BREATHLESSNESS IN THE ELDERLY DURING THE LAST YEAR OF LIFE SUFFICIENT TO RESTRICT ACTIVITY: PREVALENCE, PATTERN AND ASSOCIATED FACTORS.

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Running head: Dyspnoea in the elderly at the end of life.

Funding: National Institute on Ageing (NIA)(R37AG17560). Data were collected, in part, through the support of the Yale Claude D. Pepper Older Americans Independence Center (P30AG21342). Dr. Gill is the recipient of an Academic Leadership Award (K07AG043587)

from the National Institute on Aging.

This is the peer reviewed version of the following article: Johnson, M. J., Bland, J. M., Gahbauer, E. A., Ekström, M., Sinnarajah, A., Gill, T. M. and Currow, D. C. (2016), Breathlessness in Elderly Adults During the Last Year of Life Sufficient to Restrict Activity: Prevalence, Pattern, and Associated Factors. J Am Geriatr Soc, 64: 73–80, which has been published in final form at doi:10.1111/jgs.13865. This article may be used for non-commercial purposes in accordance With Wiley Terms and Conditions for self-archiving.

Conference presentation: Oral presentation. American Thoracic Society May 2015

International Conference, Denver, Colorado.

ABSTRACT

OBJECTIVES: Breathlessness is prevalent in older people. Symptom control at the end of life is important. This study investigated relationships between age, clinical characteristics and breathlessness sufficient to have people spend at least one half a day in that month in bed or cut down on their usual activities (restricting breathlessness) during the last year of life.

DESIGN: Secondary data-analysis

SETTING: General community

PARTICIPANTS: 754 non-disabled persons, aged 70 and older. Monthly telephone interviews were conducted to determine the occurrence of *restricting breathlessness*. The primary outcome was the percentage of months with restricting breathlessness reported during the last year of life.

RESULTS: Data regarding breathlessness were available for 548/589 (93.0%) decedents (mean age 86.7 years (range 71 to 106; males 38.8%). 311/548 (56.8%) reported restricting breathlessness at some time-point during the last year of life but no-one reported this every month. Frequency increased in the months closer to death irrespective of cause. Restricting breathlessness was associated with anxiety, (0.25 percentage point increase in months breathlessness per percentage point months reported anxiety, 95% CI 0.16 to 0.34, *P*<0.001), depression (0.14, 0.05 to 0.24, *P*=0.002) and mobility problems (0.07, 0.03 to 0.1, *P*=0.001). Percentage months of restricting breathlessness increased if chronic lung disease was noted at the most recent comprehensive assessment (6.62 percentage points, 95% CI 4.31 to 8.94, *P*<0.001), heart failure (3.34, 0.71 to 5.97, *P*<0.01), and ex-smoker status (3.01, 0.94 to 5.07, *P*=0.002), but decreased with older age (-0.19, -0.37 to -0.02, *P*=0.03).

CONCLUSION: Restricting breathlessness increased in this elderly population in the months preceding death from any cause. Breathlessness should be assessed and managed in the context of poor prognosis.

Key words: dyspnea; breathlessness; prevalence; end of life; elderly;

INTRODUCTION

Published estimates for the prevalence of breathlessness, medically known as dyspnea, in the general population vary between 9% to 59%, with a higher prevalence in older populations and in women.¹⁻⁸ A large national primary care study found that one in three people seen by their family practitioner with breathlessness was over 75 years old.⁹ Common cardio-respiratory conditions such as cancer,¹⁰ chronic non-malignant lung disease, and heart failure increase in prevalence with age and are common causes of breathlessness (60% - 88% with heart failure and 90% - 95% with late stage chronic obstructive pulmonary disease).¹¹ Breathlessness worsens in the advanced stages of disease,¹² and in the weeks prior to death.¹³ Post-bereavement interviews among informal caregivers of people with lung cancer found that 78% of decedents had experienced breathlessness in their final year.¹⁴

