

# Smoking and Risk of Coronary Heart Disease in Younger, Middle-Aged, and Older Adults

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Despite decades of attempts to reduce smoking prevalence, 20% of persons living in the United States still smoke, and smoking remains the number one cause of preventable mortality.<sup>1,2</sup> A leading cause of death attributable to smoking is coronary heart disease (CHD).<sup>3</sup>

CHD etiology differs across age groups. For instance, relatively more cases of CHD among young adults may be attributable to genetic causes.<sup>4,5</sup> Hence, among young adults, who are at low absolute risk for CHD, smoking may be considered a risk factor that does not cause disease until later in life.

At the other end of the age scale, research suggests that the relative risk of CHD associated with smoking attenuates in old age.<sup>6</sup> This finding could erroneously suggest that smoking is only a weak risk factor for the elderly and that smoking prevention should therefore be of low priority because quality-of-life issues outweigh the net gain in health. With an increasingly older population, understanding patterns in the strength of risk factors by age is of considerable interest.

The incidence of CHD varies considerably by age; it is very low in women younger than 40 years and in men younger than 50 years.<sup>7</sup> For this reason, the statistical power to investigate effects of smoking on CHD in young adults is limited. We pooled the data from 8 prospective cohort studies with information on smoking and potential confounders, including diet, to gain a sufficient sample size to investigate associations between smoking and CHD in subsets of populations defined by age.

## METHODS

The Pooling Project on Diet and Coronary Heart Disease comprised data from 12 prospective cohort studies. Each study had at least 150 incident CHD cases, assessed usual dietary intake, and conducted a validation study of the

**Objectives.** We investigated associations of smoking and coronary heart disease (CHD) by age.

**Methods.** Data came from the Pooling Project on Diet and Coronary Heart Disease (8 prospective studies, 1974–1996; n = 192 067 women and 74 720 men, aged 40–89 years).

**Results.** During follow-up, 4326 cases of CHD were reported. Relative to never smokers, CHD risk among current smokers was highest in the youngest and lowest in the oldest participants. For example, among women aged 40 to 49 years the hazard ratio was 8.5 (95% confidence interval [CI] = 5.0, 14) and 3.1 (95% CI = 2.0, 4.9) among those aged 70 years or older. The largest absolute risk differences between current smokers and never smokers were observed among the oldest participants. Finally, the majority of CHD cases among smokers were attributable to smoking. For example, attributable proportions of CHD by age group were 88% (40–49 years), 81% (50–59 years), 71% for (60–69 years), and 68% (≥ 70 years) among women who smoked.

**Conclusions.** Among smokers, the majority of CHD cases are attributable to smoking in all age groups. Smoking prevention is important, irrespective of age. (*Am J Public Health.* 2014;104:96–102. doi:10.2105/AJPH.2012.301091)

diet assessment method. The project's studies were the Adventists Health Study,<sup>8</sup> Atherosclerosis Risk in Communities Study,<sup>9</sup> Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study (ATBC),<sup>10</sup> Finnish Mobile Clinic Health Examination,<sup>11</sup> Glostrup Population Study,<sup>12</sup> Health Professionals Follow-up Study,<sup>13</sup> Israeli Ischemic Heart Disease Study,<sup>14</sup> Iowa Women's Health Study,<sup>15</sup> Nurses' Health Study (NHS),<sup>16</sup> Västerbotten Intervention Program,<sup>17</sup> and Women's Health Study.<sup>18</sup> For our analysis, we excluded data from the Adventists, Finnish, and Israeli studies because of missing information on 1 or more potential confounders (education, physical activity, alcohol intake). We also excluded the Iowa study because of self-reported information on CHD. Characteristics of the 8 included studies are presented in Table 1. We divided NHS data into 2 segments: NHSa (1980–1986) and NHSb (1986–1996) to take advantage of repeated-exposure assessment. The ATBC included only men who smoked. To verify that this did not affect our

results, we repeated the analyses without the ATBC participants, without significant changes to our results.

