Associations between mental symptoms, incident somatic disease and smoking cessation – the HUNT Study

By Oda Wullum Williams and Monika Maria Mielnik

Acknowledgements

Abstract

Objective: To assess the association of demographic variables, socioeconomic status, mental symptoms, incident somatic disease and lifestyle and smoking cessation.

Methods: We used a longitudinal data set extracted from the second (1995-1997) and third wave (2006-2008) of the Nord-Trøndelag Health Study (HUNT2 and HUNT3, respectively), which includes data from questionnaires, interviews and clinical measurements. Our study sample consisted of those who smoked in HUNT2, and also participated in HUNT3 (9554 individuals). Associations between the different independent variables and smoking cessation were estimated using logistic regression. We assessed possible effect measure modification between mental symptoms and incident somatic disease.

Results: Men, older participants and those with higher education were more likely to quit smoking compared to women, younger and the lower educated. Participants with symptoms of depression had an odds ratio (OR) of 0.76 (95% confidence interval (CI): 0.60-0.96) for smoking cessation, compared with those without depression. Incident cardiovascular disease for those without mental illness was associated with smoking cessation (OR: 2.08. 95% CI: 1.77-2.45), as was incident pulmonary disease (OR: 1.57. 95% CI: 1.18-2.08). Also for those with symptoms of mental illness, incident cardiovascular disease had a strong association with smoking cessation. Pulmonary disease did not show the same strong association. Increased alcohol intake and a problematic drinking pattern was associated with reduced likelihood of smoking cessation.

Conclusions: Symptoms of either depression or comorbid depression and anxiety were associated with increased risk of smoking continuation. Although incident somatic disease increased likelihood of smoking cessation, smoking cessation after incident somatic disease was less common among participants with mental symptoms compared to those without mental symptoms. These results might indicate the need of targeted smoking cessation interventions in people with mental health problems..

Introduction

Smoking is a worldwide health problem causing several diseases, including lung cancer, chronic obstructive pulmonary disease and cardiovascular diseases (CVD) (1-5). Several political means have been made to reduce smoking prevalence. On the 1.st of June 2004 the Norwegian government passed a law, banning smoking in all workplaces and public areas, including hospitality venues (6). This law is a part of the Tobacco Act, originally implemented in 1988, banning smoking from public areas, but not from hospitality venues. The total ban of smoking in public areas was passed due to the hazards of passive smoking, to protect people with asthma and allergies, and also to prevent young people from associating smoking with positive socializing (6). After this public policy was introduced, we have seen a decrease in the number of daily cigarette smokers in Norway. In 2015 in Norway, 13% of the population defined themselves as daily smokers, which is 12 percentage points less than in 2005 (7). Prevalence of occasional smoking has been stable since 2008, at around 10% (7). The trend with fewer daily smokers applies for the entire country, although there are regional differences in smoking prevalence (8). However, different groups of smokers might have experienced different rates of smoking cessation during this period.

Smoking is equally common among men and women in Norway, however, it is associated with lower education and higher ages groups (7). Smoking is also associated with poor mental health. Individuals with depression report greater rates of smoking than those without depression (9), and current smokers more often present with symptoms of depression and/or anxiety compared to non-smokers (10) or previous smokers (11). Several studies also indicate a dose-response relationship between anxiety and depression symptoms, and the consumption of cigarettes (12). The causality between smoking and anxiety and depression is, however, not clear. The association can be confounded by other factors such as socioeconomic status (13, 14) and demographical factors such as sex, age and living (15).

Although poor mental health has been found to be unrelated to motivation to stop smoking, depressed individuals appear to have more difficulty quitting smoking compared to individuals without depression (16, 17). An American study showed that the decrease in smoking over a period of 7 years was less among people with mental illness than mentally healthy people (18). In addition, one found that people who were treated for anxiety or depression during the last year were more likely to stop smoking than untreated people (18).

Lifestyle habits and somatic health are also associated with smoking status. Alcohol consumption and smoking are strongly associated (19, 20). Studies have shown that people who drink alcohol smoke more often and have more difficulties quitting smoking (19, 20). Especially people with alcohol problems often have great nicotine dependence, which contributes to their high mortality (21). Furthermore, there is an inverse relationship between Body Mass Index (BMI) and smoking, this is to say smokers have a lower body mass index than non-smokers (22). On the other hand, obese smokers tend to smoke more and have more difficulties quitting than lean smokers (23), although research on smoking cessation in relation to body weight is scarce.

The greatest motivation for smoking cessation is concerns about health (24), and the onset of severe smoking-related disease increases motivation to quit smoking (25, 26). Although patients with cardiovascular disease report a greater quitting rate than patients without cardiovascular disease (27), as many as one out of five patients with coronary disease continue to smoke, despite given a personal advice to stop (28). Even though hypertension is one of the greatest risk factors for cardiovascular death (29), and hypertensive patients are motivated to quit, their smoking cessation rates are almost equal to the non-hypertensive patients (25). When experiencing smoking-related somatic disease, individuals with poor mental health might quit smoking to a lesser degree than mentally healthy people (30). Still few prospective studies have considered the combination of mental symptoms and incident somatic disease in relation to smoking cessation in the general population.

The aims of the current paper were to consider the associations between demographic variables, socioeconomic status, mental and somatic health and smoking cessation over ten years in the general population. Based on previous research we expected high age, poor mental health, high body mass index, low education, high alcohol intake and high smoking intensity to be associated with decreased smoking cessation, whereas we expected onset of somatic disease to be associated with increased smoking cessation. Furthermore, we expected decreased smoking cessation after incident somatic disease among smokers with high mental symptom load compared to those without mental symptoms.

Methods

Study sample

Our study sample was derived from participants in the second and third wave of the HUNT Study (an acronym for the Norwegian name: **H**else**u**nderseøkelsen I **N**ord-**T**røndelag). Data was obtained from this total population-based cohort study carried out in Norway, respectively in 1995-1997 and 2006-2008. All inhabitants of Nord-Trøndelag aged 20 years or older were invited to the study. A total of 65 229 participated in HUNT2 (82.6 % of those invited to HUNT2) and 50 804 participated in HUNT3 (64.3% of those invited to HUNT3). The HUNT Study includes data from questionnaires, interviews, clinical measurements and biological samples (blood and urine) (31).Our study sample (n=9 554) consisted of participants who reported to smoke daily in HUNT2, and who also participated in HUNT3, independent of their smoking status in HUNT3 (Fig.1). Participants who reported to be smoking only pipe or cigars were excluded from the study sample.
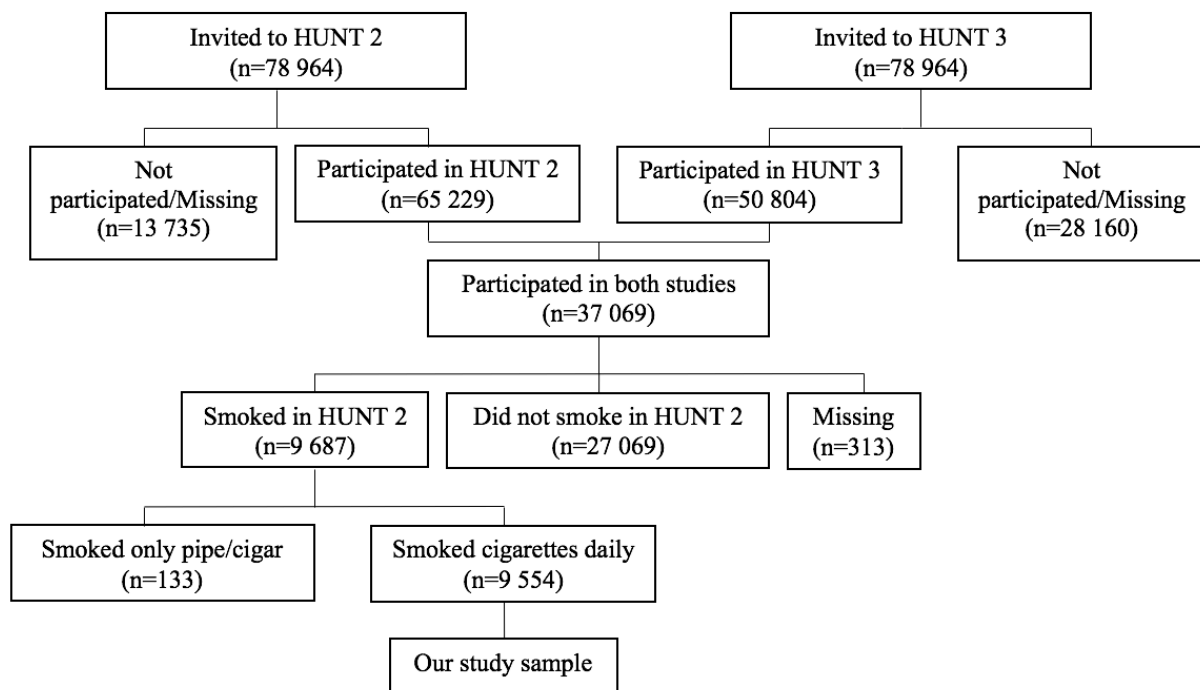

