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ORIGINAL REPORT FOR SUPPORTIVE CARE IN CANCER

The relationship between smoking and quality of life in advanced lung cancer patients: a prospective longitudinal study

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Abstract

Purpose

Smoking is a major cause of lung cancer and continued smoking may compromise treatment efficacy and quality of life (HRQoL) in patients with advanced lung cancer. Our aims were to determine i) preference for treatments which promote quality over length of life depending on smoking status, ii) the relationship between HRQoL and smoking status at diagnosis (T1), after controlling for demographic and clinical variables and iii) changes in HRQoL 6 months after diagnosis (T2) depending on smoking status.

Methods

296 patients with advanced lung cancer were given questionnaires to assess HRQoL (EORTC-QLQ-C30), time-trade off for life quality versus quantity (QQQ) and smoking history (current, former or never smoker) at diagnosis (T1) and six months later (T2). Medical data were extracted from case records.

Results

Questionnaires were returned by 202 (68.2%) patients at T1 and 114 (53.3%) at T2. Patients favoured treatments that would enhance quality of life over increased longevity. Those who continued smoking after diagnosis reported worse HRQoL than former smokers or those who never smoked. Smoking status was a significant independent predictor of coughing in T1 (worse in smokers), and Cognitive Functioning in T2 (better in never-smokers).

Conclusions

Smoking by patients with advanced lung cancer is associated with worse symptoms on diagnosis and poorer HRQoL for those who continue smoking. The results have implications to help staff explain the consequences of smoking to patients.

Keywords: Lung cancer, smoking, smoking cessation, quality of life

Relevance of manuscript: This paper assesses the relationship between smoking and HRQoL in patients with advanced lung cancer. It shows that smoking is associated with worse symptoms on diagnosis and poorer HRQoL for those who continue smoking. This knowledge can be used when smoking status and smoking cessation are discussed with patients to provide positive encouragement of the benefits of quitting.

Introduction

Lung cancer accounts for 27% of cancer deaths [1]. Five-year survival rates range from 52% for lung cancer patients with localised disease to 4% for those with distant metastases [1]. Patients often are elderly (median age 70 years), diagnosed at a late stage, and have complex medical histories and co-morbidities [2]. Patients with advanced lung cancer typically have troublesome symptoms. This, compounded with the added burden of side effects from chemotherapy and radiotherapy, can adversely impact their quality of life.

When discussing treatments for advanced lung cancer, both survival benefits and health related quality of life (HRQoL) should be considered [3]. HRQoL captures the broader consequences of illness for cognitive, social and emotional functioning in addition to physiological effects of illness and treatment [4]. Symptom palliation and HRQoL are very important to patients [5] and those who are older with incurable disease may prioritise quality over length of survival [6, 7].

Over 86% of lung cancers are attributed to smoking [8]. In early stage lung cancer, continued smoking is associated with greater post-operative morbidity [9] and a two-fold greater risk of death [10]. In more advanced disease, smoking is associated with radiation-induced pneumonitis [11], greater difficulty in administering chemotherapy due to worse baseline symptoms [12], and decreased treatment efficacy, through mechanisms such as altered pharmacokinetics [13]. Half of patients who quit smoking begin again after potentially curative surgery [14], illustrating how difficult it can be to quit even when motivation to do so is substantial.

Lung cancer patients have reported feeling more judged than breast or prostate cancer patients and are most likely to acknowledge their own behaviours as a causal

factor in disease onset [15]. Evidence suggests that perceived stigma is not constructed by patients who perhaps feel guilty or shameful themselves, but reflects opinions which are evident in the general population [16, 17] and within health care professions [18, 19]. For lung cancer patients, these opinions appear to develop because of the strong association between disease onset and smoking regardless of the patients' personal history of smoking [18].