We excluded participants younger than 40 years. Because the presence of clinical disease itself may change smoking habits, we also excluded participants who reported a history of cardiovascular disease, diabetes or cancer (except nonmelanoma skin cancer) at baseline. We excluded participants with missing information on smoking or potential confounders from further analyses.

## Measurements

We harmonized variables from the individual studies. We harmonized information on smoking into 2 variables: smoking status (never, former, current) and amount of smoking for current smokers (assuming 1 cigarette to be equivalent to 1 g of tobacco, 1 cheroot or 1 cigar to be equivalent to 3 g of tobacco, and 1 pipe to be equivalent to 5 g of tobacco). We assessed average daily alcohol intake from

**TABLE 1—Characteristics of Studies and Participants: Pooling Project on Diet and Coronary Heart Disease, 1974–1996**

Study	Participants			Study Years	Women, %	Age, Years, Mean (Range)	Current Smoker, %	Follow-Up, Person-Years	CHD Cases	
	Enrolled, No.	Step 1, <sup>a</sup> No.	Final, <sup>b</sup> No.						Deaths, No.	Total Events, No.
ARIC	15 732	11 721	11 572	1987–1989	55	53.8 (44–67)	25	102 744	68	381
ATBC	29 133	21 141	21 120	1984–1988	0	56.5 (50–70)	100	121 692	534	1338
GPS	4072	3324	2803	1974–1995	54	50.0 (35–70)	43	25 021	93	107
HPFS	51 529	41 754	38 654	1986–1988	0	52.6 (39–77)	29	354 990	384	1167
NHSa	92 468	81 415	79 479	1980–1982	100	46.8 (35–67)	29	501 752	95	390
NHSb	73 666	61 706	60 083	1986–1988	100	52.4 (40–67)	21	591 107	200	672
VIP	25 732	20 076	18 244	1992–1996	54	50.0 (39–70)	21	75 420	37	134
WHS	39 876	37 272	34 832	1992–1995	100	52.0 (38–89)	13	178 192	9	137
Total	332 208	278 409	266 787	1974–1996	58	51.8 (35–89)	35	1 950 918	1420	4326

Note. ARIC = Atherosclerosis Risk in Communities Study; ATBC = Alpha-Tocopherol Beta-Carotene Cancer Prevention Study; CHD = coronary heart disease; GPS = Glostrup Population Study; HPFS = Health Professionals Follow-up Study; NHSa = Nurses' Health Study (1980–1986); NHSb = Nurses' Health Study (1986–1996); VIP = Västerbotten Intervention Program; WHS = Women's Health Study.

<sup>a</sup>Sample size after exclusion of participants with baseline cardiovascular disease, cancer, and diabetes.

<sup>b</sup>Sample size after exclusion of participants with missing information on smoking status and other covariates.

a question about typical intake of alcohol-containing beverages. For each beverage, we calculated grams of daily alcohol intake from responses on the amount and frequency of intake and the alcohol content of the beverage (according to study-specific conversion factors). We calculated total alcohol intake (g/day) by adding the beverage-specific intakes.

Physical activity measures varied across cohorts, calculated either according to an energy expenditure score of weekly time spent on various activities during the past year (Atherosclerosis Risk in Communities Study, Health Professionals Follow-up Study, NHS, Västerbotten Intervention Program, Women's Health Study) or according to the intensity of the average weekly physical activity during the past year (ATBC, Glostrup Population Study). We harmonized these measures to a 5-level variable from 1 (least active) to 5 (most active).<sup>19–21</sup> We calculated body mass index (defined as weight in kilograms divided by the square of height in meters) from self-reported height and weight (NHS, Women's Health Study, Health Professionals Follow-Up Study) or from measurements taken during physical examinations (Glostrup Population Study, ATBC, Atherosclerosis Risk in Communities Study, Västerbotten Intervention Program).