Fig. 1 Flowchart for the selection of the study population.

Outcome

Smoking cessation

In HUNT2, participants were asked about daily smoking of cigarettes, cigars/cigarillos or pipe. In HUNT3, participants were asked about daily smoking, occasional smoking and age at smoking cessation. Participants who reported to smoke in HUNT2 but not in HUNT3 were categorized as having quit smoking, whereas daily and occasional smokers were both considered current smokers.

Independent variables

Smoking cessation was studied in relation to different independent variables. The independent variables were based on variables reported in HUNT2. The following were used in our study.

Demography

We categorized age at baseline as 20-29, 30-49, 50- 69, >70. Educational level was in HUNT2 reported as five categories; Primary School, Vocational Education, Matriculation, College/University – less than 4 years, College/University – more than 4 years. In our study we merged Vocational Education and Matriculation into "High School", and College/University – less than 4 years and College/University – more than 4 years was named "College/University", giving the three levels "Primary school", "High School" and "College/University". We included marital status in the analyses as unmarried, married/registered partner, widow/widower and separated/divorced.

Symptoms of anxiety and depression

Mental health was assessed using Hospital Anxiety and Depression Scale (HADS) (32), a 14 item Likert scale. The grade of anxiety is assessed with the following questions:

- I feel tense or wound up
- I get a sort of frightened feeling as if something bad is about to happen
- Worrying thoughts go through my mind
- I can sit at ease and feel relaxed
- I get a sort of frightened feeling like butterflies in the stomach
- I feel restless and have to be on the move
- I get sudden feelings of panic

The grade of depression is assessed with the following questions:

- I still enjoy the things I used to enjoy
- I can laugh and see the funny side of things
- I feel cheerful
- I feel as if I am slowed down
- I have lost interest in my appearance
- I look forward with enjoyment to things
- I can enjoy a good book or radio or TV program

All questions are scored on a 4-point scale from 0-3. Answering all seven questions gives a possible maximum score of 21 points in each subscale (32, 33). We used a score of 8 or above for "caseness" anxiety or depression. This gives an optimal balance between sensitivity and specificity, which lies around 0.8 for both categories. To get a valid HADS score one needs to answer 5 or more questions in each category. If participants answered only 5 or 6 questions, the missing responses were replaced by the sum of the answered questions multiplied by 7/5 or 7/6, respectively (34).

Based on the HADS score we generated four levels of anxiety and depression symptoms, respectively (<5, 5-7.99, 8-10.99, ≥11). When considering the interaction between mental symptoms and incident somatic disease, we had to collapse the two upper categories to increase the number of events in each category. We also considered four mutually exclusive categories of mental symptoms; no symptoms, caseness anxiety, caseness depression and combined caseness anxiety and depression. Only participants with valid score on both anxiety and depression subscales could be classified according to the latter category.

Somatic health
Cardiovascular disease status
Information about cardiovascular status was obtained in HUNT2 and HUNT3 from three questions: "Have you ever had a heart attack?", "Do you have or have you ever had angina?" and "Have you ever had a stroke?" Based on these questions we made a variable with participants divided into three categories: (1) No cardiovascular events, (2) Incident cardiovascular events between the time of HUNT2 and HUNT3, (3) Prevalent cardiovascular disease at the time of HUNT2.

Pulmonary disease

Information about symptoms and diseases from the airways was obtained in HUNT2 from the questions: "Do you have or have you ever had asthma?", "Are you using or have you ever used asthma medication?", "Have you had episodes with shortness of breath or wheezing during the last 12 months?", "Do you cough daily?" and "Have you had cough with expectoration in at least 3 months coherent during the last 2 years?" In HUNT3 there was also a question about obstructive pulmonary disease: "Have you ever had chronic bronchitis, emphysema or chronic obstructive pulmonary disease?" Based on these questions we made a variable with participants divided into three categories: (1) No symptoms from the airways, (2) No symptoms from the airways in HUNT2, but chronic bronchitis, emphysema or chronic obstructive pulmonary disease in HUNT3, (3) Onset of symptoms from the airways before the time of HUNT2.

Blood pressure

Blood pressure was measured at the health examination site in HUNT2. Based on these measurements combined with self-reported information about use of antihypertensives, we generated three categories of hypertension; severe hypertension, moderate hypertension and normal blood pressure. Severe hypertension was defined as systolic blood pressure ≥ 160 and/or diastolic blood pressure ≥ 100 or participant using antihypertensive medication. Moderate hypertension was defined as a systolic blood pressure $140 \leq$ and <160 and/or diastolic blood pressure $90 \leq$ and <100, not medically treated. Normal blood pressure was defined as systolic blood pressure <140 and/or diastolic blood pressure <90 and no use of antihypertensive medication.

Lifestyle
Alcohol

The quantity of alcohol consumption was assessed in HUNT2 with the question: "How many beers, glasses of wine and spirits do you consume during a usual two-week period?" There was also a question to indicate whether the participants were non-drinkers.

Problem drinkers were identified using the CAGE questions, where CAGE is an acronym of the four questions (35, 36):

- Have you ever felt you needed to **C**ut down on your drinking?
- Have people **A**nnoyed you by criticizing your drinking?
- Have you ever felt **G**uilty about drinking?

- Have you ever felt you needed a drink first thing in the morning (**E**ye-opener) to steady your nerves or to get rid of a hangover?

Answering "yes" to two or more of these questions indicates a problematic drinking pattern. Based on this, the participants were put into six categories: (1) Abstainer/≤0.5 drinks per week, (2)>0.5 and ≤ 3, (3) >3 and ≤5, (4) >5 and ≤7, (5) >7, (6) Problem drinker.

Anthropometry

Participants were weighed and measured at the health examination site, wearing light clothes without shoes; height to the nearest 1.00 cm and weight to the nearest 0.5 kg. BMI was calculated as weight in kg divided by the squared value of height in meters. Because a BMI between 25 and 30 not necessarily is an unhealthy overweight due to bad lifestyle (37), we categorized BMI≥30 as overweight (BMI≥30), 18.5>BMI<30 as normal weight and BMI≤18.5 as underweight. Waist-hip ratio might be a better way to predict health status than BMI (37). We therefore also defined normal weight and overweight based on health guidelines for waist-hip ratio for men and women. Overweight for men was defined as a waist-to-hip ratio≥0.9, and for women waist-to-hip ratio≥0.8. Normal weight was defined as waist-to-hip ratio <0.9 for men and waist-to-hip ratio <0.8 for women.

Smoking intensity

The quantity of cigarette smoking was determined in HUNT2 with the question: "How many cigarettes do you smoke a day?" Based on this the participants were put into four categories of smoking intensity: (1) ≤5, (2) >5 and ≤10, (3) >10 and ≤20, (4) >20.