Breathlessness is a frightening symptom which limits all aspects of life and is associated with poor clinical outcomes. People with breathlessness are more likely to be sent to hospital from primary care,⁹ admitted to hospital from the emergency department,¹⁵ experience an inhospital serious event ¹⁶ and have a poorer prognosis.¹⁷⁻¹⁹ The relationship between breathlessness and mortality remains relevant for older age groups; in people aged 70 or over with breathlessness, both 2-year and 10-year survival are reduced.²⁰ Good control of symptoms at the end of life is consistently rated as important by patients, caregivers, and health care providers.²¹ However, refractory breathlessness (breathlessness which persists despite optimal management of the underlying condition),²² is common and burdensome in many chronic cardio-respiratory conditions and cancer;^{12, 23} and is frequently neglected despite available effective interventions.^{24, 25} Breathlessness is likely to be particularly difficult for the elderly, where it adds burden to multiple chronic conditions with major

effects on mobility, activities of daily living, confidence, independence, care needs and the ability to remain in their own homes in those older people nearing the end of life.

Despite associations between age and breathlessness, it is unknown whether breathlessness is primarily a feature of disease or of ageing.

Aim and Objectives

Using data from a cohort of community dwelling older people, we examined monthly patterns of reported difficulty breathing or shortness of breath sufficient to restrict activities (defined as stay in bed at least half a day, or cut down on their usual activities) during the last year of life (herein as *restricting breathlessness*). We investigated associations with clinical characteristics including "condition leading to death", age and the dependent variable of restricting breathlessness reported longitudinally during the last year of life.

The study's objectives were to: describe the prevalence and temporal patterns of restricting breathlessness during the last year; describe the temporal patterns of restricting breathlessness in relation to conditions leading to death; and to identify the clinical and demographic characteristics associated with restricting breathlessness.

Hypothesis

Based on the literature, we hypothesized that several factors would be associated with restricting breathlessness during the last year of life, including the presence of co-morbid disease, cause of death, smoking status, age, sex, anxiety and depression.

As this was a cohort of elderly people living at home (at study enrolment), this would include people who were medically fit but may have intercurrent illness, and those with chronic

conditions causing breathlessness. We anticipated that during the last year of life, there would also be people who developed a condition which led to their death. Given the heterogeneity often observed in older persons, we also hypothesized that distinct trajectories of restricting breathlessness during the last year of life could be identified (no breathlessness; chronic [present at every month point]; intermittent; and crescendo breathlessness (started partway through the year and was continuously present until death).

METHODS

The study was approved by the human investigational committee at Yale University and participants provided verbal informed consent.

Design

This is a secondary analysis of data relating to the last year of life among decedents who had participated in a longitudinal cohort study of initially non-disabled, community-living persons 70 years of age or older when enrolled.²⁶

Study population

The study cohort (n = 754) was identified from a computerized list of 3157 members of a large health plan in the United States of America. Sequential screening and enrollment was conducted between March 1998 and October 1999. Data collection is ongoing. Eligible plan members, 75.2% of whom agreed to participate, were English-speaking and could bathe, walk, dress, and transfer from a chair to standing without assistance at baseline. Those who did not agree to participate were not significantly different in terms of age or sex. Members were excluded if they had: a diagnosis of a terminal illness with an expected prognosis of less than 12 months; plans to move out of the study area during the next 12 months; or significant cognitive impairment with no available proxy.

Sample for analysis

Of the 589 participants who had died between October 1998 and June 2013, 41 had withdrawn from the study, leaving 548 (93%) with data on breathlessness in the last year of

life. Of these, 50 (9.1%) died within the first year of follow up and therefore had less than one year of data.