Studies determined dietary intake at baseline with a food-frequency questionnaire or a dietary history interview. We calculated total energy intake as the sum of energy intake

derived from fat, carbohydrates, and protein. Derived exposure measures were dietary intake of saturated, monounsaturated, and polyunsaturated fatty acids; fiber; and cholesterol. We evaluated the validation and repeatability of the diet assessment methods and found them to be reasonable for population studies of the nutrients of interest.

Our outcome of interest was incident CHD events (fatal and nonfatal). We applied standardized criteria for case ascertainment.<sup>22</sup>

### Statistical Analysis

We identified all known and suspected risk factors not believed to be on the causal pathway between exposure and disease as potential confounders. Hence, our multivariate models incorporated educational level (< high school, high school, > high school), body mass index (< 18.5, 18.5–24.9, 25.0–29.9, and  $\geq 30$  kg/m<sup>2</sup>), total energy intake (kcal/day), and energy-adjusted quintiles of cholesterol, dietary fiber, saturated fat, monounsaturated fat, and polyunsaturated fat intakes. We modeled alcohol intake continuously and included a linear and root-squared term to account for the U-shaped association between alcohol and risk of CHD.<sup>23</sup>

We combined individual studies with an aggregated pooled-analysis technique allowing for calculation of a single pooled exposure–effect estimate.<sup>24</sup> We estimated hazard ratios (HRs) of CHD by Cox proportional hazards regression with age as underlying time scale,

allowing for delayed entry and including study as a fixed effect. We followed participants from baseline to date of CHD (fatal or nonfatal), death, or end of follow-up, whichever occurred first. We truncated follow-up periods longer than 10 years (Glostrup Population Study, Atherosclerosis Risk in Communities Study) to reduce heterogeneity between studies. We estimated multivariate adjusted absolute risks (incidence rates) by Poisson regression. We calculated risk differences and derived 95% confidence intervals (CIs) by bootstrap estimation (5000 replications), with the 2.5 and 97.5 percentiles of the distribution as lower and upper limits. We adjusted all models for year of baseline questionnaire, education, alcohol intake, body mass index, physical activity, total energy intake, and intakes of polyunsaturated fat, monounsaturated fat, saturated fat, fiber, and cholesterol.

We estimated the attributable fractions among current smokers as (RR-1)/RR, where RR (relative risk) was substituted with HR for CHD among current smokers relative to never smokers.<sup>25</sup> We analyzed the study population separately for 4 age groups: 40 to 49 years, 50 to 59 years, 60 to 69 years, and 70 years and older. We updated all variables during follow-up and assigned participants to the appropriate age category; thus an individual could contribute person-time at risk to more than 1 age category.

We assessed heterogeneity between study-specific effects by including an interaction term between smoking and study origin under the null hypothesis of no between-study

differences in the HRs of CHD by smoking. We also compared the pooled risk estimates after systematically excluding each study from the analysis, 1 at a time.

RESULTS

The population of the 8 included studies comprised 192 067 women and 74 720 men

**TABLE 2—Baseline Characteristics of Participants by Gender and Smoking Status: Pooling Project on Diet and Coronary Heart Disease, 1974–1996**