Where the patient perceives stigmatisation they may feel that family, friends, and medical staff are less supportive than they could be, to the detriment of HRQoL, in turn, affecting treatment decisions. Smoking cessation is one intervention which is under direct control of the patient and which could have a positive impact on their outcomes leading a patient who quits to feel empowered [20]. Equally, those who have never smoked, or continue to smoke may feel more nihilistic about their outcomes. In these situations, smokers may have different opinions about treatment options that benefit quality over length of survival compared with never smokers.

Given the established links between smoking and lung cancer, newly diagnosed patients who smoke might be especially motivated to quit, but little is currently known about the implications of smoking cessation for HRQoL in advanced lung cancer [21, 22].

We therefore undertook a longitudinal study to determine:

i) preference for treatments which promote quality over length of life depending on smoking status

ii) relationship between HRQoL and smoking status at diagnosis (T1), controlling for demographic and clinical variables

iii) changes in HRQoL 6 months after diagnosis (T2) depending on smoking status

Materials and methods

Patients

Patients (>18 years old) with a pathological diagnosis of advanced lung cancer were recruited from the North Trent Cancer Network, UK between December 2009 and January 2012. Inclusion criteria were diagnosis within 12 weeks, unsuitable for radical treatment with radiotherapy or surgery, and clinician-estimated survival of greater than six months. The pathology could be either non-small cell lung cancer (NSCLC) or small cell lung cancer (SCLC). North Sheffield Research Ethics Committee approved the study and the work was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. All patients were treated according to local guidelines.

Study procedures

Clinicians approached eligible patients with verbal and written information about the study and obtained signed consent. Patients completed questionnaires at home, or in clinic with assistance from a researcher. Assistance was only given with reading and completing the form, not in how to interpret the questions. Six months after recruitment (T2), surviving patients were sent questionnaires by post. On both occasions, reminders were sent to non-responders after two weeks. Throughout the study, patients wishing to pursue smoking cessation were supported by lung cancer clinical nurse specialists. There was no standard practice on smoking cessation services provided by the clinical team so the options were discussed with patients and individual plans designed.

Quantitative measures

The EORTC-QLQ-C30 questionnaire was used to evaluate cancer-related HRQoL [23]. This yields a Global HRQoL score, five function scales (physical, role, emotional, cognitive, and social functioning), three symptom scales (fatigue, pain, nausea and vomiting), and six single item symptom scores (dyspnoea, insomnia, appetite loss, constipation, diarrhoea, and financial difficulties). Higher scores for Global HRQoL and function scales indicate better HRQoL. High symptom scores indicate worse outcomes. The EORTC QLQ-LC13 lung cancer module [24] comprises one scale (dyspnoea) and nine single item symptom scores and was used to assess disease-specific HRQoL. The 8-item Quality-Quantity Questionnaire (QQQ) [6] was used to determine preferences for quality and length of life. This includes eight statements about accepting life-prolonging treatments at the expense of life quality or vice versa (for example, 'to live a bit longer I would try any treatment that might help', and 'I can imagine some side-effects being so bad that I would refuse treatment, even if it meant a shorter life'). Each statement is followed by a five point Likert scale. Responses are summed to produce two scales: a preference for quality of life ('Q') and a preference for length of life ('L'). A high score on the Q scale indicates a high value for quality of life over length and a high score on L indicates a preference for length of life over quality. The QQQ has demonstrated validity for use with cancer patients: internal reliability scores range from 0.68-0.75 for Quality and 0.67-0.79 for Length [6, 7, 25].

Patients provided demographic information by completing self-report questionnaires. Smoking status was self-categorised as never (smoked less than five cigarettes ever), former ('I used to smoke but have now given up) or current ('I am a smoker'). At T1 information about gender, date of birth, diagnosis, Performance Status (PS)

[26], treatment (chemotherapy, radiotherapy, other), and previous or long-term health problems were obtained from self-report questionnaires. At T2, toxicity outcomes [27] (number of events rated severe and undesirable) (3) or life-threatening or disabling (4)) and number of chemotherapy cycles were recorded by retrospective extraction of data from the notes.

