Does current smoking predict future frailty? the English Longitudinal Study of Ageing

Gotaro Kojima, MD[1]; Steve Iliffe, FRCGP[1]; Stephen Jivraj, PhD[2];
Ann Liljas, MPH[1]; Kate Walters, PhD[1].

[1] Department of Primary Care and Population Health, University College London, London, UK
[2] Department of Epidemiology and Public Health, University College London, London, UK

Corresponding Author:
Gotaro Kojima, MD
Department of Primary Care and Population Health
University College London (Royal Free Campus)
Rowland Hill Street,
London, NW3 2PF, UK
Phone: +44 (0)20 7794 0500
Fax: +44 (0)20 7472 6871
Email: gotarokojima@yahoo.co.jp

ABSTRACT

Background:

Smoking is the single most preventable cause of morbidity and mortality. The evidence on independent associations between smoking in later life and incident frailty is scarce.

Objectives:

To examine the effect of current smoking in older people on the risk of developing frailty, controlling for important confounders.

Methods:

We used data of 2,542 community-dwelling older people aged ≥60 years in England. Participants were classified as current smokers or non-smokers. Frailty was defined using modified Fried criteria. Multivariable logistic regression models were used to examine risk of four-year incident frailty in current smokers compared with non-smokers, adjusted for demographic, socioeconomic and health variables.

Results:

Of 2,542 participants, 261 and 2,281 were current smokers and non-smokers, respectively. The current smokers were significantly frailer, younger, with lower BMI, less educated, less wealthy and lonelier compared with non-smokers at baseline. In multivariable logistic regression models adjusting for age and gender, current smokers were twice as likely to develop frailty compared with non-smokers (OR=2.07, 95%CI=1.39-3.39, p=0.001). The association is attenuated largely by controlling for socioeconomic status. Smoking remains significantly associated with incident frailty in fully adjusted models including age, gender, socioeconomic status, alcohol use, education, wealth, cognitive function and loneliness (OR=1.60, 95%CI=1.02-2.51, p=0.04). The relationship is however attenuated when taking account of non-response bias through multiple imputation.

Conclusions:

Current smokers compared with non-smokers were significantly more likely to develop frailty over four years among community-dwelling older people. Given that smoking is a modifiable lifestyle factor, smoking cessation may potentially prevent or delay developing frailty, even in old age.

INTRODUCTION

When national surveys on smoking started in the UK in 1974, 41% of women and 51% of men were smokers.[1] The overall prevalence of smoking has been declining since then, down to 17% for women and 20% for men in 2014.[1] Tobacco smoking is the single most preventable cause of morbidity and mortality in the UK.[2] The National Health Service (NHS) spent £5.2 billion (approximately $7.5 billion) in treating smoking-related health conditions in 2005/06.[3]

Smoking also increases the risk of developing a number of other diseases, such as chronic obstructive pulmonary disease (COPD), coronary heart disease, stroke and peripheral vascular disease,[4] all of which can potentially have negative effects on the physical, psychological and social health of smokers. Disability itself limits autonomy, increases the risk of dependence, reduces quality of life and contributes to mortality.[5]

Frailty is considered a precursor to, but a distinct state from, disability.[6] Frailty has been described as a condition associated with decreased physiological reserve and increased vulnerability to adverse health outcomes with exposure to a stressor.[7] The outcomes include falls,[8] fractures,[9] disability,[10] hospitalisation[11] and institutionalisation.[12] Frailty has also been shown to be linked to worse psychological or cognitive outcomes, such as poor quality of life[13] and dementia.[14] Due to the potential for reversibility of frailty,[15] identifying potentially modifiable risk factors of frailty may help to develop strategies to prevent or slow progression of adverse health outcomes associated with both frailty and smoking. As maintaining independence is a key priority for older people, demonstrating links with smoking and frailty might provide additional motivation for older smokers to quit. A previous systematic review showed that only a few studies have examined longitudinal associations between smoking and risk of incident frailty.[16] Although most of these studies demonstrated that smokers were more likely to develop frailty, they provided effect measures that were unadjusted or adjusted for a limited number of confounders.[16] Therefore, the independent association of smoking with incident frailty has not been convincingly established. We thus aimed to examine the association of smoking with the risk of developing frailty, controlling for important confounding variables and using data from a nationally representative sample of community-dwelling older men and women living in England.