Characteristic	Total	Never Smokers	Past Smokers	Current Smokers, 1–14 Grams/Day	Current Smokers, ≥ 15 Grams/Day
<b>Women</b>					
Participants, no.	192 067	87 855	59 699	26 6601	17 912
Age, y, mean (SD)	50.4 (7.6)	50.5 (7.7)	50.8 (7.6)	50.8 (7.3)	47.4 (6.8)
Education < high school, no. (%)	8276 (4)	3978 (6)	1844 (3)	1937 (7)	517 (3)
Alcohol intake, g/d (5th, 95th percentile)	1.8 (0.0, 28)	0.9 (0.0, 16)	2.7 (0.0, 29)	2.2 (0.0, 35)	2.7 (0.0, 37)
BMI, kg/m <sup>2</sup> , mean (SD)	25.0 (4.7)	25.3 (4.8)	25.2 (4.7)	24.4 (4.3)	23.9 (4.1)
Physical inactivity, No. (%)	66 248 (25)	28 742 (33)	17 718 (30)	8878 (33)	10 910 (61)
Polyunsaturated fat intake, <sup>a</sup> g/d (5th, 95th percentile)	5.4 (3.3, 8.4)	5.4 (3.4, 8.3)	5.5 (3.3, 8.5)	5.5 (3.4, 8.7)	5.0 (3.0, 8.2)
Monounsaturated fat intake, <sup>a</sup> g/d (5th, 95th percentile)	13.1 (8.1, 20.5)	12.9 (8.1, 20.3)	12.6 (7.8, 19.9)	12.9 (8.5, 19.2)	16.1 (9.7, 22.7)
Saturated fat intake, <sup>a</sup> g/d (5th, 95th percentile)	12.8 (7.7, 20.0)	12.6 (7.6, 19.8)	12.3 (7.4, 19.5)	12.8 (8.1, 19.5)	15.9 (9.7, 22.1)
Fiber intake, g/d (5th, 95th percentile)	15.4 (8.4, 25.7)	15.9 (8.9, 26.2)	16.0 (8.9, 26.3)	14.7 (8.4, 24.1)	11.7 (6.4, 20.3)
Cholesterol intake, mg/d (5th, 95th percentile)	254 (139-458)	250 (136-452)	249 (137-454)	243 (139-263)	310 (173-519)
Total energy intake, Mcal/d (5th, 95th percentile)	1.60 (0.90, 2.63)	1.63 (0.92, 2.65)	1.60 (0.91, 2.61)	1.60 (0.89, 2.66)	1.49 (0.81, 2.49)
Hypertension, no. (%)	35 637 (19)	16 839 (19)	11 542 (19)	4786 (18)	2470 (14)
Dyslipidaemia, no. (%)	20 850 (11)	9637 (11)	7109 (12)	2922 (11)	1182 (7)
<b>Men</b>					
Participants, no.	74 720	24 594	21 982	7403	20 741
Age, y, mean (SD)	54.0 (8.4)	51.7 (9.1)	54.1 (9.1)	55.4 (7.8)	56.3 (5.7)
Education < high school, no. (%)	20 773 (28)	2588 (11)	2775 (13)	4082 (55)	11 328 (55)
Alcohol intake, g/d (5th, 95th percentile)	6.5 (0.0, 47)	3.1 (0.0, 32)	7.1 (0.0, 44)	6.8 (0.0, 45)	12.2 (0.0, 64)
BMI, kg/m <sup>2</sup> , mean (SD)	25.8 (3.5)	25.5 (3.4)	26.0 (3.4)	25.9 (3.5)	26.1 (3.8)
Physical inactivity, no. (%)	18 850 (25)	4466 (18)	4021 (18)	2096 (28)	8267 (40)
Polyunsaturated fat intake, <sup>a</sup> g/d (5th, 95th percentile)	5.4 (3.3, 8.9)	5.5 (3.6, 8.4)	5.6 (3.6, 8.6)	5.0 (3.2, 9.4)	4.8 (3.0, 9.8)
Monounsaturated fat intake, <sup>a</sup> g/d (5th, 95th percentile)	12.8 (8.5, 16.8)	12.4 (7.9, 16.6)	12.5 (8.0, 17.0)	13.1 (9.7, 16.9)	13.4 (10.1, 16.8)
Saturated fat intake, <sup>a</sup> g/d (5th, 95th percentile)	13.2 (7.5, 23.8)	11.5 (6.8, 17.7)	11.6 (6.9, 17.8)	16.7 (8.9, 25.2)	18.3 (10.5, 26.4)
Fiber intake, g/d (5th, 95th percentile)	19.8 (11.5, 32.3)	21.0 (12.6, 34.5)	20.2 (12.0, 33.1)	19.5 (11.4, 30.2)	18.1 (10.3, 29.0)
Cholesterol intake, mg/d (5th, 95th percentile)	322 (174-573)	283 (160-477)	291 (166-491)	352 (182-591)	403 (243-660)
Total energy intake, Mcal/d (5th, 95th percentile)	2.14 (1.15, 3.67)	1.94 (1.10, 3.20)	1.90 (1.08, 3.17)	2.41 (1.27, 3.91)	2.63 (1.45, 4.17)
Hypertension, no. (%)	14 388 (19)	4479 (18)	5038 (23)	1350 (18)	3521 (17)
Dyslipidaemia, no. (%)	5076 (9)	2052 (8)	2294 (10)	256 (8)	474 (12)