Statistical analysis

Analyses were conducted using SPSS 20.0 [28]. Skewed variables (QQQ scales (T1 and T2) and HRQoL outcomes (T1 and T2) were log-transformed where necessary. Attrition analyses were conducted to determine differences between those who responded at T1 but not T2 (non-deceased) and those who replied to both questionnaires. Differences in age, gender, PS and diagnosis were assessed with Chi-square and independent samples t-tests for number of toxic incidences, T1 HRQoL (all outcomes), and T1 QQQ.

Mixed ANOVA was used to examine relationships between QQQ and smoking status and multiple regression models to predict HRQoL. HRQoL outcomes associated with smoking status were used as dependent variables in a regression model. T-tests, correlations, and ANOVAs (with Tukey *post-hoc* analysis) determined other baseline variables associated with HRQoL or smoking which may be potential confounds, which were then included in regressions at step 1. Step 2 examined the additional effect of the smoking variables after the baseline effects were taken into account. All analyses were conducted separately at T1 and T2.

Smoking status was dummy coded in regression models. Initially 'never smoked' was the reference for comparison with current and former smokers. Models were repeated with current smokers as the reference category to provide comparison between current and former smokers. PS was dummy coded and entered into the

regression model, with PS 0 (full functioning) as the reference value. Multiple regression models included only participants with complete data on all predictor variables. The resulting number of participants included in each model is shown in Tables 2 and 3.

For ease of interpretation, non-standardised regression coefficients (b) are reported for categorical variables entered into regression models (smoking status, PS, employment status (1=not retired), sex (1=female)). Standardised regression coefficients (β) are reported for continuous variables.

Results

Sample description

The flow of patients through the study is shown in Figure 1. In total 641 possible patients were identified from medical records and 304 consented to take part. 309 were considered inappropriate to approach or ineligible by the clinician, for example if they were too unwell, had a predicted life expectancy less than six months, or were highly distressed by their diagnosis. Eight subsequently withdrew leaving a final sample of 296. Participants did not differ in age, gender, PS or diagnosis (NSCLC or SCLC) from those (n=94) who consented but did not respond. Median interval from diagnosis was 5.14 weeks (range 0.9-12.0 weeks) and did not differ by smoking status ($F(2,194)=2.05$, $p=.09$). At T1, there were 20 (10%) never-smokers, 45 (22.5%) current smokers and 135 (67.5%) former smokers, two participants did not classify their smoking behaviour and are excluded from analyses. One patient resumed smoking between T1 and T2. Participants were typically white (99.5%), male (57.7%), aged 68 years (range 43.2-85.5 years), reported no formal educational qualifications (58.9%) and had a PS of 1 (64.4%). Most patients were diagnosed with NSCLC (73.5%), 49.5% had distant metastases and 77.0% received chemotherapy. Never-smokers were more often older, female, partnered and more educated, with fewer previous medical conditions (PMC) than current or former smokers and fewer long-term health problems (LTHP) than former smokers. Baseline characteristics of patients are shown in Table 1. T2 demographic and medical variables were similar to T1. There were no significant differences on key variables between those who responded at T1 but not T2 (non-deceased) and those who replied at both times.

Data were also collected on cause of death and were as follows: death was directly attributable to the cancer in 63 cases; deaths from anticancer treatment - 2 (1 bowel perforation secondary to erlotinib, 1 neutropenic sepsis); death for other reasons - 16 (ischaemic stroke 1, pneumonia 9, pulmonary embolus 2, heart failure 1, pulmonary fibrosis 1, ruptured abdominal aortic aneurysm 1, sepsis 1); and cause of death was unknown in 1 case.

i) Preference for quality versus length of life by smoking status

At T1 and T2, there was a significant preference for quality over length of life (T1: quality=2.52(.29), length=1.85(.46); $F(1,182)=98.201$, $p<.001$; T2: quality=2.53(.30), length=1.91(.47), $F(1,99)=38.1$, $p<.001$), but no effect of smoking status (T1: $F(2,182)=.27$, $p=.77$; T2: $F(2,99)=.60$, $p=.55$) and no interaction between smoking status and time (T1: $F(2,182)=1.41$, $p=.32$; T2: $F(2,99)=.75$, $p=.48$).

ii) Associations between HRQoL and smoking status at baseline.

