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Authors
Leistikow, Bruce N.
Martin, Daniel C.
Jacobs, Jeffrey
et al.

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Smoking as a Risk Factor for Injury Death: A Meta-Analysis of Cohort Studies[1]

Bruce N. Leistikow, M.D., M.S.,[2] Daniel C. Martin, Jeffrey Jacobs, M.D., M.P.H., and David M. Rocke, Ph.D.

Department of Epidemiology and Preventive Medicine, University of California, Davis, California 95616-8638

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.**

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

[1] Supported by University of California, Davis.

[2] To whom correspondence and reprint requests should be addressed at Shields Ave., TB 168, Department of Epidemiology and Preventive Medicine, University of California, Davis, CA 95616-8638. Fax: (530) 752- 3239. E-mail: BNLeistikow@UCDavis.edu.

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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) × (years followed)) − ((years followed / 2) × (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	1.0–2.0
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	3	673[b]	1.0	
					Smoker	52	3,397[b]	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.

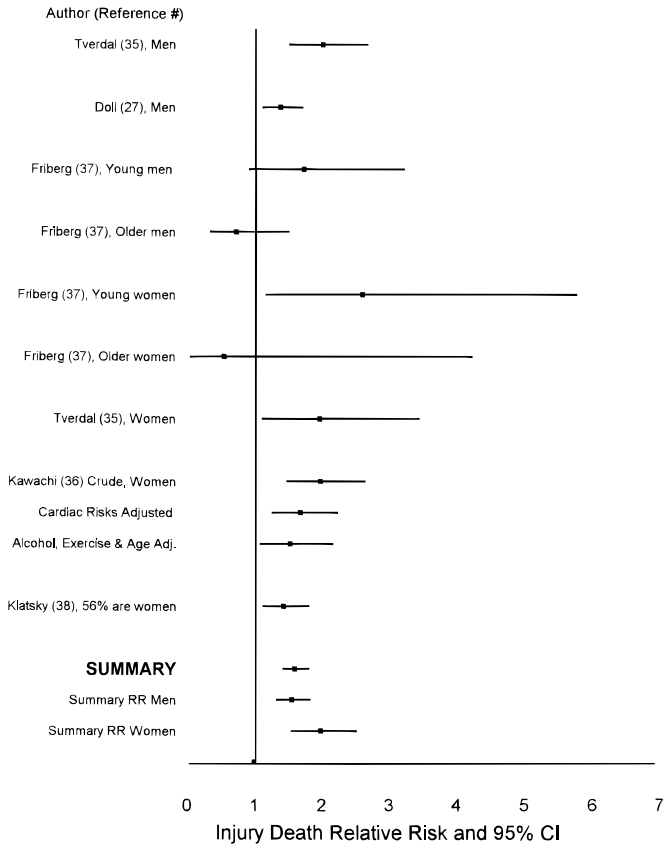


FIG. 1. Relative risks of injury death in current (vs. never) cigarette smokers. The horizontal bars represent 95% confidence intervals.