METHODS

Study Setting and Population

The English Longitudinal Study of Ageing (ELSA) is a multi-centre longitudinal panel study of a nationally representative sample of community-dwelling men and women aged 50 years and older in England and its detail has been published elsewhere.[17] The initial participants (n=11,391) at wave 1 in 2002 were recruited from households that participated in the Health Survey for England (HSE). The panel has been followed up with every two years. Ethical approval for all of the ELSA waves was obtained from the National Research and Ethics Committee and informed consent was obtained from all participants.

The current study used data of participants who were aged 60 years or older at wave 2 (baseline), since the gait speed was not measured for those aged less than 60 years, and who also participated at wave 4 (follow-up). Of 6,183 men and women aged 60 years or older who were interviewed at wave 2, those who missed any data regarding smoking status at wave 2 (n=3) and frailty components at waves 2 (n=1,688) were excluded. Those who were frail at wave 2 (n=575) were also excluded in order to examine the risk of incident frailty. Among 3,918 participants left, 1,376 could not participate at the follow-up wave due to ill health

(n=44), death (n=139), refusal (n=547), being unable to contact (n=132) or other reasons (n=514). The final analytic sample for this study was 2,542 participants.

Predictor Variable − Smoking

Participants were classified as 'current smoker' or 'non-smoker' based on answers to the question 'Do you smoke cigarettes at all nowadays?' during the interview at wave 2. To examine effects of smoking cessation on frailty, the non-smokers were divided, based on data of when they quit smoking available from wave 3 (2 years after wave 2), into two groups: past smokers and never smoker. The past smokers were further divided into another two groups: those who quit within the last 10 years and those who quit more than 10 years ago.[18]

Outcome Variable − Incident frailty

Frailty was defined using the frailty phenotype criteria that Fried et al. described in the Cardiovascular Health Study (CHS).[6] In CHS, frailty is defined using a combination of five physical frailty components: (1) unintentional weight loss, (2) self-reported exhaustion, (3) weakness, (4) slow walking speed and (5) low physical activity. Frailty is classified as having three or more of the five criteria. An individual who meets one or two criteria is classified as prefrail, and an individual with no criterion is classified as robust. Please see **Appendix 1** for detail of definitions of the CHS criteria components, covariates and statistical analysis.

RESULTS

Table 1 and **Appendix 2** present the baseline characteristics of the final analytic sample of 2,542 participants according to smoking status as well as 1,376 who were excluded at follow-up according to reasons for lost follow-up. Among the analytic sample at baseline, 2,281 participants were non-smokers (1,168 never smokers and 1,113past smokers) and 261 were current smokers. Current smokers were significantly frailer, younger, with lower BMI, less educated, less wealthy and lonelier compared with non-smokers. There were no significant differences in gender, alcohol use and cognitive function between these two groups.

In the univariate logistic regression models, various factors were significantly associated with a higher risk of incident frailty over four years. Current smoking was associated with an approximately 50% increased risk of developing frailty (OR=1.56, 95% confidence interval (CI)=1.06-2.29, p=0.02). Other factors associated with an increased risk of incident frailty were belonging to the older age group, being a female, having a higher BMI, consuming alcohol less frequently, having completed a lower level of education, having a lower level of wealth, having a lower cognitive function and having more loneliness. (**Table 2**)

Table 3 shows the results of the multivariable logistic regression models. In Model 1 adjusting for age and gender, current smokers were twice as likely to develop frailty at the time of follow-up compared with non-smokers (OR=2.07, 95%CI=1.34-3.19, p=0.001). Further adjusting for alcohol use did not change the odds ratio drastically (OR=2.17, 95%CI=1.39-3.39, p=0.001). Although adding education and wealth for adjustment in Model 3 decreased the odds ratio, current smoking remained a significant predictor of incident frailty (OR=1.62, 95%CI=1.05-2.52, p=0.03). In Model 4, cognitive function and loneliness were further adjusted for, which made little change in the association (OR=1.60, 95%CI=1.02-2.51, p=0.04). We repeated the final model (Model 4) with multiple imputation by chained equations, and this attenuated the association (OR=1.48, 95%CI=0.97-2.28, p=0.07).