There was a significant association between smoking status and physical functioning ($F(2,196)=3.52$, $p=.03$), with never-smokers (76.00 [22.93]) reporting significantly better physical functioning than former smokers (61.86 [22.93], p=.02). Coughing was also associated with smoking status ($F(2,196)=5.21$, $p=.01$), with current smokers (50.00[25.42]) reporting more coughing than former smokers (35.62 [27.79], p=.007). There were no other significant relationships between smoking status and HRQoL.

Chemotherapy was not included in regression modelling as all current smokers received chemotherapy, violating the multicollinearity assumption.

Physical functioning

Physical functioning was significantly associated with QQQ Length (r=-.21, p=.003) and PS (F(3,188)=9.30, p<.001) which were entered into the regression model along with correlates of smoking status. Clinical and demographic variables explained 24% of variance in physical functioning at step 1, but smoking status was not a significant additional predictor (step 2, Table 2).

Coughing

Male gender was associated with coughing (t(185.19)=2.25, p=.03) (equal variance not assumed) and was included in the regression model as a covariate. Being male and a current smoker (compared to never and former smokers) were independently associated with worse coughing (Table 2).

iii) Change in HRQoL at Q2 predicted by smoking status.

At T2, smoking status was associated with cognitive functioning (F(2,110)=5.22, p=.01), social functioning (F(2,110)=4.32, p=.02), and fatigue (F(2,109)=4.54, p=.01). Never-smokers (99.54[1.71]) had better cognitive functioning than former smokers (98.14[1.35], p=.008) and current smokers (97.99[1.48], p=.007). Former smokers reported better social functioning (63.93[28.19]) than current smokers (45.40[30.50], p=.01) and less fatigue (48.93[27.31] and 66.81[26.81], p=.01). There were no other significant relationships between smoking status and HRQoL.

At T2, smoking status was associated with age (F(2,111)=4.19, p=.02), employment status (χ2(2)=6.96, p=.03) and number of PMCs (F(2,104)=3.29, p=.04). These variables were included as confounders in multiple regressions to predict fatigue, cognitive and social functioning.

Cognitive functioning

LTHP (r=-.19, p=.04), T1 cognitive functioning (r=.30, p<.01) and T1 fatigue (r=-.27, p<.01) were significantly associated with T2 cognitive functioning and were included in this regression model at step 1, which significantly predicted T2 cognitive functioning (Table 3). The addition of smoking status at step 2 significantly increased the amount of variance explained (R^2Change=.08, p=.02). Former smokers (B=-1.47, p=.005) and current smokers (B=-1.43, p=.014) both independently predicted worse T2 cognitive functioning, after controlling for T1 cognitive functioning.

Social functioning

T1 social functioning (r=.36, p<.001), T1 fatigue (r=-.29, p<.01) and female gender (r=.20, p<.05) were significantly associated with T2 social functioning and were included in step 1. At step 1, being female was an independent predictor of better social functioning (B=13.06, p=.03). Smoking status did not explain additional variance in the model (R^2Change=.05, p=.08) (Table 3) although the specific comparisons indicated that former smokers had significantly better social functioning compared to current smokers (B=15.76, p=.03).

Fatigue

T1 fatigue (r=.46, p=<.01), T1 social functioning (r=-.31, p<.01), and number of toxic incidents (r=.24, p=.01) were significantly associated with T2 fatigue and were entered at step 1. T1 fatigue was the only significant independent predictor of T2 fatigue, at step 1 (β=.46, p<.001). At step 2 smoking status did not explain additional variance in the model (R^2Change=.03, p=.19) (Table 3).

