education, skills in stress reduction, problem-solving, cognitive challenging, and enhancing relationship support (Chambers, Morris, et al., 2015) and resulted in improvements in health-related stigma, as well as depression and cancer-specific distress (Chambers, Morris, et al., 2015).

Such interventions may also be delivered via the internet. Online CBT interventions have been studied in the context of mental health to treat for example depression, and anxiety (Andersson, 2009). Results demonstrate that such interventions can achieve similar outcomes as conventional face-to-face delivered therapies (Andersson, Cuijpers, Carlbring, Riper, & Hedman, 2014). Potential benefits of digital interventions could reduce health costs as less hours of therapists are required, but this largely depends on the design of the intervention (Fairburn & Patel, 2017). Furthermore, considering the stigma surrounding seeking help for mental health, the digital setting could overcome the barrier of low adherence to mental health treatments and increase its reach to people in need of psychological treatments (Muñoz et al., 2016).

Strengths and Limitations

In this study, we used a relatively large dataset from a patient sample from six hospitals and with diverse demographic and clinical characteristics that allowed for statistical examination of relationships among the multiple covariates. However, a large proportion of patients in this study received surgical treatment which is atypical for this population. Although we achieved a fairly high response rate, we are unable to make comparisons between respondents and non-respondents to identify potential bias in our sample and data. It is possible that people who did feel stigmatised in relation to their lung cancer diagnosis found the study of greater interest than those who had no LCS perceptions. Alternatively, those with experiences of LCS may have chosen not to participate.

In addition, we did not collect information on additional covariates of potential interest, such as self-esteem, self-efficacy, anxiety or treatment adherence. Therefore, future research should explore the above factors and their relationships with perceived LCS. Finally, this was a cross-sectional investigation of perceived LCS and covariates, which prevents us from establishing the “causal” pathways that involve precipitating and perpetuating triggers of LCS and its longitudinal impact on patient outcomes. Further longitudinal research is thus warranted.

Conclusions

Perceived LCS is a significant predictor of poorer outcomes (symptom burden, depression, HR-QoL) in patients with lung cancer, when controlling for demographic and clinical variables. Perceived LCS is a potentially important psychosocial factor when considering the psychosocial well-being of patients with lung cancer. Incorporating systematic assessments of perceived LCS in the plan of care for patients with lung cancer is required to ensure adverse effects are tackled in a timely fashion at the time of diagnosis, during treatment and post-treatment.

Acknowledgements

We acknowledge the support of the clinical staff who supported the recruitment to this study at the participating NHS hospitals. We also thank the participants of this study to commit their time to complete to this study.

Conflict of interest

The authors have no conflict of interest to declare.

REFERENCES

- Andersson, G. (2009). Using the Internet to provide cognitive behaviour therapy. *Behaviour Research and Therapy*, 47(3), 175-180.
- Andersson, G., Cuijpers, P., Carlbring, P., Riper, H., & Hedman, E. (2014). Guided Internet-based vs. face-to-face cognitive behavior therapy for psychiatric and somatic disorders: a systematic review and meta-analysis. *World Psychiatry*, 13(3), 288-295.
- Barbeau, E. M., Krieger, N., & Soobader, M.-J. (2004). Working class matters: socioeconomic disadvantage, race/ethnicity, gender, and smoking in NHIS 2000. *American journal of public health*, 94(2), 269-278.
- Bell, K., Salmon, A., Bowers, M., Bell, J., & McCullough, L. (2010). Smoking, stigma and tobacco 'denormalization': Further reflections on the use of stigma as a public health tool. A commentary on Social Science & Medicine's Stigma, Prejudice, Discrimination and Health Special Issue (67: 3). *Social science & medicine*, 70(6), 795-799.
- Brown, C., & Cataldo, J. (2013). Explorations of lung cancer stigma for female long-term survivors. *Nursing inquiry*, 20(4), 352-362.
- Brown Johnson, C. G., Brodsky, J. L., & Cataldo, J. K. (2014). Lung cancer stigma, anxiety, depression, and quality of life. *Journal of psychosocial oncology*, 32(1), 59-73.
- Cataldo, J. K., & Brodsky, J. L. (2013). Lung cancer stigma, anxiety, depression and symptom severity. *Oncology*, 85(1), 33-40.
- Cataldo, J. K., Jahan, T. M., & Pongquan, V. L. (2012). Lung cancer stigma, depression, and quality of life among ever and never smokers. *European Journal of Oncology Nursing*, 16(3), 264-269.
- Cataldo, J. K., Slaughter, R., Jahan, T. M., Pongquan, V. L., & Hwang, W. J. (2011). *Measuring stigma in people with lung cancer: psychometric testing of the cataldo lung cancer stigma scale*. Paper presented at the Oncology nursing forum.

