

Smoking as a Risk Factor for Injury Death: A Meta-Analysis of Cohort Studies¹

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Background. Injury and tobacco effects represent one-quarter of the global burden of disease. Understanding the causes of injury and the effects of smoking may help reduce those burdens. Some smokers have high risks of injury. We provide an initial meta-analysis of cohort associations between smoking and fatal injury.

Methods. Three authors independently searched MEDLINE, and bibliographies of the pertinent studies found, for cigarette smoker-specific injury death data which allowed estimation of an appropriate relative risk (RR) and 95% confidence interval (CI). Relative risks and dose response were summarized by fixed effects and Poisson modeling, respectively.

Results. Six studies covering 10 pertinent cohorts were located. Associations between smoking and injury death have been significant after adjustment or, in effect, stratification for age, race, sex, country, and, respectively, alcohol, marriage, education, and body mass; job and time period; job, alcohol, and exercise; etc. Summary dose-response trends were significantly positive ($P < 0.00005$). Cigarette smoking predicted summary injury death crude RRs of 1.61 (CI 1.44-1.81) vs never smokers and 1.39 (CI 1.25-1.55) vs ex-smokers.

Conclusions. Smoking has significant, consistent, dose-response, often strong and independent, prospective associations with injury death, internationally. ©1998 American Health Foundation and Academic Press

Key Words: smoking; adverse effects; epidemiology; wounds; injuries; meta-analysis.

INTRODUCTION

Injuries kill 5 million humans, including 150,000 Americans annually [1]. Globally, about half of all deaths in 10-24-year-olds are due to injuries. Injury effects are increasing from over 15% (in 1990) to over

20% (estimated for the year 2020) of the global burden of disease [2]. Injury costs hundreds of billions of dollars per year in the United States alone [3,4]. The World Health Organization recently recommended that "Possible links between . . . injury and a range of modifiable risk factors . . . should be quantified" [5].

Globally, nearly half of men and 12% of women smoke [6]. Tobacco use (mostly cigarette smoking) causes debilitating illnesses representing 3% (for 1990) to an estimated 9% (for the year 2020) of the global burden of disease (as measured in disability-adjusted life-years lost (DALYs)) [7]. Smoking is an acknowledged modifiable risk factor for fire [8], explosion [9], military [10], osteoporosis [11], hip fracture [12], and tobacco poisoning injuries [10,13-16]. Smoking causes general, often preclinical injury precursors such as debilities [5,17], distractions [8], and decrements in physiologic performance [18-21], and healing [22,23]. Smoking, or resultant withdrawal, appears to impair performance in tasks relevant to injury avoidance [24,25]. Stopping smoking relieves feelings of anxiety, self-perceived stress, and, possibly, negative affect [12].

That smokers exhibit injury, accident, and suicide excesses has been acknowledged since 1969, at least internally at Philip Morris, Inc. [26]. It has been suggested [8], and doubted [27], that smoking may cause the large injury excesses associated with being a smoker. Associations between smoking and injury are more likely to be causal if they are prospective, consistent, dose-response, strong [28], and independent from likely confounders. So we will analyze those factors in an initial meta-analysis of smoking and injury risk in cohort studies.

METHODS

Criteria for selection of published studies for meta-analysis were: (1) The ability to extract: (a) person-year-based (incidence density) relative risks (RRs) and 95% confidence intervals (CIs) for the association of current smoking and injury death; or (b) sufficient data to estimate smoker injury death incidence density RRs

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and CIs. (2) The resulting RR was from the longest follow-up for that cohort that we located. (3) The study was published or included in MEDLINE after 1965. (4) The RR were specific to cigarette smoking (as sole use of a pipe or cigars appears to have somewhat different biological effects) [29].

The studies were located via a search of MEDLINE from 1966 to August 1, 1995. Smoking, study type, and injury key words were used. The smoking key words were smoke, smoker, smoking, tobacco, or cigarette. The study type key words were cohort, prospective, longitudinal, follow-up, or review. The injury key words were suicide, violence, violent, external cause, injury, trauma, traumatic, homicide, murder, murdered, or unnatural. Three authors (B.N.L., D.C.M., and J.J.) independently reviewed the 263 studies retrieved for pertinence (prospective data on smoking and any category of injury death). Bibliographies of pertinent studies were searched for additional pertinent studies published since 1965. Pertinent studies were then selected or excluded.