When COPD was added to the Model 4, current smoking was no longer a significant predictor of incident frailty and the OR decreased by 14.4% (OR=1.37, p=0.19). In this model, COPD was strongly associated with incident frailty (OR=2.58, 95%CI=1.59-4.20, p<0.001). These findings suggest that current smokers are more likely to develop frailty due to COPD, rather than smoking itself. Adding CVD or cancers to Model 4 made little changes in the results, which suggest that CVD and cancers are not a modulator in the associations between current smoking and development of frailty.

In supplementary analyses, incident frailty risk for current and past smokers compared with never smokers was calculated. Compared with never smokers, current smokers were significantly more likely to develop frailty in Models 1 and 2, which became non-significant in Models 3 and 4. There was no significant association between past smoking and incident frailty in any models. (**Appendix 3**) Among 1,113 past smokers, 157 quit smoking within the last 10 years and 956 quit smoking for more than 10 years ago. Incident frailty risks of these two groups were not significantly different to that of non-smokers in all models. (**Appendix 4**)

DISCUSSION

This prospective panel study of 2,542 British community-dwelling men and women aged 60 years or older who were free of frailty at baseline showed that current older smokers were 60% more likely to develop frailty than non-smokers over four years, controlling for a wide range of potential confounders including age, gender, alcohol use, education, wealth, cognitive function and loneliness.

Our findings are consistent with the limited previous longitudinal research, which has shown in the majority of studies that smoking worsened subsequent frailty status,[19-23] except for one study.[15]

Mechanisms by which current smokers are more likely to develop frailty are unknown, but may be multifactorial given that tobacco smoke is a mixture of numerous kinds of toxic chemicals and compounds and can affect every organ in the body. Smoking has been shown to be associated with various physical and mental illnesses,[4] any of which can contribute to the development of frailty. These health risks can be reduced substantially by smoking cessation, according mostly to findings from studies among middle aged adults.[24] Although scarce, the evidence supports that one is never too old to quit smoking and older smokers can still benefit from quitting.[25] One study showed that the risks of myocardial infarction and stroke were reduced by 40% within five years of smoking cessation in German older people aged 50 and over.[26] Smoking cessation can potentially be an effective strategy to prevent or delay developing frailty among older smokers. This possible benefit of smoking cessation is supported by our findings that past smokers did not have higher risk of incident frailty than never smokers. Evidence suggests that older people may be less motivated by preventing disease such as heart attacks than younger people.[27] However it is their priority to remain independent, able to look after themselves and engaged socially.[28] Therefore knowledge that continued smoking in later life may increase the risk of frailty, which itself is strongly associated with increased dependency and increased risk of moving into care home settings, may provide additional motivation to encourage older smokers to quit.

In the multivariable logistic regression models, the odds ratio of developing frailty in current smokers compared with non-smokers decreased from 2.17 to 1.62 (-25.3%) when further adjusted for education and wealth, which suggests that the association between smoking and

incident frailty can partially be explained by socioeconomic status. Lower socioeconomic status has been shown to be associated with a higher prevalence of smoking[3] and a higher level and faster progression of frailty.[29] Socioeconomically disadvantaged smokers typically are found to have developed their smoking habit earlier in their lives, and are likely to be more nicotine dependent, to have less social support for smoking cessation and to be less likely to succeed in smoking cessation attempts.[30] In order to reduce the smoking-related health inequalities, smoking cessation measures should be effective on these hard-core smokers with low socioeconomic status.[30] In our supplementary analysis using multiple imputation of covariates the relationship of smoking with frailty was attenuated further and becomes non-significant.

COPD, CVD and cancers were separately added to the final multivariable logistic regression model to see if these smoking-related diseases fully explained the association between current smoking and incident frailty, or if there appeared to be a further independent effect of smoking on frailty. Only COPD changed the results significantly and current smoking no longer predicted incident frailty in that model, which suggests that the association appears to be explained by COPD. Finally our supplementary analysis suggests that the harmful effects of smoking on frailty are largely restricted to those who were currently smoking at baseline, as with even those who had more recently quit (within the last 10 years), showed no increased risk of frailty compared to never-smokers.