Baseline data collection

Comprehensive home-based assessments were completed at baseline and at 18-month intervals by trained nurses who used standard instruments to perform all interviews and assessments. Data were collected on demographic characteristics and nine self-reported chronic conditions diagnosed by a physician (hypertension; myocardial infarction; congestive heart failure; stroke; diabetes; arthritis; hip fracture, chronic lung disease, cancer), cognition (Folstein Mini-Mental State Examination) and frailty.²⁷

Follow up data collection

Telephone interviews were conducted monthly. For participants with significant cognitive impairment, data were collected from a proxy. Proxy assessments are valid for many measures, including breathlessness. ^{28, 29} Data were used from the comprehensive assessment that pre-dated death by at least one year and from the monthly interviews during the last year of life. Data for this current secondary analysis were collected until June 2013.

Condition leading to death

Decedents were identified through local obituary reviews, from the next of kin or another suitable informant during a subsequent telephone interview, or both. The classification of conditions leading to death is described elsewhere.³⁰ The approach used by Lunney³¹ was modified by adding advanced dementia as a condition leading to death, and including chronic kidney disease and cirrhosis to the category of 'organ failure'. Frailty, as a condition leading to death, was defined by the phenotype described by Fried *et al*³² using data from the

comprehensive assessments. Where data from death certificates were obtained, diagnoses were the 'immediate' or 'underlying cause' of death.

Assessment of restricting breathlessness

This analysis relates to difficulty breathing that caused restriction in activity during the previous month. During the monthly interviews, participants were asked if they had stayed in bed at least half a day or cut down on their usual activities due to an illness, injury, or other problem in the preceding month. Those who said 'yes' to either question (i.e. had restricted activity) were asked about a series of problems including whether they had experienced "difficulty breathing or shortness of breath since we last talked" *and* whether or not that problem caused restricted activity. Restricting activity has face validity as an important concern for elderly people, recognised over 30 years ago in the US Surgeon General's Healthy People Report.³³⁻³⁵ It has been extensively used in the elderly care literature where it has been a key outcome measure in several clinical trials of interventions.³⁵⁻³⁹

Statistical analysis

Using date of death as the anchor, descriptive statistics presented the number and percentage of participants reporting breathlessness at each month before death. We calculated the total number of months participants reported restricting breathlessness during the last year of life and evaluated its relationship with the condition leading to death, plotting this relationship as a percentage of the total possible number of months. If participants died during the first year of follow-up, the denominator was the number of months with available data.

We used percentage of months with restricting breathlessness during the last year as the outcome variable rather than a binary outcome (presence/absence) to provide a quantitative measure of restricting breathlessness. We investigated the relationships between percentage

months of restricting breathlessness and possible associated variables recorded before the final year (the most recent comprehensive assessment prior to the last year of life), using two sample t tests or linear regression. From the monthly follow-up data during the last year of life we calculated the percentage of months for which possible associated variables, and proxy measures were recorded and tested their associations with months of restricting breathlessness using multiple regression. Candidate variables were drawn from the literature and can be seen in table 2.

We used multiple regression to investigate demographic and associated clinical factors, which had an effect identified in the unifactorial analysis and others with a plausible biological rationale or have been previously reported in the literature.⁴⁰ These were included in a multiple regression analysis using stepwise analysis with backwards elimination. At each stage, the variable with the largest non-significant *P* value was removed and the step repeated until there were no non-significant associated factors.

To assess the effect of using a mixture of participant and proxy measures, the stepwise regression model included the proportion of proxy measures as an associated factor.

The appropriateness of the regression model was tested by examining residuals. Histograms and scatter plots were inspected for non-Normal distribution and non-linearity. Analyses were carried out by MB and MJ using Stata 12 (StataCorp, 2011, College Station, Texas).

RESULTS

Of the 548 decedents in the analytic sample, 61.2% were women. Ethnicity was coded as "white" (91.2%) or "other" (8.8%). The mean age at death was 86.7 years (SD 6.0; range 71 to 106; median age 87; IQR 83 to 91). Most were ex-smokers (59%) or current smokers (6%). This sample was representative of the main New Haven elderly cohort (64.6% women; 90.5% "white"), but has more "white" people and, as expected in an older group, more women than in the general population in that region (79.3% "white"; 51.7% female).⁴¹

Restricting breathlessness by condition leading to death

The proportion of participants reporting restricting breathlessness at each month time-point during the last year of life (Figure 1) increases closer to death.