Statistical analysis

All analyses were conducted using STATA 13.0. We used logistic regression to estimate the associations between each of the different independent variables and smoking cessation, with each independent variable considered in a separate model (see table 2). Subsequently, we estimated the risk difference for smoking cessation given the independent variables, using the margins function in STATA (adjusted average marginal effects). In our main model, we adjusted for age, sex, education and marital status. Because educational achievements or marital status can be affected by mental and somatic health, or by factors associated with early lifestyle behavior, we also performed additional analyses without adjustment for education or marital status. Participants with complete information on included variables were included in the analyses; the number thus varies between different independent variables.

To assess how mental health affected smoking cessation among those who experienced smoking-related somatic disease, we included an interaction term between incident somatic disease and mental health score, and estimated the likelihood of smoking cessation given mental symptoms and somatic health (adjusted average marginal predictions).

We looked for associations with missing information on outcome or independent variables to evaluate the appropriateness of complete case analyses. Due to incomplete participation at follow-up and some missing, and because validity of complete case analyses could not be confirmed, we also performed multiple imputation by chained equations.

Results

Out of all the participants in both HUNT2 and HUNT3, 9554 (25.8%) were daily smokers in HUNT2 and met our inclusion criteria. Results showed that men tended to smoke more cigarettes daily than women. The mean number of cigarettes smoked per day for men was 12.4 (sd 6.0), while the mean number for women was 10.0 (sd 4.5) cigarettes per day. The mean age for smoking initiation for men was 18.13 years old, while the mean age for women was 19.16 years old. In HUNT3, 3247 (34%) reported to have quit smoking. Information about smoking status in HUNT3 was missing for 328 (3.43%). Descriptive statistics of the samples are given in Table 1. Among our selection of smokers in HUNT2, 9311 (97.5%) participants had a valid HADS score, and 2154 (23.1%) reported to have either anxiety, depression or both.

Demography

Men had higher odds for smoking cessation than women (odds ratio (OR): 1.38. 95% confidence interval (CI): 1.27- 1.51), and smoking cessation increased with increasing age (see Table 2). Participants with higher education had a higher rate of smoking cessation compared to participants with lower education (OR 1.70 (95% CI: 1.48- 1.94) and OR 1.18 (95% CI: 1.07- 1.31) for College/University and High School, respectively).

Table 1
Number and percentages of participants in the different variables, and number and percentages of participants having quit smoking in relation to the different variables.

	Study sample, n = 9554		Quit smoking, n= 3247	
	N	%	N	%
Sex				
Female	5618	58.80	1723	31.83
Male	3936	41.20	1524	39.97
Age				
<30	926	9.69	277	30.88
30 -	5342	55.91	1695	32.28
50 -	3097	32.42	1199	41.17
>70	189	1.98	76	45.78
Education				
Primary School	3378	36.07	1078	33.50
High School	4685	50.03	1557	34.06
College/University	1301	13.89	556	43.47
Missing	190	1.99	56	29,47
Marital status				
Married/registered partnership	6034	63.16	2163	37.11
Unmarried	2119	22.18	631	30.72
Widow/widower	298	3.12	104	37.55
Divorced/Separated	1089	11.40	344	32.70
Missing	14	0.15	5	35,71
HADS score categories				
Symptom free	7157	76.87	2511	36.11
Depression	353	3.79	106	31.27
Anxiety	1117	12.00	364	34.11
Comorbid; depression and anxiety	684	7.35	192	29.05
Missing	243	2.54	74	30,45
Anxiety symptom score				
0-	5231	56.16	1879	36.95
5-	2283	24.51	738	33.36
8-	1131	12.14	362	33.55
11-	670	7.19	194	29.89
Missing	239	2.50	74	30,96
Depression symptom score				
0-	6374	68.25	2252	36.38
5-	1921	20.57	630	34.09
8-	756	8.10	222	30.45
11-	288	3.08	78	28.06
Missing	215	2.25	65	30,23
Cardiovascular disease (CVD)				
No cardiovascular events	8564	89.65	2783	33.57
Incidence of CVD	720	7.54	376	54.73
Prevalence of CVD	269	2.82	88	35.48
Missing	1	0.01	0	0
Blood pressure				
Normal	6570	68.95	2193	34.37
Moderate	1885	19.78	662	36.53
Severe	1073	11.26	384	38.13
Missing	26	0.27	8	30,77
Pulmonary disease				
No airway symptoms	6502	69.12	2212	35.22
Incident pulmonary disease	211	2.24	98	47.80
Prevalent airway symptoms	2694	28.64	884	33.97
Missing	425	4.45	136	32,00
Alcohol units per week				
Abstainer or <=0,5	2732	33.72	886	33.91
>0,5 to <=3	3944	48.67	1393	36.37
>3 to <=5	523	6.45	191	37.45
>5 to <=7	56	0.69	19	35.19
>7	82	1.01	27	34.18
Problem drinker	766	9.45	223	30.18
Missing	1451	15.19	508	35,01
Body Mass Index				
Underweight	103	1.08	27	27.27
Normal weight	8365	87.82	2867	35.47
Overweight	1057	11.10	341	33.63
Missing	29	0.30	12	41,38
Waist-hip Ratio				
Normal weight	5525	58.21	1896	35.45
Overweight	3966	41.79	1329	34.85
Missing	63	0.66	22	34,92
Smoking intensity				
<=5	1428	15.37	623	45.38
>5 to <=10	4127	44.41	1390	34.76
>10 to <=20	3514	37.82	1078	31.59
>20	223	2.40	73	33.64
Missing	262	2.74	83	31,68

N = number of participants

missing = number of participants who did not answer the question

Table 2
Odds ratios, 95 % confidence intervals and percentage points for smoking cessation in relation to the different variables.

Variable	Odds ratio	95% CI	Percentage points (RD)	95% CI
Sex[1]				
Female	1.0	REF	0	REF
Male	1.38	1.27- 1.51	0.07	0.05- 0.09
Age[2]				
<30	1.0	REF	0	REF
30-	1.05	0.90- 1.22	0.01	-0.02- 0.04
50-	1.50	1.28- 1.76	0.09	0.06- 0.13
>70	1.77	1.26- 2.48	0.13	0.05- 0.21
Education[3]				
Primary School	1.0	REF	0	REF
High School	1.18	1.07- 1.31	0.04	0.01- 0,06
College/University	1.70	1.48- 1.94	0.12	0.09- 0.15
HADS score categories[4]				
Symptom free	1.0	REF	0	REF
Caseness anxiety	0.99	0.86- 1.14	0.00	-0.03- 0.03
Caseness depression	0.76	0.60- 0.96	-0.06	-0.11- (-0.01)
Comorbid; depression and anxiety	0.75	0.63- 0.90	-0.06	-0.10- (-0.02)
Anxiety symptom score[4]				
0 -	1.0	REF	0	REF
5-	0.91	0.82- 1.01	-0.02	-0.05- 0.00
8-	0.92	0.80- 1.01	-0.02	-0.05- 0.01
11-	0.81	0.68- 0.97	-0.05	-0.08- (-0.01)
Depression symptom score[4]				
0-	1.0	REF	0	REF
5-	0.87	0.78- 0.97	-0.03	-0.06- (-0.01)
8-	0.75	0.63- 0.89	-0.06	-0.10- (-0.03)
11-	0.67	0.51- 0.88	-0.08	-0.14- (-0.03)
Cardiovascular disease (CVD)[4]				
No cardiovascular events	1.0	REF	0	REF
Incidence of CVD	2.08	1.77- 2.45	0.17	0.13- 0.21
Prevalence of CVD	0.89	0.68- 1.17	-0.02	-0.08- 0.03
Blood Pressure[4]				
Normal	1.0	REF	0	REF
Moderate	0.95	0.85- 1,06	-0.01	-0.04- 0.01
Severe	0.95	0.82- 1,10	-0.01	-0.04- 0.02
Pulmonary disease[4]				
No airway symptoms	1.0	REF	0	REF
Incident pulmonary disease	1.57	1.18- 2,08	0.11	0.04- 0.17
Prevalent airway symptoms	0.93	0.85- 1,03	-0.02	-0.04- 0.01
Alcohol units per week[4]				
Abstainer	1.0	REF	0	REF
>0,5 to <=3	1.06	0.95- 1.18	0.01	-0.01- 0.04
>3 to <=5	1.00	0.81- 1.22	0.00	-0.05- 0.04
>5 to <=7	0.81	0.45- 1.43	-0.05	-0.17- 0.07
>7	0.79	0.49- 1.29	-0.05	-0.15- 0.05
Problem drinker	0.72	0.60- 0.87	-0.07	-0.11- (-0.03)
Body Mass Index[4]				
Normal weight	1.0	REF	0	REF
Underweight	0.82	0.52- 1.28	-0.04	-0.14- 0.05
Overweight	0.94	0.81- 1.08	-0.01	-0.05- 0.02
Waist-Hip Ratio[4]				
Normal weight	1.0	REF	0	REF
Overweight	0.94	0.86- 1.02	-0.01	-0.03- 0.01
Smoking intensity[4]				
<=5	1.0	REF	0	REF
>5 to <=10	0.66	0.58- 0.75	-0.10	-0.13- (-0.07)
>10 to <=20	0.54	0.48- 0.62	-0.14	-0.17- (-0.11)
>20	0.53	0.39- 0.72	-0.15	-0.21- (-0.08)

