

Table. Recommendations for IVC Filter Placement

Indication for IVC Filter Placement	ACCP ¹⁰	AHA ¹¹	British Committee for Standards in Hematology ¹²	Thrombosis Interest Group of Canada ¹³
Acute VTE and contraindication to anticoagulation	Yes	Yes	Yes	Yes If proximal DVT present
VTE despite anticoagulation	Yes	Yes	Maybe High intensity oral anticoagulation or LMWH should be considered prior to placement of filter	No Anticoagulation should be intensified or alternative agent started. IVC filter will not prevent progression
Preoperatively in patients who have had recent VTE (within one month) and must have anticoagulation interrupted for surgery	NR	NR	Yes (VTE within 4 weeks prior to surgery)	YES (VTE within 2 weeks prior to major surgery)
Proximal DVT in patient with poor cardiopulmonary reserve	NR	Yes	NR	There is no agreement on definition of poor reserve
Free-floating thrombus	NR	NR	No	No
Thrombolysis with proximal DVT	NR	NR	No	No
Primary prophylaxis in selected high risk patients (surgical, trauma, etc)	No	NR	NR	No

Abbreviations: ACCP, American College of Chest Physicians; AHA, American Heart Association; DVT, deep venous thrombosis; IVC, inferior vena cava; LMWH, low-molecular-weight heparin; NR, not reported; VTE, venous thromboembolism.

has not been associated with increased risk of embolization and is not an indication for device placement. Inferior vena cava filters are often considered in patients with recent PE, poor cardiopulmonary reserve, and residual proximal DVT, but the lack of demonstrated mortality benefit challenges this practice.

IVC Filter Retrieval. Because retrievable filters often become permanent, the risk-benefit analysis performed prior to placement should involve weighing the long-term consequences of recurrent DVT and IVC thrombosis with reduction in nonfatal PE. Inferior vena cava filters should be used primarily in patients who have acute VTE with an absolute contraindication to anticoagulation and should be removed as soon as full-dose anticoagulation can be safely tolerated. Health care providers should remember that while these devices may decrease the risk of PE, they do not prevent DVT nor are they a substitute for anticoagulant treatment of VTE. While recommended retrieval time varies by filter type, Godoy-Garcia and colleagues⁷ offer data to suggest that later removal was relatively safe for those devices studied. Through a combination of increasing appropriate use, increased retrieval, and more data on safety and efficacy, we can optimize patient benefit from use of these filters.

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RESEARCH LETTER

Cigarette Smoking Cessation and Total and Cause-Specific Mortality: A 22-Year Follow-up Study Among US Male Physicians

Since the 1950s, studies have linked cigarette smoking to total and cause-specific mortality. Few studies have comprehensively presented patterns of total and cause-specific mortality reduction

on smoking cessation^{1,2} or age at quitting³, comparing risks with both never and current smokers. We thus assessed the relationship of time since quitting and age at smoking cessation with total and cause-specific mortality of major noncommunicable diseases among 19 705 US male physicians.

See also pages 1887, 1894, 1901, and 1950

Methods. The methods of the Physicians' Health Study (PHS), an institutional review board–approved trial of aspirin and beta carotene use among 22 071 physicians starting 1982 to 1984, have been described previously.⁴ Detailed smoking information was collected from 20 148 men on their 60-month questionnaire. Death certificates were obtained for confirmation and review of cause of death. All mortality end points are adjudicated by the PHS Endpoints Committee. The main outcome was death between 3 years after the date of the 60-month questionnaire return and March 9, 2010. A total of 19 705 eligible participants were included in the analysis.

We calculated “years since quitting” among past smokers by subtracting the age at quitting from the age at the date of the 60-month questionnaire return. Cox proportional hazards models were used to calculate hazard ratios (HRs) for smoking status, years since quitting, and age at quitting on total and/or cause-specific mortality. Person-years were accrued from the date of return of the 60-month questionnaire until either the date of death or the end of follow-up. We adjusted baseline variables including aspirin and beta carotene treatment; body mass index (<25, 25-30, ≥30 [calculated as weight in kilograms divided by height in meters squared]); alcohol intake (<daily or ≥daily); vigorous exercise (<1, 1-4, or ≥5 times/wk); history of diabetes, hypertension, and high cholesterol; parental history of myocardial infarction prior to age 60 years; age at start of smoking; and number of cigarette pack smoked per day. We assessed effect modification by age at start of smoking (≥20 and <20 years) and smoking dose (≥1 vs <1 pack/d) on the association between years since quitting and total mortality. All analyses were conducted using SAS version 9.1 (SAS Institute Inc, Cary, North Carolina).