<< insert Fig.1 about here>>

Temporal patterns of restricting breathlessness

Overall, 311/548 (56.8%) participants were reported to have restricting breathlessness at some point during the last year of life. Table 1 shows the participants who reported restricting breathlessness in the month before death and who reported this symptom in *consecutive* months prior to death, that is, those who presented with new breathlessness during the last year of life and continued with this symptom until death. No participant had restricting breathlessness reported at every month, and very few fitted the category "breathlessness that commenced partway through the year and continued", for example, only 4 participants developed breathlessness during the last year *and continued* with reported breathlessness until death.

<< insert Table 1 about here>>

Some of these participants may have had earlier restricting breathlessness episodes as well. Only about half (148/311) of those who reported restricting breathlessness at some time in the last year, were restricted by breathlessness one month before death. From the original hypotheses regarding temporal patterns of breathlessness during the last year, only "intermittent" and "crescendo" were observed.

When displayed as restricting breathlessness per month according to the condition leading to death, breathlessness was most commonly reported for those who died from organ failure. This can be seen graphically in Figure 2, which shows increasing prevalence as death nears.

<<insert Fig.2 about here>>

Selection of potential variables associated with restricting breathlessness during the last year of life: unifactorial analyses

Candidate factors with a plausible rationale and a statistically significant association with breathlessness in the last year of life on unifactorial analysis were: i) (when a problem was identified in the monthly report) mobility problems; depression; anxiety and, from death certificate data, the condition leading to death; and ii) from the most recent comprehensive assessment prior to the last year of life: age; frailty; gender; physicians' diagnoses; peak expiratory flow rate (PEFR); smoking status. The condition leading to death was a six-level factor (cancer, dementia, organ failure, frailty, sudden, other) and was tested together, rather than by individual t tests. Smoking was a three-level factor (current, ex-smoker, never) and was also treated as a composite. Educational level was included due to its plausible impact and reported association with breathlessness in previous work.⁴⁰. Other physician-diagnosed conditions such as arthritis, hip fracture, hypertension or diabetes mellitus had no rationale, nor unifactorial significance and were excluded. Ethnicity was not significant on unifactorial analysis. (See Table 2)

<< insert Table 2 about here>>

Predictors of restricting breathlessness during the last year of life: multifactorial analysis

The final multifactorial model is shown in Table 3. Percentage months of restricting breathlessness was associated with percentage months of anxiety, depression, and mobility problems reported during the last year of life, and a history of chronic lung disease, congestive heart failure, being an ex-smoker from the most recent comprehensive assessment, and having cancer, organ failure or other categories as the condition leading to death rather than frailty, dementia or sudden death. Percentage months of restricting breathlessness decreased with higher educational attainment and age at death.

For associated factors identified from the comprehensive assessment recorded as present or absent e.g. chronic lung disease, the coefficient represents the change in percentage of months with breathlessness if the diagnosis is present. For associated factors recorded as percentage of months where the factor is reported during the last year of life, the coefficient represents the change in percentage months with breathlessness for each percentage point of months with this report. Thus an increase of one percentage point in months of anxiety is related to an increase of 0.25 in percentage months of breathlessness. Age is in years, so an increase of one year is related to a 0.23 reduction in percentage months with breathlessness. Testing of the regression model confirmed acceptable analyses.

<<insert Table 3 about here>>

Proxy measures for restricting breathlessness were obtained for 418 participants, including 177 with partial proxy data and 241 with complete proxy data. In the last year of life, the proportion of proxy measures increased slowly for the first nine months from (37% to 45%), and more rapidly over the last three months of life (49%; 57%; 70%). To assess the effect of

using a mixture of participant and proxy measures, stepwise regression included the proportion of proxy measures as an associated factor. It did not contribute to the final model. We also regressed the percentage of months with breathlessness on proportion of proxies but the relationship was not significant (P=0.40). It was felt that, in such a regression analysis, this approach was an appropriate and sufficiently robust method to assess the influence of proxy measurement and demonstrated that the analysis was not materially affected by proxy measures.