[1]Adjusted for age
[2]Adjusted for sex
[3]Adjusted for age, sex and marital status
[4]Adjusted for age, sex, marital status and education

Mental health

Participants with caseness depression had an OR of 0.76 (95% CI: 0.60-0.96) for smoking cessation, while caseness anxiety was not associated with smoking cessation (OR: 0.99. 95% CI: 0.86-1.14). Participants with both depression and anxiety had an OR of 0.75 (95% CI: 0.63-0.90) for smoking cessation. Increasing degree of depressive symptoms was associated with a lower likelihood of smoking cessation. A similar trend was found for anxiety, but less pronounced (see Table 2).

Somatic health

Incident cardiovascular disease between HUNT2 and HUNT3 was associated with a higher likelihood of smoking cessation (OR: 2.08. 95% CI: 1.77-2.45), as was incident pulmonary disease (OR: 1.57. 95% CI: 1.18-2.08). On the contrary, prevalent cardiovascular disease or prevalent pulmonary symptoms at baseline were not associated with smoking cessation (OR: 0.89 (95% CI: 0.68-1.17) and OR: 0.93 (95% CI: 0.85- 1.03), respectively). Hypertension at baseline was not associated with smoking cessation compared to normotensive participants (OR: 0.95 (95% CI: 0.82-1.10) for severe hypertension and OR: 0.95 (95% CI: 0.85-1.06) for moderate hypertension).

Lifestyle

Increasing quantity of alcohol consumption was associated with a lower likelihood of smoking cessation. Compared to those who were abstainers, the ORs were 0.81 (95% CI: 0.45- 1.43), 0.79 (95% CI: 0.49- 1.29) and 0.72 (95% CI: 0.60- 0.87) for >5 and ≤7 alcohol units per week, >7 alcohol units per week and problem drinkers, respectively. Increasing quantity of cigarettes smoked daily was inversely associated with smoking cessation. Compared to those who smoked 5 cigarettes or less daily, the ORs were 0.66 (95% CI: 0.58-0.75), 0.54 (95% CI: 0.48-0.62) and 0.53 (95% CI: 0.39-0.72) for >5 and ≤10 cigarettes per day, >10 and ≤20 cigarettes per day and >20 cigarettes per day, respectively.

Incident somatic disease with or without poor mental health

Figure 3.1-5. show the predicted probability of smoking cessation given different somatic and mental health status. Incident cardiovascular disease was associated with smoking cessation among those without symptoms of depression or anxiety (OR 2.08, 95% CI: 1.77-2.45). Participants with no symptoms of anxiety or depression had the highest probability of smoking cessation, compared to those with mental health symptoms (fig. 3.1). For those with symptoms of mental illness, incident cardiovascular disease had a stronger association with

smoking cessation than incident pulmonary disease (fig. 3.2-3.5). Higher levels of anxiety were associated with a lower probability of smoking cessation among those who experienced incident cardiovascular disease (fig. 3.2). Incident pulmonary disease seemed not to be associated with smoking cessation among participants with symptoms of anxiety or depression, however, confidence intervals were wide (fig. 3.4-3.5).
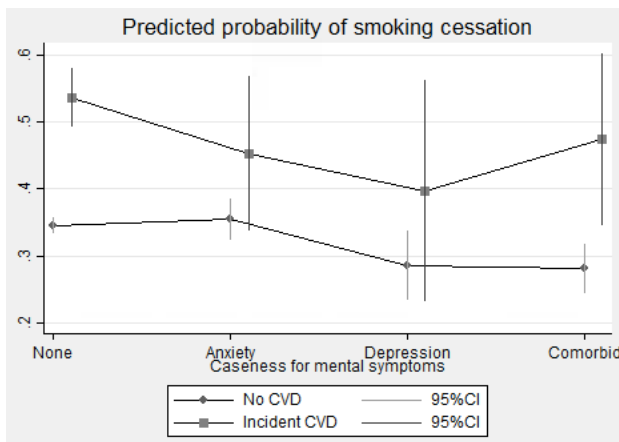

Fig. 3.1 The graph shows predicted probability of smoking cessation with 95% confidence intervals among participants with no cardiovascular disease and incident cardiovascular disease, given different categories based on the HADS score.
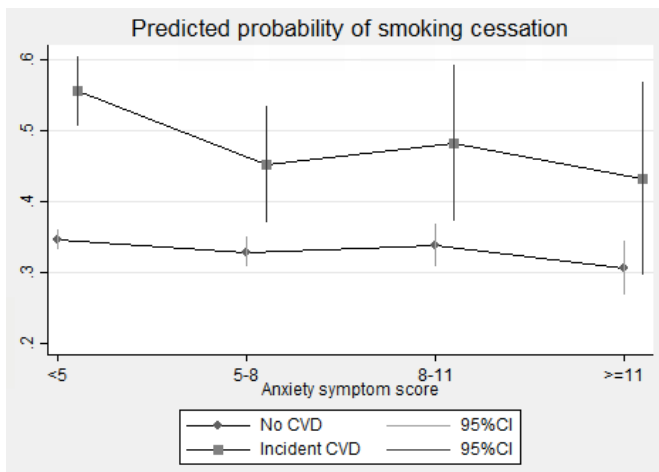

