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# Smoking and cancer, cardiovascular and total mortality among older adults: The Finrisk Study

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## ABSTRACT

Little information is available about the deleterious effect of smoking in older adults. The objective of this study was to assess the relationship of smoking habits with cancer, CVD and all-cause mortality in late middle-age (45–64 years) and older (65–74) people. This cohort study of 6516 men and 6514 women studied the relationship of smoking habits with cancer, cardiovascular disease (CVD) and all-cause mortality among middle-aged and older Finnish men and women during 1997–2013. The study cohort was followed up until the end of 2013 (median follow-up time was 11.8 years). Mortality data were obtained from the National Causes of Death Register and data on incident stroke events from the National Hospital Discharge Register. Adjusted Hazard ratios (HR) for total mortality were 2.61 (95% Confidence interval 2.15–3.18) among 45–64 years-old men and 2.59 (2.03–3.29) in 65–74 years-old men. The corresponding HRs for women 45–64 years-of-age were 3.21 (2.47–4.19) and 3.12 (2.09–4.68) for those 65–74 years-old, respectively. Adjusted HRs for CVD mortality in the 45–64 years-old and 65–74 years-old groups were 2.67 (1.92–2.67) and 1.95 (1.33–2.86) in men, and 4.28 (2.29–7.99) and 2.67 (1.28–5.58) in women, respectively. Among men, the risk difference between never and current smokers was 108/100.000 in the age-group 45–64 years, and 324/100.000 in the age group 65–74 years. Among women the differences were 52/100.000 and 196/100.000, respectively. In conclusion, absolute risk difference between never and current smokers are larger among the older age group. Smoking cessation counseling should routinely target also older adults in primary health-care.

## 1. Introduction

Tobacco smoking causes many chronic diseases, such as many cancers, cardiovascular disease (CVD) and chronic obstructive pulmonary disease (COPD), and increases markedly all-cause mortality (Mitchell et al., 2010; Doll et al., 2004). Even though the age-standardized smoking prevalence has decreased worldwide during the past three decades, the absolute number of smokers has increased with almost one billion daily smokers worldwide in 2012 (Ng et al., 2014).

Even though a number of the studies have shown the deleterious effect of smoking in the middle-aged population, less information is available in older adults (Kelly et al., 2008; Myint et al., 2008; Parish et al., 1995; Thun et al., 2013a; Gellert et al., 2012a). A recent meta-analysis revealed that smoking, even among older adults, considerably

advances, and cessation delays, the risk of all-cause, CVD and cancer death (Ordóñez-Mena et al., 2016; Mons et al., 2015; Müezziner et al., 2015). However, scientific evidence in regard the risk estimates of CVD, cancer and all-cause mortality between middle-aged and older adults in the same population cohort is scarce.

As the number of older adults is globally increasing, it must be of great public health interest to get estimates of the association between smoking, morbidity and mortality in the older adult population.

The objective of this study was to assess the relationship of smoking habits with cancer, CVD and all-cause mortality and to compare whether the smoking related health risk differs between late middle-age (45–64 years) and older (65–74) people.

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## 2. Methods

### 2.1. Study participants

The National FINRISK Study has been conducted every five years since 1972 in order to monitor cardiovascular and other non-communicable disease risk factors and other health related factors among the Finnish adult population (Borodulin et al., 2015). An independent random sample has been drawn from the national population register for each survey. The samples were stratified by sex and 10-year age categories according to the World Health Organization Multinational Monitoring (WHO MONICA) of trends and determinants of CVD protocol (Vartiainen et al., 2010). The current study cohort consists of participants who were aged 45–74 years sampled in 1997, 2002, and 2007 in five study areas (provinces of North Karelia and North Savo in Eastern Finland, Turku-Loimaa area in Southwestern Finland, cities of Helsinki and Vantaa in Southern Finland and Oulu province in Northern Finland). People who participated more than once in the surveys are included in their first study cohort, and those with missing information on any of the variables needed for the analysis or those with an acute CHD, stroke event prevalent heart failure or cancer before the baseline survey, were excluded from the analysis. The final sample size of the follow-up cohort consisted of 6516 men and 6514 women.