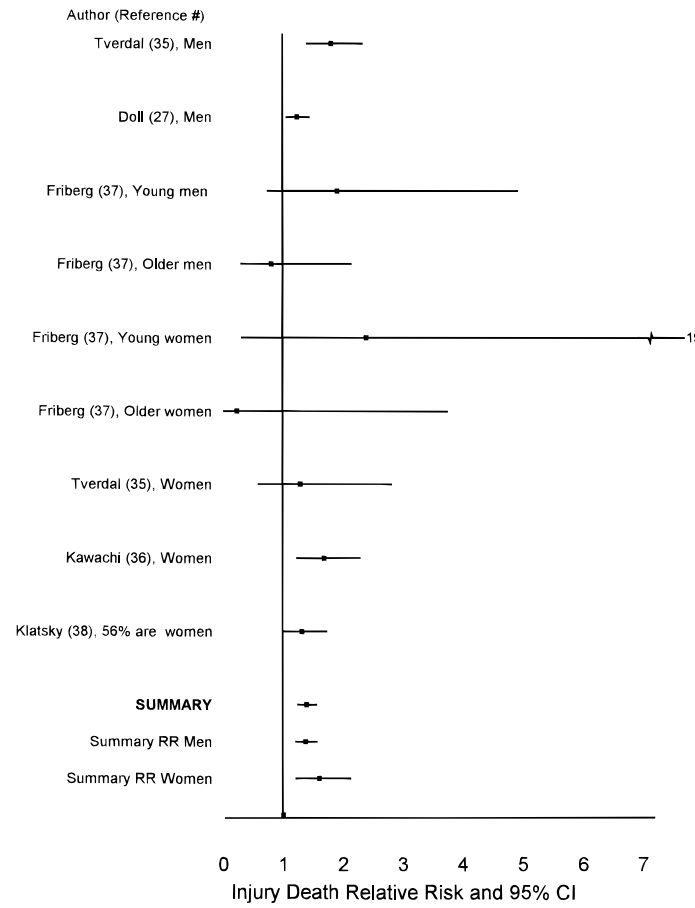


FIG. 2. Relative risks of injury death in current (vs. ex-) cigarette smokers. The horizontal bars represent 95% confidence intervals.

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 nonsignificant 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*]), crosssectional, 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.

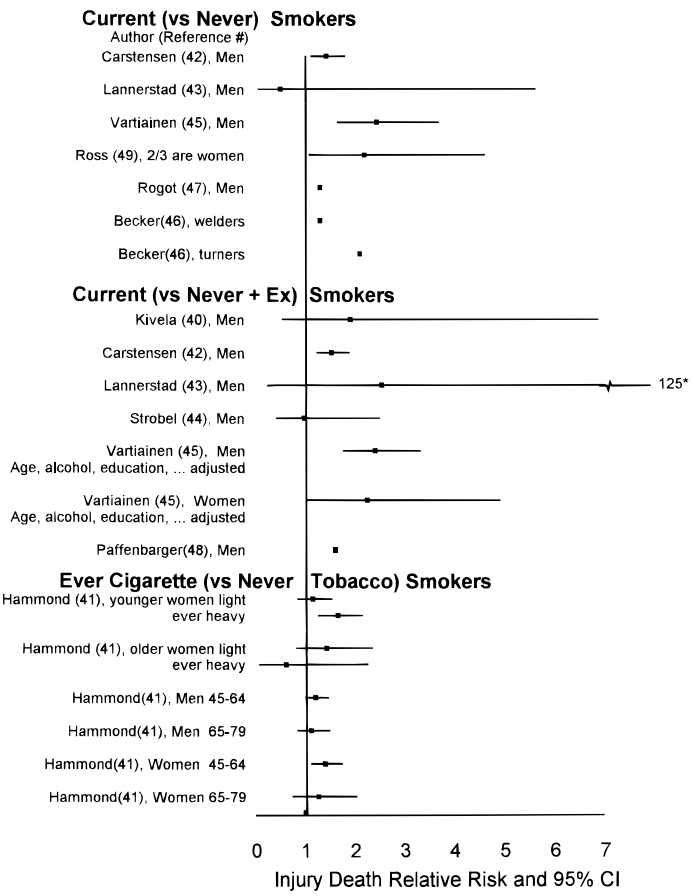
Yet numerous injury deaths are closely and independently related to smoking. Smoking seems to contribute to multiple debilitations, diseases, and other risk factors for adverse injury outcomes. Smoking cessation has numerous great benefits, including improved metabolic

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 strateg[y]. . ." [*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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REFERENCES