<sup>a</sup>Energy adjusted.

(Table 1). The mean age was 51.8 years (range = 38–77 years). At baseline, 35% were current smokers.

Distributions of covariates according to smoking status were comparable across cohorts. For example, current smokers generally drank more alcohol than never smokers, were less physically active, and had lower intakes of fiber and saturated fat (Table 2).

During a mean follow-up time of 7.2 years among women and 8.0 years among men, studies reported 1365 and 2961 CHD cases, respectively. In pooled analysis, the multivariate adjusted HR (relative to female never smokers) was 1.30 (95% CI = 1.11, 1.51) among women who were past smokers, 4.12 (95% CI = 3.57, 4.76) among women who smoked 1 to 14 grams per day, and 4.85 (95% CI = 4.00, 5.88) among women who smoked more than 15 grams per day. Corresponding HRs among men were 1.16 (95% CI = 1.03, 1.30), 1.95 (95% CI = 1.66, 2.28), and 2.35 (95% CI = 2.03, 2.71; Table 3). We detected no sign of heterogeneity between studies ( $P = .3$  in women and

$P = .11$  in men). Regressions that excluded each study in turn confirmed that no single study had particular influence on the pooled estimates. Hence, we considered the pooled HRs to be appropriate summaries of the study-specific data.

We estimated multivariate-adjusted HRs, incidence rate differences, and attributable fractions of CHD in 4 age groups (40–49, 50–59, 60–69, and  $\geq 70$  years; Figures 1 and 2). The HR of CHD in current smokers, relative to never smokers, was highest in the youngest and lowest in the oldest women and men. For example, the HR among female current smokers aged 40 to 49 years was 8.5 (95% CI = 5.0, 14) and 3.1 (95% CI = 2.0, 4.9) among those aged 70 years and older. By contrast, we observed higher incidence rate differences in the oldest women and men. For example, the incidence rate differences (per 10 000 person-years) between women who smoked and never smokers were 4.4 (95% CI = 2.8, 6.4) among participants aged 40 to 49 years and 32 (95% CI = 15, 54) among those aged 70 years and older. The

CHD-attributable fractions among smokers were highest among the youngest and lowest among the oldest women and men. However, in all age groups and among both men and women, a substantial proportion of cases among smokers could be attributed to smoking. For example, attributable fractions among women who smoked were 88% (95% CI = 82%, 94%) for participants aged 40 to 49 years, 81% (95% CI = 77%, 85%) for those aged 50 to 59 years, 71% (95% CI = 65%, 76%) for those aged 60 to 69 years, and 68% (95% CI = 53%, 82%) for those aged 70 years and older.

## DISCUSSION

In our pooled data set of 192 067 women and 74 720 men, we found that a large proportion of CHD cases among smokers were attributable to smoking in all age groups. This proportion was highest among currently smoking women (88%) and men (79%) aged 40 to 49 years. We also found that although the HR attenuated with increasing age, the rate difference increased with age. As a measure of absolute risk, the rate difference is usually considered a more relevant effect measure to public health than a relative measure such as HR because it is a more direct indication of the number of individuals affected.