### 2.2. Baseline assessment of cardiovascular risk factors

A self-administered questionnaire was mailed to the participants in advance. The questionnaire included standardized questions on health behavior, including smoking habits, and other health related and sociodemographic factors. Smoking habits were classified to three categories: never smokers, ex-smokers (stopped more than six months ago) and current smokers (currently smoking or stopped smoking within the last 6 months). Education level, measured as the total number of school years, was divided into birth cohort-specific thirds. Marital status was categorized according to married, unmarried, divorced or widowed. At the study site, specially trained nurses checked that the questionnaire was fully completed and measured height, weight, and blood pressure using a standardized protocol (Vartiainen et al., 2010). Height and weight were measured in light clothing without shoes and body mass index (BMI) was calculated ( $\text{kg}/\text{m}^2$ ). Blood pressure was measured with mercury sphygmomanometer twice in 1997 and three times in 2002 and 2007 from the right arm of the participant in a seated position after at least 5 min of rest. The mean value of the first and second systolic blood pressure measurement was used in the analysis. After clinical measurements, a venous blood specimen was taken for laboratory analysis. Serum total cholesterol level was analyzed by using enzymatic method. All laboratory analyses were done in the same central laboratory of the National Institute for Health and Welfare.

### 2.3. Outcome definition

The study cohort was followed up until the end of 2013. Mortality data were obtained from the National Causes of Death Register. The median follow-up time was 11.8 years. End points were defined ICD-10 coding and the number of end point events during the follow-up was: 3454 deaths (all deaths), 1362 CVD deaths (ICD-10: I20–I25, R98, I61, I63, not I636, I64) and 1172 cancer deaths (ICD-10: C00–C97).

### 2.4. Statistical analysis

Statistical analyses were performed with SAS for Windows 9.3 (Cary, NC). The Cox proportional hazards model was used to estimate the association between smoking status at baseline and the risk for the above mentioned endpoints during the follow-up. For each endpoint, two models were applied: A: adjusted for age, study area and study year; B: Model A with additional adjustments for BMI, total cholesterol,

systolic blood pressure, education and marital status. All analysis was done separately for men and women, and by age-group, 45–64 years and 65–74 years. Smoking status was treated as ordinal variable in the model, and the statistical significance of the different smoking categories was tested in the same models, with the category never smoking as reference group. The proportional hazards assumption in the Cox model was tested graphically using Kaplan-Meier curves. The *p*-value for statistical significance was set as 0.05. Finally, the incidence rates were calculated dividing the number of new cases by the follow-up time of the people for each smoking category separately for sex and the two age-groups. In addition, the corresponding 95% confidence intervals for each incidence rate was calculated.

### 2.5. Ethical issues

The study was conducted according to the Helsinki Declaration of the World Medical Association. The study protocol was approved by the ethics committee as defined by the Finnish law during each study year. All participants gave an informed consent. The study report is written by following the STROBE guidelines for prospective cohort studies (Von Elm et al., 2007).

## 3. Results

Table 1 shows the characteristics of the study population according to sex and age-group at baseline. The prevalence of current smoking was 30% in men 45–64 years-of-age and 15% in men 65–74 years-of-age. The corresponding prevalence in women were as 18% and 7%, respectively.

Multifactorial adjusted (age, area, study year, BMI, systolic blood pressure, serum cholesterol, education and marital status) hazard ratios (HR) for current smoking, compared to never smoking were 2.61 (95% CI 2.15–3.18) among 45–64 years-old men and 2.59 (95% CI 2.03–3.29) in 65–74 years-old men (Table 2). The corresponding HRs for women were 3.21 (95% CI 2.47–4.19) and 3.12 (95% CI 2.09–4.68), respectively. Ex-smoking men, had a significant 30–38% increased hazard of total mortality, whereas a non-significant increase in HRs was found among older ex-smoker women only.