There are some limitations and strengths of this study. First, due to the limited availability of data at the baseline wave, only current smokers and non-smokers were defined. We had to retrieve data from a later wave to create past and never smoker groups. We had no information on the extent of smoking exposure (quantity of cigarettes consumed or length of exposure) and we were therefore unable to explore a 'dose-response' relationship. It should be noted that the information on smoking status was self-reported and potentially subject to response bias. Second, our sample was restricted to those who had completed measurements of frailty status (e.g. gait speed, handgrip strength) in nurse interviews at two time points in ELSA. Those who were excluded due to missing data at follow-up were significantly frailer and more likely to be current smokers compared with those who were included, which suggests that those excluded were missing data that were not random. Therefore, this exclusion is likely to attenuate an association between smoking status and incident frailty. Whilst we attempted to account for attrition bias by using non-response weights, this differential loss to follow-up may have underestimated the associations between frailty and smoking. Third, the ELSA cohort only includes the English population and may not be generalisable to other populations. Fourth, as in other studies, components of CHS criteria were slightly modified according to availability of ELSA data, which may have affected the findings.[31] Fifth, we used to only two time points four years apart to assess incident frailty risk according to smoking. Given that COPD may be an important mediator in the association between smoking and frailty, over many years, a study with a longer follow-up period and multiple data collection time points would be justified.

The major strengths of this analysis are a large sample size, a prospective study design and the use of a wide range of potential confounders for adjustment.

In conclusion, current smokers compared with non-smokers were significantly more likely to develop frailty over four years among British community-dwelling older people. This result is in line with findings of a recent systematic review.[16] Given that smoking is a modifiable

lifestyle factor, smoking cessation may potentially prevent or delay developing frailty, even in old age.

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Table 1. Summary of the baseline characteristics of analytic sample (N=2,542)

Variable*	Entire sample	Non-smoker			Current smoker
	N=2,542	Total non-smoker n=2,281	Never smoker n=1,168 (51.2%)	Past smoker n=1,113 (48.8%)	n=261
Frailty status					
Robust	1,430 (56.3%)	1,319 (57.8%)	698 (59.8%)	621 (55.8%)	111 (42.5%)
Prefrail	1,112 (43.7%)	962 (42.2%)	470 (40.2%)	492 (44.2%)	150 (57.5%)
Age group					
60-64	611 (24.0%)	526 (23.1%)	276 (23.6%)	250 (22.5%)	85 (32.6%)
65-65	825 (32.5%)	739 (32.4%)	409 (35.0%)	330 (29.6%)	86 (33.0%)
70-74	542 (21.3%)	498 (21.8%)	257 (22.0%)	241 (21.7%)	44 (16.9%)
75-79	354 (13.9%)	320 (14.0%)	140 (12.0%)	180 (16.2%)	34 (13.0%)
80+	210 (8.3%)	198 (8.7%)	86 (7.4%)	112 (10.1%)	12 (46%)
Gender					
Male	1,150 (45.2%)	1,032 (45.2%)	421 (36.0%)	611 (54.9%)	118 (45.2%)
Female	1,392 (54.8%)	1,249 (54.8%)	747 (64.0%)	502 (45.1%)	143 (54.8%)
BMI	27.6 ± 4.4	27.7 ± 4.4	27.5 ± 4.5	28.0 ± 4.4	26.8 ± 4.3
<=25	706 (27.8%)	613 (26.9%)	353 (30.2%)	260 (23.4%)	93 (35.6%)
25<, <=30	1180 (46.4%)	1071 (47.0%)	541 (46.3%)	530 (47.6%)	109 (41.8%)
>30	656 (25.8%)	597 (26.2%)	274 (23.5%)	323 (29.0%)	59 (22.6%)
Alcohol					
None	223 (9.4%)	192 (9.0%)	123 (11.1%)	69 (6.7%)	31 (13.0%)
1/year - 2/month	690 (29.0%)	617 (28.8%)	363 (32.6%)	254 (24.7%)	73 (30.5%)
1/month - 4/week	877 (36.8%)	794 (37.1%)	409 (36.7%)	385 (37.4%)	83 (36.8%)
5/week or more	592 (24.9%)	541 (25.2%)	218 (19.6%)	322 (31.3%)	52 (21.8%)
Education					
Higher education	322 (12.7%)	306 (13.4%)	164 (14.0%)	142 (12.8%)	16 (6.1%)
Intermediate	1,314 (51.7%)	1,201 (52.7%)	610 (52.2%)	591 (53.1%)	113 (43.3%)
No qualification	906 (35.6%)	774 (33.9%)	394 (33.7%)	380 (34.1%)	132 (50.6%)
Wealth quintile					
Richest	661 (26.3%)	619 (27.5%)	327 (28.3%)	292 (26.6%)	42 (16.3%)
2nd	569 (22.7%)	528 (23.4%)	258 (22.3%)	270 (24.6%)	41 (16.0%)
3rd	523 (20.8%)	474 (21.0%)	261 (22.6%)	213 (19.4%)	49 (19.1%)
4th	446 (17.7%)	393 (17.4%)	187 (16.2%)	206 (18.7%)	53 (20.6%)
Poorest	312 (12.4%)	240 (10.7%)	122 (10.6%)	118 (10.7%)	72 (28.0%)
Cognitive function score	48.9 ± 10.4	49.2 ± 10.3	49.5 ± 10.2	48.8 ± 10.4	46.9 ± 10.8
Loneliness score	3.9 ± 1.4	3.9 ± 1.3	3.9 ± 1.3	3.9 ± 1.3	4.3 ± 1.6
COPD	153 (6.0%)	113 (5.0%)	53 (4.5%)	60 (5.4%)	40 (15.3%)