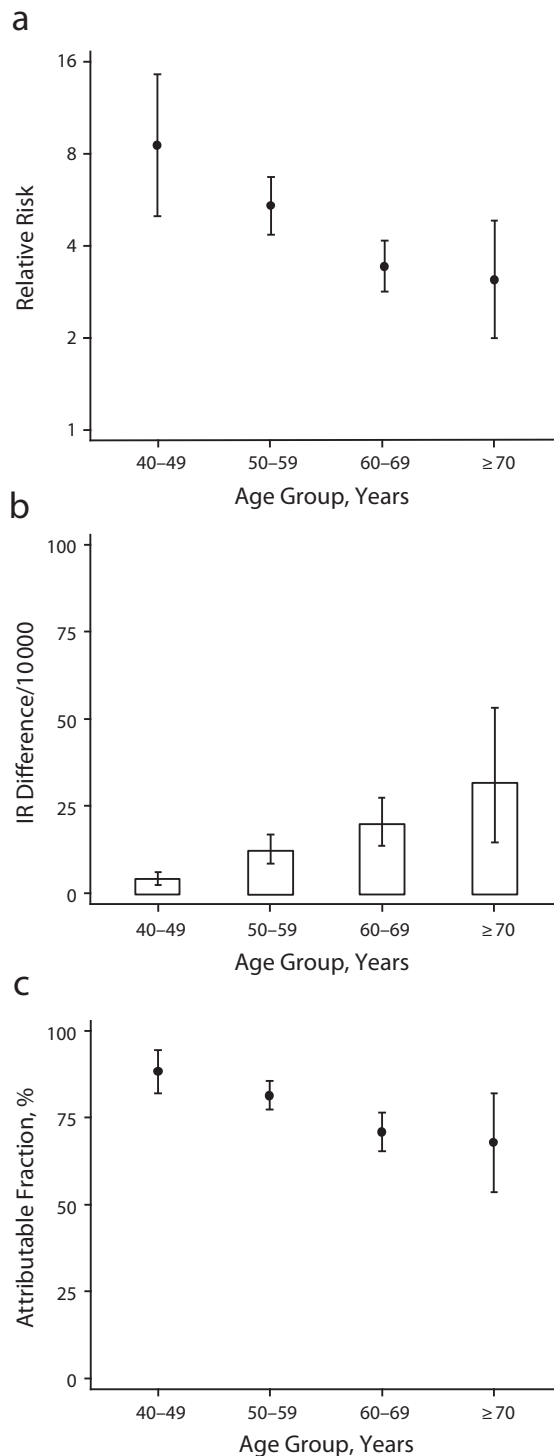
These results have important public health implications. First, smoking prevention should remain a high priority, and equally so in all age groups. CHD events caused by smoking also occur in young adults, in our study defined as age 40 to 49 years. This finding does not support the standard belief that smoking-related CHD does not occur until old age. The incidence of CHD may be low in this age group, and hence the burden of disease is much smaller than in the older age groups, but this finding constitutes important knowledge for public health.

Ours was one of only a few studies to focus on the effect of smoking on CHD according to age.<sup>26–28</sup> We analyzed a large body of data with thorough assessments of relevant potential confounders, including diet. The size of the study population allowed us to perform subset analyses exploring the association between smoking and CHD in strata of younger men and women, which even large individual

**TABLE 3—Study-Specific and Adjusted Pooled Hazard Ratios of Coronary Heart Disease by Smoking Status: Pooling Project on Diet and Coronary Heart Disease, 1974–1996**