B.N.L. and D.C.M. independently extracted the data using EpiInfo [30] software, with consensus reached thereafter. Results were then exported to Excel software where algebraic calculations were completed. When needed, person-year counts were estimated to equal injury deaths/rate or, if count or rate data were missing, person-years = ((total persons followed) \times (years followed)) - ((years followed / 2) \times (total deceased in follow-up)). Among California narcotic addicts, we assumed that three of the four nonsmoker deaths were due to injury, the proportion that was observed across that population as a whole (a conservative assumption if smokers have excess injuries) [31]. Crude RRs and CIs that were missing in the original sources were then estimated using Stata software [32] for Table 1. When lack of deaths in a smoker and referent group would have precluded calculation of a RR, the RR was estimated after adding 1 to each death and person-year number in that RR estimation. Dose-response trends were calculated using Stata's Poisson regression program, adjusting for person-years of exposure [33].

RevMan software [34] was used to summarize the RRs. Fixed effects summary RRs are presented, as no statistically significant heterogeneity between studies' RRs was noted.

RESULTS

Six studies covering 10 age-sex specific populations met these criteria and are described in Table 1 [27,31,35-38]. The mortality follow-up rates were greater than 93% in each study except, perhaps, the Swedish twins (who presumably had a high follow-up rate due to the Swedish population registries) [37]. All included studies assessed smoking only at baseline, except Kawachi who used the smoking status recorded at

the beginning of each biennium of follow-up [36] and Doll who used the smoking status at last follow-up [27]. Whenever possible, published adjusted RR are presented in Table 1 in order to show their independence from confounding.

The populations' average smoker crude injury RR ranged from 1.40 to 2.62, except for male and female Swedish twins born 1901-1910 who had RRs of 0.7 and 0.5, respectively, not significantly different from 1. Figures 1 and 2 summarize the associations using the crude RR (they were most uniformly available). Two studies published data allowing comparison of their crude and age, alcohol, etc., adjusted RR. Both adjusted RR were statistically significant. Those adjusted RR were included in Fig. 1 [36] or Table 1 [38], though they were excluded from the summary calculations. In Figs. 1 and 2, current cigarette smokers demonstrated statistically significant (significant) excesses of injury death incidence in summary, versus either never (RR = 1.61 (CI 1.44-1.81)) or ex-smokers (RR = 1.39 (CI 1.25-1.55)). For men the summary RR vs never smokers was 1.56 (CI 1.34-1.83). For women that RR was 1.99 (CI 1.56-2.52). These associations are paralleled by excesses of injury death in heavier cigarette smokers in Swedish smoking discordant twinships (RR = 2.1 (CI 1.1-4) for all twinships, RR = 1.6 (CI 0.5 - 6, χ^2 probability=0.41) for monozygotic twinships) [37].

A dose-response trend, using adjusted data when available, from referent, to current lightest, . . . most heavily cigarette smoking was also present ($P < 0.00005$) versus never, never + ex, or lightest-smoking referents. Nurses who quit cigarettes had injury death RR of 0.81 at 2-4 years, 0.55 at 5-9 years, and 0.41 at 10-14 years versus continuing smokers, after adjustment for age. Those RR were 0.99, 0.63, and 0.70, respectively, versus continuing smokers, after adjustment for cardiac risks including their daily number of cigarettes smoked in the period before stopping smoking. Nurse current smokers who began cigarette smoking before age 15 years had an age-adjusted injury death RR of 5.39 (CI 1.84-15.78) relative to never smokers.(36)

DISCUSSION

We found published, prospective, consistently positive, significant associations between cigarette smoking and injury death independent of multiple potential confounders (when assessed), in multiple U.S. and European populations (Table 1). The included associations are strongly positive in the heaviest smokers (RRs of 1.9 to 3.9 in larger studies). Heavy smokers' age-adjusted injury RRs are higher than their total mortality RR in doctors [27], nurses [36], and Norwegian women (but not men) [35].