Discussion

Our data indicate a significant preference for quality over length of life up to six months post-diagnosis in advanced lung cancer patients, which is a new finding supported by previous related literature [6, 7, 25]. Preference for quality was independent of smoking status. At T1, smokers had worse coughing compared with former or never smokers. At T2, former and current smoking was predictive of worse cognitive functioning than never smoking. These findings provide staff with information that could help them to explain the effects of lung cancer beyond physical symptoms and help patients make informed choices about their smoking behaviour to enhance their HRQoL. This understanding of a holistic effect on HRQOL may provide a 'teachable moment' for patients newly diagnosed with advanced lung cancer who are likely to view favourably those treatments which enhance life quality.

Our data involving newly-diagnosed lung cancer patients with advanced disease complement previous findings by Garces et al. [29], who reported that HRQoL differed by smoking status in lung cancer patients who survived over a longer period of time (> 5 years) with smokers reporting worse HRQoL. Other studies have found no association between smoking and HRQoL [30, 31], but may be explained in terms of different patient groups.

Furthermore, these data are consistent with previous findings that smokers present with more co-morbidities including respiratory and cerebrovascular disease which are probably attributable to chronic cigarette use [32]. It should also be noted that self-rated physical symptoms of pain and dysphagia are negative prognostic factors for survival in NSCLC [33]. The finding that those who continue to smoke after diagnosis report significant deterioration across some HRQoL domains could be due

to higher levels of co-morbidity or that tumours of never-smokers have different biology than in smokers. Never-smokers who develop lung cancer may be particularly susceptible to environmental tobacco exposure, and there is some evidence that this may be mediated by polymorphisms in detoxification enzymes [34]. This may also make these individuals more susceptible to the toxic effects of anticancer treatments. Tumours in never-smokers sometimes exhibit different molecular changes, such as EGFR activating mutations and ALK translocations [35] that make them more likely to respond to less toxic, outpatient targeted therapy than tumours in smokers. Further, smoking itself can reduce the likelihood of success of systemic treatment [13].

We conclude that continued smoking has adverse implications for both physiological and psychological health of lung cancer patients, raising questions of whether, and how, staff might encourage patients to quit. In a large scale, prospective cohort study, Williams et al. [36], found no statistical evidence of increased, spontaneous smoking cessation among those who received a cancer diagnosis compared to the general population. In support of this, cancer survivors have reported that they would find it beneficial to receive lifestyle advice from health care professionals [37]. Thus, diagnosis could present a 'teachable moment' when patients are receptive to smoking cessation interventions, particularly older patients with advanced disease [38]. In addition, the 'teachable moment' might be relevant to patients with other types of tumour where active smoking during treatment may also be detrimental in their situation [39].

The challenge to any 'teachable moment' may especially be among those patients who argue that quitting would be detrimental to their remaining HRQoL [40]. These

patients may benefit from data such as those reported describing physical and psychological symptoms typical of smokers and non-smokers undergoing treatment.

Perhaps more than other cancers, lung cancer carries a potential blame among patients, their families and staff, given the strong association between smoking and disease onset. Where patients do acknowledge the presence of stigma due to the association between smoking and lung cancer, there can be negative psychosocial outcomes such as depressed mood [41] and illness intrusiveness [42] which may be related to lower HRQoL. In the context of this study, cognitive functioning is indicative of capacity for recollection and concentration. Of course, while we do not know what the causal pathway is between these variables [stigma, mood/intrusiveness, cognitive functioning] we could postulate that perceived stigmatisation, and associated rumination, leads to mood disturbance and illness intrusiveness, subsequently decreasing cognitive functioning and HRQoL resources

Research on the psychological theory of 'ego-depletion' [43] may offer a framework for thinking about these pathways and subsequent interventions to use in the teachable moment, to assist smoking cessation attempts, and improve or maintain HRQoL. This theory suggests that we have a limited amount of capacity to control our motives, intentions and behaviour and that this may be depleted by distractive, intrusive or negative thoughts, as well as experiences of stigmatisation [44]. It may be that, in trying to supress thoughts of stigmatisation, depressed mood or the impact of illness intrusions, patients are drawing upon their limited self-control resources and experiencing ego-depletion. When ego-depletion occurs, a person's attention to cues which signal the need for control are compromised [45]. In the example of smoking cessation this may mean that people are less successful in controlling their impulse to smoke.