- Centers for Disease Control. (2008). Cigarette smoking among adults--United States, 2007. *MMWR. Morbidity and mortality weekly report*, 57(45), 1221.
- Chambers, S. K., Baade, P., Youl, P., Aitken, J., Occhipinti, S., Vinod, S., . . . Ball, D. (2015). Psychological distress and quality of life in lung cancer: the role of health-related stigma, illness appraisals and social constraints. *Psycho-Oncology*, 24(11), 1569-1577.
- Chambers, S. K., Morris, B. A., Clutton, S., Foley, E., Giles, L., Schofield, P., . . . Dunn, J. (2015). Psychological wellness and health-related stigma: a pilot study of an acceptance-focused cognitive behavioural intervention for people with lung cancer. *European journal of cancer care*, 24(1), 60-70.
- Chapple, A., Ziebland, S., & McPherson, A. (2004). Stigma, shame, and blame experienced by patients with lung cancer: qualitative study. *bmj*, 328(7454), 1470.
- Corner, J., Hopkinson, J., & Roffe, L. (2006). Experience of health changes and reasons for delay in seeking care: a UK study of the months prior to the diagnosis of lung cancer. *Social science & medicine*, 62(6), 1381-1391.
- Else-Quest, N. M., LoConte, N. K., Schiller, J. H., & Hyde, J. S. (2009). Perceived stigma, self-blame, and adjustment among lung, breast and prostate cancer patients. *Psychology and Health*, 24(8), 949-964.
- Fairburn, C. G., & Patel, V. (2017). The impact of digital technology on psychological treatments and their dissemination. *Behaviour Research and Therapy*, 88(Supplement C), 19-25.
doi:<https://doi.org/10.1016/j.brat.2016.08.012>
- Ferrell, B. R., Wisdom, C., & Wenzl, C. (1989). Quality of life as an outcome variable in the management of cancer pain. *Cancer*, 63(11), 2321-2327.
- Goffman, E. (2009). *Stigma: Notes on the management of spoiled identity*: Simon and Schuster.
- Gonzalez, B. D., & Jacobsen, P. B. (2012). Depression in lung cancer patients: the role of perceived stigma. *Psycho-Oncology*, 21(3), 239-246.

- Hamann, H. A., Ostroff, J. S., Marks, E. G., Gerber, D. E., Schiller, J. H., & Lee, S. J. C. (2014). Stigma among patients with lung cancer: a patient-reported measurement model. *Psycho-Oncology*, 23(1), 81-92.
- Hewitt, M., Rowland, J. H., & Yancik, R. (2003). Cancer survivors in the United States: age, health, and disability. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*, 58(1), M82-M91.
- Hollen, P., Gralla, R., Kris, M., McCoy, S., Donaldson, G., & Moinpour, C. (2005). A comparison of visual analogue and numerical rating scale formats for the Lung Cancer Symptom Scale (LCSS): does format affect patient ratings of symptoms and quality of life? *Quality of Life Research*, 14(3), 837-847.
- Lehto, R. H. (2014). Patient views on smoking, lung cancer, and stigma: a focus group perspective. *European Journal of Oncology Nursing*, 18(3), 316-322.
- Link, B. G., & Phelan, J. C. (2006). Stigma and its public health implications. *The Lancet*, 367(9509), 528-529.
- Maguire, R., Stoddart, K., Flowers, P., McPhelim, J., & Kearney, N. (2014). An interpretative phenomenological analysis of the lived experience of multiple concurrent symptoms in patients with lung cancer: a contribution to the study of symptom clusters. *European Journal of Oncology Nursing*, 18(3), 310-315.
- Marlow, L. A., Waller, J., & Wardle, J. (2010). Variation in blame attributions across different cancer types. *Cancer Epidemiology and Prevention Biomarkers*, 19(7), 1799-1805.
- Marlow, L. A., Waller, J., & Wardle, J. (2015). Does lung cancer attract greater stigma than other cancer types? *Lung Cancer*, 88(1), 104-107.
- Milbury, K., Badr, H., & Carmack, C. L. (2012). The role of blame in the psychosocial adjustment of couples coping with lung cancer. *Annals of Behavioral Medicine*, 44(3), 331-340.