Study	Total	Never Smokers	Past Smokers	Current Smokers, 1–14 g/d	Current Smokers, $\geq 15$ g/d
<b>Women, No. or HR (95% CI)</b>					
CHD cases		378	306	454	227
ARIC	6406	1.00 (Ref)	0.61 (0.32, 1.18)	3.68 (2.26, 6.00)	3.48 (2.17, 5.58)
GPS	1509	1.00 (Ref)	2.76 (1.18, 6.48)	3.35 (1.45, 7.75)	1.68 (0.72, 3.96)
NHS (1980–1986)	79 479	1.00 (Ref)	1.53 (1.12, 2.09)	2.92 (1.98, 4.30)	5.42 (4.16, 7.05)
NHS (1986–1996)	60 083	1.00 (Ref)	1.32 (1.07, 1.63)	4.20 (3.47, 5.08)	NA
VIP	9758	1.00 (Ref)	2.85 (0.68, 2.00)	7.82 (2.18, 28.0)	NA
WHS	34 832	1.00 (Ref)	1.37 (0.89, 2.13)	5.63 (3.67, 8.65)	NA
Pooled	192 067	1.00 (Ref)	1.30 (1.11, 1.51)	4.12 (3.57, 4.76)	4.85 (4.00, 5.88)
<b>Men, No. or HR (95% CI)</b>					
CHD cases		567	672	375	1347
ARIC	5166	1.00 (Ref)	1.49 (1.05, 2.12)	1.06 (0.54, 2.06)	2.91 (2.01, 4.21)
GPS	1294	1.00 (Ref)	1.41 (0.39, 5.11)	2.30 (0.91, 5.83)	1.16 (0.34, 3.96)
HPFS	38 654	1.00 (Ref)	1.13 (0.99, 1.28)	1.59 (1.16, 2.18)	2.24 (1.83, 2.73)
VIP	8486	1.00 (Ref)	1.01 (0.63, 1.61)	2.86 (1.80, 4.52)	NA
Pooled	74 720	1.00 (Ref)	1.16 (1.03, 1.30)	1.95 (1.66, 2.28)	2.35 (2.03, 2.71)

Note. ARIC = Atherosclerosis Risk in Communities Study; CHD = coronary heart disease; CI = confidence interval; GPS = Glostrup Population Study; HPFS = Health Professionals Follow-up Study; HR = hazard ratio; NA = not applicable because of limited number of cases; NHS = Nurses' Health Study; VIP = Västerbotten Intervention Program; WHS = Women's Health Study. Multivariable hazard ratios were adjusted for age, year of baseline questionnaire, study origin, alcohol intake, body mass index, education, physical activity, and energy, polyunsaturated fat, monounsaturated fat, saturated fat, fiber, and cholesterol intake.



Note. Vertical bars represent 95% confidence intervals. Analyses adjusted for year of baseline questionnaire, study origin, education, alcohol intake, body mass index, physical activity, total energy intake, and polyunsaturated fat, monounsaturated fat, saturated fat, fiber, and cholesterol intake.

**FIGURE 1—Coronary heart disease (CHD) among women by (a) relative risk among current smokers relative to never smokers, (b) incidence rate (IR) differences among current smokers relative to never smokers, and (c) attributable fractions among current smokers.**

cohorts do not have the power to address. Our findings were strengthened by the prospective design, which provided information on the sequence of events, allowing for conclusions on causality, assuming proper confounding control.

