Testing differential associations between smoking and chronic disease across socioeconomic groups: pooled data from 15 prospective studies

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Running Head: Socioeconomic position, smoking and mortality

Abstract

Background: For the same quantity of cigarettes smoked, relative to more affluent people, socioeconomically disadvantaged people have higher levels of smoking biomarkers. This may be ascribed to inhaling cigarette smoke more deeply and more frequently and/or choosing higher tar-containing brands. We investigated whether this increased tobacco load, as captured using cotinine measurements, is associated with a greater risk of mortality in lower social groups.

Methods: We used Cox proportional hazards models stratified by socioeconomic position to calculate hazard ratios in a pooled sample of 15 English and Scottish prospective cohort studies (N=81476).

Results: During a mean (SD) follow-up of 10.3 (4.4) years, 8234 deaths occurred. Risk of total mortality (hazard ratio; 95% confidence interval) for smokers relative to never-smokers in the high (2.5; 2.1, 3.1), intermediate (2.1; 1.8, 2.4), and low (2.0; 1.9, 2.2) educational groups did not differ markedly (*p for interaction=0.61*). Similar findings emerged when using cause-specific outcomes, and occupational social class and housing tenure as socioeconomic indices.

Conclusion: Contrary to our hypothesis, we found no indication that chronic disease mortality associated with smoking was higher in disadvantaged people.

Keywords: cotinine; smoking; socioeconomic position; cancer; cardiovascular disease; mortality

Introduction

It is well documented that cigarette smoking is markedly associated with increased risk of developing chronic diseases, particularly several cancers and cardiovascular disease (CVD).[1] It is also well known that people in lower socioeconomic groups are much more likely to smoke than those from advantaged backgrounds[2]—in 2016, for instance, 21% of adults in England without formal qualifications smoked, compared with only 9% of those with a university degree.[3] This inequality has increased in recent years—between 2001 and 2012, smoking prevalence decreased among those with managerial or professional occupations (from 20% to 14%) while it remained unchanged among people in routine and manual occupations in the UK (33%).[4] Accordingly, the population impact of smoking is greater in socioeconomically disadvantaged groups.[2,5] In addition to a greater population prevalence of smoking among people in lower socioeconomic groups, there is evidence that, for the same number of cigarettes smoked, less advantaged people have higher levels of smoking biomarkers than more advantaged people.[2] This may be due to the manner in which individuals from lower socioeconomic groups smoke—for example by inhaling more deeply and more frequently and/or by choosing higher tar-containing brands.[2] This increased tobacco load may lead to a greater risk of mortality—that is, higher smoking-related vulnerability—among disadvantaged groups. The few studies that have tested this hypothesis have revealed inconsistent findings. For instance, in a large Danish cohort, Nordahl *et al*. found that self-reported smoking carried a greater risk of stroke mortality among lower educated groups compared with higher educated groups.[6] However, in a large Belgian cohort, Charafeddine *et al*. found no evidence of differential vulnerability to self-reported smoking on all-cause mortality.[7] Crucially, studies have exclusively relied on self-reported smoking,[6-8] which is subject to reporting bias, particularly among people with lower education,[9] and this may

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generate an inflated hazard in poorer individuals. Thus, we pooled a series of cohort studies with cause-specific mortality and measured cotinine data to test the hypothesis that smoking may exert a greater influence on health in disadvantaged populations.

Methods

Participants originated from the Health Survey for England (HSE) and the Scottish Health Survey (SHS), both of which have been described in detail elsewhere.[10,11] These are population-representative, cross-sectional health examination studies conducted in private households in England and Scotland. We pooled data from 12 HSE (1994 to 2008), and three SHS (1995, 1998, and 2003) studies in which response ranged from 68% to 77%.[10,12] Following participation in these surveys, consenting participants (88%) were linked to National Health Service mortality records up to December 2009 (SHS)[12] and mid-February 2011 (HSE).[10]

We created a baseline smoking variable by cross-referencing participants' self-reported smoking against their measured salivary or serum cotinine levels (the correlation between salivary and cotinine levels is very high)[13]: 1) never smokers were defined by self-reported "never smoker" *and* salivary cotinine below 12 ng/mL or serum cotinine below 9 ng/mL; 2) ex-smokers self-reported being an "ex-smoker" *and* had salivary cotinine below 12 ng/mL or serum cotinine below 9 ng/mL; and 3) current smokers comprised self-reported smokers and individuals with salivary cotinine ≥12 ng/mL, or serum cotinine ≥9 ng/mL. We selected endpoints that are known to have a relationship with cigarette smoking:[14] death from all causes, certain cancers (lung, pancreas, esophagus, bladder, kidney, oral, liver, stomach, leukemia), all CVD, coronary heart disease (CHD), stroke, and chronic obstructive pulmonary disease (COPD). We used three socioeconomic position variables, including: age when finished full-time education: high (18 years or above), intermediate (16-17 years), and low (15 years or less);

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occupational social class based on the UK Registrar's General categories: high (professional, managerial and technical), intermediate (skilled non-manual), and low (manual occupations); and housing tenure (owner or renter). As covariates, we included sex, age at baseline (continuous), body mass index (weight in kilograms divided by height in meters squared), and dichotomized physical activity (any weekly moderate to vigorous exercise) and excessive alcohol intake (as ≥168 grams/week for men, and ≥112 grams/week for women).