Multifactorial adjusted HRs of CVD mortality for current smoking in the 45–64 years-old and 65–74 years-old men were 2.67 (95% CI

**Table 1**  
Baseline characteristics of men and women aged 45–74 years in Finland, 1997, 2002 and 2007.

Age group (years)	Men		Women	
	45–64	65–74	45–64	65–74
	(n = 4885)	(n = 1631)	(n = 5209)	(n = 1305)
Age, mean (years)	55,0	69,0	54,7	69,2
Smoking, %				
Never	37,6	37,0	65,2	79,8
Ex-smokers	32,8	47,6	17,1	12,8
Current	29,6	15,4	17,7	7,4
BMI, mean ( $\text{kg}/\text{m}^2$ )	27,8	27,8	27,6	28,5
Cholesterol, mean (mmol/l)	5,70	5,42	5,75	5,80
Systolic blood pressure, mean (mmHg)	141,1	150,3	138,1	151,2
Education, %				
Lowest tertile	31,9	28,8	32,5	31,0
Middle tertile	34,1	36,4	34,2	36,3
Highest tertile	34,0	34,9	33,4	32,6
Marital status, %				
Married	79,3	78,9	72,0	54,2
Unmarried	9,7	7,7	7,9	7,9
Divorced	9,9	6,9	14,6	11,6
Widow	1,1	6,5	5,6	26,4

**Table 2**  
Hazard ratios for total mortality among men and women according to baseline smoking status, with various forms of adjustment, Finland, 1997–2013.

	Model A <sup>a</sup>		Model B <sup>b</sup>	
	HR	(95% CI)	HR	(95% CI)
<b>Men 45–64 years</b>				
Never	1	Ref	1	Ref
Ex-smokers	1.31	(1.06–1.62)	1.30	(1.05–1.60)
Current smokers	2.86	(2.36–3.47)	2.61	(2.15–3.18)
P for trend		< 0.001		< 0.001
<b>Men 65–74 years</b>				
Never	1	Ref	1	Ref
Ex-smokers	1.42	(1.16–1.73)	1.38	(1.13–1.69)
Current smokers	2.55	(2.02–3.23)	2.59	(2.03–3.29)
P for trend		< 0.001		< 0.001
<b>Women 45–64 years</b>				
Never	1	Ref	1	Ref
Ex-smokers	0.93	(0.63–1.39)	0.96	(0.64–1.43)
Current smokers	3.09	(2.39–4.00)	3.21	(2.47–4.19)
P for trend		< 0.001		< 0.001
<b>Women 65–74 years</b>				
Never	1	Ref	1	Ref
Ex-smokers	1.27	(0.86–1.88)	1.27	(0.86–1.88)
Current smokers	2.85	(1.92–4.23)	3.12	(2.09–4.68)
P for trend		< 0.001		< 0.001

Abbreviations: CI, confidence interval; HR, hazard ratio.

<sup>a</sup> Adjusted for age, area, survey year.

<sup>b</sup> Additional adjustments for body mass index, serum cholesterol, systolic blood pressure, education and marital status.

**Table 3**  
Hazard ratios for cardiovascular disease mortality among men and women according to baseline smoking status, with various forms of adjustment, Finland, 1997–2013.

	Model A <sup>a</sup>		Model B <sup>b</sup>	
	HR	(95% CI) <sup>†</sup>	HR	(95% CI)
<b>Men 45–64 years</b>				
Never	1	Ref	1	Ref
Ex-smokers	1.28	(0.90–1.83)	1.19	(0.83–1.71)
Current smokers	3.02	(2.18–4.18)	2.67	(1.92–3.72)
P for trend		< 0.001		< 0.001
<b>Men 65–74 years</b>				
Never	1	Ref	1	Ref
Ex-smokers	1.20	(0.89–1.63)	1.15	(0.85–1.56)
Current smokers	1.98	(1.36–2.89)	1.95	(1.33–2.86)
P for trend		0.001		0.002
<b>Women 45–64 years</b>				
Never	1	Ref	1	Ref
Ex-smokers	0.39	(0.09–1.62)	0.37	(0.09–1.59)
Current smokers	3.47	(1.91–6.29)	4.28	(2.29–7.99)
P for trend		< 0.001		< 0.001
<b>Women 65–74 years</b>				
Never	1	Ref	1	Ref
Ex-smokers	0.71	(0.32–1.56)	0.72	(0.33–1.59)
Current smokers	2.13	(1.04–4.37)	2.67	(1.28–5.58)
P for trend		0.064		0.017

Abbreviations: CI, confidence interval; HR, hazard ratio.