Strengths and limitations

Smoking can be an emotive issue and patients with advanced lung cancer often have a high level of functional impairment. Despite this, only five patients refused to take part and we achieved a good response rate (68% at T1), suggesting that it is possible to enrol patients with advanced lung cancer into studies evaluating smoking status and HRQoL. Strengths of this study include the longitudinal design and relatively large sample size compared with previous research [31, 46-48]. In using a cancer specific HRQoL instrument with an additional lung cancer module we gained a greater depth of understanding, compared with relying on a generic measure of HRQoL or symptom reports. Inclusion of quality versus length of life trade-offs also provides valuable insight into the preferences of these patients.

Limitations include that we relied on self-reporting which may be subject to bias, such as common method variance effects. However, clinical practice routinely relies on self-report. Inevitably, and as with similar studies [30, 31, 47] we recruited only a small sample of never smokers (approximately 10%). However, absolute numbers of never smokers were small, limiting our power to make comparisons between groups. Our power was further compromised by unequal sample sizes across smoking groups. The sample size was greater than in other studies of this hard to reach population, but was smaller than ideal for longitudinal analyses. Loss-to-follow up meant that the number of observations was low for the number of independent variables in each model, limiting our ability to detect small effects. However, attrition of this sort will be inherent in a population with such poor prognosis, even over a relatively short six month follow-up period. It is possible that our findings may not represent the views of HRQoL among those who survive longer and our results

would benefit from replication in a larger sample. Further work would also benefit from adopting alternative designs. For example, a randomised controlled trial of a smoking cessation intervention would provide the leverage to test causal hypotheses about the effects of smoking on HRQoL. The current observational study is valuable in providing a justification for hypothesis formation in an experimental study of this sort.

Conclusion

These findings contribute significantly to understanding the experiences of advanced lung cancer patients. Newly diagnosed lung cancer patients report a significant preference for treatments that enhance life quality rather than increase longevity irrespective of their smoking status. HRQoL is dependent on smoking status at diagnosis and worse among those who continue to smoke. These data could help staff to explain the positive implications of smoking cessation for HRQoL.

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Table 1: Patient and tumour characteristics at Q1.

(Frequencies (%) unless otherwise stated)

	Current smokers (*n*=45)	Quit smoking (*n*=135)	Never smoked (*n*=20)	Test	*p*-value
Age (years)				***F*(2,197)=4.08**	**.03**
(Mean (S.D) Median (range)	65.66$_{a*}$(6.70), 65.80 (51-80.3)	68.69 (7.45) 68.00 (44.2-85.5)	70.79$_{a*}$(9.21) 73.25 (43.2-81.3)		
Gender				$\chi^2(2)=1.54$	.46
Male	26 (57.8)	80 (59.7)	9 (45.0)		
Ethnicity					-
White	43 (100.0)	131 (99.2)	19 (100.0)		
Education	(*n*=44)	(*n*=127)	(*n*=19)	$\chi^2(2)=4.26$	.12
No formal educational qualifications	27 (61.4)	78 (61.4)	7 (36.8)		
Marital status	(*n*=44)	(*n*=132)	(*n*=19)	$\chi^2(2)=4.80$	.09
Living as married / partner	31 (70.5)	95 (72.0)	18 (94.7)		
Other	13 (29.5)	37 (28.0)	1 (5.3)		
Employment	(*n*=44)	(*n*=129)	(*n*=19)	**$\chi^2(2)=7.31$**	**.03**
Retired	27 (61.4)	101 (78.3)	17 (89.5)		
Other	17 (38.6)	28 (21.7)	2 (10.5)		
Diagnosis					
NSCLC+	32 (71.1)	102 (75.6)	16 (80.0)	$\chi^2(2)=1.00$	.61
SCLC+	13 (28.9)	29 (21.5)	4 (20.0)		
Not specified	0 (0.0)	4 (3.0)	0 (0.0)		
Staging (M)				$\chi^2(2)=1.55$	.46
Localised+	13 (28.9)	37 (27.4)	4 (20.0)		
Metastatic+	23 (51.1)	62 (45.9)	14 (70.0)		
Not specified	9 (20.0)	36 (26.7)	2 (10.0)		
Treatment					
Chemotherapy	(*n*=41)	(*n*=115)	(*n*=16)	**χ2(2)=6.78**	**.03**
	41 (100.0)	100 (87.0)	13 (81.2)		
Radiotherapy	(*n*=41)	(*n*=114)	(*n*=16)	χ2(2)=.99	.61
	26 (63.4)	71 (62.3)	8 (50)		
Other	(*n*=40)	(*n*=115)	(*n*=16)	χ2(2)=2.57	.28
	6 (15.0)	18 (15.7)	5 (31.2)		