* Mean + standard deviation or n (%), COPD: chronic obstructive pulmonary disease

Table 2. Risk factors of incident frailty by univariate logistic regression models (N=2,542).
* ref: reference group

Variable	Odds ratio (95%CI)	p value
Smoking Status		
Never/past	ref*	
Current	1.56 (1.06-2.29)	0.02
Age group		
60-64	ref*	
65-69	1.07 (0.63-1.83)	0.80
70-74	2.70 (1.64-4.44)	<0.001
75-79	5.16 (3.13-8.51)	<0.001
80+	11.88 (7.09-19.92)	<0.001
Gender		
Male	ref*	
Female	1.69 (1.28-2.23)	<0.001
BMI	1.08 (1.04-1.11)	<0.001
<=25	ref	
25<, <=30	0.90 (0.63-1.27)	0.53
>30	1.64 (1.16-2.34)	<0.01
Alcohol		
None	ref*	
1/year - 2/month	0.57 (0.37-0.88)	0.01
1/month - 4/week	0.46 (0.30-0.70)	<0.001
5/week or more	0.31 (0.19-0.51)	<0.001
Education		
Higher education	ref*	
Intermediate	1.48 (0.88-2.51)	0.14
No qualification	3.73 (2.23-6.25)	<0.001
Wealth quintile		
Richest	ref*	
2nd	1.92 (1.20-3.07)	<0.01
3rd	1.96 (1.23-3.14)	<0.01
4th	2.65 (1.68-4.18)	<0.001
Poorest	5.96 (3.81-9.34)	<0.001
Cognitive function score	0.94 (0.92-0.95)	<0.001
Loneliness score	1.27 (1.17-1.38)	<0.001

Table 3. Incident frailty risk of current smoking by multivariable logistic regression models (N=2,542).

	Odds Ratio (95%CI)	p value
Model 1	2.07 (1.34-3.19)	0.001
Model 2	2.17 (1.39-3.39)	0.001
Model 3	1.62 (1.05-2.52)	0.03
Model 4	1.60 (1.02-2.51)	0.04

Model 1: Adjusted for age and gender
Model 2: Further adjusted for alcohol
Model 3: Further adjusted for education and wealth
Model 4: Further adjusted for cognitive function and loneliness

Appendix 1. Methods

Outcome Variable − Incident frailty

In the current study, the five phenotype components are slightly modified according to data availability. At baseline, weight loss was defined as loss of 5% or more of body weight since HSE in 1998, 1999 or 2001, or body mass index (BMI) of less than 18.5 kg/m^2. At follow-up, weight loss was defined as loss of 5% or more of body weight since baseline or BMI of less than 18.5 kg/m^2. Exhaustion was defined based on responses to two questions from the eight-item Center for Epidemiologic Studies Depression Scale (CES-D) on whether much of the time during the past week (1) they felt that everything they did was an effort and (2) they could not get going. Exhaustion was considered to be present if the participant answered YES to either or both of these questions. Handgrip strength was measured three times on each hand using a dynamometer and the highest measurement was used for this criterion. Weakness was defined as having the handgrip measurement in the lowest 20%, stratified by gender and BMI quartiles. Gait speed was calculated according to the average time taken to walk eight feet at a usual pace following two attempts. Slow walking speed was defined as having gait speed in the lowest 20%, stratified by gender and median height. Those who were in wheelchair, were bed-bound or were unable to walk without assistance were considered to have slow walking speed. Physical activity was ranked based on a combination of intensity (vigorous; moderate; mild exercise) and frequency (more than once a week; once a week; one to three times a month; hardly ever or never) of usual exercise involved. Low physical activity was defined as being in the lower two ranks out of the possible four.