DISCUSSION

These data show that during the last year of life, over 50% of community-living elderly people experienced breathlessness severe enough to restrict activity. Only half of those who reported breathlessness at some point during their last year had breathlessness during their last month. Few people (10%) had restricting breathlessness until a few months before their death. This prevalence may be considered lower than expected given previous community studies of older people (e.g. 32.3 to 37%)^{4, 6}, but these studies used an outcome of MRC \geq 3 ("On level ground, I walk slower than people of the same age because of breathlessness, or have to stop for breath when walking at my own pace") which is likely to represent a much less severe level of breathlessness than that measured in this study.

The prevalence of breathlessness increased in the last few months prior to death for all conditions leading to death, including dementia and sudden death. Sudden death due to cardiac arrhythmia is associated with heart failure and an increase in breathlessness could reflect worsening of the heart condition. The finding that breathlessness increased prior to death in people dying with dementia is consistent with a retrospective study of nursing home residents with advanced dementia which found the presence of breathlessness to be a poor prognostic indicator.⁴² Even in the setting of dementia, the impact of increasing breathlessness speaks to the prevalence of this symptom irrespective of the underlying etiology, and the importance of breathlessness as a prognostic factor.

Although the prevalence of breathlessness is known to be higher in older people when compared with younger people, *within* this elderly population, age was *inversely* related to restricting breathlessness during their last year. Restricting breathlessness was also associated with a diagnosis of heart and lung disease, mobility problems, anxiety and depression, smoking status and with cancer as a condition leading to death. It may be that those living to older old age have lived to such an age because they do not have the medical conditions associated with restricting breathlessness.

The strong association between anxiety documented during monthly interviews and restricting breathlessness during the last year is consistent with other literature which describes anxiety as both a driver and a consequence of breathlessness,⁴³ although causality cannot be inferred from these data. The similarly strong association seen for depression noted at monthly interviews and restricting breathlessness during the last year, was not found for depression reported at the last comprehensive assessment prior to death. This may indicate that breathlessness *contributes to* depression in this population. Depression is prevalent in people with chronic conditions and cancer, adversely impacting on quality of life, adherence with management and days at home.⁴⁴ These new data confirm the importance of diagnosis and management of this potentially reversible co-morbidity.

Although there are reports that women report more dyspnea for the same workload than men,^{40, 45, 1, 8} we did not find an excess of reported breathlessness in women. Mobility problems were associated with breathlessness; it is interesting to note that there is trial evidence to support the use of mobility *aids* to improve breathlessness.⁴⁶

Implications for clinical practice and future research

The increased prevalence of restricting breathlessness in the months prior to death in each of the etiological sub-groups suggests that breathlessness is part of a final common pathway at the end of life. The presence, therefore, of this symptom should be systematically identified, assessed and managed in order to ensure optimal symptom management at the end of life, and optimal care planning in the light of its association with poor prognosis. However, although a trajectory pattern of escalating breathlessness was seen in some individuals, it was not

inevitable that a participant reporting restricting breathlessness would continue with this symptom until death.

Strengths and Limitations

Strengths of the present study include its prospective, repeated-measures design with standardized and comprehensive assessments including monthly reports with high rates of participation and follow up. Prospective assessment of self-reported symptoms, rather than a reliance on administrative or registry based data, is vital as older persons may not seek medical attention despite severe and prolonged symptomatology.⁴⁹ With the exception of ethnicity, the cohort demographics reflect the US general population well.²⁶ The study cohort oversampled people at enrollment with an intermediate and high risk for disability, but rates of disability or symptoms were not affected.⁵⁰

"Restricting breathlessness" is not a familiar outcome in the palliative care or respiratory literature, in which measures of intensity, mastery or exercise tolerance are more often used such as the MRC dyspnea scale. ⁴⁷ Like the MRC scale, it is a subjective measure and relative to what the participant counts as usual daily activities. These results indicate that restricted activity is a practical way to quantify the impact on people who experience restricting breathlessness. Functional status is known to be a useful prognostic indicator,⁴⁸ and further work is indicated to explore further whether breathlessness sufficient to affect function is also a useful marker of deterioration.