- Muñoz, R. F., Bunge, E. L., Chen, K., Schueller, S. M., Bravin, J. I., Shaughnessy, E. A., & Pérez-Stable, E. J. (2016). Massive open online interventions: A novel model for delivering behavioral-health services worldwide. *Clinical Psychological Science, 4*(2), 194-205.
- Ostroff, J., Riley, K., Shen, M., Atkinson, T., Williamson, T., & Hamann, H. (2019). Lung cancer stigma and depression: Validation of the Lung Cancer Stigma Inventory. *Psycho-Oncology*.
- Rose, S., Kelly, B., Boyes, A., Cox, M., Palazzi, K., & Paul, C. (2018). *Impact of Perceived Stigma in People Newly Diagnosed With Lung Cancer: A Cross-Sectional Analysis*. Paper presented at the Oncology nursing forum.
- Sarna, L., Brown, J. K., Cooley, M. E., Williams, R. D., Chernecky, C., Padilla, G., & Danao, L. L. (2005). *Quality of life and meaning of illness of women with lung cancer*. Paper presented at the Oncology nursing forum
- Sasco, A., Secretan, M., & Straif, K. (2004). Tobacco smoking and cancer: a brief review of recent epidemiological evidence. *Lung Cancer, 45*, S3-S9.
- Satin, J. R., Linden, W., & Phillips, M. J. (2009). Depression as a predictor of disease progression and mortality in cancer patients. *Cancer, 115*(22), 5349-5361.
- Sheehan, T. J., Fifield, J., Reisine, S., & Tennen, H. (1995). The measurement structure of the Center for Epidemiologic Studies Depression scale. *Journal of personality assessment, 64*(3), 507-521.
- Siminoff, L. A., Wilson-Genderson, M., & Baker, S. (2010). Depressive symptoms in lung cancer patients and their family caregivers and the influence of family environment. *Psycho-Oncology, 19*(12), 1285-1293.
- Stuber, J., Galea, S., & Link, B. G. (2008). Smoking and the emergence of a stigmatized social status. *Social science & medicine, 67*(3), 420-430.
- Sullivan, D., Forsberg, C., Ganzini, L., Au, D., Gould, M., Provenzale, D., . . . Slatore, C. (2016). Depression symptom trends and health domains among lung cancer patients in the CanCORS study. *Lung Cancer, 100*, 102-109.

- Taylor, C. L. C., Badr, H., Lee, J. H., Fossella, F., Pisters, K., Gritz, E. R., & Schover, L. (2008). Lung cancer patients and their spouses: psychological and relationship functioning within 1 month of treatment initiation. *Annals of Behavioral Medicine, 36*(2), 129.
- Tod, A. M., Craven, J., & Allmark, P. (2008). Diagnostic delay in lung cancer: a qualitative study. *Journal of advanced nursing, 61*(3), 336-343.
- Van Brakel, W. H. (2006). Measuring health-related stigma—a literature review. *Psychology, health & medicine, 11*(3), 307-334.
- Von Elm, E., Altman, D. G., Egger, M., Pocock, S. J., Gøtzsche, P. C., Vandenbroucke, J. P., & Initiative, S. (2014). The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. *International Journal of Surgery, 12*(12), 1495-1499.
- Weiss, J., Yang, H., Weiss, S., Rigney, M., Copeland, A., King, J. C., & Deal, A. M. (2017). Stigma, self-blame, and satisfaction with care among patients with lung cancer. *Journal of psychosocial oncology, 35*(2), 166-179.
- Weiss, M. G., Ramakrishna, J., & Somma, D. (2006). Health-related stigma: rethinking concepts and interventions. *Psychology, health & medicine, 11*(3), 277-287.
- Zabora, J., BrintzenhofeSzoc, K., Curbow, B., Hooker, C., & Piantadosi, S. (2001). The prevalence of psychological distress by cancer site. *Psycho-Oncology, 10*(1), 19-28.
- Zolnierok, K. B. H., & DiMatteo, M. R. (2009). Physician communication and patient adherence to treatment: a meta-analysis. *Medical care, 47*(8), 826.