Fig. 3.2 Predicted probability of smoking cessation with 95% confidence intervals among participants with no cardiovascular disease and incident cardiovascular disease, given different anxiety symptom scores based on the HADS score.
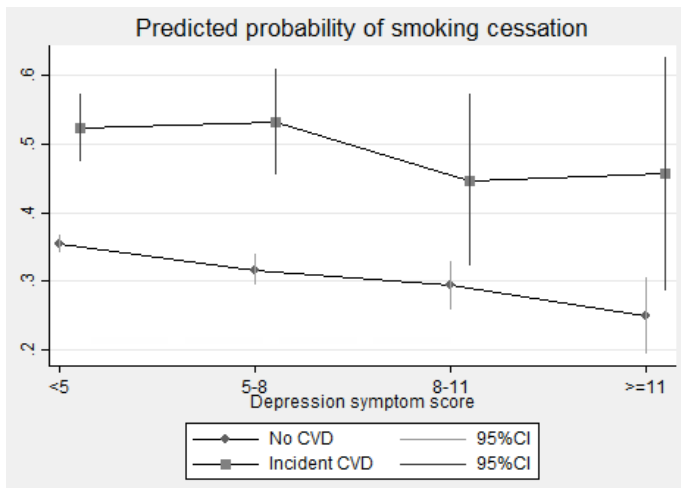
Fig. 3.3 Predicted probability of smoking cessation with 95% confidence intervals among participants with no cardiovascular disease and incident cardiovascular disease, given different depression symptom scores based on the HADS score.
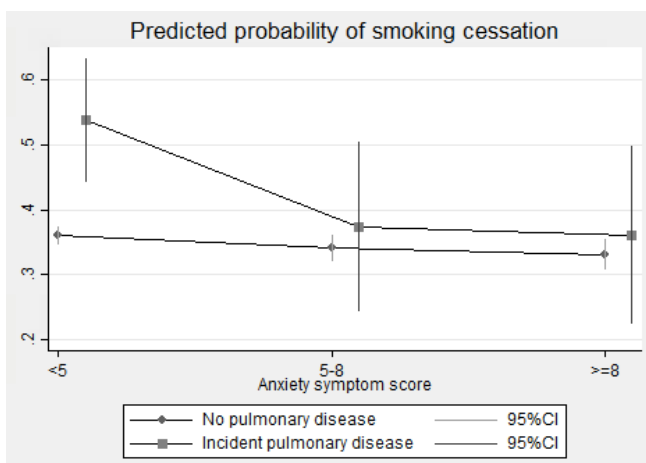

Fig. 3.4 Predicted probability of smoking cessation with 95% confidence intervals among participants with no pulmonary disease and incident pulmonary disease, given different anxiety symptom scores based on the HADS score.
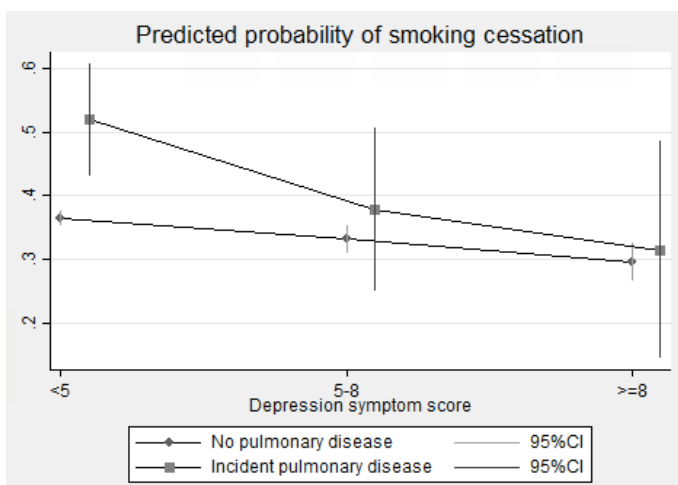

Fig. 3.5 Predicted probability of smoking cessation with 95% confidence intervals among participants with no pulmonary disease and incident pulmonary disease, given different depression symptom scores based on the HADS score.

Additional analyses

Our results were not substantially different after performing analysis without adjustment for education and marital status (see appendix, S1). Comparing those who did not respond to the smoking status question with those who had responded, we found that the non-responders had lower education and more symptoms of mental illness than the responders. Results from analyses of imputated datasets were mostly consistent with results from complete case analyses. However, the associations of high school education compared to primary school only (OR 1.56, 95% CI 1.05-1.28) and prevalent cardiovascular disease at baseline (OR 1.13. 95% CI 0.95-1.34) with smoking cessation might have been underestimated in complete case analyses (see appendix, S2). The association between caseness depression and smoking cessation was slightly weaker in analyses of imputed datasets (OR 0.81. 95% CI 0.67-0.98) compared to complete case analyses (OR 0.76. 95% CI 0.60-0.96).

Discussion

Main findings

We found that men, older participants, and participants with higher education were more likely to quit smoking than women, younger participants and those with lower education. Participants with symptoms of either depression or comorbid depression and anxiety had an increased risk of smoking continuation, but we did not find the same association for those with only symptoms of anxiety. We also found that incident somatic disease was positively associated with smoking cessation. However, smoking cessation after incident somatic disease was less common among participants with mental symptoms compared to those without mental symptoms. Lifestyle habits such as alcohol consumption showed an inverse association between increasing consumption and smoking cessation.

Strengths and limitations

The information about smoking, lifestyle, mental and somatic health, except blood pressure and BMI, was based on self-reporting questionnaires. Misclassification is thus possible, which might have biased our results. However, a complete health examination in a study sample this large, would not be feasible. The questions about symptoms of the respiratory system in HUNT2 and HUNT3 were not the same. There was no question about chronic obstructive pulmonary disease in HUNT2, which may have led to misclassification of the pulmonary disease variable. Furthermore, occasional smokers could not be identified in HUNT2. However, the study is based on a large population sample, with a high response rate. It is therefore likely to believe that the findings are not due to chance only.

There was a decline in participation rate from 71% in HUNT2 to 54% in HUNT3 (38). As participation was moderate in HUNT3, participants might not be representative of the entire population, and estimated probability of smoking cessation might thus be biased. Langhammer et al. (2012) compared nonparticipants in HUNT3 with participants (38). They found that nonparticipants had lower education, higher prevalence of cardiovascular disease and mental distress. We might have underestimated associations with mental symptoms and overestimated associations with sex if smoking cessation, being a woman and at good mental health all increase participation at follow-up (see fig. 4). However, results from multiple imputations suggest this was not the case. Complete case analyses provide valid results if missing exposure information is unrelated to the outcome and vice versa (39). This could not

be fully assessed, as there were missing in both exposure and outcome variables, but associations between independent variables and missing outcome data suggests complete cases analyses might be biased. However, the number of missing is quite low and is not likely to substantially affect the estimates. Our conclusions are further supported by similar results from analyses of original and imputed datasets. However, multiple imputation analyses assumes data to be missing at random given other fully observed variables, an assumption which cannot be proven. It is possible that people with mental illness were underrepresented in the questionnaires due to nonresponse problems. Our study included the non-hospitalized population, and will therefore not include participants with somatic or mental health problems in the hospital setting.

There is always potential residual confounding in observational studies. For instance, socioeconomic status might not be fully captured by educational level. We might also have overestimated the associations between mental symptoms and smoking cessation due to residual confounding.
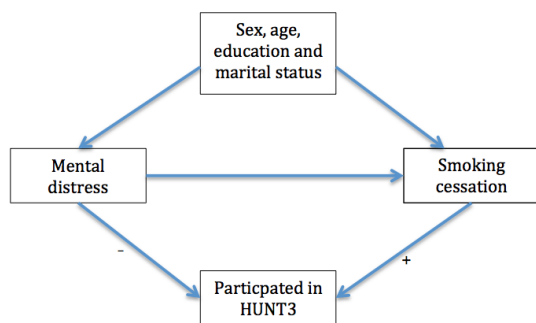

Fig. 4 Directed acyclic graph presenting assumed causal relationships between mental distress and smoking cessation, participation at follow-up, sex, age, education and marital status. Assumed direction of effects on participation at follow-up is indicated.

Demography

We found that men have a greater likelihood of smoking cessation than women. Honjo et al. (2010) on the other hand, found that female gender was significantly associated with smoking cessation (40). The observed difference in smoking cessation among men and women could be explained by differences in smoking intensity. A small number of cigarettes smoked per day were associated with smoking cessation, probably because this indicates lower nicotine dependence. This is consistent with earlier studies (40, 41). Another potential explanation

could be that men tend to precede women in the different phases of the smoking epidemic (42).

Contrary to our expectation, but supported by the findings of Hymowitz et al. (24) and Lund et al. (14), increasing age was associated with smoking cessation. This may be because the greatest motivation for smoking cessation is concerns about health, and it is likely to believe that these concerns increase with increasing age. Similar to findings of others (14, 24, 43), the current study showed that higher education is associated with smoking cessation. This may be because highly educated people respond more favorably to medical advices.