<sup>a</sup> Adjusted for age, area, survey year.

<sup>b</sup> Additional adjustments for body mass index, serum cholesterol, systolic blood pressure, education and marital status.

1.92–2.67) and 1.95 (95% CI 1.33–2.86), 4.28 (95% CI 2.29–7.99) and 2.67 (95% CI 1.28–5.58) in women, respectively (Table 3). Ex-smokers did not have an increased hazard of CVD mortality compared to never smoking during the follow-up in women. In men the increase in the hazard was not significant.

Multifactorial adjusted HRs of cancer for current smoking were 3.00 (95% CI 2.15–4.18) among 45–64 years-old men and 4.15 (95% CI 2.82–6.10) in 65–74 years-old men. The corresponding HRs for women

**Table 4**  
Hazard ratios for cancer mortality among men and women according to baseline smoking status, with various forms of adjustment, Finland, 1997–2013.

	Model A <sup>a</sup>		Model B <sup>b</sup>	
	HR	(95% CI)	HR	(95% CI)
<b>Men 45–64 years</b>				
Never	1	Ref	1	Ref
Ex-smokers	1.40	(0.98–1.99)	1.40	(0.98–2.00)
Current smokers	3.08	(2.22–4.27)	3.00	(2.15–4.18)
P for trend		< 0.001		< 0.001
<b>Men 65–74 years</b>				
Never	1	Ref	1	Ref
Ex-smokers	1.69	(1.20–2.38)	1.64	(1.16–2.31)
Current smokers	3.91	(2.68–5.70)	4.15	(2.82–6.10)
P for trend		< 0.001		< 0.001
<b>Women 45–64 years</b>				
Never	1	Ref	1	Ref
Ex-smokers	1.00	(0.61–1.65)	0.98	(0.59–1.61)
Current smokers	2.37	(1.64–3.41)	2.37	(1.64–3.44)
P for trend		< 0.001		< 0.001
<b>Women 65–74 years</b>				
Never	1	Ref	1	Ref
Ex-smokers	1.48	(0.78–2.79)	1.42	(0.74–2.70)
Current smokers	4.13	(2.36–7.21)	4.45	(2.50–7.93)
P for trend		0.064		< 0.001

Abbreviations: CI, confidence interval; HR, hazard ratio.

<sup>a</sup> Adjusted for age, area, survey year.

<sup>b</sup> Additional adjustments for body mass index, serum cholesterol, systolic blood pressure, education and marital status.

45–64 years-of-age were 2.27 (95% CI 1.64–3.44) and 4.45 (95% CI 2.50–7.93) for the 65–74 years-old, respectively (Table 4). Past smoking was statistically significantly associated with an increased hazard of cancer mortality in men 65–74 years-of-age only (HR 1.64; 95% CI 1.16–2.31).

Even though the HRs of deaths due to smoking were quite similar in both age groups (Tables 2–4), the absolute differences were much larger in the older age-group (Table 5). Among men, the risk difference between never and current smokers was 108/100.000 in the age-group 45–64 years, and 324/100.000 in the age group 65–74 years. Among women the differences were 52/100.000 and 196/100.000, respectively. In both sexes, cancer mortality was only slightly higher among never-smokers in the older age group, compared to the smokers in the younger age group.

#### 4. Discussion

Smoking related hazard of all-cause mortality was fairly similar in the 45–64 years-old and 65–74 years-old age groups, in cardiovascular mortality the hazard was higher in the younger age group and in cancer mortality in the older age group. Absolute risk difference between never and current smokers, however, were much larger among the older age group.

The following two examples demonstrate the negative public health effect of tobacco smoking: (i) Cancer mortality among never smokers in the older age group was fairly similar with the current smokers in the younger age group, i.e. smoking increases the risk of cancer death as much as 10 years of age. (ii) Men have higher CVD mortality than women, in general, but among smoking women CVD mortality was nearly as high as among never smoking men, i.e. in CVD mortality smoking is quite similar risk factor as male gender.