Covariates

Baseline covariates that could potentially have a confounding effect on the associations between smoking and frailty available in ELSA, include age, gender, BMI, alcohol consumption, education, wealth, cognitive function, and loneliness. ELSA participants were asked if they were ever told by a doctor that they had or had had COPD, cardiovascular diseases (CVD) (angina, myocardial infarction, congestive heart failure or stroke) and cancers.

Participants were classified into five age groups based on their age at baseline:(1) 60-64 years old, (2) 65-69 years old, (3) 70-74 years old (4) 75-79 years old and (5) 80 years or older. BMI was calculated as weight in kilograms divided by the square of height in metres. Alcohol use was categorised into four groups based on frequency of alcohol consumption: (1) not at all, (2) once a year to twice a month, (3) once a week to four days a week and (4) five days a week or more. Education was classified into three groups: (1) higher education, (2) intermediate and (3) no qualification. The quintiles of the net total wealth, which was calculated as the sum of savings, investments, physical wealth and housing wealth deducting financial debt and mortgage debt, were used. Cognitive function was assessed using a composite score, summing up scores of four tests covering three domains of cognitive function: (1) executive function (animal naming task, distribution range: 0-57), (2) processing speed (letter cancellation task, distribution range: 0-64) and (3) memory (immediate and delayed recall tasks, distribution range: both 0-10, together 0-20), with a higher score suggestive of better cognitive function.[17] Loneliness was assessed using a three-item short form of the Revised UCLA Loneliness Scale, with the score ranging from three to nine.

Statistical Analyses

Baseline characteristics were compared according to smoking status (current smoker or non-smoker) using a t-test for continuous variables and a chi square test for categorical variables. Univariate logistic regression models were used to examine the risk of incident frailty for

baseline characteristics. Multivariable logistic regression models were used to examine the risk of incident frailty for being a current smoker compared with a non-smoker, adjusted for age, gender and other variables that were significantly associated with a risk of incident frailty in the univariate analyses. The longitudinal weighting was used for all analyses to reduce any bias caused by non-response. The longitudinal weights are created sequentially on top of the previous wave's weights for the core members who have participated in all the previous waves, in order to minimize bias from sample loss due to attrition and be representative of those living in England (i.e. 2002).[17]

We conducted several supplementary analyses. The fully adjusted model was repeated using multiple imputation by chained equations for missing value of the covariates used for adjustment. It is based on the assumption of missing at random where the probability of missing data does not depend on unobserved data but on observed data. We also repeated the main analysis in order to explore the degrees to which smoking-related diseases explained the association between current smoking and subsequent incident frailty. Three diseases: COPD, CVD and cancers, were chosen because smoking is known to increase the risk of these diseases and they can increase the risk of frailty. These diseases were separately added to the final model and changes in the odds ratios before and after the addition were compared. We conducted a further supplementary analysis to explore if the relationships change when non-smokers were reclassified as either ‘never smokers’ or ‘past smokers’ using data of when they quit smoking from another wave two years later (these data were not available for our main cohort at baseline). The past smokers were further divided into two groups: those who quit within 10 years and those who quit more than 10 years ago. The multivariable logistic regression models were repeated using these three and four smoking groups.

All statistical analyses were conducted using StataSE 14 (StataCorp LP, College Station, Texas, USA) based on 2-tailed significance. The level of significance was set at $p<0.05$.

Appendix 2. The full version of baseline characteristics of analytic sample (N=2,542) and those who lost follow-up (N=1,376)