Performance status	(*n*=44)	(*n*=127)	(*n*=20)	$\chi 2(2)=1.80$	.41
0	7 (15.9)	24 (18.9)	6 (30.0)	*(PS 1,2,3 grouped and compared with 0 for analysis)*	
1	33 (75.0)	77 (60.6)	12 (60.0)		
2	3 (6.8)	23 (18.1)	1 (5.0)		
3	1 (2.3)	3 (2.4)	1 (5.0)		
Number previous cancers	(*n*=45)	(*n*=134)	(*n*=20)	F(2,197)=.02	.98
0	37 (82.2)	114 (84.4)	17 (85.5)		
1	7 (15.6)	17 (12.6)	2 (10.0)		
2	1 (2.2)	4 (3.0)	1 (5.0)		
(mean (S.D))	.20 (.46)	.19 (.46)	.20 (.52)		
Number previous medical conditions	(*n*=42)	(*n*=130)	(*n*=19)	**F(2,188)=6.83**	**<.01**
(Mean (S.D))	1.95 $(1.29)_{b^*}$	2.17$(1.28)_{a^{**}}$	1.05$(.71)_{a^{**}b^*}$		
Number long term health problems				**F(2,197)=3.35**	**.04**
(Mean (S.D))	1.49 (.17)	1.53 $(1.51)_{a^*}$	.60 $(.88)_{a^*}$		

*p<.05; **p<.01.

[+] Groups that were compared for statistical analysis if not all groups were used.

Note: Means with corresponding subscripts are significantly different from each other

Table 2: Q1 multiple regression analyses predicting Physical Functioning and Coughing.

	Physical Functioning (*n*=168)								Coug
	Step 1			Step 2			Step 1		
	B	*SE B*	β	*B*	*SE B*	β	*B*	*SE B*	β
Age	-0.25	0.27	-0.09	-0.33	0.27	-0.12	-0.44	0.32	-0.13
Employment status (not retired)	-4.22	4.59	-0.08	-3.96	4.59	-0.08	-3.71	5.58	-0.06
LTHP	-0.20	1.10	-0.01	-0.02	1.10	0.00	-1.37	1.39	-0.08
PMC	-3.55	1.31	**-0.21****	-3.11	1.33	**-0.18****	2.87	1.69	0.14
PS 1	-7.85	3.93	**-0.17***	-6.95	3.95	-0.15	-	-	-
PS 2	-24.18	5.65	**-0.36*****	-22.66	5.69	**-0.34*****	-	-	-
PS 3	-24.35	9.80	**-0.19***	-24.48	9.76	**-0.19****	-	-	-
QQQL	-9.61	3.48	**-0.20****	-9.35	3.47	**-0.19****	-	-	-
Gender (Female)	-	-	-	-	-	-	-10.09	4.00	**-0.19**
Current smoking (versus never)	-	-	-	-9.47	5.46	-0.20	-	-	-
Current smoking (versus never)	-	-	-	-10.92	6.13	-0.21	-	-	-
Quit smoking (versus current)	-	-	-	1.45	3.78	0.03	-	-	-
	R^2 =.24 (F=6.18)***			**R^2 =.25 (F=5.33)***** **R^2Change=.02**			**R^2 =.06 (F=2.31)***		