We included study members in the analytical sample if they had data on cotinine, self-reported smoking, socioeconomic variables, covariates (eFigure 1; http://links.lww.com/EDE/B412) and if they consented to mortality data linkage. For each socioeconomic and smoking group, we calculated age-standardized mortality rates per 10000 person-years (for five age groups) with the direct method using the 2015 European Standard Population as the standard. Subsequently, having ascertained via Schoenfeld residuals that the proportional hazards assumption was not violated, we calculated hazard ratios (HR) and associated 95% confidence intervals (95% CI) using Cox proportional hazard models. We stratified the analysis by socioeconomic position, adjusting the effect estimate first for age, sex, and cohort, then additionally for BMI, physical activity, and excessive alcohol intake. We imputed missing values for the last three variables using five imputations. Statistical significance for multiplicative interaction was assessed using the likelihood ratio test comparing the models with and without the product term of smoking and socioeconomic position. We also tested for additive interaction by calculating the Relative Excess Risk due to Interaction, the Proportion of Disease Attributable to Interaction, and the Synergy Index. In sensitivity analyses, we repeated the analysis focusing on premature all-cause and cause-specific mortality and three types of smoking exposure (number of cigarettes smoked per day; cotinine level; and self-reported

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smoking). Analyses were conducted using Stata statistical software version 14 (StataCorp,

College Station, TX).

Results

Our analytical sample comprised 81476 participants with complete data on cotinine, self-reported smoking, education, age, sex, and mortality (eFigure 1;

http://links.lww.com/EDE/B412). The mean age of participants at baseline was 46 years (range:

16 to 97 years), and 53% were women (eTable 1; http://links.lww.com/EDE/B412). During a

mean (SD) follow-up time of 10.3 (4.4) years, 8234 deaths occurred (1170 from smoking-related

cancers, 4078 from CVD, 690 from stroke, 1412 from CHD, and 2568 from COPD). The age-standardized mortality rate was highest among smokers in lower socioeconomic groups. Thus,

the rate (95% CI) per 10000 person-years for death from all causes was 243 (230, 256) among

smokers with low education versus 182 (156, 208) among smokers with high education; for

smoking-related cancer, the corresponding rates were 47 (42, 52) versus 28 (20, 36); and for

CVD, 110 (102, 118) versus 95 (74, 116) (Figure). Both the basic and multivariable models

yielded similar findings, thus we present results from the latter only. As anticipated, relative to

non-smokers, cigarette smoking was related to an elevated risk of death from all causes in the

high- (HR; 95% CI: 2.5; 2.1, 3.1), intermediate- (2.1; 1.8, 2.4), and low-education group (2.0;

1.9, 2.2). HRs (95% CI) for smoking-related cancers were 4.4 (3.0, 6.5) in the high-education

group, 4.4 (3.0, 6.6) in the medium group, and 4.3 (3.5, 5.2) in the low group; and, for CVD, 3.8

(2.6, 5.5), 2.4 (1.8, 3.2), and 2.5 (2.2, 2.9) (Figure). There was, however, no indication that

smoking in the more basic educational group was more strongly associated with mortality in

comparison to the higher educational categories as based on tests for interaction, multiplicative

or additive (p-values for interaction ≥0.21). We observed similar patterns of association and

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mortality rates for death from stroke, CHD, and COPD (eFigure 2;

http://links.lww.com/EDE/B412). Results were also similar when substituting educational level

for occupational social class (eFigure 3; http://links.lww.com/EDE/B412) and housing tenure

(eFigure 4; http://links.lww.com/EDE/B412) as the socioeconomic measure of interest. Our

findings were robust under a range of sensitivity analyses, including three types of smoking

exposure (eFigure 5-19; http://links.lww.com/EDE/B412). Finally, we found no strong evidence

of heterogeneity in the association between mortality and smoking across the 15 included cohort

studies.