"All data underpinning this publication are openly available from the University of Strathclyde at:

<https://doi.org/10.15129/286a189f-07be-466c-8cca-bb0de1a8bdc0>"

Table 1 Descriptive statistics for the CLCSS total and component scores

CLCSS Component (N=201)	N items	Mean (SD); Median	Actual range	Possible range
Component 1 – Social Isolation	14	22.1 (7.6); 20.0	14-48	14-56
Component 2 – Smoking	3	7.6 (2.4); 8.0	3-12	3-12
Component 3 – Stigma and Shame	8	12.6 (4.2); 12.0	8-26	8-32
Component 4 – Healthcare provider Stigma	2	3.6 (1.5); 3.0	2-8	2-8
Component 5 – Discrimination	4	7.2 (2.3); 7.0	4-16	4-16
Scale	31	53.1 (14.1); 53.0	31-94	31-124

Note: CLCSS=Cataldo Lung Cancer Stigma Scale

Table 2 Characteristics of all study participants (n=201)

Variable	Mean (SD); Median	Min-Max
Age in years (N=190)	69.2 (9.1); 70.5	41-89
Years since diagnosis (N=187)	2.6 (1.8); 1.9	0.2-11.0
Variable	N	%
Gender (N=196)		
Male	94	48.0
Female	102	52.0
Age categories (N=190)		
41-50 years	8	4.2

51-60 years	25	13.2
61-70 years	62	32.6
71-80 years	75	39.5
>80 years	20	10.5
Ethnicity (N=198)		
White	196	99.0
Other	2	1.0
Marital Status (N=200)		
Married/partnered	127	63.5
Divorced/separated	24	12.0
Widowed	36	18.0
Single	13	6.5
Living status (N=198)		
Alone	57	28.8
With partner/family/friend	141	71.2
Highest educational attainment (N=197)		
Primary school	28	14.2
High school	122	61.9
Higher Education College	33	16.8
University	14	7.1
Employment status (N=199)		
Employed (full-time/part-time)	24 (18/6)	12.0

Unemployed	17	8.5
Retired	149	75.0
Other (e.g. home maker)	9	4.5
Annual income in £ (N=164)		
<10,000	64	39.0
10,001-20,000	65	39.6
20,001-50,000	30	18.3
>50,000	5	3.1
Deprivation Index (SIMD)* (N=185)		
Fifth 1 (most deprived)	71	38.4
Fifth 2	35	18.8
Fifth 3	29	15.7
Fifth 4	24	13.0
Fifth 5 (least deprived)	26	14.1
Smoking status (N=195)		
Ever smoker	185	94.9
Smoking quitter	150	76.9
Current smoker	36	18.5
Never-smoker	10	5.1
Symptomatic prior to diagnosis (N=199)		
Yes	153	76.9
Presentation (N=195)		