### Limitations

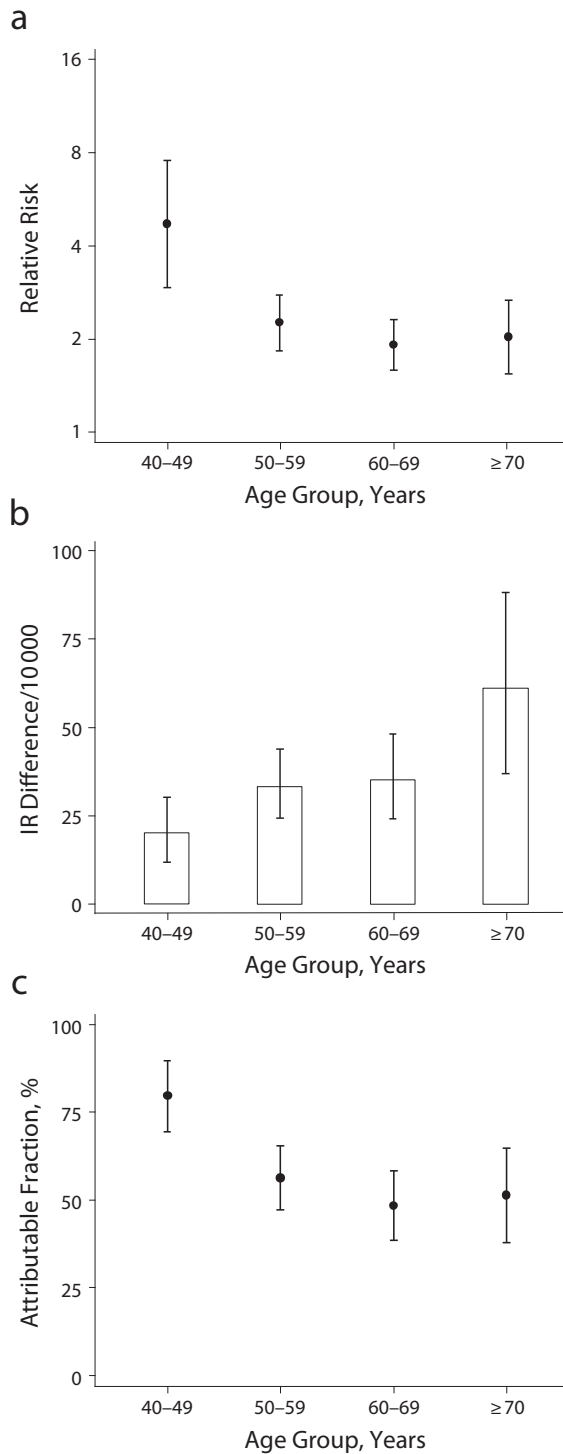
Only information on smoking status and amount of current smoking was available, and we had no information on smoking duration. Naturally, smoking duration varies widely, especially among older individuals, who may have started to smoke at very different ages (or have quit for a time and started again). It is plausible that measuring smoking in dimensions of both duration and amount (e.g., pack-years) will more accurately capture the risk associated with smoking than does a measure of current smoking only.

Information on smoking status was available at baseline only. Thus, participants who quit smoking during the follow-up period ( $\leq 10$  years) were categorized as smokers and not, more correctly, as ex-smokers. This would lead to some underestimation of the risk among current smokers. Naturally, participants who were never smokers at baseline could have started to smoke during follow-up, but this is less likely because most smokers start early in life; more than 80% of adult smokers began smoking before age 18 years.<sup>29</sup>

Residual confounding from psychosocial factors such as stress cannot be excluded. Stress has been shown to be associated with both smoking and CHD, so it is possible that increased stress among the smokers was responsible for some of the effect.<sup>30</sup> Furthermore, the majority of the cohorts in our data set were not representative of the general population, and participants may have had a more healthy distribution of lifestyle factors than did the general population; hence other risk factors may have contributed less and smoking more to disease. If so, we overestimated the fractions attributable to smoking.

### Conclusions

Our results indicate that smoking causes the majority of CHD events among smokers in all age groups. This important public health finding adds to the voluminous data on the hazardous effects of smoking. ■



Note. Vertical bars represent 95% confidence intervals. Analyses adjusted for year of baseline questionnaire, study origin, education, alcohol intake, body mass index, physical activity, total energy intake, and polyunsaturated fat, monounsaturated fat, saturated fat, fiber, and cholesterol intake.

**FIGURE 2—Coronary heart disease (CHD) among men by (a) relative risk among current smokers relative to never smokers, (b) incidence rate (IR) differences among current smokers relative to never smokers, and (c) attributable fractions among current smokers.**

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### Contributors

J. S. Tolstrup originated the study. J. S. Tolstrup and U. A. Hvidtfeldt conducted the analyses and wrote the article, with input from all authors. E. M. Flachs and D. Spiegelman provided advice on the statistical analyses.

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### Human Participant Protection

The study protocol was approved by the review board of the Pooling Project on Diet and Coronary Heart Disease.

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