Positive, usually significant, average smoker (see Appendix) or dose-response cohort associations between

TABLE 1
Populations with Injury Death Relative Risks Included in the Summarizations

| Author, year [Ref.] | Enrollee sex and ages (years) | Population studied | Study enrollment to end of follow-up | Adjusted/ stratified for | Cigarettes daily | Injury deaths | Person- years | Relative risk | 95% CI ^a |
|------------------------|-------------------------------------|--|--|--------------------------------|----------------------------------|------------------|--|---------------------|------------------------|
| Kawachi, 1993 [36] | Females 30-55 | U.S. nurses' health study 98% White | 1976 to 1988 | Age, job | Never | 90 | 591,634 | 1.0 | |
| | | | | | Ex | 68 | 375,844 | 1.2 | 0.8-1.9 |
| | | | | | 1-14 | 27 | 110,931 ^b | 1.6 | 1.1-3.1 |
| | | | | | 15-24 | 28 | 164,343 ^b | 1.1 | 0.7-2.2 |
| | | | | | 25-34 | 20 | 71,844 ^b | 1.8 | 1.0-3.7 |
| 35+ | 24 | 40,247 ^b | 3.9 | 2.3-7.6 | | | | | |
| Klatsky, 1993 [38] | 44% male 14-98 | Northern CA Permanente Medical Care program patients | 1978-1985 to 1988 | Crude | Never | 164 | 496,970 ^b | 1.0 | |
| | | | | | Ex | 82 | 227,778 ^b | 1.1 | 0.8-1.4 |
| | | | | | 1-19 | 69 | 176,923 ^b | 1.2 | 0.9-1.6 |
| | | | | | 20+ | 61 | 96,825 ^b | 1.9 | 1.40-2.58 |
| | | | | | Alcohol, age, sex, married . . . | 20+ | 61 | 96,825 ^b | 1.4 |
| Tverdal, 1993 [35] | Males 35-49 | Norwegians in five areas | 1972-1978 to 1988 or emigrate | Age, area | Never | 60 | 127,325 | 1.0 | |
| | | | | | Ex | 77 | 144,776 | 1.1 | 0.8-1.6 |
| | | | | | 1-9 | 48 | 56,350 | 1.8 | 1.2-2.7 |
| | | | | | 10-19 | 124 | 135,167 | 1.9 | 1.4-2.7 |
| | | | | | 20+ | 68 | 56,441 | 2.6 | 1.8-3.7 |
| Tverdal, 1993 [35] | Females 35-49 | Norwegians in three areas | 1972-1978 to 1988 or emigrate | Age, area | Never | 21 | 157,431 | 1.0 | |
| | | | | | Ex | 8 | 38,953 | 1.5 | 0.6-3.6 |
| | | | | | 1-9 | 8 | 57,810 | 1.0 | 0.4-2.4 |
| | | | | | 10+ | 22 | 55,809 | 3.0 | 1.6-5.7 |
| Hser, 1994 [31] | Males 36.7 mean age | CA Civil Addict Program | 1974-1975 to 1985-86 | Addiction | Non Smoker | 3 52 | 673 ^b 3,397 ^b | 1.0 3.4 | 1.1-17.2 |
| Friberg, 1973 [37] | Males 35-50 | Swedish Twin Registry, born 1911-1925 | 1961 to 1972 | Crude | Never | 15 | 18,529 ^b | 1.0 | |
| | | | | | Ex | 5 | 2,574 ^b | 0.9 | 0.3-2.7 |
| | | | | | 1-10 | 16 | 13,445 ^b | 1.5 | 0.7-3.2 |
| | | | | | 11+ | 15 | 8,477 ^b | 2.2 | 1.0-4.8 |
| Friberg, 1973, [37] | Males 51-60 | Swedish Twin Registry, born 1901-1910 | 1961 to 1972 | Crude | Never | 19 | 9,215 ^b | 1.0 | |
| | | | | | Ex | 0 | 979 ^b | 0.9 | 0.3-2.4 |
| | | | | | 1-10 | 4 | 5,587 ^b | 0.3 | 0.1-1.0 |
| | | | | | 11+ | 8 | 2,277 ^b | 1.7 | 0.7-4.1 |
| Friberg, 1973, [37] | Females 35-50 | Swedish Twin Registry, born 1911-1925 | 1961 to 1972 | Crude | Never | 14 | 51,898 ^b | 1.0 | |
| | | | | | Ex | 0 | 474 ^b | 1.1 | 0.0-7.2 |
| | | | | | 1-10 | 7 | 12,071 ^b | 2.1 | 0.7-5.7 |
| | | | | | 11+ | 5 | 3,473 ^b | 5.3 | 1.5-15.7 |
| Friberg, 1973, [37] | Females 51-60 | Swedish Twin Registry, born 1901-1910 | 1961 to 1972 | Crude | Never | 14 | 29,864 ^b | 1.0 | |
| | | | | | Ex | 0 | 94 ^b | 2.4 | 0.1-15.7 |
| | | | | | 1-10 | 1 | 3,056 ^b | 0.7 | 0.0-4.6 |
| | | | | | 11+ | 0 | 765 ^b | 0.0 | 0.0-11.8 |
| Doll, 1994 [27] | Males 35-94 | British MDs | 1951 to 1991 | Age, job calendar period | Never | 114 | 158,333 ^b | 1.0 | |
| | | | | | Ex | 165 | 196,429 ^b | 1.1 | 0.9-1.4 |
| | | | | | 1-14 | 81 | 78,641 ^b | 1.4 | 1.1-1.9 |
| | | | | | 15-24 | 80 | 88,889 ^b | 1.2 | 0.9-1.7 |
| | | | | | 25+ | 93 | 54,070 ^b | 2.4 | 1.8-3.2 |