The dataset has proved immensely valuable in increasing understanding of the experience of the elderly over time, and the effect of many health issues on their independence and ability to conduct activities of daily living. Furthermore, we specifically wished to investigate

breathlessness which was bad enough to potentially affect independent living, and thus this definition of restricting breathlessness was fit for our purpose.

We cannot comment on the number of days with restricted activity or the symptom severity, except that all reports relate to breathlessness sufficient to restrict activities, therefore all reports are of direct relevance to the respondents.

CONCLUSION

This analysis of data from a longstanding longitudinal study adds to the understanding of clinically relevant breathlessness in the elderly in the last year of life. Restricting breathlessness increased in this elderly population in the months preceding death from any cause. The data suggest that ageing *per se* may not cause breathlessness in the absence of other pathology. Data may indicate that depression was a response to restricting breathlessness. These data suggest that breathlessness may be part of a final common pathway very late in life. This symptom should therefore be systematically assessed and managed in the likely context of poor prognosis.

ACKNOWLEDGMENTS:

The work for this article was funded by a grant from the National Institute on Ageing (NIA)(R37AG17560). TG is the recipient of an Academic Leadership Award (K07AG043587) from the National Institute on Aging. The PEP study was conducted at the Yale Claude D. Pepper Older Americans Independence Center (P30AG21342).

Author Contributions:

DC and MJ had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: DC, MJ, ME

Acquisition of data and funding: TG.

Analysis and interpretation of data: MB, MJ

Statistical expertise: MB

Drafting of the manuscript: MJ

Critical revision of the manuscript for important intellectual content: all authors

Sponsor's Role:

The sponsors did not have any role in the design, conduct, interpretation, review, approval, or control of this article.

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 Table 1. The Month of First Restricting Breathlessness which continued until the Month of Death.

	frequency	percentage
Not breathless in last month	400	73.0
Breathless reported in the last month	148	27.0
Breathless for 4 months before death		4 0.7
Breathless for 3 months before death		12 2.2
Breathless for 2 months before death		29 5.3
Breathless for month in which death	10)3 18.9
occurred but not previous month		
Tota	al 548	100.0

Candidate predictor	coefficient	95% confidence	Unifactorial analysis (P		
variables, and source		intervals	value)		
FACTORS FROM MOST REC	FACTORS FROM MOST RECENT COMPREHENSIVE ASSESSMENT PRIOR TO LAST YEAR OF L				
Age	-0.32	-0.53 to -0.12	0.002		
			NB – inverse relationship		
Frailty*	-0.56	-3.13 to 2.02	0.7		
Mobility **	0.080	0.042 to 0.118	< 0.001		
Gender(female)	0.79	-1.70 to 3.78	0.5		
Proxy measures	1.18	-1.64 to 4.00	0.41		
Peak expiratory flow rate	-0.04	-0.08 to 0.01	0.1		
Smoking status	4.40	1.90 to 6.91	0.001		
Congestive Heart failure	3.68	0.39 to 6.97	0.03		
Chronic Lung disease	8.73	6.00 to 11.45	< 0.001		
Heart attack	2.24	-0.56 to 5.04	0.1		
Cancer	1.67	-1.12 to 4.46	0.2		
Stroke	3.62	0.30 to 6.95	0.03		
Arthritis	1.43	-0.99 to 3.85	0.2		
Hip fracture	0.38	-3.52 to 4.27	0.9		
Hypertension	-0.69	-3.20 to 1.81	0.6		
Diabetes mellitus	0.25	-2.60 to 3.10	0.9		
Condition leading to					
death:					