*Note: *p*<.05, **p*<.01, ***p*<.001*
Abbreviations: LTHP= Long term health problems, PMC=previous medical conditions; PSxxx = Performance status 1, 2, or 3 (dummy coded – PS 0 as reference value). QQQ L=preference for treatments which increase length of life over quality.
Interpretation: B = a change in dependent variable (e.g., Coughing) per unit change in predictor variable. β = change in standard deviation of dependent variable per change in standard deviation of predictor variable.

Table 3: Q2 multiple regression analyses.

	Cognitive Functioning (*n*=92)						Social F		
	Step 1			Step 2			Step 1		
	B	*SE B*	β	*B*	*SE B*	β	*B*	*SE B*	β
Age	0.01	0.03	0.06	0.00	0.03	0.02	0.47	0.51	0.1
Employment status (not retired)	-0.05	0.50	-0.01	-0.11	0.49	-0.03	-13.49	9.73	-0.1
PMC	-0.11	0.13	-0.09	-0.03	0.13	-0.03	-1.87	2.23	-0.0
LTHP	-0.09	0.10	-0.11	-0.09	0.10	-0.10	-	-	-
T1 Cognitive Functioning	0.21	0.11	0.22	0.13	0.11	0.14	-	-	-
T1 Social Functioning	-	-	-	-	-	-	0.23	0.13	0.2
T1 Fatigue	-0.01	0.01	-0.15	-0.01	0.01	-0.19	-0.19	0.15	-0.1
Gender (Female)	-	-	-	-	-	-	13.06	5.95	**0.2**
Quit smoking (versus Never)	-	-	-	-1.47	0.51	**-0.47****	-	-	-
Current smoker (versus Never)	-	-	-	-1.43	0.57	**-0.40***	-	-	-
Quit smoking (versus Current)	-	-	-	-0.04	0.37	-0.01	-	-	-
	R^2 =.15 (F=2.48)*			**R^2 =.23 (F=3.10)** R^2Change=.08***			**R^2 =.25 (F=4.57)****		

*Note: *p*<.05, **p*<.01, ***p*<.001*
Abbreviations: LTHP= Long term health problems, PMC=previous medical conditions.
Interpretation: B = a change in dependent variable (e.g., Coughing) per unit change in predictor variable. β = change in standard deviation of dependent variable per change in standard deviation of predictor variable.

Table 3: Q2 multiple regression analyses (continued).

	Fatigue (*n*=92)					
	Step 1			Step 2		
	B	*SE B*	β	*B*	*SE B*	β
Age	-0.15	0.43	-0.04	-0.06	0.44	-0.02
Employment status (not retired)	15.84	8.33	0.23	13.28	8.42	0.20
PMC	0.66	1.96	0.03	0.48	2.01	0.02
T1 Social Functioning	0.00	0.11	0.00	-0.02	0.11	-0.03
T1 Fatigue	0.48	0.12	**0.46*** **	0.46	0.12	**0.44*** **
Number of toxicities	6.00	3.30	0.17	6.48	3.28	0.18
Quit smoking (versus Never)	-	-	-	0.39	8.31	0.01
Current smoker (versus Never)	-	-	-	11.72	9.37	0.18
Quit smoking (versus Current)	-	-	-	-11.33	6.32	-0.19
	R^2 =.33, (F=6.94)* **			**R^2 =.36, (F=5.71)*** ** **R^2Change=.03**		

Figure 1: Recruitment and participation throughout the study.