GP	151	77.4
Emergency	8	4.1
Incidental	36	18.5
Suspected Asbestos exposure (N=197)	36	18.3
Disease status (N=183)		
Local	95	51.9
Locally advanced	52	28.4
Metastatic	31	16.9
Not staged	5	2.8
Treatment (N=195)		
Surgery only	62	31.8
Surgery in combination with other treatment	35	17.9
Chemotherapy	87	44.6
Radiotherapy	74	37.9
No. of comorbid illnesses (N=188)		
None	40	21.3
One	83	44.1
Two	44	23.4
Three or more	21	11.2
<p><i>Notes: SD=Standard Deviation; 'Local disease' is defined as any tumour that has not spread to the nodes; 'Locally advanced' is defined as the spread to lymph nodes; 'Metastatic' is defined as disease that is not localised and has spread to other parts of the body.</i></p>		

*<http://assign-score.com/estimate-the-risk/simd/>

Table 1. Descriptive statistics for depression, symptom burden, and HR-QoL

Variable (N=201)	Mean (SD); Median	Actual range	Possible range
Depression	16.2 (10.9); 14.0	0-48	0-60
Symptom Overall score	32.1 (18.0); 31.6	0-84	0-100
Symptom Burden Index	31.1 (17.2); 29.7	0-85	0-100
Symptom Severity	21.9 (5.4); 22.0	16-89	0-100
Individual Symptoms			
Appetite loss	31.9 (26.9); 27.0	0-96	0-100
Fatigue	49.1 (28.3); 49.0	0-100	0-100
Cough	29.5 (28.5); 21.0	0-100	0-100
Shortness of breath	49.2 (32.1); 51.0	0-100	0-100
Haemoptysis	4.8 (12.5); 1.0	0-83	0-100
Pain	23.0 (29.2); 8.0	0-100	0-100
Quality of life			
Overall score	5.8 (1.4); 5.8	0-9	0-10
Physical	6.5 (1.8); 6.4	1-10	0-10
Psychological	5.5 (1.7); 5.6	0-10	0-10
Social	6.7 (1.9); 7.0	0-10	0-10
Spiritual	4.7 (2.1); 4.4	0-10	0-10
<i>Notes: LCS=LC Stigma, HR-QoL=health-related quality of life</i>			

Table 2. Relationships among the study variables

Variable	LCS	Depression	HR-QoL
Age (N=190)	$r=-0.28^{**}$	$r=-0.19^*$	$r=0.35^{**}$
Time since diagnosis (N=187)	$r=0.09$	$r=0.17$	$r=-0.02$
Gender (N=196)	$t=0.08$	$t=-2.22^*$	$t=0.93$
Marital status (N=200)	$F=1.15$	$F=1.93$	$F=0.75$
Living status (N=198)	$t=0.97$	$t=2.95^{**}$	$t=-1.23$
Highest educational attainment (N=197)	$F=0.57$	$F=0.61$	$F=0.02$
Employment status (N=199)	$F=8.81^{***}$	$F=6.88^{**}$	$F=13.51^{***}$
Annual income (N=164)	$F=0.52$	$F=4.18^*$	$F=2.28$
Deprivation Index (SIMD) (N=185)	$t=2.23^*$	$t=1.50$	$t=-0.79$
Ever smoker (N=195)	$t=0.91$	$t=1.18$	$t=-0.97$
Smoking quitter (N=195)	$t=-1.64$	$t=-3.43^{**}$	$t=3.00^{**}$
Current smoker (N=194)	$t=1.81$	$t=3.56^{***}$	$t=-3.12^{**}$
Symptomatic prior to diagnosis (N=199)	$t=0.20$	$t=0.66$	$t=-1.98^*$
Presentation (N=195)	$F=0.43$	$F=0.26$	$F=1.02$
Asbestos exposure (N=197)	$t=0.43$	$t=-1.09$	$t=1.08$
Localised disease (N=183)	$t=-1.55$	$t=-0.65$	$t=1.83$
Locally advanced (N=183)	$t=1.20$	$t=0.25$	$t=-1.22$
Metastatic disease (N=183)	$t=0.59$	$t=0.56$	$t=-0.93$
Surgery only (N=195)	$t=-0.32$	$t=-0.98$	$t=1.84$
Surgery in combination with other treatment (N=195)	$t=0.75$	$t=0.42$	$t=-0.35$
Chemotherapy (N=195)	$t=0.68$	$t=0.68$	$t=-1.18$
Radiotherapy (N=195)	$t=0.64$	$t=0.90$	$t=-2.04^*$
No. of comorbid illnesses (N=188)	$F=0.94$	$F=0.17$	$F=0.25$
Quality of life (N=201)			
Overall score	$r=-0.52^{***}$	$r=-0.69^{**}$	-