^a CI are calculated 95% confidence intervals, when published CI are unavailable. Please see Methods.

^b Values were estimated from published data. Please see Methods.

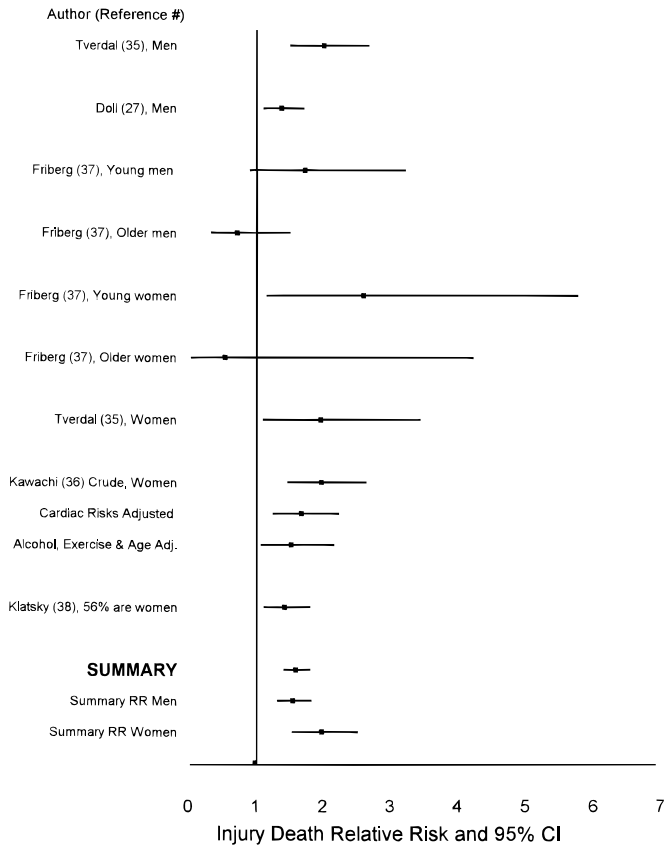


FIG. 1. Relative risks of injury death in current (vs. never) cigarette smokers. The horizontal bars represent 95% confidence intervals.