Mental health

Our results indicated that participants with symptoms of depression had lower odds for smoking cessation than participants without such symptoms. These findings are consistent with other studies (9, 16). Nicotine might act as an antidepressant, thus smoking can function as a form of self-medication (11). Anxiety and depression will both increase the risk of smoking, and determine how much one smokes. The antidepressant effect of nicotine is supported by evidence that transdermal nicotine gives less depressive symptoms in non-smokers (44), and that smoking cessation can precipitate depressive symptoms (44, 45). These results support our findings of lower smoking cessation among individuals with mental symptoms. On the other hand, several observational studies have indicated that smokers have a greater risk of developing depression than non-smokers (11, 46-49), which would suggest an even greater benefit of smoking cessation among people with symptoms of depression. The association between smoking and mental health has been suggested to be mediated through poor physical health, or by a long-term biological impact on transmitter levels (50). However, the causal effect of smoking on symptoms of anxiety or depression has not been supported in instrumental variable analyses (51).

Cardiovascular disease

Incident cardiovascular events and first time hospitalization is shown to increase the likelihood of smoking cessation, both in our study and in others (28, 41). Cardiovascular events are often traumatic for the patients and leads to increased concerns about own health, and therefore increased rate of smoking cessation. Furthermore, the doctors are keen to achieve appropriate risk factor management and will focus on lifestyle advices (28).

On the other hand, prevalent cardiovascular events are inversely associated with smoking cessation. As a cardiovascular event is a strong predictor of smoking cessation, smokers with

prevalent cardiovascular disease are a selected group who has continued smoking despite a strong incentive to quit. It might therefore not be surprising that they have lower odds of smoking cessation. Hospitalization with myocardial infarction might give a relatively higher proportion of patients who stop smoking compared to patients hospitalized with angina (28). Our variable does not distinguish between stroke, angina and heart attack. This has to be kept in mind when comparing our estimates to results from other studies.

Blood pressure

Hypertension, on the other hand, was not associated with changes in smoking status. The reason for this is not certain, but there are some theories. Doctors might not convey the association between smoking, hypertension and cardiovascular disease good enough (52). There has also been discussed if hypertension normally is a "silent" disease with no traumatic incidents, and therefore does not induce enough "fear or motivation" to quit smoking (41). These findings are in line with observations made both by Tsai et al. (2012) and Honjo et al. (2010) (40, 41). There is, however, good reason to urge hypertensive patients to quit smoking, both because of the increased risk of cardiovascular death caused by the combination of smoking and hypertension, and because smoking contributes to the development of hypertension (53).

Lifestyle

Our analyses showed that a large number of alcohol units consumed per week are inversely associated with smoking cessation. This is consistent with other studies that have shown that a greater use of alcohol reduces the odds of quitting smoking (20, 24). Our study extended those of previously published studies on alcohol use and smoking cessation by comparing the abstinent with both weekly quantities of consumption and persons with a problematic drinking pattern. Participants with a problematic drinking pattern had lower odds for smoking cessation than those with a large number of alcohol units consumed per week. This might be because smoking and having a problematic drinking pattern are similar lifestyle vices. It is likely to believe that people who are problem drinkers are more likely to get treatment for their drinking habits rather than their smoking habits. Also, it is likely to believe that arguments concerning health effects caused by smoking cessation will not have an impact on their smoking status because their main challenge is the large amount of alcohol consumption. Quitting alcohol drinking increases the likelihood of smoking cessation (41), possibly because abstinence leads to better judgment and willpower. Also, smoking cessation leads to less

alcohol consumption (54). These two findings might reflect that participants who quit either smoking or drinking, are motivated to make lifestyle changes and therefore we see a positive synergistic effect.

Mental symptoms and incident somatic disease
Incident cases of both cardiovascular disease and pulmonary disease were associated with smoking cessation among both participants with symptoms of depression and symptoms of anxiety. However, incident pulmonary disease did not have as great effect on smoking cessation as incident cardiovascular disease. Pulmonary diseases are often slowly developing illnesses. One might imagine that the patients gradually accustom to the pulmonary symptoms, and therefore do not experience the symptoms as traumatic as patients with cardiovascular symptoms. But even though somatic disease was associated with smoking cessation, the association was weaker among participants with symptoms of depression or anxiety. Other studies have also found that depressive symptoms were associated with a lower likelihood of smoking cessation in patients with either incident cardiovascular disease or pulmonary disease (30, 43, 55, 56).

Participants with symptoms of both depression and anxiety had a higher likelihood of smoking cessation than those with only symptoms of depression, but given the low precision, this might be a chance finding. We need a greater understanding of the differences in these two groups, to be able to determine why there is a difference in likelihood for smoking cessation.

Conclusion

During a decade where the prevalence of smoking has decreased substantially, vulnerable groups, such as those with low socioeconomic status or poor mental health, have accomplished smoking cessation to a lesser degree than others. Thus, current initiatives, including general population advice, seem to be insufficient in order to reduce smoking among these groups. People with poor mental health quit smoking less than mentally healthy, even after incidence of severe, smoking-related somatic disease. Further research is needed to evaluate the effect of different smoking cessation initiatives at both individual and group levels.

Regarding individual level initiatives, smoking cessation among hypertensive patients seem to be underachieved. Clinicians should urge hypertensive patients to quit smoking to prevent further cardiovascular events. Furthermore, mental distress might preclude smoking cessation, and should be taken into consideration when supporting patients through smoking cessation.

References

1.   Doll R, Peto R, Boreham J, Sutherland I. Mortality in relation to smoking: 50 years' observations on male British doctors. BMJ (Clinical research ed). 2004;328(7455):1519.

2.   National Center for Chronic Disease P, Health Promotion Office on S, Health. Reports of the Surgeon General. The Health Consequences of Smoking-50 Years of Progress: A Report of the Surgeon General. Atlanta (GA): Centers for Disease Control and Prevention (US); 2014.

3.   (CDC) CfDCaP. Smoking-attributable mortality, years of potential life lost, and productivity losses--United States, 2000-2004. MMWR Morbidity and mortality weekly report. 2008;57(45):1226-8.

4.   Ezzati M, Lopez AD. Estimates of global mortality attributable to smoking in 2000. Lancet (London, England). 2003;362(9387):847-52.

5.   Peto R, Lopez AD, Boreham J, Thun M, Heath C, Jr., Doll R. Mortality from smoking worldwide. British medical bulletin. 1996;52(1):12-21.

6.   Gursli-Berg G. Røykeloven. 2014.

7.   sentralbyrå S. Røykevaner, 2015 https://www.ssb.no/helse/statistikker/royk/aar/2016-01-14 - content: Statistisk sentralbyrå; 2015 [

8.   Folkehelseinstituttet S. Rusmidler i Norge [Available from: http://www.sirus.no/publikasjon/rusmidler-i-norge/3-tobakk/.

9.   Weinberger AH, Pilver CE, Desai RA, Mazure CM, McKee SA. The relationship of major depressive disorder and gender to changes in smoking for current and former smokers: longitudinal evaluation in the US population. Addiction (Abingdon, England). 2012;107(10):1847-56.

10.   Lawrence D, Mitrou F, Zubrick SR. Smoking and mental illness: results from population surveys in Australia and the United States. BMC public health. 2009;9:285.

11.   Mykletun A, Overland S, Aaro LE, Liabo HM, Stewart R. Smoking in relation to anxiety and depression: evidence from a large population survey: the HUNT study. European psychiatry : the journal of the Association of European Psychiatrists. 2008;23(2):77-84.

12.   Lawrence D, Considine J, Mitrou F, Zubrick SR. Anxiety disorders and cigarette smoking: Results from the Australian Survey of Mental Health and Wellbeing. The Australian and New Zealand journal of psychiatry. 2010;44(6):520-7.

13.   Hiscock R, Bauld L, Amos A, Fidler JA, Munafo M. Socioeconomic status and smoking: a review. Annals of the New York Academy of Sciences. 2012;1248:107-23.

