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Research report

Cigarette smoking and completed suicide: Results from 3 prospective cohorts of American adults

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ABSTRACT

Background: Prior reports have indicated a potential dose–response relationship between smoking and suicide. However, this relationship is controversial.
Methods: This study evaluated the association between smoking and risk of death from suicide in three large-scale cohorts of U.S. men and women ($n=253,033$). Suicides were identified from death certificates among 43,816 men enrolled in the Health Professionals Follow-up Study (HPFS) between 1986 and 2008, 116,566 women in the Nurses' Health Study (NHS) between 1976 and 2008, and 92,651 women in the NHS II between 1989 and 2007. Information on smoking was obtained at baseline and updated every 2 years. Relative risks (RRs) of suicide were estimated using Cox proportional hazards regression models. Cohort specific RRs were pooled using random-effects models. Suicide deaths were determined by physician review of death certificates.
Results: A total of 457 deaths from suicide were documented. Compared to never smokers, the pooled multivariate RR (95% confidence interval [CI]) of suicide was 1.15 (0.91–1.45) for former smokers and 2.69 (2.11–3.42) for current smokers. A nonmonotonic dose–response relationship was noted between the number of cigarettes smoked per day (CPD) and suicide risk ($P_{trend} < 0.001$). Compared to never smokers, the pooled multivariate RR (95% CI) was 2.59 (1.77–3.79) for those with 1–14 CPD, 2.03 (1.39–2.94) for those with 15–24 CPD, and 4.13 (2.96–5.78) for those with ≥ 25 CPD.
Limitations: Smoking was self-reported and had some degree of measurement error. Participants were not a representative sample of the U.S. population.
Conclusions: Results from three large cohorts suggest a nonmonotonic dose–response association between smoking and suicide risk.

1. Introduction

Tobacco use is the leading preventable cause of death in the U.S., killing an estimated 443,000 Americans each year and is responsible for approximately one in every five deaths (Ezzati and Lopez, 2003; U.S. Department of Health and Human Services, 2010; Oza et al., 2011). In many low- and middle-income countries, use of tobacco products is increasing, while it is steadily and slowly decreasing in many high-income countries (World Health Organization, 2008). In 2007, the prevalence of smokers in U.S. adults (except California) was established at 17.9%, with 5.3% of low-intensity (0–9 cigarettes smoked per day (CPD)), 5.4% of moderate-intensity (10–19 CPD), and 7.2% of high-intensity smokers (≥ 20 CPD) (Pierce et al., 2011).

Suicide is a major cause of death and an important public health problem (Hawton and van Heeringen, 2009). In the U.S., suicide is the 10th leading cause of death, with a rate of 11.9 per 100,000 persons in 2010 (Murphy et al., 2012). The rate of smoking and nicotine dependence are significantly higher for subjects with psychiatric disorders (Lasser et al., 2000; Grant et al., 2004; Pulay et al., 2010) and affective disorders are well-known risk factors for suicide or suicidal behaviors (Kessler et al., 2005). Smoking is one of the leading behavioral causes of ongoing morbidity (U.S. Department of Health and Human Services, 2010) and serious physical illness might predispose to higher risk of suicide or suicidal behaviors (Hawton and van Heeringen, 2009).

Smoking as a risk factor for suicide has been proposed by cohort studies that found a positive association between cigarette

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smoking and suicide or suicidal behaviors (Hemenway et al., 1993; Tverdal et al., 1993; Doll et al., 1994; Miller et al., 2000a, 2000b; Tanskanen et al., 2000; Breslau et al., 2005; Iwasaki et al., 2005; Yaworski et al., 2011). However, this relationship is controversial and the explanations for this association remain unclear (Hughes, 2008). On the other hand, smoking cessation is often associated with a greater likelihood of experiencing withdrawal syndrome symptoms and depression, which might increase risk of suicide (Glassman et al., 1990; Laje et al., 2001). We therefore accessed data from three large U.S. cohorts in which cigarette smoking was assessed every 2 years to investigate prospectively and over a long follow-up period the association between smoking and quitting smoking and risk of deaths from suicide. The present work represents an extension of a previous brief report in the NHS (Hemenway et al., 1993) and a report based on only 8 years of follow-up in the HPFS (Miller et al., 2000b).

2. Methods

2.1. Study population

The designs of the Health Professionals Follow up Study (HPFS), Nurses' Health Study (NHS) and Nurses' Health Study-II (NHS II) have been described previously (Ascherio et al., 2001; Colditz and Hankinson, 2005). The NHS is a prospective cohort study comprising 121,700 female U.S. registered nurses aged 30–55 years in 1976. The HPFS is a prospective cohort study comprising 51,529 male U.S. health professionals aged 40–75 years in 1986. The NHS II is a prospective cohort study comprising 116,671 female U.S. registered nurses aged 25–42 years in 1989. Participants in all cohorts were followed with biennial questionnaires on lifestyle (including diet every 4 years), medication use, and disease incidence.