Our findings in regard all-cause mortality in 45–74 years-old men and women who were smoking at baseline parallels the ones of studies among different population groups of similar age (Thun et al., 2013b; Doll et al., 1994; Pirie et al., 2013; Jha et al., 2013; Nash et al., 2017). In a pooled data analysis from five contemporary cohort studies in the United States among men 55 to 74 years of age and women 60 to

**Table 5**

Age-adjusted all-cause, cardiovascular disease and cancer mortality rates in men and women according to baseline smoking status, Finland, 1997–2013.

	All-cause mortality		Cancer mortality		CVD <sup>c</sup> mortality	
	Rate <sup>a</sup>	(95% CI) <sup>b</sup>	Rate	(95% CI)	Rate	(95% CI)
<b>Men (45–64 years-old)</b>						
Never smokers	75	(63–86)	25	(19–32)	26	(19–33)
Ex-smokers	103	(88–117)	37	(28–45)	35	(27–44)
Current smokers	183	(162–203)	65	(52–77)	64	(51–76)
<b>Men (65–74 years-old)</b>						
Never smokers	250	(211–289)	78	(56–100)	115	(88–141)
Ex-smokers	335	(294–376)	128	(103–154)	131	(105–156)
Current smokers	574	(474–674)	276	(207–345)	203	(144–263)
<b>Women (45–64 years-old)</b>						
Never smokers	40	(33–46)	22	(17–26)	7	(5–10)
Ex-smokers	29	(18–39)	19	(10–27)	2	(0–5)
Current smokers	92	(74–110)	43	(31–55)	18	(10–26)
<b>Women (65–74 years-old)</b>						
Never smokers	173	(148–198)	55	(41–69)	73	(57–90)
Ex-smokers	196	(127–265)	76	(33–119)	44	(11–77)
Current smokers	369	(241–496)	207	(112–303)	104	(36–171)

Abbreviations: CI, confidence interval; CVD, cardiovascular disease.

<sup>a</sup> Per 10,000 person-years.<sup>b</sup> Confidence interval.<sup>c</sup> Cardiovascular disease.

74 years of age, (Thun et al., 2013b) all-cause mortality was at least three times as high among current smokers than among those who had never smoked. Lower risk estimates compared with ours were found in some previous studies and meta-analysis (LaCroix et al., 1991; Gellert et al., 2012b). LaCroix et al. found that smokers' mortality rates were twice those of never smokers in a prospective study of 7178 persons aged 65 years or older (LaCroix et al., 1991). Finally, The recent findings of the Consortium on Health and Ageing: Network of Cohorts in Europe and the U.S. (CHANCES) that included 489,056 participants aged  $\geq 60$  years at baseline from 22 population-based cohort studies, also from the Finnish Study, revealed that current smokers had 2-fold and former smokers had 1.3-fold increased mortality compared with never smokers (Müezzinler et al., 2015). Even though some data of our study were included in the results of the CHANCES meta-analysis, their follow-up ended in 2007, whereas our study included information on follow-up time and events until the end of 2013. In our study, former smoking was significantly associated with an increased hazard of total mortality among older men only.

Only a few prospective cohort studies have been published on the association of smoking with CVD mortality specifically focused on older adult populations (Gellert et al., 2012b; Beer et al., 2011; Gellert et al., 2013; Iso et al., 2005). A recent random effects meta-analysis of the association of smoking status with CVD mortality yielded a summary hazard ratio of 2.07 (95% CI 1.82 to 2.36) for current smokers and 1.37 (1.25 to 1.49) for former smokers compared with never smokers (Mons et al., 2015). Our results are basically in line with these findings, however, the hazard ratios among older women were much higher compared with the findings of that particular meta-analysis. Moreover our findings support results of a meta-analysis of 19 population-based prospective cohort studies with individual participant data for 897,021 European and American adults (46–74 years-old) revealing that smoking even among older adults' advances and cessation delays the hazard of developing and dying from cancer (Ordóñez-Mena et al., 2016).