Results. Among the 19 705 male physicians, 41.7% were past and 6.7% were current smokers with a mean age of 58.3 years at the beginning of the follow-up. Past and current smokers had a similar mean number of packs smoked per day and age at start of smoking, but the mean total years of smoking among current smokers was almost twice as long as that of past smokers. Compared with never smokers, both current and past smokers had higher BMIs, were more likely to consume alcohol daily, and were more likely to have a history of hypertension or diabetes. Never and past smokers were more likely to vigorously exercise 5 or more times a week than current smokers.

A total of 5594 deaths occurred during the 386 772 person-years of follow-up. The crude mortality rates were 11.5, 16.6, and 26.1 per 1000 person-years for

never, past, and current smokers, respectively. Among 612 deaths in current smokers, 13.7% died before the age of 65 years, compared with 8.3% in never smokers. Current smokers had significantly higher risks of major cause-specific mortalities compared with never smokers, including all cardiovascular diseases and sudden death (HR, 3.42; 95% CI, 2.26-5.20); pulmonary disease (HR, 8.27; 95% CI, 5.76-11.86); lung cancer (HR, 16.43; 95% CI, 11.28-23.93); smoking-related cancers including larynx, kidney, acute myeloid leukemia, oral cavity, esophageal, pancreatic, bladder, and stomach cancer (HR, 2.74; 95% CI, 1.97-3.83); colorectal cancer (HR, 3.59; 95% CI, 2.25-5.71); and prostate cancer (HR, 1.79; 95% CI, 1.14-2.81).

Compared with current smokers, the risk of dying was significantly reduced among past smokers within 10 years of quitting (HR, 0.60; 95% CI, 0.54-0.68). By 20 years of quitting, the risk was further reduced (HR, 0.48; 95% CI, 0.43-0.54) to the level of never smokers (HR, 0.44; 95% CI, 0.40-0.50) (**Figure, A**).

Compared with current smokers, quitting after age 50 or 60 years significantly reduced risk of total mortality (HR, 0.54; 95% CI, 0.48-0.61; and HR, 0.61; 95% CI, 0.54-0.70; respectively) among past smokers. However, only quitting before age 50 years could completely eliminate the excess risk of mortality due to smoking (**Figure, B**).

The pattern of total mortality reduction on smoking cessation were similar in those who initiated smoking before and after age 20 years. Although current heavy smokers (≥1 pack/d) had the highest risk of dying compared with current light and past smokers, it could be reduced by 44% within 10 years of quitting and reach a similar risk as never smokers after more than 20 years (vs 10 years for light smokers).

Among past smokers, the risks of dying were quickly reduced to the level of never smokers within 10 years of quitting for cerebrovascular disease, sudden death, and colorectal cancer; after 10 years for smoking-related cancers other than lung cancer; after 20 years for coronary heart disease, pulmonary disease, and lung cancer; and after 30 years of cessation for prostate cancer (**Figure, C-J**).

Comment. Our findings in the US male physicians are consistent with the results from the US female nurses, such that the risk of total mortality decreased to the level of never smokers 20 years after quitting.^{1,2} Our analysis also conveyed a clear public health message on the benefit of quitting smoking at an early age, suggesting that even men who quit after age 60 years had a 39% lower risk of death compared with those who continued to smoke. In addition, this study provided new evidence on the patterns of cause-specific mortality reduction with smoking cessation, such as sudden death, colorectal cancer, and prostate cancer.