Physical	$r=-0.32^{***}$	$r=-0.61^{**}$	-
Psychological	$r=-0.49^{***}$	$r=-0.65^{**}$	-
Social	$r=-0.52^{***}$	$r=-0.58^{**}$	-
Spiritual	$r=-0.18^{**}$	$r=-0.16^{**}$	-
Depression (N=201)	$r=0.40^{***}$	-	$r=-0.69^{**}$
Symptom Overall score (N=201)	$r=0.29^{***}$	$r=0.67^{**}$	$r=-0.67^{**}$
Symptom Burden Index (N=201)	$r=0.26^{***}$	$r=0.64^{**}$	$r=-0.61^{**}$
Symptom Severity (N=201)	$r=0.07$	$r=0.10$	$r=-0.07$
Individual Symptoms			
Appetite loss (N=201)	$r=0.14$	$r=0.47^{**}$	$r=-0.42^{**}$
Fatigue (N=201)	$r=0.21^{***}$	$r=0.56^{**}$	$r=-0.53^{**}$
Cough (N=201)	$r=0.19^{***}$	$r=0.34^{**}$	$r=-0.31^{**}$
Shortness of breath (N=201)	$r=0.15^*$	$r=0.38^{**}$	$r=-0.40^{**}$
Haemoptysis (N=201)	$r=0.19^{***}$	$r=0.26^{**}$	$r=-0.21^{**}$
Pain (N=201)	$r=0.16^*$	$r=0.46^{**}$	$r=-0.46^{**}$
<p><i>Notes: LCS=LC Stigma; GP=General Practitioner; QoL=Quality of Life; SIMD=Scottish Index of Multiple Deprivation, 'Local disease' is defined as any tumour that has not spread to the nodes; 'Locally advanced' is defined as the spread to lymph nodes; 'Metastatic' is defined as disease that is not localised and has spread to other parts of the body. *$p<0.05$; **$p<0.01$; ***$p<0.001$</i></p>			

Table 5. Summary of hierarchical regression analysis for symptom burden predicting LCS

Step	Predictor	β	ΔR^2
1	Socio-demographic characteristics		0.13***
	Age	-0.23**	
	Unemployed or home maker	0.11	
	Most deprived socioeconomic area	-0.12	
2	Patient outcome variables		0.05***

	Symptom burden index	0.22***	
	Cumulative R ²		0.18***
Dependent variable: LCS			
Notes: Betas shown are for the last step; Employment status was coded as a binary variable (unemployed/home maker v. employed/retired); Social deprivation was coded as a binary variable (1 st fifth v. all other).			
*p<0.05; **p<0.01; ***p<0.001			

Table 6. Summary of hierarchical regression analysis for LCS predicting depression and QoL