There were two major changes during the study period in the Finnish Tobacco Act, passed in 1976 in an effort to reduce smoking among Finns (Heloma et al., 2012). In 2004, the indoor smoking ban was extended to all restaurants in Finland and in 2010, the public display of cigarette products at shops was banned completely (Heloma et al., 2012; Männistö et al., 2016). Thus, the results observed in 45–64 years-old ex-smoking women may be due to a shorter smoking

exposure time. Furthermore, a very recent study of randomly selected pregnancies from 1987 to 2011 observed a reduction in active cigarette smoking during pregnancy among women aged  $\geq 30$  years in Finland (Männistö et al., 2016). This may explain partially our findings in that particular group.

Surprisingly, unlike most previous studies, we did not find a higher hazard of death among men compared with women. (Kelly et al., 2008; Myint et al., 2008; Parish et al., 1995; Gellert et al., 2012a; Ordóñez-Mena et al., 2016; Mons et al., 2015; Müezzinler et al., 2015; Thun et al., 2013b) Moreover, the hazard of death seemed to be higher in women in most of our models. However, it has to be kept in mind that the 95% confidence intervals of the hazards were less precise in women and overlapped with the corresponding confidence intervals of the hazard ratios in men indicating no statistically significant difference in the hazard of death between sexes. In addition, as outlined by Thun et al., one possible reason for the increased relative risk of dying may be that in contemporary birth cohorts women had typically started smoking in their teenage whereas in earlier birth cohorts range of age at initiation was wider (Thun et al., 2013a).

Relative effect of smoking is higher, but the absolute mortality is lower in women. As smoking prevalence has decreased in men and increased in women in both the US and Finland, this result can probably be expected as the pathophysiological mechanism between smoking and adverse health effects are the same for both men and women.

Our results challenge the primary health-care systems to implement smoking cessation activities among older adult population. Previous studies have effectively shown that smoking cessation is highly and rapidly beneficial for health even at the oldest ages (Gellert et al., 2012a). As older adults who smoke often believe that they are too old to receive a benefit from stop smoking, interventions targeting them may need to be age-tailored as their motivation and behavioral certainly are different compared with younger population groups (Lam, 2012).

One of the main strengths of our study was that our analyses were conducted among large, representative population samples of middle-aged and older men and women. The follow-up was comprehensive and relatively long, enabling to apply the results directly to the general population.

However, several limitations of this study need to be considered. The assessment of our cohort is limited to a single examination performed when the participants entered the study as it is usual for large prospective studies. Information on smoking status is available only at



baseline, and therefore any modification during follow up cannot be accounted for. In general, this can lead to non-differential misclassification bias of the exposure, which in most cases could bias results towards no differences between exposure groups. A relative large proportion of smokers have quit during the follow-up but starting smoking after the age of 45 years is very rare. In addition, assessing smoking habits by questionnaire may lack validity of the participants' responses in the questionnaires. No information on package-years of smokers or ex-smokers was available in our study participants, either. However, self-reported smoking habits are commonly used in epidemiological studies and seem to be rather accurate when compared with biochemical markers of tobacco use. Another limitation is the lack of detailed information on smoking cessation. For example, differences in the HR for former versus never smoking in men and women may reflect differences in the age at which men and women quit smoking in this population. Thus, future studies may include information on age of cessation to the statistical models upon availability of data.

Finally, we cannot completely exclude either effects of residual confounding attributable to the measurement error in the assessment of confounding factors or some unmeasured dietary factors.

In conclusion, smoking increases the hazard of all-cause, CVD and cancer mortality both middle-age population and older adults. Compared with younger age groups, the relative risk of death for current smokers is similar for older age groups as health among non-smokers deteriorates as well. However, absolute risk difference between never and current smokers are larger among the older age groups due to their increased overall risk of death.

Smoking cessation seems to be beneficial also among older adult population in order to reduce CVD, cancer and total mortality. Thus, we recommend to advice routinely older adults to quit smoking and to implement special tailored interventions to reduce the smoking prevalence among that specific age group.

## Conflict of interest

Conflict of interest.

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