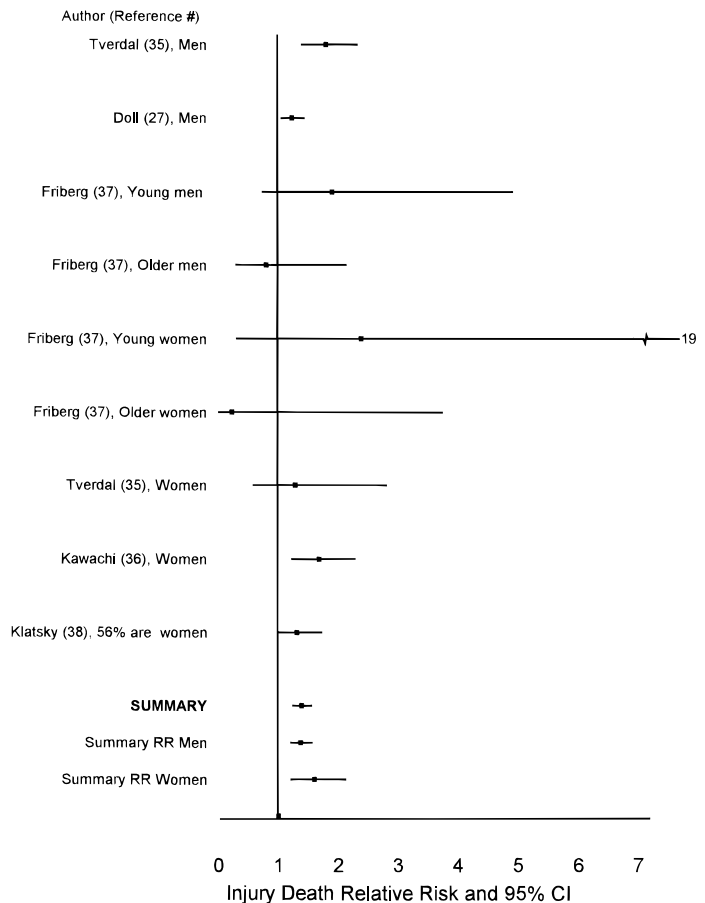


FIG. 2. Relative risks of injury death in current (vs. ex-) cigarette smokers. The horizontal bars represent 95% confidence intervals.

smoking and injury were also present in all but 1 [39] of 18 populations [39–51] excluded from quantitative summarization. Six populations were excluded due to equating pipe or cigar with cigarette smoking (Finnish women [45] (or men [40,45]), Swiss male doctors [44], and Swedish men [42,43]). Twelve populations were excluded for lack of available incidence density current smoker relative risk or confidence interval data (middle-aged (or elderly) U.S. women (or men) [41]; insured U.S. veterans [47]; West German welders (or turners) [46]; Southern California retirees [49]; or Harvard [48], Honolulu [50], Italian [39], or Lithuanian men [51]). Subsequent to our literature search, significantly positive cohort associations between smoking and injury death were reported in white men, or white women, from the U.S. Cancer Prevention Study I [52], and non-significant positive [53] and negative [54] associations were reported in Shanghai men. Smoking was significantly associated with both nonfatal injuries and accidents, independent of drug use, job, exercise, and age, in a U.S. postal worker cohort [56]. In case-control studies, smoking was positively associated with injury in elderly Greeks [55] and people with sleep disorders [57].

Suicides account for less than half of smokers' excess

injury deaths in large studies where data are available to assess this [27,35,52]. Homicide represented only 4% of the Norwegian [35,58] and 14% of Kaiser [38] injury deaths studied and occurs rarely in British doctors.

Though possible, suggestions that the injury/smoking association might be noncausal, e.g., explained by familial [59] or personality [27] factors or publication bias, are weakened by the above facts, other study types (see below), and these considerations. A funnel plot [60] for Fig. 1 is not consistent with publication bias, though few points are available to plot. Associations between personality and smoking are described as "very slight" [61] and "weak" [62]. Assertions that it is improbable and implausible that smoking causes suicides or impossible for smoking to cause homicides [63] ignore addiction's prominent roles in smoking [64], suicide [65], and homicide [66]; ignore smoking's roles in feelings of anxiety, stress, and possibly negative affect [12]; are somewhat based on specificity of association (a "weak" criterion [28] discredited by smoking's many components and effects); and are insufficient in magnitude to explain away smoking/injury associations.