14.   Lund M, Lund KE, Rise J. [Socioeconomic differences in smoking cessation among adults]. Tidsskrift for den Norske laegeforening : tidsskrift for praktisk medicin, ny raekke. 2005;125(5):564-8.

15.   McBride CM, Emmons KM, Lipkus IM. Understanding the potential of teachable moments: the case of smoking cessation. Health education research. 2003;18(2):156-70.

16.   Hitsman B, Papandonatos GD, McChargue DE, DeMott A, Herrera MJ, Spring B, et al. Past major depression and smoking cessation outcome: a systematic review and meta-analysis update. Addiction (Abingdon, England). 2013;108(2):294-306.

17.   Prochaska JJ, Rossi JS, Redding CA, Rosen AB, Tsoh JY, Humfleet GL, et al. Depressed smokers and stage of change: implications for treatment interventions. Drug and alcohol dependence. 2004;76(2):143-51.

18.   Cook BL, Wayne GF, Kafali EN, Liu Z, Shu C, Flores M. Trends in smoking among adults with mental illness and association between mental health treatment and smoking cessation. Jama. 2014;311(2):172-82.

19.   McKee SA, Hinson R, Rounsaville D, Petrelli P. Survey of subjective effects of smoking while drinking among college students. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2004;6(1):111-7.

20.   Kahler CW, Borland R, Hyland A, McKee SA, Thompson ME, Cummings KM. Alcohol consumption and quitting smoking in the International Tobacco Control (ITC) Four Country Survey. Drug and alcohol dependence. 2009;100(3):214-20.

21.   Yokoyama A, Mizukami T, Nakayama H, Takimura T, Sakuma H, Yoshimura A, et al. [Concurrent inpatient smoking cessation and alcohol abstinence programs for alcoholics and their outcomes]. Nihon Arukoru Yakubutsu Igakkai zasshi = Japanese journal of alcohol studies & drug dependence. 2014;49(6):381-90.

22.   Pieroni L, Minelli L, Salmasi L. Economic Evaluation of the effect of Quitting Smoking on Weight Gains: Evidence from the United Kingdom. Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research. 2015;18(6):791-9.

23.   Rupprecht LE, Donny EC, Sved AF. Obese Smokers as a Potential Subpopulation of Risk in Tobacco Reduction Policy. The Yale journal of biology and medicine. 2015;88(3):289-94.

24.   Hymowitz N, Cummings KM, Hyland A, Lynn WR, Pechacek TF, Hartwell TD. Predictors of smoking cessation in a cohort of adult smokers followed for five years. Tobacco control. 1997;6 Suppl 2:S57-62.

25.   Wilkes S, Evans A. A cross-sectional study comparing the motivation for smoking cessation in apparently healthy patients who smoke to those who smoke and have ischaemic heart disease, hypertension or diabetes. Family practice. 1999;16(6):608-10.

26.   Wilson K, Gibson N, Willan A, Cook D. Effect of smoking cessation on mortality after myocardial infarction: meta-analysis of cohort studies. Archives of internal medicine. 2000;160(7):939-44.

27.   Rigotti NA, McKool KM, Shiffman S. Predictors of smoking cessation after coronary artery bypass graft surgery. Results of a randomized trial with 5-year follow-up. Annals of internal medicine. 1994;120(4):287-93.

28.   Scholte op Reimer W, de Swart E, De Bacquer D, Pyorala K, Keil U, Heidrich J, et al. Smoking behaviour in European patients with established coronary heart disease. European heart journal. 2006;27(1):35-41.

29.   Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet (London, England). 2002;360(9349):1903-13.

30.   Doyle F, Rohde D, Rutkowska A, Morgan K, Cousins G, McGee H. Systematic review and meta-analysis of the impact of depression on subsequent smoking cessation in patients with coronary heart disease: 1990 to 2013. Psychosom Med. 2014;76(1):44-57.

31.   Krokstad S, Langhammer A, Hveem K, Holmen TL, Midthjell K, Stene TR, et al. Cohort Profile: the HUNT Study, Norway. International journal of epidemiology. 2013;42(4):968-77.

32.   Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta psychiatrica Scandinavica. 1983;67(6):361-70.

33.   Herrmann C. International experiences with the Hospital Anxiety and Depression Scale--a review of validation data and clinical results. Journal of psychosomatic research. 1997;42(1):17-41.

34.   Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. Journal of psychosomatic research. 2002;52(2):69-77.

35.   Ewing JA. Detecting alcoholism. The CAGE questionnaire. Jama. 1984;252(14):1905-7.

36.   O'Brien CP. The CAGE questionnaire for detection of alcoholism: a remarkably useful but simple tool. Jama. 2008;300(17):2054-6.

37.   Petursson H, Sigurdsson JA, Bengtsson C, Nilsen TI, Getz L. Body configuration as a predictor of mortality: comparison of five anthropometric measures in a 12 year follow-up of the Norwegian HUNT 2 study. PloS one. 2011;6(10):e26621.

38.   Langhammer A, Krokstad S, Romundstad P, Heggland J, Holmen J. The HUNT study: participation is associated with survival and depends on socioeconomic status, diseases and symptoms. BMC medical research methodology. 2012;12:143.

39.   White IR, Carlin JB. Bias and efficiency of multiple imputation compared with complete-case analysis for missing covariate values. Statistics in medicine. 2010;29(28):2920-31.

40.   Honjo K, Iso H, Inoue M, Tsugane S. Smoking cessation: predictive factors among middle-aged Japanese. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2010;12(10):1050-4.

41.   Tsai AC, Lin YA, Tsai HJ. Predictors of smoking cessation in 50-66-year-old male Taiwanese smokers: a 7-year national cohort study. Archives of gerontology and geriatrics. 2012;55(2):295-300.

42.   Lopez ADC, N. E.; Piha, T. A descripitve model of the cigarette epidemic in developed countries. Tobacco control. 1994;3(3):242 - 7.

43.   Brummett BH, Babyak MA, Mark DC, Williams RB, Siegler IC, Clapp-Channing N, et al. Predictors of smoking cessation in patients with a diagnosis of coronary artery disease. Journal of cardiopulmonary rehabilitation. 2002;22(3):143-7.

44.   Salin-Pascual RJ, Rosas M, Jimenez-Genchi A, Rivera-Meza BL, Delgado-Parra V. Antidepressant effect of transdermal nicotine patches in nonsmoking patients with major depression. The Journal of clinical psychiatry. 1996;57(9):387-9.

45.   Laje RP, Berman JA, Glassman AH. Depression and nicotine: preclinical and clinical evidence for common mechanisms. Current psychiatry reports. 2001;3(6):470-4.

46.   Klungsoyr O, Nygard JF, Sorensen T, Sandanger I. Cigarette smoking and incidence of first depressive episode: an 11-year, population-based follow-up study. American journal of epidemiology. 2006;163(5):421-32.

47.   Korhonen T, Broms U, Varjonen J, Romanov K, Koskenvuo M, Kinnunen T, et al. Smoking behaviour as a predictor of depression among Finnish men and women: a prospective cohort study of adult twins. Psychological medicine. 2007;37(5):705-15.

48.   Wu LT, Anthony JC. Tobacco smoking and depressed mood in late childhood and early adolescence. American journal of public health. 1999;89(12):1837-40.

49.   Haukkala A, Uutela A, Vartiainen E, McAlister A, Knekt P. Depression and smoking cessation: the role of motivation and self-efficacy. Addict Behav. 2000;25(2):311-6.

50.   Bjorngaard JH, Gunnell D, Elvestad MB, Davey Smith G, Skorpen F, Krokan H, et al. The causal role of smoking in anxiety and depression: a Mendelian randomization analysis of the HUNT study. Psychological medicine. 2013;43(4):711-9.

51.   Taylor AE, Fluharty ME, Bjorngaard JH, Gabrielsen ME, Skorpen F, Marioni RE, et al. Investigating the possible causal association of smoking with depression and anxiety using Mendelian randomisation meta-analysis: the CARTA consortium. BMJ open. 2014;4(10):e006141.