Table 2. Unifactorial analysis of candidate predictors

death:

cancer	1.17	-3.11 to 5.45	< 0.001	
dementia	-5.35	-9.66 to -1.04		
organ failure	5.46	1.31 to 9.60		
sudden death	-7.18	-15.20 to 0.84		
frailty	-2.30	-6.25 to 1.66		
Educational level	-0.05	-0.47 to 0.36	0.8	
"White" Ethnicity	-0.24	-0.50 to 0.02	0.07	
Depression (Center for	1.35	-1.42 to 4.13	0.3	
Epidemiologic Studies-				
Depression Scale) yes/no				
FACTORS FROM MONTHLY INTERVIEWS DURING THE LAST YEAR OF LIFE				
Self report anxiety,	0.44	0.38 to 0.50	< 0.001	
present or absent				
Self report depression,	0.49	0.33 to 0.46	< 0.001	
present or absent				
Problems with mobility	0.08	0.04 to 0.12	< 0.001	

*Frailty = >3 of: Slow gait, weight loss, exhaustion, inactivity and reduced grip strength **Mobility problems= the need for personal assistance or unable to walk one quarter of a mile or unable to climb one flight of stairs

Table 3. Final Regression Model investigating Factors Associated with the Presence ofPercentage Months of Reported Breathlessness during the Last Year of Life

	Coefficient	Standard	t	<i>P</i> > t	[95% Confidence
		Error			Interval]
PREDICTIVE FACTORS FROM MO	ONTHLY INTER	VIEWS DURING TH	HE LAS	ST YEAR OF	LIFE
Depression*	0.14	0.05	3.0	0.003	0.05 to 0.24
(Self report, present or absent)			2		
Mobility problems*	0.07	0.02	3.8	< 0.001	0.03 to 0.11
(Self report, present or absent)			5		
Anxiety*	0.25	0.05	5.2	< 0.001	0.16 to 0.34
(Self report, present or absent)			4		
PREDICTIVE FACTORS FROM MC) OST RECENT CO	OMPREHENSIVE AS	SSESSI	MENT PRIO	R TO LAST YEAR OF LIFE
Educational attainment	-0.47	0.17	-2.	0.006	-0.80 to -0.13
			76		
Chronic lung disease	6.62	1.18	5.6	< 0.001	4.31 to 8.94
			2		
Congestive heart failure	3.34	1.34	2.5	0.013	0.71 to 5.97
			0		
Condition leading to death					
Cancer	3.25	1.53	2.1	0.034	0.24 to 6.25
			2		
Other condition	3.64	1.71	2.1	0.034	0.27 to 7.00
			2		

Dementia	-0.81	1.49	— 0.	0.586	-3.75 to 2.12
			54		
Organ failure	4.19	1.41	2.9	0.003	1.41 to 6.96
			7		
Sudden death	0.32	3.26	0.1	0.923	-6.08 to 6.
			0		
Age one year prior to death	-0.19	0.09	-2.	0.030	-0.37 to -0.02
			17		
Smoking status					
Ex-smoker	3.01	1.05	2.8	0.004	0.94 to 5.07
			6		
Never smokers	1.28	2.17	0.5	0.554	-2.97 to 5.54
			9		
constant	16.48	8.02	2.0		0.73 to 32.24
			6		

*percentage months reported during the last year of life

P =probability

For an explanation of the meaning of the co-efficient, see text

Figure 1. Percentage of participants reporting restricting breathlessness at each month during the last year of life

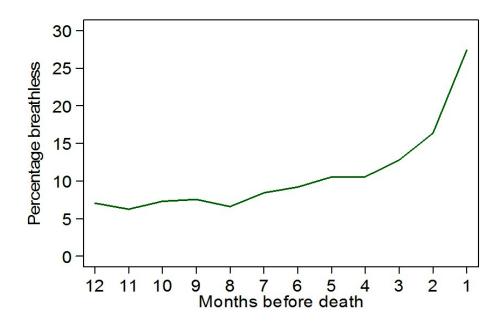


Figure 2. The percentage of participants reporting restricting breathlessness at each month during the last year of life by condition leading to death