Supportive data from physical, biologic/toxicologic (*in*

vitro and challenge–rechallenge [22]), cross-sectional, cotwin control, and randomized controlled trial (RCT) research suggest that smoking may cause many injuries. Smoking physically ignites fires and explosions, biologically poisons and debilitates animals and humans, and is associated with suggestive, but not statistically significant, injury excesses in identical twin [37] and RCT data.

Physical evidence of smoking's contributions to fires, explosions, and resulting injuries has resulted in widespread posting of no-smoking areas (gas stations, grain mills, commercial airplanes during landings, etc.) and campaigns for less fire-prone cigarettes. Smoking continues to be “the leading cause of fire deaths in the West” [67] (totaling a third of fire and 1% of all injury deaths in the United States and a cause of devastating explosions [8,9]).

The remarkable toxicities of tobacco and/or nicotine have led to their over 300 years of ongoing commercial use in poisoning various animals [15,68]. Tobacco and/or nicotine also cause acknowledged, clinical, poisoning injuries in, at least, children [13], workers [14], pets [68,69], and those who attempt to overdose on nicotine [15,16].

Perhaps more importantly, the smoking of tobacco and/or nicotine causes performance decrements [18–21] that may reduce the smoker's ability to avoid or survive injury. Smoking is associated with cohort accident incidence excesses (independent of age, drug use, etc.) [56] and cross-sectional impaired performance on “tests of muscle strength, agility and coordination, gait and balance, and self-reported functional status. . . after adjusting for age, . . . activity, and alcohol use ($P < 0.05$)” [70]. Young nonsmokers were able to escape from a simulated danger in half the time that smokers took [24]. Aggressiveness, confusion, and impulsivity reportedly increase during smoking withdrawal [25].

Smoking may increase the risk of serious complications [71–74] and death [75,76] from injuries that do occur. Smoking impairs the metabolic efficiency [18–20] and fitness [21] that may be needed to survive the acute physiologic stress of trauma. Smoking (or nicotine [77,78]) impairs the healing of diverse wounds in rats [79–81], hamsters [82], pigs [78], and rabbits [77,83]. Smoking (or perhaps nicotine [22]) impairs human blood flow [84,85], tissue oxygenation [86], bone healing [22], and pulmonary toilet [71]. Smoking may thus cause smokers' up to 10-fold excesses of wound infections [23], traumatic skin [87] and muscle sloughs [88,89], bone fractures and nonunions [22,90], and severe pulmonary complications following unconsciousness and trauma [71,74]. Smoking is believed to cause combat injury and death [10].

The above evidence of contributions of smoking to injuries qualitatively support, but limitedly quantify the magnitude of possible causal associations between

smoking and injury. RCT data may be the ultimate way to quantify the impact of the myriad ways that smoking may contribute to injury. Secondary analysis of injury data in RCTs using effective smoking cessation interventions found a suggestive, but not statistically significant, association between usual care (excess continued smoking) and excess injury death (RR = 1.54 (95% CI 0.84–2.78)) [91].

This report has limitations. Only 44 Asian and no South American or African injury deaths were discussed. Summary relative risk estimates are based on only nine populations. RRs from cohort studies are too high if not adjusted for confounders, and too low if adjusted for effects of the exposure, e.g., smoking-caused cardiac, lung, cancer, . . . disease [92]. The analysis addresses injury. It provides little data on associations between smoking and injury subtypes.

In their 1969 annual Research Center presentation, the Philip Morris, Inc., Board of Directors was prominently told that smokers exhibit excesses of injuries, accidents, and suicides [26]. The medical literature reviewed above increasingly allows physicians and the public access to studies supporting that recently released tobacco company document.