Almost consistent but with an early decline compared with the US national trend, smoking prevalence peaked at 1960 (35.4%) and decreased to 6.7% in 1988 in these US male physicians. The observed reduction in mortality as a result of smoking cessation could in part explain the national decline in total mortality, mortality from cardiovascular diseases,⁵ smoking-related cancers,⁶ and colorectal and prostate

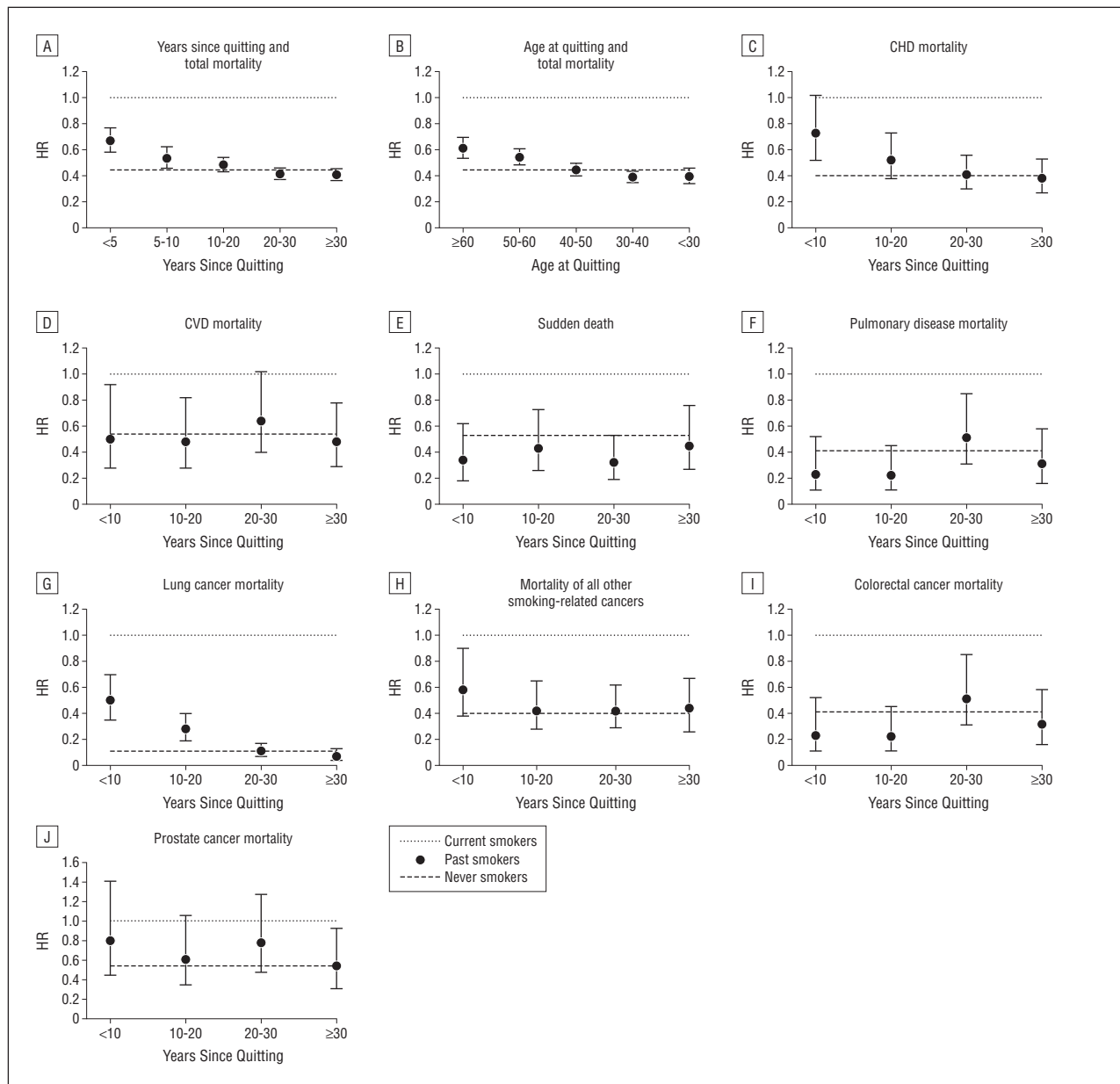


Figure. Time since quitting, age at quitting, and total and cause-specific mortality. A, Years since quitting and total mortality; B, age at quitting and total mortality; C, coronary heart disease (CHD) mortality; D, cerebrovascular disease (CVD) mortality; E, sudden death; F, pulmonary disease mortality; G, lung cancer mortality; H, mortality of all other smoking-related cancers; I, colorectal cancer mortality; and J, prostate cancer mortality. Current smokers were the reference category, and the horizontal dashed line refers to hazard ratio in never smokers. The multivariate model was adjusted for baseline characteristics, including body mass index, exercise, alcohol intake, history of diabetes, history of hypertension, history of high cholesterol, parental history of myocardial infarction prior to 60 years, aspirin treatment, beta carotene treatment, packs of cigarettes smoked per day, age when started smoking, and age at 60-month questionnaire return. Smoking-related cancers include larynx, kidney, acute myeloid leukemia, oral cavity, esophageal, pancreatic, bladder, and stomach cancer.

cancer.⁷ Our study reinforces the critical need for tobacco control, especially in countries where the smoking prevalence is high, to reduce the global burden of noncommunicable diseases.

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Author Contributions: Dr Ma had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Cao and Ma. *Acquisition of data:* Sesso, Gaziano, and Ma. *Analysis and interpretation of data:* Cao, Kenfield, Song, Rosner, Qiu, Sesso, and Ma. *Drafting of the manuscript:* Cao. *Critical revision of the manuscript for important intellectual content:* Cao, Kenfield, Song, Rosner, Qiu, Sesso, Gaziano, and Ma. *Statistical analysis:* Cao, Song, Rosner, Qiu, and Sesso. *Obtained funding:* Ma. *Administrative, technical, and material support:* Sesso, Gaziano, and Ma. *Study supervision:* Gaziano and Ma.

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COMMENTS AND OPINIONS

Adverse Drug Events Due to Potentially Inappropriate Medications