1. World Health Report 1997: Conquering suffering, enriching humanity. Geneva: World Health Organization, 1997.
2. Berger LR, Mohan D. Injury control: a global view. Oxford: Oxford Univ. Press, 1996.
3. Max W, Rice DP, MacKenzie EJ. The lifetime cost of injury. Inquiry 1990;27:332–43.
4. Leigh JP, Markowitz SB, Fahs M, Shin C, Landrigan PJ. Occupational injury and illness in the United States: estimates of costs, morbidity, and mortality. Arch Intern Med 1997;157: 1557–68.
5. Investing in health research and development. Geneva: World Health Organization, 1996.
6. The global tobacco epidemic. Geneva: World Health Organization, 1996.
7. Murray CJ, Lopez AD. Global mortality, disability, and the contribution of risk factors: global burden of disease study. Lancet 1997;349:1436–42.
8. Sacks JJ, Nelson DE. Smoking and injuries: an overview. Prev Med 1994;23:515–20.
9. Stephens HW. The Texas City disaster, 1947. Austin: Univ. of Texas Press, 1997.
10. Amoroso PJ, Reynolds KL, Barnes JA, White DJ. Tobacco and injury: an annotated bibliography. Natick, MA: U.S. Army Research Institute of Environmental Medicine, 96–1, 1996.
11. Law MR, Hackshaw AK. A meta-analysis of cigarette smoking, bone mineral density and risk of hip fracture: recognition of a major effect. BMJ 1997;315:841–5.
12. Report of the Scientific Committee on Tobacco and Health. London: Department of Health, The Stationery Office, 1998.
13. Ingestion of cigarettes and cigarette butts by children—Rhode Island, January 1994–July 1996. MMWR Morb Mortal Weekly Rep 1997;46:125–8.
14. Green tobacco sickness in tobacco harvesters—Kentucky, 1992. MMWR Morb Mortal Weekly Rep 1993;42:237–40.
15. Hayes W, Jr, Laws E, Jr. Handbook of pesticide toxicology. San Diego: Harcourt Brace Jovanovich, 1991:1318–1339.
16. Woolf A, Burkhart K, Caraccio T, Litovitz T. Self-poisoning among adults using multiple transdermal nicotine patches. J Toxicol Clin Toxicol 1996;34:691–8.
17. The health benefits of smoking cessation: a report of the Surgeon General. Washington, DC: Department of Health and Human Services, Public Health Service, CDC, DCDPHP, Office on Smoking and Health, 1990.
18. Perkins KA, Epstein LH, Marks BL, Stiller RL, Jacob RG. The effect of nicotine on energy expenditure during light physical activity. N Engl J Med 1989;320:898–903.
19. Hirsch GL, Sue DY, Wasserman K, Robinson TE, Hansen JE. Immediate effects of cigarette smoking on cardiorespiratory responses to exercise. J Appl Physiol 1985; 58:1975–81.
20. Morton AR, Holmik EV. The effects of cigarette smoking on maximal oxygen consumption and selected physiological responses of elite team sportsmen. Eur J Appl Physiol 1985; 53:348–52.
21. Sandvik L, Erikssen G, Thaulow E. Long term effects of smoking on physical fitness and lung function: a longitudinal study of 1393 middle aged Norwegian men for seven years. BMJ 1995;311:715–8.