Variable*	Entire cohort	Analytic sample	Non-smoker			Current smoker	Lost f/u			
	N=3,918	N=2,542	Total non-smoker n=2,281	Never smoker n=1,168 (51.2%)	Past smoker n=1,113 (48.8%)	n=261	Total lost f/u N=1,376	Died n=139 (10.1%)	Ill health n=44 (3.2%)	Other reasons n=1,193 (86.7%)
Frailty status										
Robust	2054 (52.4%)	1,430 (56.3%)	1,319 (57.8%)	698 (59.8%)	621 (55.8%)	111 (42.5%)	624 (45.4%)	40 (28.8%)	17 (38.6%)	567 (47.5%)
Prefrail	1864 (47.6%)	1,112 (43.7%)	962 (42.2%)	470 (40.2%)	492 (44.2%)	150 (57.5%)	752 (54.7%)	99 (71.2%)	27 (61.4%)	626 (52.5%)
Age group										
60-64	875 (22.3%)	611 (24.0%)	526 (23.1%)	276 (23.6%)	250 (22.5%)	85 (32.6%)	264 (19.2%)	15 (10.8%)	2 (4.5%)	247 (20.7%)
65-65	1202 (30.7%)	825 (32.5%)	739 (32.4%)	409 (35.0%)	330 (29.6%)	86 (33.0%)	377 (27.4%)	19 (13.7)	11 (25.0%)	347 (29.1%)
70-74	826 (21.1%)	542 (21.3%)	498 (21.8%)	257 (22.0%)	241 (21.7%)	44 (16.9%)	284 (20.6%)	37 (26.6%)	14 (31.8%)	233 (19.5%)
75-79	583 (14.9%)	354 (13.9%)	320 (14.0%)	140 (12.0%)	180 (16.2%)	34 (13.0%)	229 (16.6%)	30 (21.6%)	10 (22.7%)	189 (15.8%)
80+	432 (11.0%)	210 (8.3%)	198 (8.7%)	86 (7.4%)	112 (10.1%)	12 (46%)	222 (16.1%)	38 (27.3%)	7 (15.9%)	177 (14.8%)
Gender										
Male	1790 (45.7%)	1,150 (45.2%)	1,032 (45.2%)	421 (36.0%)	611 (54.9%)	118 (45.2%)	640 (46.5%)	75 (54.0%)	15 (34.1%)	550 (46.1%)
Female	2128 (54.3%)	1,392 (54.8%)	1,249 (54.8%)	747 (64.0%)	502 (45.1%)	143 (54.8%)	736 (53.5%)	64 (46.0%)	29 (65.9%)	643 (53.9%)
BMI	27.7 ± 4.5	27.6 ± 4.4	27.7 ± 4.4	27.5 ± 4.5	28.0 ± 4.4	26.8 ± 4.3	27.8 ± 4.5	26.9 ± 4.4	27.8 ± 5.3	27.9 ± 4.5
<=25	1099 (28.0%)	706 (27.8%)	613 (26.9%)	353 (30.2%)	260 (23.4%)	93 (35.6%)	393 (28.6%)	51 (36.7%)	16 (36.4%)	326 (27.3%)
25<, <=30	1761 (45.0%)	1180 (46.4%)	1071 (47.0%)	541 (46.3%)	530 (47.6%)	109 (41.8%)	581 (42.2%)	56 (40.3%)	13 (29.6%)	512 (42.9%)
>30	1058 (27.0%)	656 (25.8%)	597 (26.2%)	274 (23.5%)	323 (29.0%)	59 (22.6%)	402 (29.2%)	32 (23.0%)	15 (34.1%)	355 (29.8%)
Alcohol										
None	363 (9.3%)	223 (9.4%)	192 (9.0%)	123 (11.1%)	69 (6.7%)	31 (13.0%)	140 (10.2%)	22 (19.5%)	9 (23.7%)	109 (10.2%)
1/year - 2/month	1034 (26.4%)	690 (29.0%)	617 (28.8%)	363 (32.6%)	254 (24.7%)	73 (30.5%)	344 (25.0%)	27 (23.9%)	5 (13.2 %)	312 (29.2%)
1/month - 4/week	1322 (33.7%)	877 (36.8%)	794 (37.1%)	409 (36.7%)	385 (37.4%)	83 (36.8%)	445 (32.3%)	34 (30.1%)	14 (36.8%)	397 (37.1%)
5/week or more	884 (22.6%)	592 (24.9%)	541 (25.2%)	218 (19.6%)	322 (31.3%)	52 (21.8%)	292 (21.2%)	30 (26.5%)	10 (26.3%)	252 (23.6%)
Education										
Higher education	437 (11.2%)	322 (12.7%)	306 (13.4%)	164 (14.0%)	142 (12.8%)	16 (6.1%)	637 (46.3%)	70 (50.4%)	21 (47.7%)	546 (45.8%)
Intermediate	1937 (49.4%)	1,314 (51.7%)	1,201 (52.7%)	610 (52.2%)	591 (53.1%)	113 (43.3%)	623 (45.3%)	54 (38.8%)	18 (40.9%)	551 (46.2%)
No qualification	1543 (39.4%)	906 (35.6%)	774 (33.9%)	394 (33.7%)	380 (34.1%)	132 (50.6%)	115 (8.4%)	15 (10.8%)	5 (11.4%)	95 (8.0%)
Wealth quintile										
Richest	912 (23.3%)	661 (26.3%)	619 (27.5%)	327 (28.3%)	292 (26.6%)	42 (16.3%)	251 (18.2%)	26 (18.7%)	8 (19.0%)	217 (18.3%)
2nd	878 (22.4%)	569 (22.7%)	528 (23.4%)	258 (22.3%)	270 (24.6%)	41 (16.0%)	309 (22.5%)	26 (18.7%)	11 (26.2%)	272 (23.0%)
3rd	824 (21.0%)	523 (20.8%)	474 (21.0%)	261 (22.6%)	213 (19.4%)	49 (19.1%)	301 (21.9%)	31 (22.3%)	5 (11.9%)	265 (22.4%)
4th	706 (18.0%)	446 (17.7%)	393 (17.4%)	187 (16.2%)	206 (18.7%)	53 (20.6%)	260 (18.9%)	27 (19.4%)	6 (14.3%)	227 (19.2%)
Poorest	557 (14.2%)	312 (12.4%)	240 (10.7%)	122 (10.6%)	118 (10.7%)	72 (28.0%)	245 (17.8%)	29 (20.9%)	12 (28.6%)	204 (17.2%)
Cognitive function score	47.6 ± 11.0	48.9 ± 10.4	49.2 ± 10.3	49.5 ± 10.2	48.8 ± 10.4	46.9 ± 10.8	45.0 ± 11.8	41.8 ± 12.7	44.8 ± 11.5	45.4 ± 11.6
Loneliness score	4.0 ± 1.4	3.9 ± 1.4	3.9 ± 1.3	3.9 ± 1.3	3.9 ± 1.3	4.3 ± 1.6	4.0 ± 1.5	4.2 ± 1.6	3.8 ± 1.4	4.0 ± 1.5
COPD	270 (6.9%)	153 (6.0%)	113 (5.0%)	53 (4.5%)	60 (5.4%)	40 (15.3%)	117 (8.5%)	20 (14.4%)	9 (20.5%)	88 (7.4%)