Hamilton et al¹ assessed whether potentially inappropriate medications (PIMs) defined by STOPP (Screening Tool of Older Persons' Potentially Inappropriate Prescriptions) criteria are significantly associated with adverse drug events (ADEs) in elderly patients with acute illness. They showed that the likelihood of an ADE significantly increased with receiving STOPP criteria PIMs (odds ratio [OR], 1.8; 95% CI, 1.5-2.3) but not with Beers criteria PIMs (OR, 1.3; 95%

CI, 0.9-1.7) and claimed that STOPP criteria are more sensitive to PIMs that result in ADEs compared with Beers criteria.

There are 2 caveats to keep in mind when interpreting their results. First, they retrospectively collected the ADEs after the index hospital admission, which may bias toward the collection of more ADEs according to STOPP criteria PIMs than to other criteria. Actually, 52% (170 of 329) of ADEs were due to STOPP criteria PIMs, while 20% (67 of 329) were due to Beers criteria PIMs. Second, they calculated ORs by multivariate logistic model, which examined the effects of such PIMs on ADEs. Because ADEs were not necessarily caused by PIMs, the results indicated that STOPP criteria PIMs might be associated with patients who are likely to have ADEs from any drug.

We recently reported a prospective cohort study on all ADEs among adult inpatients² and examined the burden of Beers criteria PIMs in relation to ADE occurrence in an elderly subgroup.³ We identified 37 ADEs due to Beers criteria PIMs in 36 of 922 patients who were administered at least 1 such PIM (4 ADEs per 100 patients who were administered Beers criteria PIMs), while overall 746 ADEs occurred in 523 of 2155 elderly inpatients (35 ADEs per 100 patients hospitalized).^{2,3} The same multivariate logistic model analysis of our data showed that the presence of at least 1 Beers criteria PIM had a significant association with ADEs due to any drug (OR, 2.1; 95% CI, 1.7-2.6). Our findings suggested that Beers criteria PIM prescriptions were not directly associated with an increasing incidence of ADEs due to such PIMs, but that elderly patients prescribed these PIMs were likely to have ADEs due to any drug during their hospitalization.

Both studies indicated that patients who were administered PIMs defined by either STOPP criteria or Beers criteria had a higher risk of ADEs due to any drug, but the study by Hamilton et al¹ might overestimate the prevalence of STOPP criteria PIMs among all ADEs, and the high prevalence might inflate the significant association between such PIMs and ADEs. Thus, the utility of STOPP criteria PIMs to avoid ADEs needs further investigations.

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