22. Kwiatkowski TC, Hanley EN, Jr, Ramp WK. Cigarette smoking and its orthopedic consequences. Am J Orthop 1996;25:590–7.
23. Kurz A, Sessler DI, Lenhardt R. Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization: Study of Wound Infection and Temperature Group [see comments]. N Engl J Med 1996;334:1209–15.
24. Fowler RL. Smoking and performance on simulated firefighting tasks. Percept Mot Skills 1989:1302.
25. Sommese T, Patterson JC. Acute effects of cigarette smoking withdrawal: a review of the literature. Aviat Space Environ Med 1995;66:164–7.
26. Wakeham H. Presentation and report to the Philip Morris Board of Directors: Minnesota and Minnesota Blue Cross vs Philip Morris, *et al*. Trial Exhibit 10299—"Smoker psychology research" by: Dr. H. Wakeham, presented to the PM board of directors 691126, http://www.mnbluecrosstobacco.com/toblit/trialnews/docs/TE10299.pdf accessed 2/24/98, 1969.
27. Doll R, Peto R, Wheatley K, Gray R, Sutherland I. Mortality in relation to smoking: 40 years' observations on male British doctors. BMJ 1994;309:901–11.
28. Hill AB. The environment and disease: association or causation? Proc R Soc Med 1965:295–300.
29. Wald NJ, Watt HC. Prospective study of effect of switching from cigarettes to pipes or cigars on mortality from three smoking related diseases. BMJ 1997;314:1860–3.
30. EpiInfo, 6.01 ed. Atlanta, GA: Centers for Disease Control, 1996.
31. Hser YI, McCarthy WJ, Anglin MD. Tobacco use as a distal predictor of mortality among long-term narcotics addicts. Prev Med 1994;23:61–9.
32. Stata, 3.1 ed. College Station, TX: Stata Corporation, 1993.
33. Selvin S. Practical biostatistical methods. Belmont, CA: Duxbury Press, 1995.
34. RevMan, 3.1 ed. Oxford, UK: Cochrane Collaboration, 1998.
35. Tverdal A, Thelle D, Stensvold I, Leren P, Bjartveit K. Mortality in relation to smoking history: 13 years' follow-up of 68,000 Norwegian men and women 35–49 years. J Clin Epidemiol 1993;46:475–87.
36. Kawachi I, Colditz GA, Stampfer MJ, Willett WC, Manson JE, Rosner B, Hunter DJ, Hennekens CH, Speizer FE. Smoking cessation in relation to total mortality rates in women: A prospective cohort study. Ann Intern Med 1993;119:992–1000.
37. Friberg L, Cederlof R, Lorich U, Lundman T, De Faire U. Mortality in twins in relation to smoking habits and alcohol problems. Arch Environ Health 1973;27:294–304.
38. Klatsky AL, Armstrong MA. Alcohol use, other traits, and risk of unnatural death: a prospective study. Alcohol Clin Exp Res 1993;17:1156–62.
39. Menotti A, Matiotti S, Seccareccia S, Giampaoli S. The 25 year estimated probability of death from some specific causes as a function of twelve risk factors in middle aged men. Eur J Epidemiol 1988;4:60–7.
40. Kivela SL, Nissinen A, Ketola A, Punsar S, Puska P, Karvonen M. Alcohol consumption and mortality in aging or aged Finnish men [published erratum appears in J Clin Epidemiol 1989; 42(7):701]. J Clin Epidemiol 1989;42:61–8.
41. Hammond EC. Smoking in relation to the death rates of one million men and women. Natl Cancer Inst Monogr 1966;19: 127–204.
42. Carstensen JM, Pershagen G, Eklund G. Mortality in relation to cigarette and pipe smoking: 16 years' observation of 25,000 Swedish men. J Epidemiol Community Health 1987;41:166–72.