Disputes continue over the exact level of smoking (or other tobacco [10]) caused injury RRs in various populations, at various levels of tobacco, for various types of injury, etc. Even small smoking-caused excess injury RRs have large global health implications. If smoking causes adult only (age 15+ years) injury relative risks of 1.25–1.75, as seems plausible, then smoking-caused injuries would represent 5–12% of injury; 0.8–2.1% of total global DALYs; or about 16–31% of all reported illness and injury DALYs from tobacco in the year 2000 [93]. In the year 2020, given stable men and women's smoking prevalences, these proportions would be 6–15% of injury, 1–3% of total, and 10–26% of tobacco-caused burdens from illness and injury (assuming that the global burden of disease baseline estimates for DALYs are correct). The effects of cigar, pipe, or chewing tobacco; increases in smoking [6]; youth smoking; or smoking-caused injuries to ex- or never smokers [94] are excluded from the above potential smoking-caused injury tolls.

Analyses of smoking and injury risks from additional continents, smoking discordant monozygotic twinships, populations, and injury subtypes seem merited. Research prospectively assessing injury precursors and injuries as smoking begins and ceases in both observational and (smoking prevention or cessation) randomized controlled intervention trials also seems merited.

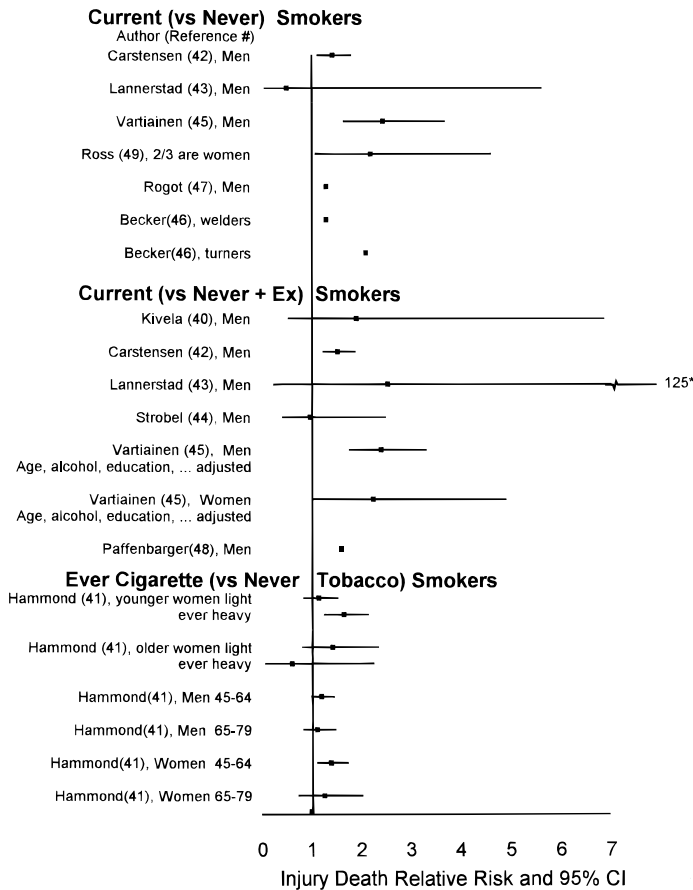
Yet numerous injury deaths are closely and independently related to smoking. Smoking seems to contribute to multiple debilitations, diseases, and other risk factors for adverse injury outcomes. Smoking cessation has numerous great benefits, including improved metabolic

efficiency and stress test performance [18], increased tissue perfusion [84,86], reduced cortisol [95], reduced immunosuppression [95], and, possibly, reduced self-perceived stress [96] and injury death rates [36,97,98] (Fig. 2).

“Raising body resistance that is abnormally low (as in hemophilia treatment or, e.g., smoking cessation [99]) or preventing its decline. . . (e.g., by preventing smoking) is a sometimes useful . . . injury control strategy[. . .] [100]. Tobacco control is an injury control strategy practiced by many organizations [97,101] and physicians [87,99]. It seems prudent to warn the general population, smokers, physicians, and policy makers of smoking’s associations with, and possibly immense contributions to, injuries.

APPENDIX

Populations excluded from quantitative summaries. Relative risks of injury death in smokers. The horizontal bars represent 95% confidence intervals.



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