52.   Heymann AD, Gross R, Tabenkin H, Porter B, Porath A. Factors associated with hypertensive patients' compliance with recommended lifestyle behaviors. The Israel Medical Association journal : IMAJ. 2011;13(9):553-7.

53.   Talukder MA, Johnson WM, Varadharaj S, Lian J, Kearns PN, El-Mahdy MA, et al. Chronic cigarette smoking causes hypertension, increased oxidative stress, impaired NO bioavailability, endothelial dysfunction, and cardiac remodeling in mice. American journal of physiology Heart and circulatory physiology. 2011;300(1):H388-96.

54.   Berg KM, Piper ME, Smith SS, Fiore MC, Jorenby DE. Defining and predicting short-term alcohol use changes during a smoking cessation attempt. Addict Behav. 2015;48:52-7.

55.   Ho SY, Alnashri N, Rohde D, Murphy P, Doyle F. Systematic review and meta-analysis of the impact of depression on subsequent smoking cessation in patients with chronic respiratory conditions. General hospital psychiatry. 2015;37(5):399-407.

56.   Gerber Y, Koren-Morag N, Myers V, Benyamini Y, Goldbourt U, Drory Y. Long-term predictors of smoking cessation in a cohort of myocardial infarction survivors: a longitudinal study. European journal of cardiovascular prevention and rehabilitation : official journal of the European Society of Cardiology, Working Groups on Epidemiology & Prevention and Cardiac Rehabilitation and Exercise Physiology. 2011;18(3):533-41.

Appendix

Supplementary Table 1

Odds ratio, 95% confidence intervals and percentage points for smoking cessation in relation to the different variable. Not adjusted for education and marital status.

Variable	Odds ratio	95% CI	Percentage points (RD)	95% CI
Sex[1]				
Female	1.0	REF	0	REF
Male	1.38	1.27- 1.51	0.07	0.05- 0.09
Age[1]				
<30	1.0	REF	0	REF
30-	1.05	0.90- 1.22	0.01	-0.02- 0.04
50-	1.50	1.28- 1.76	0.09	0.06- 0.13
>70	1.77	1.26- 2.48	0.13	0.05- 0.21
Education[1]				
Primary School	1.0	REF	0	REF
High School	1.17	1.06- 1.30	0.03	0.01- 0.06
College/University	1.70	1.48- 1.95	0.12	0.09- 0.15
HADS score categories[1]				
Symptom free	1.0	REF	0	REF
Caseness anxiety	0.97	0.85- 1.12	-0.01	-0.04- 0.02
Caseness depression	0.73	0.58- 0.93	-0.07	-0.12- (-0.02)
Comorbid; depression and anxiety	0.72	0.69- 0.86	-0.07	-0.11- (-0.03)
Anxiety symptom score[1]				
0 -	1.0	REF	0	REF
5-	0.90	0.81- 1.00	-0.02	-0.05- 0.00
8-	0.90	0.78- 1.04	-0.02	-0.05- 0.01
11-	0.78	0.65- 0.94	-0.05	-0.09- (-0.02)
Depression symptom score[1]				
0 -	1.0	REF	0	REF
5-	0.85	0.76- 0.95	-0.04	-0.06- (-0.01)
8-	0.73	0.62- 0.86	-0.69	-0.10- (-0.03)
11-	0.64	0.49- 0.84	-0.10	-0.15- (-0.04)
Cardiovascular disease[1]				
No cardiovascular events	1.0	REF	0	REF
Incidence of CVD between H2 and H3	2.04	1.74- 2.40	0.17	0.13- 0.21
Prevalent CVD in H2	0.85	0.64- 1.11	-0.04	-0.09- 0.02
Pulmonary disease[1]				
No airway symptoms	1.0	REF	0	REF
Incidence of pulmonary disease	1.53	1.16- 2.03	0.10	0.03- 0.17
Prevalent airway symptoms	0.92	0.84- 1.02	-0.02	-0.04- 0.00
Blood pressure[1]				
Normal	1.0	REF	0	REF
Moderate	1.01	0.84- 1.22	0.00	-0.04- 0.04
Severe	0.95	0.82- 1.10	-0.01	-0.05- 0.02
Alcohol units per week[1]				
Abstainer	1.0	REF	0	REF
>0,5 to <=3	1.10	0.98- 1.22	0.02	-0.00- 0.04
>3 to <=5	1.07	0.87- 1.30	0.01	-0.03- 0.06
>5 to <=7	0.90	0.51- 1.60	-0.02	-0.15-0.10
>7	0.87	0.54- 1.41	-0.03	-0.13- 0.07
Problem drinker	0.75	0.63- 0.91	-0.06	-0.10- (-0.02)
Weight[1]				
Normal weight	1.0	REF	0	REF
Underweight	0.80	0.50- 1.23	-0.05	-0.01- 0.04
Overweight	0.91	0.80- 1.05	-0.02	-0.05- 0.01
Waist-hip Ratio[1]				
Normal weight	1.0	REF	0	REF
Overweight	0.92	0.84- 1.01	-0.18	-0.04- 0.00
Smoking intensity[1]				
<=5	1.0	REF	0	REF
>5 to <=10	0.63	0.56- 0.72	-0.11	-0.14- 0.08
>10 to <=20	0.52	0.45- 0.59	-0.15	-0.18- (-0.12)
>20	0.50	0.37- 0.68	-0.16	-0.22- (-0.09)

1. Adjusted for sex and age

Supplementary table 2
Multiple imputation by chained equations on outcome and independent variables

Variable	Odds ratio	95 % CI
Sex[1]		
Female	1.0	REF
Male	1.38	1.26-1.50
Age[2]		
<30	1.0	REF
30-	1.08	0.92-1.25
50-	1.56	1.30-1.88
70-	2.26	1.74-2.92
Education[3]		
Primary school	1.0	REF
High school	1.56	1.05- 1.28
College/University	1.66	1.45- 1.90
HADS score categories[4]		
Symptom free	1.0	REF
Caseness anxiety	0.94	0.82- 1.07
Caseness depression	0.81	0.67- 0.98
Comorbid; depression and anxiety	0.73	0.63- 0.85
Anxiety symptom score[4]		
0-	1.0	REF
5-	0.92	0.84- 1.01
8-	0.88	0.77- 1.00
11-	0.77	0.66- 0.90
Depression symptom score[4]		
0-	1.0	REF
5-	0.88	0.79- 0.98
8-	0.77	0.67- 0.90
11-	0.68	0.55- 0.84
Cardiovascular disease[4]		
No cardiovascular events	1.0	REF
Incidence of CVD	2.02	1.73- 2.37
Prevalence of CVD	1.13	0.95- 1.34
Pulmonary disease[4]		
No airway symptoms	1.0	REF
Incident pulmonary disease	1.55	1.15- 2.09
Prevalent airway symptoms	0.93	0.86- 1.01
Blood pressure[4]		
Normal	1.0	REF
Moderate	0.97	0.87- 1.09
Severe	1.04	0.90- 1.20
Alcohol units per week[4]		
Abstainer	1.0	REF
>0,5 to <=3	1.02	0.92- 1.13
>3 to <= 5	0.95	0.78- 1.15
>5 to <=7	0.78	0.46- 1.33
>7	0.80	0.49- 1.30
Problem drinker	0.72	0.60- 0.86
Weight[4]		
Normal weight	1.0	REF
Underweight	0.90	0.63- 1.29
Overweight	0.98	0.86- 1.11
Waist- Hip Ratio[4]		
Normal weight	1.0	REF
Overweight	0.97	0.89- 1.05
Smoking intensity[4]		
<=5	1.0	REF
>5 to <=10	0.75	0.67- 0.84
>10 to <=20	0.61	0.54- 0.68
>20	0.47	0.35- 0.62

[1]Adjusted for age, marital status and education
[2]Adjusted for sex, marital status and education
[3]Adjusted for sex, age and marital status
[4]Adjusted for sex, age, marital status and education