To identify a healthy population, participants with diagnoses of cardiovascular disease or cancer at baseline were excluded. After further exclusion of participants with missing information on smoking at baseline, data from 43,816 participants in HPFS (1986–2008), 116,566 in NHS (1976–2008) and 92,651 in NHS II (1989–2007) were available for analysis. The study protocol was approved by the institutional review boards of Brigham and Women's Hospital and Harvard School of Public Health.

2.2. Assessment of smoking

Smoking status was assessed at baseline in each cohort and was updated on subsequent biennial questionnaires. The initial cohort questionnaires also asked for age at which regular smoking began, age at quitting, and the usual number of cigarettes smoked per day. The number of cigarettes smoked per day was reported every 2 years by category (1–4, 5–14, 15–24, 25–34, 35–44, $\geq$45). For smoking status and CPD, the last value was carried forward to replace missing values. Duration of smoking and years since quitting were derived based on the information from the initial and subsequent questionnaires and updated during each follow-up cycle, and, therefore, their accuracy is within 2 years. Duration of smoking was calculated as the difference between age at smoking initiation and current age for current smokers, or between age at onset and cessation for former smokers. Years since cessation were obtained for former smokers by deducting the age of quitting smoking from current age. Ages at smoking initiation and cessation were continuous values in the NHS cohort but were collected categorically in NHS II ($<$15, 15–19, 20–24, 25–29, 30–35 years) and HPFS ($<$15, 15–19, 20–29, 30–39, 40–49, 50–59, $\geq$60 years).

2.3. Ascertainment of death from suicide

Deaths were identified by next of kin or postal authorities, or by searching the National Death Index. At least 98% of deaths among the study participants were identified (Rich-Edwards et al., 1994). Physicians reviewed death certificates to classify individual causes of death. The end point of this study comprised all death cases of suicide and self-inflicted injuries (*Eighth Revision International Classification of Diseases* [ICD] codes E950 to E959) (US Dept of Health, Education, and Welfare, 1963). Suicide might refer to several terminologies, e.g. behavior, ideation, plan, attempt, and completed suicide. In this study, the term "suicide" refer to death or completed suicide and "suicidal behaviors" for nonfatal suicidal thought, ideation, plan, and/or attempt.

2.4. Statistical analysis

Person-years of follow-up were calculated from the date of return of the baseline questionnaire (1986 for HPFS, 1976 for NHS, and 1989 for NHS II) to the earliest of: date of death from suicide or another cause; end of follow-up (January 1, 2008 for HPFS, June 30, 2008 for NHS and, June 30, 2007 for NHS II); or return date of the last questionnaire received during follow-up. Cox proportional hazards models, stratified on age in months and questionnaire cycle, were used to estimate relative risks (RRs) and 95% confidence intervals (CIs). Linear trends were tested by modeling medians of categories of exposure. Analyses were performed separately in each cohort and cohort-specific estimates were pooled using random-effect summaries.

Clinical relevance guided the choice of covariates (Hernan et al., 2002). The multivariate models were adjusted for time varying confounders using simple updating information at each 2-year and 4-year questionnaire cycle, including high alcohol consumption ($\geq$30 g/day, $<$30 g/day), caffeinated coffee consumption (continuous, cup/d), body-mass index ($<$25.0, 25.0–29.9, $\geq$30.0 kg/m^2), physical activity (quintiles), marital status (married/partnered or widowed/separated/divorced/single), and reported regular use of antidepressants (yes or no) and minor tranquilizers such as benzodiazepines (yes or no). In NHS II, hormonal status (post-menopausal with or without hormonal therapy, pre-menopausal or never used hormonal therapy) was also included. Sensitivity analyses including factors that can mediate the effects of smoking, such as self-reported high blood pressure, myocardial infarction or angina, stroke, and cancer (all yes/no) were preformed. All analyses were performed with SAS software, version 9.2 (SAS Institute Inc., 2003). All *P* values reported are 2-sided.

3. Results

Participant characteristics according to smoking status are presented in Table 1. At baseline, prevalence of current smokers was 32% for NHS, 12.8% for NHS II, and 10.3% for HPFS. Compared to never smokers, current smokers were more likely to consume more alcohol and caffeine, reported a higher prevalence of regular use of antidepressants and minor tranquilizers, and a lower prevalence of married/partnership status.

A total of 457 deaths from suicide were documented among the 253,033 participants: 221 in NHS (rate=6.3/100,000 person-years), 71 in NHS II (rate=4.3/100,000), and 165 in HPFS (rate=19.2/100,000). After multivariate adjustment, current smoking was associated with a higher suicide risk in all cohorts (Table 2). Compared to never smokers, the pooled multivariate RR of suicide was 1.15 (95% CI, 0.91–1.45) for former smokers and 2.69 (95% CI, 2.11, 3.42) for current smoker. The risk of suicide was higher as the number of CPD increased ($P_{trend}<0.001$), and was the highest