43. Lannerstad O, Isacsson SO, Lindell SE. Risk factors for premature death in men 56–60 years old: a prospective study of men born 1914, living in Malmo, Sweden. Scand J Soc Med 1979; 7:41–7.
44. Strobel M, Gsell O. Mortality in relation to tobacco smoking: 9 years of observations of physicians in Switzerland. Helv Med Acta 1965;32:547–92.
45. Vartiainen E, Puska P, Pekkanen J, Tuomilehto J, Lonnqvist J, Ehnholm C. Serum cholesterol concentration and mortality from accidents, suicide, and other violent causes [see comments]. 1994:445–7.
46. Becker N, Chang-Claude J, Frentzel-Beyme R. Risk of cancer for arc welders in the Federal Republic of Germany: results of a second follow up (1983–8). Br J Ind Med 1991;48:675–83.
47. Rogot E, Murray JL. Smoking and causes of death among U.S. veterans: 16 years of observation. Public Health Rep 1980; 95:213–22.
48. Paffenbarger RS, King SH, Wing AL. Chronic disease in former college students. IX. Characteristics in youth that predispose to suicide and accidental death in later life. Am J Pub Health 1969;59:900–8.
49. Ross RK, Bernstein L, Trent L, Henderson BE, Paganini-Hill A. A prospective study of risk factors for traumatic deaths in a retirement community. Prev Med 1990;19:323–34.
50. Iribarren C, Reed DM, Wergowske G, Burchfiel CM, Dwyer JH. Serum cholesterol level and mortality due to suicide and trauma in the Honolulu Heart Program. Arch Intern Med 1995;155: 695–700.
51. Prokhorskas RP, Grabauskas VI, Baubinene AV, Glazunov IS, Domarkene SB. Chief risk factors of ischemic heart disease and mortality of the middle-aged male population of Kaunas. Kardiologiia 1987;27:14–9.
52. Changes in cigarette-related disease risks and their implication for prevention and control. Bethesda, MD: National Cancer Institute, NIH, PHS, DHHS, 1997.
53. Yuan J, Ross RK, et al. Morbidity and mortality in relation to cigarette smoking in Shanghai, China. JAMA 1996;275:1646.
54. Chen ZM, Xu Z, Collins R, Li WX, Peto R. Early health effects of the emerging tobacco epidemic in China: a 16-year prospective study [see comments]. JAMA 1997;278:1500–4.
55. Petridou E, Polychronopoulou A, Dounis E, Tsampira P, Revinthi K, Trichopoulos D. Risk factors for injuries among the elderly in Greece. Accid Anal Prev 1996;28:333–8.
56. Ryan J, Zwerling C, Orav EJ. Occupational risks associated with cigarette smoking: a prospective study. Am J Pub Health 1992;82:29–32.
57. Phillips BA, Danner FJ. Cigarette smoking and sleep disturbance [see comments]. Arch Intern Med 1995;155:734–7.
58. Tverdal A. A mortality follow-up of persons invited to a cardiovascular disease study in five areas in Norway. Oslo: National health screening service, 1989.
59. Kendler KS, Neale MC, MacLean CJ, Heath AC, Eaves LJ, Kessler RC. Smoking and major depression: a causal analysis. Arch Gen Psychiatry 1993;50:36–43.
60. Egger M, Davey Smith G, Schneider M, Minder C, Smith GD. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997;315:629–34.
61. Dunn WL. Behavioral research annual report. Richmond, VA: Philip Morris, Inc. Research Center, www.philipmorris.com/Document 1003288521 3/1/98, 1974.
62. Patton D, Barnes GE, Murray RP. A personality typology of smokers. Addict Behav 1997;22:269–73.
63. Smith GD, Phillips AN, Neaton YD. Smoking as "independent" risk factor for suicide: illustration of an artifact from observational epidemiology? Lancet 1992;340:709–12.