Discussion

We found no support for the hypothesis of differential vulnerability to the effects of

smoking on several chronic disease outcomes across different socioeconomic groups. Comparing

our results to the literature is not straightforward due to differing methodologic approaches,

different smoking and socioeconomic indicators, and a range of mortality outcomes. However,

Lewer *et al*.,[15] in a similar analysis to ours, also found no evidence of interaction between

smoking and socioeconomic position on death from all causes and from COPD, while revealing

higher absolute risk of smoking among more disadvantaged groups.

Some strengths of our study include the large and representative sample size which

provided sufficient power to test for interaction, the use of an array of smoking-related chronic

disease outcomes, and, for the first time to our knowledge, the utilization of an objective

indicator of smoking exposure. Our work is of course not without its shortcomings. Smoking was

only measured at baseline and, given the continuous decline of smoking prevalence in the

population, it is likely that many participants decreased their intake or ceased completely during

follow-up.

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In conclusion, in a large and representative series of cohorts of the English and Scottish populations, we found no indication of differential association by socioeconomic disadvantage between smoking and death from a range of major chronic diseases known to be related to tobacco smoking.

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Figure footnote

Association between cigarette smoking and death from all causes, smoking-related cancer, and CVD, according to educational level, from pooled cohort samples of 12 Health Survey for England and 3 Scottish Health Survey studies conducted between 1994 and 2008 (N = 81476). Educational level derived from age when finished full-time education: high (18 years or above), intermediate (16-17 years), and low (15 years or below). Hazards ratios (95% CI) from Cox proportional hazards model are adjusted for age, sex, cohort, body mass index, physical activity and excessive alcohol, and are indicated by squares and the 95% confidence interval by the horizontal lines. X-axes are natural log-scaled. ASMR: Age-standardized mortality rates calculated using the 2015 European Standard Population as the standard.

Figure

ALL CAUSE

	Deaths / persons at risk	HR (95% CI)		ASMR (95% CI)
High education				
Never smoker	301 / 13960	1.0 (ref.)		97 (86, 108)
Former smoker	244 / 3859	1.1 (0.9, 1.4)		111 (97, 125)
Smoker	188 / 5400	2.5 (2.1, 3.1)		182 (156, 208)
Intermediate education				
Never smoker	429 / 12043	1.0 (ref.)		101 (91, 111)
Former smoker	401 / 4964	1.2 (1.1, 1.4)		128 (115, 141)
Smoker	364 / 9332	2.1 (1.8, 2.4)		215 (193, 237)
Low education				
Never smoker	1304 / 8350	1.0 (ref.)		123 (116, 130)
Former smoker	1410 / 6510	1.2 (1.1, 1.3)		153 (145, 161)
Smoker	1412 / 7449	2.0 (1.9, 2.2)		243 (230, 256)

HR (95% CI) — 1 2 3 4 5 6 7

SMOKING-RELATED CANCER

	Deaths / persons at risk	HR (95% CI)		ASMR (95% CI)
High education				
Never smoker	22 / 15378	1.0 (ref.)		3 (2, 4)
Former smoker	36 / 4285	2.5 (1.5, 4.3)		11 (7, 15)
Smoker	50 / 5944	4.4 (3.0, 6.5)		28 (20, 36)
Intermediate education				
Never smoker	41 / 13269	1.0 (ref.)		6 (4, 8)
Former smoker	71 / 5602	2.2 (1.5, 3.3)		17 (13, 21)
Smoker	79 / 10256	4.4 (3.0, 6.6)		35 (27, 43)
Low education				
Never smoker	135 / 9592	1.0 (ref.)		10 (8, 12)
Former smoker	272 / 8058	2.0 (1.6, 2.5)		20 (18, 22)
Smoker	391 / 8705	4.3 (3.5, 5.2)		47 (42, 52)

HR (95% CI) — 1 2 3 4 5 6 7

CARDIOVASCULAR DISEASE

	Deaths / persons at risk	HR (95% CI)		ASMR (95% CI)
High education				
Never smoker	120 / 14795	1.0 (ref.)		49 (40, 58)
Former smoker	91 / 3955	1.2 (0.9, 1.8)		47 (37, 57)
Smoker	79 / 5764	3.8 (2.6, 5.5)		95 (74, 116)
Intermediate education				
Never smoker	169 / 12538	1.0 (ref.)		51 (43, 59)
Former smoker	169 / 5024	1.3 (1.0, 1.7)		63 (54, 72)
Smoker	137 / 9939	2.4 (1.8, 3.2)		91 (76, 106)
Low education				
Never smoker	600 / 8125	1.0 (ref.)		62 (57, 67)
Former smoker	673 / 6395	1.4 (1.2, 1.6)		77 (71, 83)
Smoker	658 / 7752	2.5 (2.2, 2.9)		110 (102, 118)

HR (95% CI) — 1 2 3 4 5 6 7