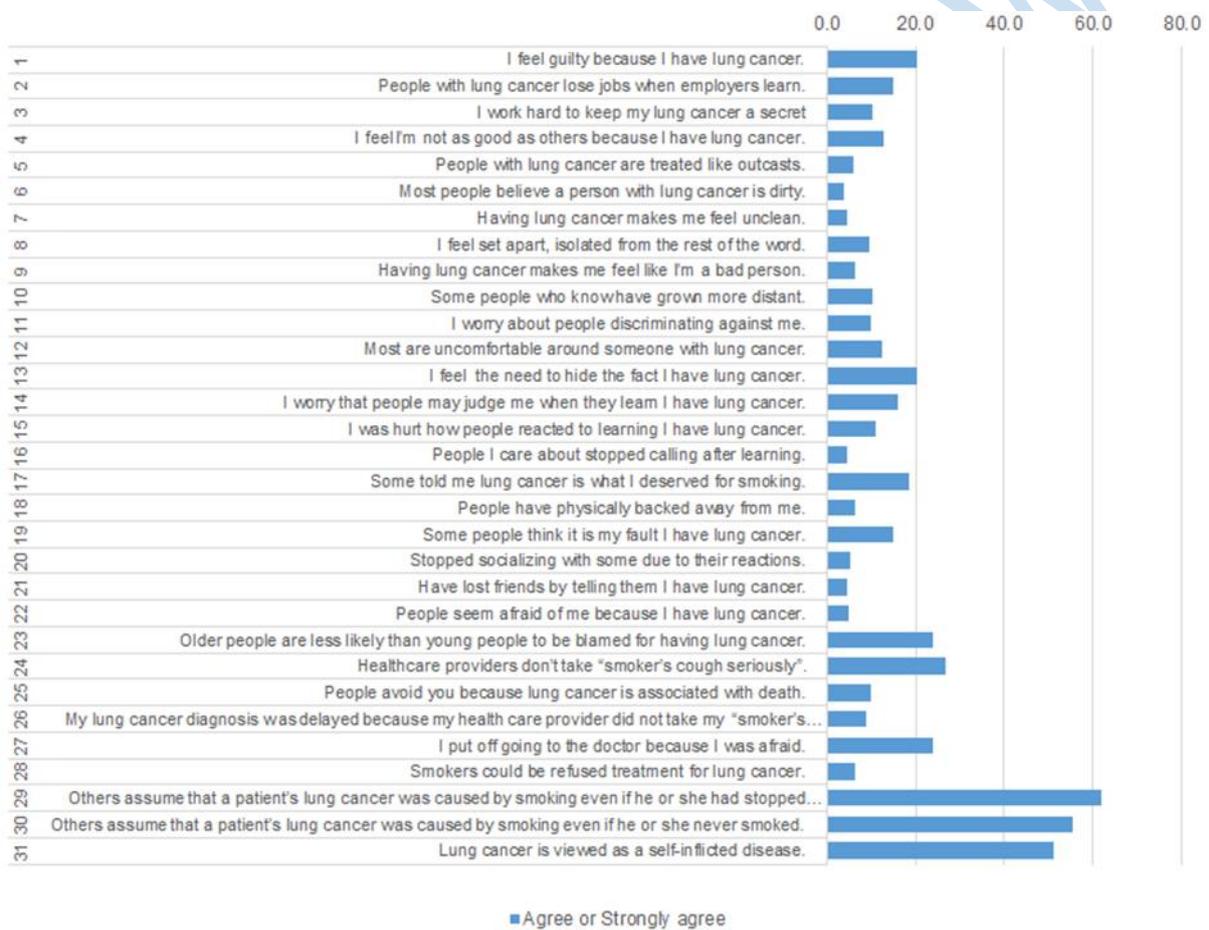
Regression 1 - Dependent variable: Depression			
Step	Predictor	β	ΔR^2
1	Socio-demographic characteristics		0.12**
	Age	-0.07	
	Female	0.16*	
	Living alone	-0.11	
	Unemployed or home maker	-0.01	
	Earning <£10,000 annually	0.20	
	Earning £10,001-20,000 annually	0.12	
2	Clinical factors		0.02
	Current smoker	-0.15	
3	Patient outcome variables		0.09***
	Perceived LCS	0.31***	
	Cumulative R ²		0.23***
Regression 2 - Dependent variable: QoL			
Step	Predictor	β	ΔR^2
1	Socio-demographic characteristics		0.14***
	Age	0.15*	
	Unemployed or home maker	-0.10	
2	Clinical factors		0.06**
	Current smoker	0.12	
	Symptomatic prior to LC diagnosis	0.13*	
	Previous radiotherapy	0.12	
3	Patient outcome variables		0.15***

	Perceived LCS	-0.40***	
	Cumulative R ²		0.35***

Notes: Betas shown are for the last step; Employment status was coded as a binary variable (unemployed/home maker v. employed/retired).

*p<0.05; **p<0.01; ***p<0.001

Figure 1. Item-by-item prevalence of “agree” or “strongly agree” responses (indicating perceived LCS) on the LCSS.



For Peer Review