* Mean + standard deviation or n (%), COPD: chronic obstructive pulmonary disease

Appendix 3. Incident frailty risk for current and past smokers by multivariable logistic regression models (N=2,542).*

	Current smoker n=261		Past smoker n=1,113	
	Odds Ratio (95%CI)	p value	Odds Ratio (95%CI)	p value
Model 1	1.93 (1.22-3.04)	0.005	0.86 (0.63-1.18)	0.35
Model 2	2.11 (1.32-3.37)	0.002	0.94 (0.67-1.31)	0.71
Model 3	1.56 (0.97-2.49)	0.06	0.92 (0.64-1.30)	0.62
Model 4	1.55 (0.96-2.50)	0.08	0.94 (0.65-1.35)	0.72

* Never smoker (n=1,168) as reference group
Model 1: Adjusted for age and gender
Model 2: Further adjusted for alcohol
Model 3: Further adjusted for education and wealth
Model 4: Further adjusted for cognitive function and loneliness

Appendix 4. Incident frailty risk for past smokers who quit within the last 10 years and who quit more than 10 years ago by multivariable logistic regression models (N=2,542).*

	Quit <= 10 years ago n=157		Quit > 10 years ago n=956	
	Odds Ratio (95%CI)	p value	Odds Ratio (95%CI)	p value
Model 1	0.88 (0.46-1.69)	0.70	0.86 (0.62-1.19)	0.36
Model 2	1.01 (0.51-2.00)	0.97	0.93 (0.65-1.32)	0.67
Model 3	0.85 (0.43-1.69)	0.64	0.93 (0.64-1.33)	0.68
Model 4	0.88 (0.43-1.79)	0.73	0.95 (0.65-1.38)	0.77

* Never smoker (n=1,168) as reference group
Model 1: Adjusted for age and gender
Model 2: Further adjusted for alcohol
Model 3: Further adjusted for education and wealth
Model 4: Further adjusted for cognitive function and loneliness