64. The health consequences of smoking: nicotine addiction. Washington, DC: U.S. Gov. Printing Office, 1988.
65. Moscicki EK. Epidemiology of suicidal behavior. Suicide Life Threat Behav 1995;25:22–35.
66. Rivara FP, Mueller BA, Somes G, Mendoza CT, Rushforth NB, Kellermann AL. Alcohol and illicit drug abuse and the risk of violent death in the home. JAMA 1997;278:569–75.
67. Whidden P, Whidden M. Fire-safe cigarettes. Helsinki: abstract presented at the Conference for a Smoke-free Europe, www.health.fi/tkk/smoke_free/tupakkakirja.html 12/9/97, 1996.
68. Farm chemicals handbook. Willoughby, OH: Meister Publishing, 1997.
69. Vig MM. Nicotine poisoning in a dog. Vet Hum Toxicol 1990; 32:573–5.
70. Nelson HD, Nevitt MC, Scott JC, Stone KL, Cummings SR. Smoking, alcohol, and neuromuscular and physical function of older women: Study of Osteoporotic Fractures Research Group [see comments]. JAMA 1994;272:1825–31.
71. Warner MA, Offord KP, Warner ME, Lennon RL, Conover MA, Jansson SU. Role of preoperative cessation of smoking and other factors in postoperative pulmonary complications: a blinded prospective study of coronary artery bypass patients. Mayo Clin Proc 1989;64:609–16.
72. Underwood MJ, Bailey JS. Coronary bypass surgery should not be offered to smokers [see comments]. BMJ 1993;306:1047–9.
73. Griepp RB, Ergin MA, Galla JD, Lansman S, Khan N, Quintana C, McCollough J, Bodian C. Looking for the artery of Adamkiewicz: a quest to minimize paraplegia after operations for aneurysms of the descending thoracic and thoracoabdominal aorta. J Thorac Cardiovasc Surg 1996;112:1202–13, discussion 1213–5.
74. Forrest JB, Rehder K, Cahalan MK, Goldsmith CH. Multicenter study of general anesthesia. III. Predictors of severe perioperative adverse outcomes [published erratum appears in Anesthesiology 1992 Jul;77(1):222] [see comments]. Anesthesiology 1992;76:3–15.
75. Dombi GW, Nandi P, Saxe JM, Ledgerwood AM, Lucas CE. Prediction of rib fracture injury outcome by an artificial neural network. J Trauma 1995;39:915–21.
76. Raff T, Germann G, Barthold U. Factors influencing the early prediction of outcome from burns. Acta Chir Plast 1996;38: 122–7.
77. Silcox DH, Daftari T, Boden SD, Schimandle JH, Hutton WC, Whitesides TEJ. The effect of nicotine on spinal fusion. Spine 1995;20:1549–53.
78. Forrest CR, Xu N, Pang CY. Evidence for nicotine-induced skin flap ischemic necrosis in the pig. Can J Physiol Pharmacol 1994;72:30–8.
79. van Adrichem LN, Hoegen R, Hovius SE, Kort WJ, van Strik R, Vuzevski VD, van der Meulen JC. The effect of cigarette smoking on the survival of free vascularized and pedicled epigastric flaps in the rat. Plast Reconstr Surg 1996;97:86–96.
80. Nolan J, Jenkins RA, Kurihara K, Schultz RC. The acute effects of cigarette smoke exposure on experimental skin flaps. Plast Reconstr Surg 1985;75:544–51.
81. Gu YD, Zhang GM, Zhang LY, Li FG, Jiang JF. Clinical and experimental studies of cigarette smoking in microvascular tissue transfers. Microsurgery 1993;14:391–7.
82. Craig S, Rees TD. The effects of smoking on experimental skin flaps in hamsters. Plast Reconstr Surg 1985;75:842–6.
83. Ueng SW, Lee MY, Li AF, Lin SS, Tai CL, Shih CH. Effect of intermittent cigarette smoke inhalation on tibial lengthening: experimental study on rabbits. J Trauma 1997;42:231–8.
84. Sarin CL, Austin JC, Nickel WO. Effects of smoking on digital blood-flow velocity. JAMA 1974;229:1327–8.
85. Mosely LH, Finseth F. Cigarette smoking: impairment of digital blood flow and wound healing in the hand. Hand 1977;9:97–101.
86. Jensen JA, Goodson WH, Hopf HW, Hunt TK. Cigarette smoking decreases tissue oxygen. Arch Surg 1991;126:1131–4.
87. Rees TD, Liverett DM, Guy CL. The effect of cigarette smoking on skin-flap survival in the face lift patient. Plast Reconstr Surg 1984;73:911–5.
88. Kroll SS. Necrosis of abdominoplasty and other secondary flaps after TRAM flap breast reconstruction. Plast Reconstr Surg 1994;94:637–43.
89. Lovich SF, Arnold PG. The effect of smoking on muscle transposition. Plast Reconstr Surg 1994;93:825–8.
90. Cobb TK, Gabrielsen TA, Campbell DC, 2nd, Wallrichs SL, Ilstrup DM. Cigarette smoking and nonunion after ankle arthrodesis. Foot Ankle Int 1994;15:64–7.
91. Leistikow B. Might smoking cessation reduce injury mortality? A meta-analysis of randomized, controlled trials. In press, 1998.
92. Davey Smith G, Egger M, Phillips AN, Smith GD. Meta-analysis. Beyond the grand mean? BMJ 1997;315:1610–4.
93. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990–2020: global burden of disease study. Lancet 1997;349:1498–504.
94. Aligne CA, Stoddard JJ. Tobacco and children: an economic evaluation of the medical effects of parental smoking. Arch Pediatr Adolesc Med 1997;151:648–53.
95. Meliska CJ, Stunkard ME, Gilbert DG, Jensen RA, Martinko JM. Immune function in cigarette smokers who quit smoking for 31 days. J Allergy Clin Immunol 1995;95:901–10.
96. Parrott AC. Smoking cessation leads to reduced stress, but why? Int J Addict 1995;30:1509–16.
97. White GJ, Pedersen DM, Wood SD, Warden DR, Thiese SM. Cigarette smoking and combat injuries [editorial]. Mil Med 1988;153:381–2.
98. Multiple Risk Factor Intervention Trial Research Group. Multiple risk factor intervention trial: Risk factor changes and mortality results. JAMA 1982;248:1465–77.
99. Munday IT, Desai PM, Marshall CA, Jones RM, Phillips ML, Rosen M. The effectiveness of pre-operative advice to stop smoking: a prospective controlled trial. Anaesthesia 1993;48:816–8.
100. Haddon WJ. Advances in the epidemiology of injuries as a basis for public policy. Pub Health Rep 1980;95:411–21.
101. Tsai SP, Gilstrap EL, Cowles SR, Waddell LC, Jr, Ross CE. Personal and job characteristics of musculoskeletal injuries in an industrial population. J Occup Med 1992;34:606–12.